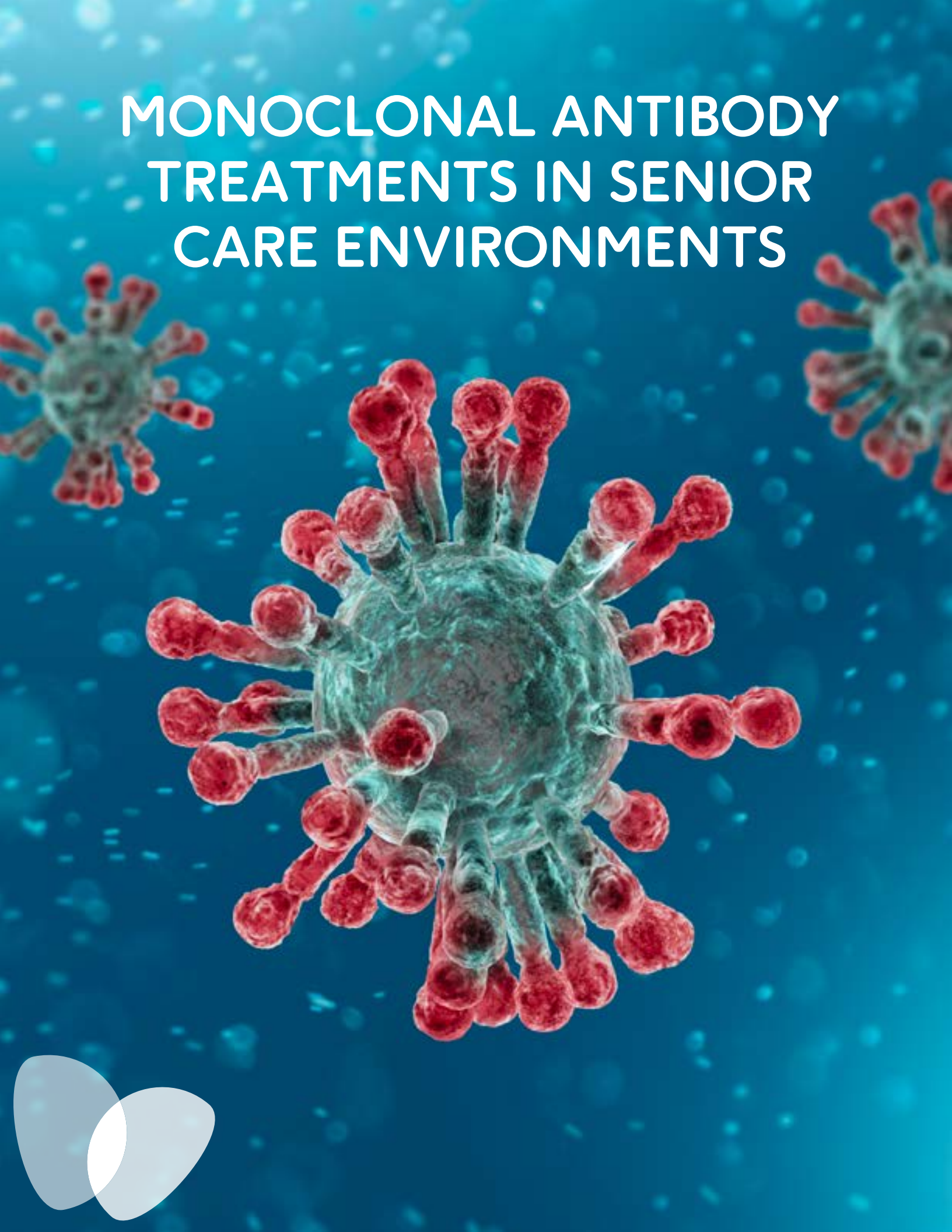
MONOCLONAL ANTIBODY TREATMENTS IN SENIOR CARE ENVIRONMENTS



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MONOCLONAL ANTIBODY TREATMENTS IN SENIOR CARE ENVIRONMENTS

Two investigational SARS-CoV-2 neutralizing antibody treatments, bamlanivimab and casirivimab plus imdevimab are now available through Emergency Use Authorization (EUA) from the FDA for use in eligible outpatients with mild to moderate disease who are at high risk for disease progression and/or hospitalization. Both neutralizing antibodies might reduce the rate of hospitalizations and emergency room visits in high risk patients defined as age >65 years and underlying illnesses listed below.[1]

At the present time, due to insufficient data the National Institute of Health (NIH) COVID-19 Treatment Guidelines Panel (the Panel) does not recommend either for or against the use of neutralizing antibodies (bamlanivimab or casirivimab plus imdevimab), though preliminary data suggests that outpatients may benefit from receiving anti-SARS-CoV-2 monoclonal antibodies early in the course of infection.[2]

MONOCLONAL ANTIBODY INFUSIONS ARE NOT A PROPHYLAXIS AGAINST COVID-19.

Residents of skilled nursing facilities (SNFs) are ideal for these novel therapies and long-term care (LTC) pharmacies provide intravenous medications (IV) routinely in SNF environments. In order to best deploy these solutions, state departments of health should engage with LTC pharmacies who can work with their contracted SNFs to obtain orders for the products and convey those orders to the states for allocation from the distributor (AmerisourceBergen). The LTC pharmacies can acquire, safely compound (using clean rooms and aseptic technique), dispense (with patient specific labeling and data tracking) and delivery (appropriately in accordance with required storage and handling specifications) these products with their associated tubing, IV poles, and any required pumps into skilled nursing facilities and other appropriate settings per FDA EUA label.

EMERGENCY USE AUTHORIZATIONS (APPROVED USE):

In patients who are ≥12 years of age and weighing ≥40 kilograms (about 88 pounds), and who are at high risk for progressing to severe COVID-19 and/or hospitalization

Anti-SARS-CoV-2 antibody-based therapies may have their greatest likelihood of having an effect in the earliest stages of infection, before the host has mounted an effective immune response. The treatment is a one dose, infused therapy that should be administered as soon as possible after a confirmed positive SARS-CoV-2 test result.

SAFETY:

Infusion-related reactions have been observed and there is potential for severe reactions, including anaphylaxis. Monoclonal antibody treatment may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS). Post-acute and long-term care settings with access to such expertise and resources may be able to administer monoclonal antibody in their own facilities.

www.fda.gov/media/143603/download

www.fda.gov/media/143892/download

VACCINE CONSIDERATION:

The CDC's Advisory Committee on Immunization Practices has recommended that COVID-19 vaccine should be deferred until 90 days after the administration of monoclonal antibody treatment. [3]

References:
1. www.covid19treatmentguidelines.nih.gov/therapeutic-management/
2. www.covid19treatmentguidelines.nih.gov/therapeutic-management
3. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-12/slides-12-12/COVID-03-Mbaeyi.pdf

FEDERAL ALLOCATION PROGRAM: SPECIAL PROJECTS FOR EQUITABLE AND EFFICIENT DISTRIBUTION (SPEED) - APPENDIX 3D

On Monday, December 14th, the Chief Medical Officer of the Office of the Assistant Secretary for Preparedness and Response at HHS (HHS/ASPR), sent a communication to all State and Territorial Health Officials concerning their oversight of the allocation and distribution of COVID-19 therapeutics administered under Emergency Use Authorization. In support of this responsibility and to assist states and territories with their allocation and distribution efforts, HHS/ASPR is implementing a new federal allocation program called the Special Projects for Equitable and Efficient Distribution (SPEED).

The goal of SPEED is to assist states and territories with identifying and allocating monoclonal antibodies (mAbs) to non-hospital facilities that serve priority populations, including nursing homes and federally qualified health centers (FQHCs). **It should be noted that SPEED is separate and complementary to the state-based mAb allocation system**.

SPEED will be conducted in partnership with national organizations and associations that will assist with educating members (and non-members) and identifying those who are able and willing to administer these infusions. Membership in participating associations is not required for participation as a SPEED facility.

The first two SPEED initiatives will be launched this week and include:

1. **Home infusion in nursing homes and assisted living facilities**
   a. Description: Home infusion providers in 46 states and the District of Columbia will dispense and provide nursing support for administration of mAbs to residents of nursing homes and assisted living facilities
   b. Patient courses (initial): 560
   c. Launch date: 12/12/20
   d. Partner: National Home Infusion Association
2. Direct allocation to long-term care pharmacies
   e. Description: mAbs will be pre-positioned with long-term care pharmacies for ready deployment when cases occur in nursing homes and assisted living communities served by each pharmacy
   f. Patient courses: TBD
   g. Launch date: Week of 12/14/20
   h. Partners: American Society of Consultant Pharmacists (ASCP); AMDA – The Society for Post-Acute and Long-Term Care Medicine

For LTCFs that do not have the capability of infusing this therapy and are not contracted with a participating LTC pharmacy, they can access mAbs thru the SPEED Home infusion in nursing homes and assisted living facilities. Information about this program can be found on the NHIA website.[4]

Additional SPEED initiatives are being explored for Federally Qualified Health Centers, state/local correctional facilities, dialysis centers, and other settings. Treatment courses allocated through SPEED will be communicated with states for tracking and coordinating purposes.

The information herein this document has been prepared by the American Society of Consultant Pharmacists in consultation with federal agencies to help provide regulatory guidance and should not be taken as legal advice.

ALLOCATION SYSTEMS BY STATE JURISDICTION

The initial distribution of the monoclonal antibody treatments has been allocated through the state jurisdictions. Due to limited state capacity, state jurisdiction have allocated treatments to acute care hospital centers even though the EUAs specifically indicate that these therapies be reserved for non-hospitalized patients. This has led to stockpiling and subsequently led to the development of the SPEED program.

Some states have been deploying treatments to long term care and infusion pharmacies. It is important to understand that these processes and those of SPEED are separate and distinct at this time. Pharmacies that desire to acquire these treatments should pursue relationships with both project SPEED and their local state jurisdiction. At some time downstream, HHS will coordinate with the states to distribute product in collaboration.

APPENDIX 3E is a list of state pharmacy executives that may help with contact to the state jurisdictions.

Reference:
4. www.nhia.org/news/bam-pilot-program/

ASCP PROCESS FOR PROJECT SPEED PARTICIPATION (IN PROCESS)

Pharmacies interested in participating this this federal allocation need to submit information to ASCP (Email Chad Worz cworz@ascp.com) including name of individual location, address, contact person and email address. Request initial allocation which is based on pharmacy size: >5000 SNF beds serviced – 48 doses, 2500 – 5000 SNF beds serviced – 30, <2000 SNF beds serviced – 20. It is critical that does aren't wasted or that the product isn't placed into environments that cannot manage the administration.

If the location is already an Amerisource Bergen customer, please include your customer ID.

If location is not an Amerisource Bergen customer, please include pharmacy license number for that location. HHS will work to expediate a relationship with Amerisource Bergen Specialty so you may receive the product.

ASCP will keep this information confidential and only be used to communicate to HHS for this program.

HEALTH AND HUMAN SERVICES GUIDANCE

During the COVID-19 public health emergency (PHE), Medicare will cover and pay for these infusions (when furnished consistent with their respective EUAs) the same way it covers and pays for COVID-19 vaccines.

This will allow a broad range of providers and suppliers, including pharmacies, freestanding and hospital-based infusion centers, home health agencies, nursing homes, and entities with whom nursing homes contract for this, to administer these treatments in accordance with the EUA. While Medicare will not pay for the COVID-19 monoclonal antibody products that providers receive for free, Medicare will pay for the infusion. If a change occurs and providers begin to purchase COVID-19 monoclonal antibody products, Medicare anticipates setting the payment rate for the products at 95% of the average wholesale price (AWP), consistent with usual vaccine payment methodologies. Additionally, Medicare anticipates establishing codes and rates for the administration of the products at that time.

In order to facilitate the efficient administration of COVID-19 vaccines to SNF residents, CMS will exercise enforcement discretion with respect to certain statutory provisions. Through the exercise of that discretion, CMS is allowing Medicare-enrolled immunizers including, but not limited to, pharmacies working with the United States, as well as infusion centers, and home health agencies to *bill directly and receive direct reimbursement from the Medicare program for vaccinating Medicare SNF residents*.

Health care providers administering the COVID-19 monoclonal antibody infusions will follow the same enrollment process as those administering the other COVID-19 vaccines. Review provider enrollment information.[5]

Reimbursement (which falls outside of the Part A bundled payment) ideally would be split through Medicare Part B into a pharmacist professional fee for acquisition, compounding, handling and delivery and an administration fee to nursing staff at the SNF. Currently there is an absence of a split payment from CMS, so reimbursement could be provided to the dispensing pharmacy who could in turn reimburse the SNF for administration services based on guidance from CMS.

MONOCLONAL ANTIBODY SPECIFICATIONS

On November 9, 2020, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy, bamlanivimab, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients with positive COVID-19 test results who are at high risk for progressing to severe COVID-19 and/or hospitalization. Bamlanivimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. More information for health care providers and practitioners is available for review from the manufacturer[6] (Appendix 3F) and additional materials can be found throughout this packet.

References:

5. www.cms.gov/medicare/covid-19/enrollment-administering-covid-19-vaccine-shots
6. pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf

BAMLANIVIMAB (LILLY)

- The FDA issued an EUA[7] to permit the emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct viral testing and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
- Bamlanivimab is not authorized for use in patients who are hospitalized, require oxygen therapy, or who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

On November 21, 2020, the FDA issued an emergency use authorization (EUA) for casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age or older weighing at least 40 kilograms [about 88 pounds]) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19. This includes those who are 65 years of age or older or who have certain chronic medical conditions. Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. More information for health care providers and practitioners is available for review from the manufacturer[8] (Appendix 3G) and additional materials can be found throughout this packet.

CASIRIVIMAB AND IMDEVIMAB (REGENERON)

- The FDA issued an EUA[9] for this combination for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age or older weighing at least 40 kilograms [about 88 pounds]) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19 (Appendix 3B).
- Not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. There was no evidence of benefit in these patients in randomized, double-blind, placebo-controlled clinical trials conducted with 799 non-hospitalized adults with mild to moderate COVID-19 symptoms.

PREPARATION AND ADMINISTRATION OF BAMLANIVIMAB (LILLY)

Bamlanivimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

- Remove the bamlanivimab vial from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat.
- Inspect bamlanivimab visually for particulate matter and discoloration.
  - Bamlanivimab is a clear to slightly opalescent and colorless to slightly yellow to slightly brown solution.
- Gently invert vial by hand approximately 10 times. Do not shake.
- Dilute bamlanivimab using a 250 mL prefilled 0.9% Sodium Chloride Injection bag for intravenous infusion according to Table 1.
  - Withdraw and discard required volume of 0.9% Sodium Chloride Injection from infusion bag.
  - Withdraw required volume of bamlanivimab from the vial using an appropriately sized syringe.
  - Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.
  - Discard any product remaining in the vial.
- Gently invert IV bag by hand approximately 10 times to mix. Do not shake.
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.
- Gather the recommended materials for infusion:
  - Polyvinylchloride (PVC) infusion set containing a 0.20/0.22 micron in-line polyether sulfone (PES) filter.
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the infusion solution via pump or gravity over at least 60 minutes.

References:
7. www.fda.gov/media/143603/download
8. pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf
9. www.fda.gov/media/143892/download

Treatment	Dose/Volume of Bamianivimab (# of vials)	Volume of 0.9% Sodium Chloride to Discard from a 250 mL IV Bag	Total Volume for Infusion	Minimum Infusion Rate	Minimum Infusion Time
Bamianvimab	700 mg/20 mL (1 vial)	70 mL	200 mL	200 mL/hr	60 minutes

- Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

PREPARATION AND ADMINISTRATION OF CASIRIVIMAB AND IMDEVIMAB (REGENERON)

Casirivimab and imdevimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

a. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat. Do not shake the vials.

b. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.

c.Obtain an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab solutions according to Table 2.

d. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the infusion bag containing 0.9% Sodium Chloride Injection, see Table 2. Discard any product remaining in the vial.

e. Gently invert infusion bag by hand approximately 10 times to mix. Do not shake. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Casirivimab and imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

a. Gather the recommended materials for infusion:
   - Polyvinyl chloride (PVC), Polyethylene (PE)-lined PVC, or Polyurethane (PU) infusion set
   - In-line or add-on 0.2-micron polyether sulfone (PES) filter

b. Attach the infusion set to the IV bag.

c. Prime the infusion set.

d. Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyether sulfone (PES) filter.

	Antibody Dose	Volume to Withdraw from Vial	Number of Vials Needed[b]	Volume of 0.9% Sodium Chloride to Discard from a 250 mL Infusion Bag	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Casirivimab and Imdevimab 2,400 mg Dose[a]	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL or 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL or 4 vials of 2.5 mL				

Note: Casirivimab = REGN10933; Imdevimab = REGN10987

a. 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

b. One 11.1 mL vial of on antibody may be prepared with four 2.5 mL viles of the other antibody to create one treatment course.

e. The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.
f. After infusion is complete, flush with 0.9% Sodium Chloride Injection.
g. Discard unused product.
h. Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

CONSIDERATIONS

- Bamlanivimab storage: Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze, shake, or expose to direct light.
- Casirivimab and imdevimab must be administered together intravenously over 60 minutes.
- Casirivimab and imdevimab vials must be stored in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze, shake, or expose to direct light.
- May only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

MONITORING AND REPORTING OF ADVERSE REACTIONS

- Patients treated with monoclonal antibody treatment should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.
- Clinically monitor patients, including vital signs during administration and observe patients for at least 1 hour after infusion is complete.
- There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of monoclonal antibody treatment. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration, and initiate appropriate medications and/or supportive care.

Suggested medications to be available in Nursing home infusion site: E-Box for MAb infusions:	
Medication	**Number of doses**
Epinephrine 0.3 mg IM	
Methylprednisolone 125mg	
Albuterol neb 2.5 mg INH	
Diphenhydramine 50 mg IV	
Famotidine 20 mg IV	
Albuterol syr 2 mg PO	
Diphenhydramine 25mg PO	

An FDA MedWatch Form[10] (Appendix 3H) must be completed to report all medication errors and serious adverse events that occur with treatment of bamlanivimab or casirivimab and imdevimab use and considered to be potentially related to bamlanivimab or casirivimab and imdevimab is mandatory and must be done by the prescribing healthcare provider and/or the provider's designee. These adverse events must be reported within 7 calendar days from the onset of the event.

***Serious Adverse Events are defined as:**
- Death
- A life-threatening adverse event
- inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

In addition, please provide a copy of all FDA MedWatch forms to:
Eli Lilly and Company, Global Patient Safety
Fax: 1-317-277-0853
E-mail: mailindata_gsmtindy@lilly.com
Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.
or
Regeneron Pharmaceuticals, Inc
Fax: 1-888-876-2736
E-mail: medical.information@regeneron.com
Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

Reference:
10. www.fda.gov/safety/medical-product-safety-information/medwatch-forms-fda-safety-reporting

MONOCLONAL ANTIBODY ELIGIBILITY CRITERIA CHECKLIST (ALSO APPENDIX 3J)

Several monoclonal antibodies have received emergency use authorization from the FDA for the treatment of mild to moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Resident Name:	**Room:**	**Date:**
InclusionCriteria *(Must Meet All 3 Criteria)*	**Yes**	**No**
Mild to moderately symptomatic COVID-19[1]		
Within 10 days of symptom onset, preferably in the first 3 days		
Positive direct test for SARS-CoV-2 (*either A or B*) A) If no outbreak present in the building, PCR positive B) If outbreak is present in the building, PCR or antigen positive		
High Risk Criteria forAdults *(Must Have 1 of the Following)*	**Yes**	**No**
Body mass index ≥ 35		
Age ≥ 65		
Chronic kidney disease		
Diabetes		
Immunosuppressive disease or currently receiving immunosuppressive treatment		
≥ 55 years of age AND have: · Cardiovascular disease, OR · Hypertension, OR · Chronic obstructive pulmonary disease/other chronic respiratory disease		
Exclusion Criteria *(May Not Have Any of the Following)*	**Yes**	**No**
Patient is hospitalized or meets hospitalization criteria[2]		
Patient requires oxygen due to COVID-19 (Pulse ox ≤ 93% on room air)		
If on chronic oxygen, patient requires an increase in oxygen therapy due to COVID-19		
Patient is on hospice, is hospice eligible, had a palliative care/hospice consult within the prior 6 months, or has a life expectancy less than 6 months (clinician judgement or MDS J1400), inclusions of these residents can be decided on a case by case basis		

DEFINITIONS	
Mild to Moderate Symptoms (1 or more of the following)	**Hospitalization Criteria Definition (1 or more of the following)**
• Fever (99.0 or greater) • New cough • Sore throat • Malaise • Headaches • Muscle pain/aches • Gastrointestinal symptoms • Shortness of breath with exertion • Loss of smell and taste	• RR≥30 • HR ≥ 130 • SBP < 90 despite fluid resuscitation

Infusion-related reactions have been observed and there is potential for severe reactions, including anaphylaxis. Monoclonal antibody treatment may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS).

Several monoclonal antibodies have received emergency use authorization from the FDA for the treatment of mild to moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Post-acute and long-term care settings with access to such expertise and resources may be able to administer monoclonal antibody in their own facilities.

Administration of monoclonal antibody treatment requires documentation of:

1. Patient has been given FDA Fact sheet for patient.
2. Patient has been informed of alternatives to receiving monoclonal antibody treatment,
3. Patient has been informed that this is an unapproved drug that is authorized for use under the FDA Emergency Use Authorization (EUA)
4. Reporting of adverse events to FDA MedWatch, following the requirements under Emergency Use Authorizations (see last page for details).

COVID-19 OUTPATIENT MONOCLONAL ANTIBODY INFUSION ORDERS - APPENDIX 3K

MEDICARE PAYMENT FOR MONOCLONAL COVID-19 INFUSION

In order to ensure immediate access during the COVID-19 PHE, Medicare will cover and pay for these infusions in accordance with Section 3713 of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act). CMS intends to address potential refinements to payment for COVID-19 monoclonal antibody infusions and their administration through future notice and comment rulemaking.

PAYMENT FOR INFUSION

Initially, for the infusion of bamlanivimab and casirivimab and imdevimab (administered together), the Medicare national average payment rate for the administration will be approximately $310. This payment rate is based on one hour of infusion and post-administration monitoring in the hospital outpatient setting. At a later date, CMS may use a similar methodology to determine the payment rate for the infusion of additional monoclonal antibody products based on the expected infusion time, consistent with the FDA EUA or FDA approval of such products.

PAYMENT FOR PRODUCT

As noted above, Medicare will not provide payment for the COVID-19 monoclonal antibody products that health care providers receive for free, as will be the case upon the product's initial availability in response to the COVID-19 PHE. If health care providers begin to purchase these monoclonal antibody products, CMS anticipates setting the payment rate in the same way we set the payment rate for COVID-19 vaccines. For example, Medicare will pay 95% of AWP for COVID-19 vaccines furnished in the physician office setting and pay hospital outpatient departments at reasonable cost for COVID-19 vaccines. Because COVID-19 monoclonal antibody products are considered COVID-19 vaccines, they are not eligible for the New COVID-19 Treatments Add-on Payment (NCTAP) under the Inpatient Prospective Payment System (IPPS).[11]

Should there be additional products that come to market, get the most up to date list of billing codes, payment allowances and effective dates.[12]

People with Medicare pay no cost sharing for these COVID-19 monoclonal antibody infusion therapy products:

- No copayment/coinsurance
- No deductible

References:

11. Note: CMS also anticipates addressing coding and payment rates for administration of monoclonal antibody products through future notice-and- comment rulemaking
12. www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/covid-19-vaccines-and-monoclonal-antibodies

The ASCP Memorandum on Vaccine Distribution Liability Under Prep Act (Appendix 3L) applies also to the monoclonal antibody treatments.

BILLING FOR MONOCLONAL ANTIBODY COVID-19 INFUSION ADMINISTRATION

Health care providers can bill for the administration of the COVID-19 monoclonal antibody infusion on a single claim for COVID-19 monoclonal antibody administration or submit claims on a roster bill, in accordance with the FDA EUA for each product.

- The EUA for COVID-19 monoclonal antibody treatments contain specific requirements for administration that are considerably more complex than for other services that are billed using roster billing. CMS expects that health care providers will maintain appropriate medical documentation that supports the medical necessity of the service. This includes documentation that supports that the terms of the EUAs are met. The documentation should also include the name of the practitioner who ordered or made the decision to administer the infusion, even in cases where claims for these services are submitted on roster bills.
- When COVID-19 monoclonal antibody doses are provided by the government without charge, providers should only bill for the administration. Health care providers should not include the COVID- 19 monoclonal antibody codes on the claim when the product is provided for free.

Health care providers who provide these services to enrollees in a Medicare Advantage Plan should submit claims for monoclonal antibodies to treat COVID-19 that are covered by Part B in accordance with Section 3713 of the CARES Act to Original Medicare for all patients enrolled in Medicare Advantage in 2020 and 2021.

CODING FOR MONOCLONAL ANTIBODY COVID-19 INFUSIONS

CMS identified specific code(s) for each COVID-19 monoclonal antibody product and specific administration code(s) for Medicare payment:

Eli Lilly and Company's Antibody Bamlanivimab (LY-CoV555)[13], EUA effective November 10, 2020

Q0239:
Long descriptor: Injection, bamlanivimab-xxxx, 700 mg
Short descriptor: bamlanivimab-xxxx

M0239:
Long Descriptor: intravenous infusion, bamlanivimab-xxxx, includes infusion and post administration monitoring

Short Descriptor: bamlanivimab-xxxx infusion

Regeneron's Antibody casirivimab & imdevimab (REGN-COV2)[14], EUA effective November 21, 2020

Q0243:
Long descriptor: Injection, casirivimab and imdevimab 2400 mg

Short descriptor: casirivimab and imdevimab

M0243:
Long Descriptor: intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring

Short Descriptor: casirivi and imdevi infusion

BILLING MEDICARE AS A MASS IMMUNIZER

Pharmacies must register as a Mass Immunizer to bill for vaccination administration. Monoclonal antibody treatments are being classified as vaccinations for the purposes of access and reimbursement as well.

Even pharmacies with the ability to bill Medicare Part B must separately register as a mass immunizer.

- Receiving Part B reimbursement includes 2 steps:
  1. Pharmacy must have a National Provider Identification number (NPI). Click here for more information.[15]
  2. Apply for a Medicare Part B Provider status: application is CMS Form 855I. (Appendix 3M)
  3. Apply for Mass Immunization Provider Status: application is CMS Form 855B.[16] Click here for this form. (Appendix 3N)

To enroll over the phone as a mass immunizer — call your MAC-specific enrollment hotline[17] and give your valid Legal Business Name (LBN), National Provider Identifier (NPI), Tax Identification Number (TIN), practice location and state license, if applicable.

References:

13. www.fda.gov/media/143602/download
14. www.fda.gov/media/143891/download
15. nppes.cms.hhs.gov/NPPES/StaticForward.do?forward=static.instructions
16. www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms855i.pdf
17. www.cms.gov/files/document/covid-19-mac-webpages-and-hotlines.pdf

ADDITIONAL INFORMATION ON ROSTER BILLING FROM CMS[18]

- Medicare will cover the cost monoclonal antibody therapy for COVID-19 treatments, and coverage is extended to beneficiaries in nursing homes at no cost during the public health emergency.[19]
- Health care providers can bill for the administration of the COVID-19 monoclonal antibody infusion on a single claim for COVID-19 monoclonal antibody administration or submit claims on a roster bill, in accordance with the FDA EUA for each product. Providers should only bill for the administration and should not include the COVID-19 monoclonal antibody codes on the claim.

PER THERAPY COMPOUNDED AND DELIVERED FOR ADMINISTRATION:

In the absence of a split reimbursement fee designated by CMS for the pharmacy costs and the administration costs, ASCP has proposed the following as a guideline to CMS.

PHARMACIST PROFESSIONAL FEE:

- Consistent with pharmacy costs associated with the following necessary elements:
- Drug Utilization Review (allergies, vaccine specifications, etc.)
- Order entry into system for patients (data collection)
- Product ordering and receiving, with appropriate storage
- Pharmacist aseptic preparation and compounding (clean room)
- Verification/ checking of process
- Labeling of product
- Delivery to facility with appropriate storage of product and supplies (which is often a separate delivery and can be a long distance from the pharmacy)
- Includes appropriate pumps/poles/tubing
- Appropriate billing (Medicare Part B / Nursing facility direct / Commercial or Medicare Part D)

ASCP suggested a total pharmacy cost per therapy of $147.68 to CMS on 11/24/2020.

Because on the reimbursement structure, either the skilled nursing facility or the pharmacy can bill for the therapy. The product has generally been allocated to pharmacies due to the storage, handling, and compounding of the intravenous (IV) treatment. In skilled nursing environments, nurses are capable of administering and monitoring IV medications. In this described situation, the pharmacy may contract with the nursing facility to reimburse for this administration and monitoring. The rate should be determined fairly between those parties.

APPENDIX 3P is a sample contract between the pharmacy and the LTC facility for reimbursement for the administration and monitoring of the therapy.

Just as with COVID-19 vaccines, the liability for health care providers providing and administering treatments for COVID-19 are protected under the PREP Act provided that they meet the requirements outlines in the EUA. Pharmacies should work with the medical director on an individual basis when dispensing monoclonal antibody treatments to ensure that each facility meets the requirements outlined in the respective EUA.

For skilled nursing facilities and for most assisted living facilities, pharmacies can provide nursing support for the vaccines or can refer those facilities to infusion pharmacies who can provide end-to-end services around the monoclonal antibody treatments.

Provision requirements outside of Skilled Nursing Facilities (ALF, PACE, Community)

For LTCFs that do not have the capability of infusing this therapy and are not contracted with a participating LTC pharmacy, they can access mAbs thru the SPEED Home infusion in nursing homes and assisted living facilities. Information about this program can be found on the NHIA website.[20]

DATA REPORTING

At this point, data reporting is not a requirement of Project SPEED. This document **APPENDIX 3Q** represents what CDC is considering for reporting in the future. Most of this data is reportable from pharmacy dispensing systems and is documented as part of normal nursing practice in skilled nursing facilities.

References:
18. www.cms.gov/medicare/preventive-services/roster-billing-mass-immunizers
19. www.cms.gov/files/document/covid-medicare-monoclonal-antibody-infusion-program-instruction.pdf
20. www.nhia.org/news/bam-pilot-program/

Medicare Monoclonal Antibody COVID-19 Infusion Program Instruction
Updated: December 3, 2020

On November 9, 2020, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy, bamlanivimab, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients with positive COVID-19 test results who are at high risk for progressing to severe COVID-19 and/or hospitalization. Bamlanivimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. Review the Fact Sheet for Health Care Providers EUA of Bamlanivimab regarding the limitations of authorized use.

On November 21, 2020, the FDA issued an EUA for the investigational monoclonal antibody therapy, casirivimab and imdevimab, administered together, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients with positive COVID-19 test results who are at high risk for progressing to severe COVID-19 and/or hospitalization. Similar to bamlanivimab, casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. Review the Fact Sheet for Health Care Providers EUA of Casirivimab and Imdevimab regarding the limitations of authorized use when administered together.

During the COVID-19 public health emergency (PHE), Medicare will cover and pay for these infusions (when furnished consistent with their respective EUAs) the same way it covers and pays for COVID-19 vaccines.

This would allow a broad range of providers and suppliers, including freestanding and hospital-based infusion centers, home health agencies, nursing homes, and entities with whom nursing homes contract for this, to administer these treatments in accordance with the EUA. Medicare will not pay for the COVID-19 monoclonal antibody products that providers receive for free. If providers begin to purchase COVID-19 monoclonal antibody products, Medicare anticipates setting the payment rate for the products, which will be 95% of the average wholesale price (AWP) for many health care providers, consistent with usual vaccine payment methodologies. Additionally, Medicare anticipates establishing codes and rates for the administration of the products.

In order to facilitate the efficient administration of COVID-19 vaccines to SNF residents, CMS will exercise enforcement discretion with respect to certain statutory provisions as well as any associated statutory references and implementing regulations, including as interpreted in pertinent guidance (collectively, "SNF Consolidated Billing Provisions"). Through the exercise of that discretion, CMS will allow Medicare-enrolled immunizers including, but not limited to, pharmacies working with the United States, as well as infusion centers, and home health agencies to bill directly and receive direct reimbursement from the Medicare program for vaccinating Medicare SNF residents.

Health care providers administering the COVID-19 monoclonal antibody infusions will follow the same enrollment process as those administering the other COVID-19 vaccines. Review provider enrollment information.

Coding for Monoclonal Antibody COVID-19 Infusions

CMS identified specific code(s) for each COVID-19 monoclonal antibody product and specific administration code(s) for Medicare payment:

Eli Lilly and Company's Antibody Bamlanivimab (LY-CoV555), EUA effective November 10, 2020

Q0239:

Long descriptor: Injection, bamlanivimab-xxxx, 700 mg
Short descriptor: bamlanivimab-xxxx

M0239:

Long Descriptor: intravenous infusion, bamlanivimab-xxxx, includes infusion and post administration monitoring
Short Descriptor: bamlanivimab-xxxx infusion

Regeneron's Antibody casirivimab and imdevimab (REGN-COV2) , EUA effective November 21, 2020

Q0243:

Long descriptor: Injection, casirivimab and imdevimab, 2400 mg

Short descriptor: casirivimab and imdevimab

M0243:

Long Descriptor: intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring
Short Descriptor: casirivi and imdevi infusion

Medicare Payment for Monoclonal COVID-19 Infusion

In order to ensure immediate access during the COVID-19 PHE, Medicare will cover and pay for these infusions in accordance with Section 3713 of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act). CMS intends to address potential refinements to payment for COVID-19 monoclonal antibody infusions and their administration through future notice and comment rulemaking.

Payment for Infusion

Initially, for the infusion of bamlanivimab and casirivimab and imdevimab (administered together), the Medicare national average payment rate for the administration will be approximately $310. This payment rate is based on one hour of infusion and post-administration monitoring in the hospital outpatient setting. At a later date, we may use a similar methodology to determine the payment rate for the infusion of additional monoclonal antibody products based on the expected infusion time, consistent with the FDA EUA or FDA approval of such products.

Payment for Product

As noted above, Medicare will not provide payment for the COVID-19 monoclonal antibody products that health care providers receive for free, as will be the case upon the product's initial availability in response to the COVID-19 PHE. If health care providers begin to purchase these monoclonal antibody products, CMS anticipates setting the payment rate in the same way we set the payment rate for COVID-19 vaccines. For example, Medicare will pay 95% of AWP for COVID-19 vaccines furnished in the physician office setting, and pay hospital outpatient departments at reasonable cost for COVID-19 vaccines. Because COVID-19 monoclonal antibody products are considered COVID-19 vaccines, they are not eligible for the New COVID-19 Treatments Add-on Payment (NCTAP) under the Inpatient Prospective Payment System (IPPS).

Note: We also anticipate addressing coding and payment rates for administration of monoclonal antibody products through future notice-and-comment rulemaking.

Should there be additional products that come to market, get the most up to date list of billing codes, payment allowances and effective dates.

People with Medicare pay no cost sharing for these COVID-19 monoclonal antibody infusion therapy products:

- No copayment/coinsurance
- No deductible

Billing for Monoclonal Antibody COVID-19 Infusion Administration

Health care providers can bill for the administration of the COVID-19 monoclonal antibody infusion on a single claim for COVID-19 monoclonal antibody administration or submit claims on a roster bill, in accordance with the FDA EUA for each product.

- The EUA for COVID-19 monoclonal antibody treatments contain specific requirements for administration that are considerably more complex than for other services that are billed using roster billing. CMS expects that health care providers will maintain appropriate medical documentation that supports the medical necessity of the service. This includes documentation that supports that the terms of the EUAs are met. The documentation should also include the name of the practitioner who ordered or made the decision to administer the infusion, even in cases where claims for these services are submitted on roster bills.

- When COVID-19 monoclonal antibody doses are provided by the government without charge, providers should only bill for the administration. Health care providers should not include the COVID-19 monoclonal antibody codes on the claim when the product is provided for free.

Health care providers who provide these services to enrollees in a Medicare Advantage Plan should submit claims for monoclonal antibodies to treat COVID-19 that are covered by Part B in accordance with Section 3713 of the CARES Act to Original Medicare for all patients enrolled in Medicare Advantage in 2020 and 2021.

FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab and imdevimab to be administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

Casirivimab and imdevimab have been authorized by FDA for the emergency uses described above.

Casirivimab and imdevimab are not FDA-approved for these uses.

Casirivimab and imdevimab are authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of casirivimab and imdevimab under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

This EUA is for the use of the unapproved products, casirivimab and imdevimab, to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease

- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to casirivimab and imdevimab. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

- The authorized dosage is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous (IV) infusion as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.
- Casirivimab and imdevimab solutions must be diluted prior to administration.
- Administer 1,200 mg of casirivimab and 1,200 mg of imdevimab together as a single IV infusion over at least 60 minutes via pump or gravity.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

The authorized dosage may be updated as additional data from clinical trials becomes available.

For information on clinical trials that are testing the use of casirivimab and imdevimab in COVID-19, please see www.clinicaltrials.gov.

Contraindications

None.

Dosing

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved products, casirivimab and imdevimab, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Dosage

The dosage in adults and in pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion over at least 60 minutes. Casirivimab and imdevimab solutions must be diluted prior to administration. Casirivimab and imdevimab should be given together as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Dosage Adjustment in Specific Populations

No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment *[see Full EUA Prescribing Information, Use in Specific Populations (11)]*.

Preparation and Administration

Preparation

Casirivimab and imdevimab are each supplied in individual single-dose vials. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials**.
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared.
   - The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.
3. Obtain an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab solutions according to **Table 1**.
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the infusion bag containing 0.9% Sodium Chloride Injection, see **Table 1**. Discard any product remaining in the vial.
5. Gently invert infusion bag by hand approximately 10 times to mix. **Do not shake**. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

Table 1: Recommended Dilution Instructions for Casirivimab and Imdevimab for IV Infusion

Casirivimab and Imdevimab 2,400 mg Dose[a]	Antibody Dose	Volume to Withdraw from Vial	Number of Vials Needed[b]	Volume of 0.9% Sodium Chloride to Discard from a	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time

				250 mL Infusion Bag			
	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL				

NOTE: casirivimab = REGN10933; imdevimab = REGN10987

[a] 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

[b] One 11.1 mL vial of one antibody may be prepared with four 2.5 mL vials of the other antibody to create one treatment course.

Administration

Casirivimab and imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), Polyethylene (PE)-lined PVC, or Polyurethane (PU) infusion set
  - In-line or add-on 0.2 micron polyethersulfone (PES) filter
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see **Table 1**).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.
- After infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

Storage

Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the individual original carton to protect from light. Do NOT freeze, shake, or expose to direct light.

Warnings

There are limited clinical data available for casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

Infusion-related reactions have been observed with administration of casirivimab and imdevimab.

Signs and symptoms of infusion-related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab are not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Side Effects

Adverse events have been reported with casirivimab and imdevimab [*see Full EUA Prescribing Information, Clinical Trials Experience (6.1)*].

Additional adverse events associated with casirivimab and imdevimab, some of which may be serious, may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the health care provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving casirivimab and imdevimab, including:

- FDA has authorized the emergency use of casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

- The patient or parent/caregiver has the option to accept or refuse casirivimab and imdevimab.
- The significant known and potential risks and benefits of casirivimab and imdevimab, and the extent to which such risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.

For information on clinical trials that are testing the use of casirivimab and imdevimab related to COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR CASIRIVIMAB AND IMDEVIMAB UNDER EMERGENCY USE AUTHORIZATION:

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of casirivimab and imdevimab to be administered together, the following items are required. Use of casirivimab and imdevimab under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.
2. As the health care provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to the patient receiving casirivimab and imdevimab. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
    a. Given the "Fact Sheet for Patients, Parents and Caregivers",
    b. Informed of alternatives to receiving casirivimab and imdevimab, and
    c. Informed that casirivimab and imdevimab are unapproved drugs that are authorized for use under this Emergency Use Authorization.
3. Patients with known hypersensitivity to any ingredient of casirivimab and imdevimab must not receive casirivimab and imdevimab.
4. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of casirivimab and imdevimab.
5. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to casirivimab and imdevimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.

- Submit adverse event reports to FDA MedWatch using one of the following methods:
    - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
    - By using a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
    - Call 1-800-FDA-1088 to request a reporting form
    - Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)."

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

6. OTHER REPORTING REQUIREMENTS
   In addition, please provide a copy of all FDA MedWatch forms to:
   Regeneron Pharmaceuticals, Inc
   Fax: 1-888-876-2736
   E-mail: medical.information@regeneron.com
   Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved and available alternatives to casirivimab and imdevimab to be administered together for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html. The health care provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Regeneron Pharmaceuticals, Inc. for the unapproved products, casirivimab and imdevimab, to be administered together, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral

testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. [1] As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that casirivimab and imdevimab, administered together, may be effective for the treatment of COVID-19 in patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for casirivimab and imdevimab will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

CONTACT INFORMATION

For additional information visit www.REGENCOV2.com
If you have questions, please contact Regeneron at 1-844-734-6643.

END SHORT VERSION FACT SHEET
Long Version Begins on Next Page

[1] The health care provider should visit https://clinicaltrials.gov/ to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

FULL EUA PRESCRIBING INFORMATION

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

1 AUTHORIZED USE

Casirivimab and imdevimab are authorized to be administered together for use under an EUA for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19 *[see Warnings and Precautions (5.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

The optimal dosing regimen for treatment of COVID-19 has not yet been established.
The recommended dosing regimen may be updated as data from clinical trials become available.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved products, casirivimab and imdevimab, to be administered together, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

2.2 Dosage

The dosage in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab should be given as soon as possible after a positive viral test for SARS-CoV-2 and within 10 days of symptom onset.

2.3 Dose Adjustment in Specific Populations

Pregnancy or Lactation

No dosage adjustment is recommended in pregnant or lactating women *[see Use in Specific Populations (11.1, 11.2)]*.

Pediatric Use

No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg and are older than 12 years of age. Casirivimab and imdevimab are not recommended for pediatric patients weighing less than 40 kg or those less than 12 years of age *[see Use in Specific Populations (11.3)]*.

Renal Impairment

No dosage adjustment is recommended in patients with renal impairment *[see Use in Specific Populations (11.5)]*.

2.4 Dose Preparation and Administration

Preparation

Casirivimab and imdevimab are each supplied in individual single-dose vials. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique:

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials.**
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.
3. Obtain an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab according to **Table 2**.
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the infusion bag containing 0.9% Sodium Chloride Injection, see **Table 2**. Discard any product remaining in the vial.
5. Gently invert infusion bag by hand approximately 10 times. **Do not shake.**
   This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C

(36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Table 2: Recommended Dilution Instructions for Casirivimab and Imdevimab for IV Infusion

Casirivimab and Imdevimab 2,400 mg Dose[a]	**Antibody Dose**	**Volume to Withdraw from Vial**	**Number of Vials Needed[b]**	**Volume of 0.9% Sodium Chloride to Discard from a 250 mL Infusion Bag**	**Total Volume for Infusion**	**Maximum Infusion Rate**	**Minimum Infusion Time**
	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL				

NOTE: casirivimab = REGN10933; imdevimab = REGN10987

[a] 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

[b] One 11.1 mL vial of one antibody may be prepared with four 2.5 mL vials of the other antibody to create one treatment course.

Administration

Casirivimab and imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), Polyethylene (PE)-lined PVC, or Polyurethane (PU) infusion set
  - In-line or add-on 0.2 micron polyethersulfone (PES) filter
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see **Table 2**).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.

- After infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

Storage

This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

3 DOSAGE FORMS AND STRENGTHS

Casirivimab is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution available as:

- Injection: 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) in a single-dose vial

Imdevimab is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution available as:

- Injection: 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) in a single-dose vial

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

There are limited clinical data available for casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

5.1 Hypersensitivity including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reactions, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant

hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of casirivimab and imdevimab.

Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

5.2 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab are not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

6 OVERALL SAFETY SUMMARY

Overall more than 2,100 subjects have been exposed to IV casirivimab and imdevimab in clinical trials in both hospitalized and non-hospitalized patients.

6.1 Clinical Trials Experience

The safety of casirivimab and imdevimab is based on analysis from one phase 1/2 trial of 799 ambulatory (non-hospitalized) subjects with COVID-19.

R10933-10987-COV-2067 is a randomized, double-blind, placebo-controlled clinical trial in ambulatory adults with mild to moderate COVID-19 symptoms who had a sample collected for the first positive SARS-CoV-2 viral infection determination within 3 days prior to the start of the infusion. Subjects were treated with a single infusion of 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) (N=258) or 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) (N=260), or placebo (n=262). The adverse events collected were infusion-related reactions and hypersensitivity reactions of moderate severity or higher through day 29, all serious adverse events (SAEs); and in phase 1 only, all grade 3 and 4 treatment-emergent adverse events.

Serious adverse events were reported in 4 subjects (1.6%) in the casirivimab and imdevimab 2,400 mg group, 2 subjects (0.8%) in the casirivimab and imdevimab 8,000 mg group, and 6 subjects (2.3%) in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg casirivimab and imdevimab), intestinal obstruction and dyspnea (8,000 mg casirivimab and imdevimab) and COVID-19, pneumonia and hypoxia (placebo). Casirivimab and imdevimab are not authorized at the 8,000 mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).

Hypersensitivity Including Anaphylaxis and Infusion-related Reactions

One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and include pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm and none were reported in the 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm.

In two subjects receiving the 8,000 mg dose of casirivimab and imdevimab, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved [*see Warnings and Precautions (5.1)*].

7 PATIENT MONITORING RECOMMENDATIONS

Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete *[see Warnings and Precautions (5.1) and Clinical Trials Experience (6.1)]*.

8 ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS AND INSTRUCTIONS

Clinical trials evaluating the safety of casirivimab and imdevimab are ongoing *[see Overall Safety Summary (6)]*.

Completion of FDA MedWatch Form to report all medication errors and serious adverse events* occurring during casirivimab and imdevimab use and considered to be potentially related to casirivimab and imdevimab is mandatory and must be done by the prescribing healthcare provider and/or the provider's designee. These adverse events must be reported within 7 calendar days from the onset of the event:

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;

- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

If a serious and unexpected adverse event occurs and appears to be associated with the use of casirivimab and imdevimab, the prescribing health care provider and/or the provider's designee should complete and submit a MedWatch form to FDA using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Use a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form

IMPORTANT: When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient initials, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of casirivimab and imdevimab
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In section A, box 1, provide the patient's initials in the Patient Identifier
2. In section A, box 2, provide the patient's date of birth or age
3. In section B, box 5, description of the event:
    a. Write "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)" as the first line
    b. Provide a detailed report of medication error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved drug. Please see information to include listed above.
4. In section G, box 1, name and address:
    a. Provide the name and contact information of the prescribing health care provider or institutional designee who is responsible for the report
    b. Provide the address of the treating institution (NOT the health care provider's office address).

9 OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:
Regeneron Pharmaceuticals, Inc
Fax: 1-888-876-2736
E-mail: medical.information@regeneron.com
Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

10 DRUG INTERACTIONS

Casirivimab and imdevimab are 2 monoclonal antibodies (mAbs) which are not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Casirivimab and imdevimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Nonclinical reproductive toxicity studies have not been conducted with casirivimab and imdevimab. In a tissue cross-reactivity study with casirivimab and imdevimab using human fetal tissues, no binding of clinical concern was detected. Human immunoglobulin G1 (IgG1) antibodies are known to cross the placental barrier; therefore, casirivimab and imdevimab have the potential to be transferred from the mother to the developing fetus. It is unknown whether the potential transfer of casirivimab and imdevimab provides any treatment benefit or risk to the developing fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

11.2 Nursing Mothers

Risk Summary

There are no available data on the presence of casirivimab and/or imdevimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of

breastfeeding should be considered along with the mother's clinical need for casirivimab and imdevimab and any potential adverse effects on the breastfed child from casirivimab and imdevimab or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

11.3 Pediatric Use

The safety and effectiveness of casirivimab and imdevimab have not been assessed in pediatric patients. The recommended dosing regimen is expected to result in comparable serum exposures of casirivimab and imdevimab in patients 12 years of age and older and weighing at least 40 kg as observed in adults, since adults with similar body weight have been included in Trial R10933-10987-COV-2067.

11.4 Geriatric Use

Of the 799 patients with SARS-CoV-2 infection randomized in Trial R10933-10987-COV-2067, 7% were 65 years or older, and 2% were 75 years of age or older. The difference in PK of casirivimab and imdevimab in geriatric patients compared to younger patients is unknown.

11.5 Renal Impairment

Casirivimab and imdevimab are not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of casirivimab and imdevimab.

11.6 Hepatic Impairment

The effect of hepatic impairment on PK of casirivimab and imdevimab is unknown.

11.7 Other Specific Populations

The effect of other covariates (e.g., sex, race, body weight, disease severity) on PK of casirivimab and imdevimab is unknown.

12 OVERDOSAGE

Doses up to 8,000 mg (4,000 mg each of casirivimab and imdevimab, greater than 3 times the recommended dose) have been administered in clinical trials without dose-limiting toxicity. Treatment of overdose should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with casirivimab and imdevimab.

13 PRODUCT DESCRIPTION

Casirivimab, a human immunoglobulin G-1 (IgG1) monoclonal antibody (mAb), is a covalent heterotetramer consisting of 2 heavy chains and 2 light chains produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture and has an approximate molecular weight of 145.23 kDa.

Casirivimab injection is a sterile, preservative-free, clear to slightly opalescent and colorless to pale yellow solution in a single-dose vial for intravenous infusion after dilution available as a 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) solution and must be administered with imdevimab.

- Casirivimab: Each 2.5 mL of solution contains 300 mg of casirivimab, L-histidine (1.9 mg), L-histidine monohydrochloride monohydrate (2.7 mg), polysorbate 80 (2.5 mg), sucrose (200 mg), and Water for Injection, USP. The pH is 6.0.

- Casirivimab: Each 11.1 mL of solution contains 1,332 mg of casirivimab, L-histidine (8.3 mg), L-histidine monohydrochloride monohydrate (12.1 mg), polysorbate 80 (11.1 mg), sucrose (888 mg), and Water for Injection, USP. The pH is 6.0.

Imdevimab, a human IgG1 mAb, is a covalent heterotetramer consisting of 2 heavy chains and 2 light chains produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture and has an approximate molecular weight of 144.14 kDa.

Imdevimab injection is a sterile, preservative-free, clear to slightly opalescent and colorless to pale yellow solution in a single-dose vial for intravenous infusion after dilution available as a 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) solution and must be administered with casirivimab.

- Imdevimab: Each 2.5 mL of solution contains 300 mg of imdevimab, L-histidine (1.9 mg), L-histidine monohydrochloride monohydrate (2.7 mg), polysorbate 80 (2.5 mg), sucrose (200 mg), and Water for Injection, USP. The pH is 6.0.

- Imdevimab: Each 11.1 mL of solution contains 1,332 mg of imdevimab, L-histidine (8.3 mg), L-histidine monohydrochloride monohydrate (12.1 mg), polysorbate 80 (11.1 mg), sucrose (888 mg), and Water for Injection, USP. The pH is 6.0.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

Casirivimab (IgG1κ) and imdevimab (IgG1λ) are two recombinant human mAbs which are unmodified in the Fc regions. Casirivimab and imdevimab bind to non-overlapping epitopes of the spike protein receptor binding domain (RBD) of SARS-CoV-2 with dissociation constants K_D = 45.8 pM and 46.7 pM, respectively. Casirivimab, imdevimab and the casirivimab + imdevimab combination blocked RBD binding to the human ACE2 receptor with IC_{50} values of 56.4 pM, 165 pM and 81.8 pM, respectively [*see Microbiology/Resistance Information (15)*].

14.2 Pharmacodynamics

Trial R10933-10987-COV-2067 evaluated casirivimab and imdevimab with doses of 1 and 3.33 times the recommended doses (1,200 mg casirivimab and 1,200 mg imdevimab; 4,000 mg casirivimab and 4,000 mg imdevimab) in ambulatory patients with COVID-19. A flat dose-response relationship for efficacy was identified for casirivimab and imdevimab at those two doses, based on viral load and clinical outcomes.

14.3 Pharmacokinetics

Pharmacokinetic profiles of casirivimab and imdevimab are expected to be consistent with the profile of other IgG1 mAbs.

Specific Populations

The effect of different covariates (e.g., age, sex, race, body weight, disease severity, hepatic impairment) on the PK of casirivimab and imdevimab is unknown. Renal impairment is not expected to impact the PK of casirivimab and imdevimab, since mAbs with molecular weight >69 kDa are known not to undergo renal elimination. Similarly, dialysis is not expected to impact the PK of casirivimab and imdevimab.

Drug-Drug Interactions

Casirivimab and imdevimab are mAbs which are not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely *[see Drug Interactions (10)]*.

15 MICROBIOLOGY/RESISTANCE INFORMATION

Antiviral Activity

In a SARS-CoV-2 virus neutralization assay in Vero E6 cells, casirivimab, imdevimab, and the casirivimab + imdevimab combination neutralized SARS-CoV-2 (USA-WA1/2020 isolate) with EC_{50} values of 37.4 pM (0.006 μg/mL), 42.1 pM (0.006 μg/mL), and 31.0 pM (0.005 μg/mL) respectively.

Antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) were assessed using Jurkat target cells expressing SARS-CoV-2 spike protein. Casirivimab, imdevimab and the casirivimab + imdevimab combination mediated ADCC with human natural killer (NK) effector cells. Casirivimab, imdevimab and the casirivimab + imdevimab combination mediated ADCP with human macrophages. Casirivimab, imdevimab and the casirivimab + imdevimab combination did not mediate complement-dependent cytotoxicity in cell-based assays.

Antibody Dependent Enhancement (ADE) of Infection

The potential of casirivimab and of imdevimab to mediate viral entry was assessed in immune cell lines co-incubated with recombinant vesicular stomatitis virus (VSV) pseudoparticles expressing SARS-CoV-2 spike protein at concentrations of mAb(s) down to approximately 10-fold below the respective neutralization EC_{50} values. The casirivimab + imdevimab combination and imdevimab alone, but not casirivimab alone, mediated entry of pseudoparticles into $Fc\gamma R2^+$ Raji and $Fc\gamma R1^+/Fc\gamma R2^+$ THP1 cells (maximum infection in total cells of 1.34% and 0.24%, respectively, for imdevimab; 0.69% and 0.06%, respectively for the casirivimab + imdevimab combination), but not any other cell lines tested (IM9, K562, Ramos and U937 cells).

Antiviral Resistance

There is a potential risk of treatment failure due to the development of viral variants that are resistant to the casirivimab + imdevimab combination.

Escape variants were identified following passage in cell culture of recombinant VSV encoding SARS-CoV-2 spike protein in the presence of casirivimab or imdevimab individually, but not following passage in the presence of the casirivimab + imdevimab combination. Variants which showed reduced susceptibility to casirivimab included spike protein amino acid substitutions K417E, Y453F, L455F, F486V and Q493K, and variants which showed reduced susceptibility to imdevimab included K444Q and V445A substitutions. Each variant showing reduced susceptibility to one mAb retained susceptibility to the other, and all variants retained susceptibility to the casirivimab + imdevimab combination.

In neutralization assays using VSV pseudotyped with 37 different receptor binding domain (RBD) variants identified as the most common RBD variations in circulation as of late March 2020, and D614G, D614N spike protein variants, casirivimab had reduced susceptibility (4.5-fold) to G476S and S494P variants, and imdevimab had reduced susceptibility (463-fold) to the N439K variant. The casirivimab + imdevimab combination retained activity against all variants tested.

In clinical trial R10933-10987-COV-2067, interim data indicated only one variant (G446V) occurring at an allele fraction ≥15%, which was detected in 3/66 subjects who had nucleotide sequencing data, each at a single time point (two at baseline in subjects from placebo and 2,400 mg casirivimab + imdevimab combination groups, and one at Day 25 in a subject from the 8,000 mg casirivimab + imdevimab combination group). The G446V variant had reduced susceptibility to imdevimab of 135-fold compared to wild-type in a VSV pseudoparticle neutralization assay but retained susceptibility to casirivimab and the casirivimab + imdevimab combination.

It is possible that resistance-associated variants to the casirivimab + imdevimab combination could have cross-resistance to other mAbs targeting the receptor binding domain of SARS-CoV-2. The clinical impact is not known.

Immune Response Attenuation

There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to re-infection.

16 NONCLINICAL TOXICOLOGY

Carcinogenicity, genotoxicity, and reproductive toxicology studies have not been conducted with casirivimab and imdevimab.

In a toxicology study in cynomolgus monkeys, casirivimab and imdevimab had no adverse effects when administered intravenously. Non-adverse liver findings (minor transient increases in AST and ALT) were observed.

In tissue cross-reactivity studies with casirivimab and imdevimab using human adult and fetal tissues, no binding of clinical concern was detected.

17 ANIMAL PHARMACOLOGIC AND EFFICACY DATA

The casirivimab + imdevimab combination has been assessed in rhesus macaque and Syrian golden hamster treatment models of SARS-CoV-2 infection. Therapeutic administration of the casirivimab + imdevimab combination at 25 mg/kg or 150 mg/kg into rhesus macaques (n=4 for each dosing group) 1-day post infection resulted in approximately 1-2 $\log_{10}$ reductions in genomic and sub-genomic viral RNA in nasopharyngeal swabs and oral swabs at Day 4 post-challenge in most animals, and reduced lung pathology relative to placebo-treated animals. Therapeutic administration of the casirivimab + imdevimab combination at 5 mg/kg and 50 mg/kg doses to hamsters 1-day post infection resulted in reduced weight loss relative to placebo treated animals, but had no clear effects on viral load in lung tissue. The applicability of these findings to a clinical setting is not known.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Mild to Moderate COVID-19 (R10933-10987-COV-2067)

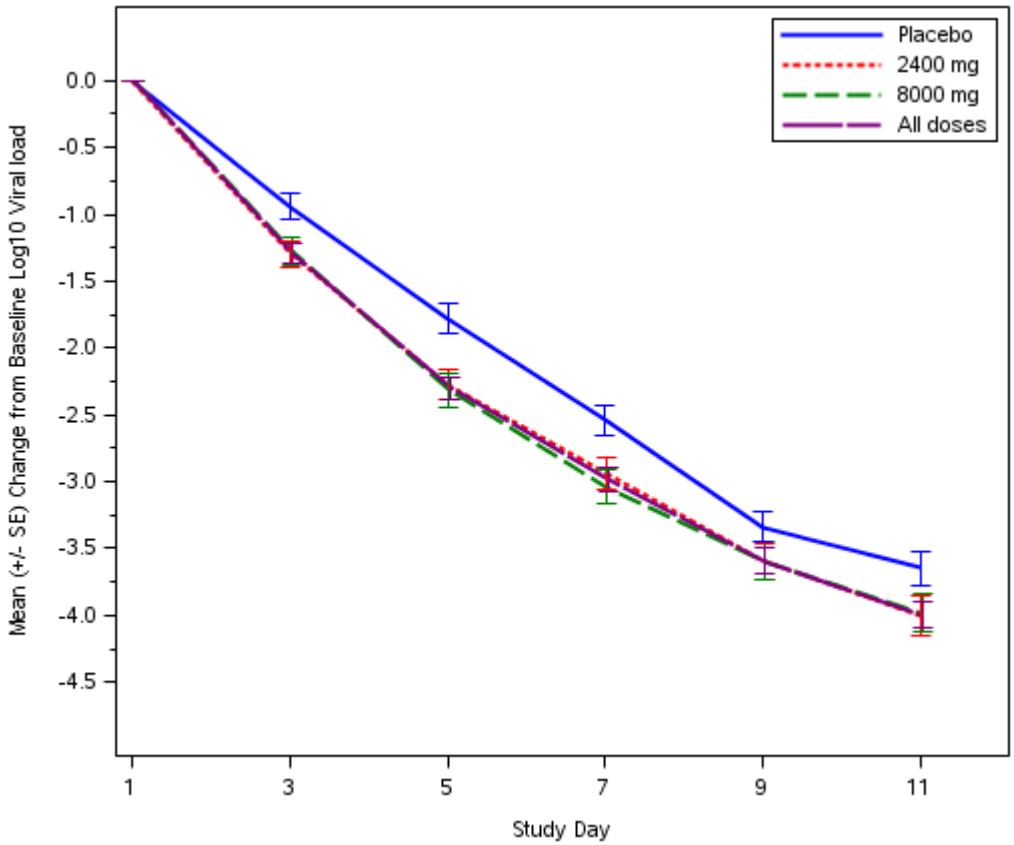
The data supporting this EUA are based on the analysis of Phase 1/2 from trial R10933-10987-COV-2067, that occurred after 799 enrolled subjects had completed at least 28 days of study duration. R10933-10987-COV-2067 is a randomized, double-blinded, placebo-controlled clinical trial studying casirivimab and imdevimab for the treatment of adult subjects with mild to moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized). The trial enrolled adult subjects who were not hospitalized and had at least 1 or more COVID-19 symptoms that were at least mild in severity. Treatment was initiated within 3 days of obtaining a positive SARS-CoV-2 viral infection determination. Subjects were randomized in a 1:1:1 manner to receive a single intravenous (IV) infusion of 2,400 mg of casirivimab and imdevimab (1,200 mg of each) (n=266), or 8,000 mg of casirivimab and imdevimab (4,000 mg of each) (n=267), or placebo (n=266).

At baseline, the median age was 42 years (with 7% of subjects ages 65 years or older), 53% of the subjects were female, 85% were White, 50% were Hispanic or Latino, and 9% were Black;

34% were considered high risk (as defined in Section 2). Approximately 31% of subjects reported at least 1 severe symptom at baseline, 36% reported at least 1 moderate symptom and no severe symptoms, and 13% reported only mild symptoms. The median duration of symptoms was 3 days; mean viral load was 5.8 $\log_{10}$ copies/mL at baseline. The baseline demographics and disease characteristics were well balanced across the casirivimab and imdevimab and placebo treatment groups.

The pre-specified primary endpoint in Phase 1/2 of trial R10933-10987-COV-2067 was the time weighted average (TWA) change from baseline in viral load ($\log_{10}$ copies/mL), as measured by RT-qPCR in nasopharyngeal swab samples, in subjects with a positive baseline RT-qPCR value, i.e., the modified full analysis set (mFAS). In the mFAS for the Phase 1/2 analysis, the difference in TWA from Day 1 through Day 7 for the pooled doses of casirivimab and imdevimab compared with placebo (n=665) was -0.36 $\log_{10}$ copies/mL ($p<0.0001$). The largest reductions in viral load relative to placebo occurred in patients with high viral load (-0.78 $\log_{10}$ copies/mL) or who were seronegative (-0.69 $\log_{10}$ copies/mL) at baseline. Reductions occurring from Day 1 through Day 11 were similar to those for Day 1 through Day 7. **Figure 1** shows the mean change from baseline in SARS-COV-2 viral load over time.

Figure 1. Mean Change from Baseline in SARS-COV-2 Viral Load Over Time



While viral load was used to define the primary endpoint in the Phase 1/2 analysis, clinical evidence demonstrating that casirivimab and imdevimab may be effective came from the predefined secondary endpoint, medically attended visits (MAV) related to COVID-19.

Medically attended visits comprised hospitalizations, emergency room visits, urgent care visits, or physician office/telemedicine visits for COVID-19. A lower proportion of subjects treated with casirivimab and imdevimab had COVID-19 related MAVs (2.8% for combined treatment arms vs 6.5% placebo). In post-hoc analyses, a lower proportion of subjects treated with casirivimab and imdevimab had COVID-19-related hospitalizations or emergency room visits compared to placebo, see Table 3. Results for this endpoint were suggestive of a relatively flat dose-response relationship. The absolute risk reduction for casirivimab and imdevimab compared to placebo was greater in subjects at high risk for progression to severe COVID-19 and/or hospitalization, according to the criteria outlined in section 2 (Table 4).

Table 3: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment[a]

Treatment	N[b]	Events	Proportion of subjects
Placebo	231	10	4%
2,400 mg[c] casirivimab and imdevimab	215	4	2%
8,000 mg[d] casirivimab and imdevimab	219	4	2%
All doses casirivimab and imdevimab	434	8	2%

[a] Hospitalization and emergency room visits were a subset of a key secondary endpoint, Medically-Attended Visits, which also included urgent care visits, physician's office visits and telemedicine visits.
[b] N = number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization
[c] 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab)
[d] 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab)

Table 4: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment for Subjects at Higher Risk of Hospitalization[a]

Treatment	N[b]	Events	Proportion of subjects
Placebo	78	7	9%
2,400 mg[c] casirivimab and imdevimab	70	2	3%
8,000 mg[d] casirivimab and imdevimab	81	2	2%
All doses casirivimab and imdevimab	151	4	3%

[a] Hospitalization and emergency room visits were a subset of a key secondary endpoint, Medically-Attended Visits, which also included urgent care visits, physician's office visits and telemedicine visits.
[b] N = number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization
[c] 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab)
[d] 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab)

The median time to symptom improvement, as recorded in a trial-specific daily symptom diary, was 5 days for casirivimab and imdevimab-treated subjects, as compared with 6 days for placebo-treated subjects. Symptoms assessed were shortness of breath or difficulty breathing, chills, feverish, sore throat, cough, nausea, vomiting, diarrhea, headache, red or watery eyes, body and muscle aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum/phlegm, runny nose. Symptom improvement was defined as symptoms scored as moderate or severe at baseline being scored as mild or absent, and symptoms scored as mild or absent at baseline being scored as absent.

19 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Casirivimab injection is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution supplied in a single-dose vial. Refer to Table 5.

Imdevimab injection is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution supplied in a single-dose vial. Refer to Table 5.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER.

Table 5: How Casirivimab and Imdevimab are Supplied

Antibody	Concentration	Package Size	NDC Number
Casirivimab REGN 10933	1332 mg/11.1 mL (120 mg/mL)	1 vial per pack	61755-024-01
	300 mg/2.5 mL (120 mg/mL)	1 vial per pack	61755-026-01
Imdevimab REGN10987	1332 mg/11.1 mL (120 mg/mL)	1 vial per pack	61755-025-01
	300 mg/2.5 mL (120 mg/mL)	1 vial per pack	61755-027-01

Storage and Handling

Casirivimab is preservative-free. Discard any unused portion.
Imdevimab is preservative-free. Discard any unused portion.

Store unopened casirivimab and imdevimab vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE. DO NOT SHAKE. DO NOT EXPOSE TO DIRECT LIGHT.

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted casirivimab and imdevimab solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for no more

than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

20 PATIENT COUNSELING INFORMATION

Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines. Also see Fact Sheet for Patients, Parents and Caregivers.

21 CONTACT INFORMATION

For additional information visit www.REGENCOV2.com
If you have questions, please contact Regeneron at 1-844-734-6643.

REGENERON

Manufactured by:
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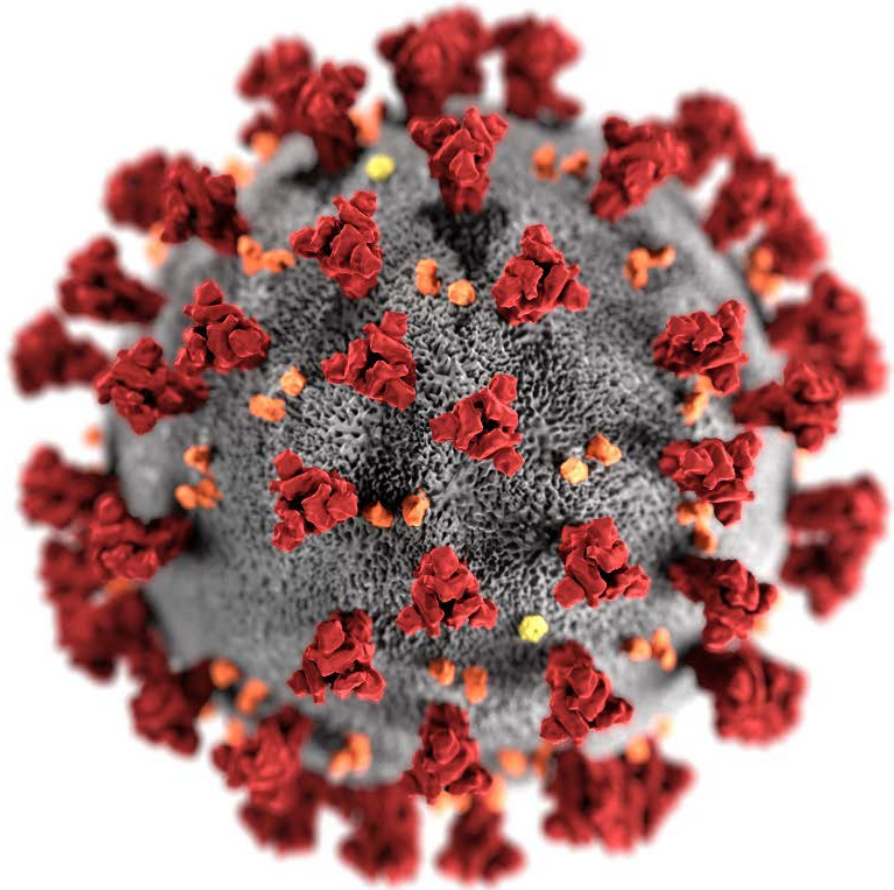
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

Authorized: 11/2020

ACIP COVID-19 Vaccines Work Group

Use of Pfizer-BioNTech COVID-19 Vaccine: Clinical Considerations



Sarah Mbaeyi, MD MPH

December 12, 2020

Clinical considerations for use of Pfizer-BioNTech COVID-19 vaccine

- Clinical considerations are based on information submitted to the Food and Drug Administration for Emergency Use Authorization (EUA) of the vaccine
  - May be updated as further information becomes available

- In addition to these considerations, the EUA conditions of use and the package insert should be referenced when using the vaccine

https://www.fda.gov/media/144412/download
https://www.fda.gov/media/144413/download

Administration

Administration

- 2-dose series administered intramuscularly 3 weeks apart
- Administration of 2nd dose within 4-day grace period (e.g., day 17-21) considered valid
- If >21 days since 1st dose, 2nd dose should be administered at earliest opportunity (but no doses need to be repeated)
- Both doses are necessary for protection; efficacy of a single dose has not been systematically evaluated

Interchangeability with other COVID-19 vaccine products

- Pfizer-BioNTech COVID-19 vaccine not interchangeable with other COVID-19 vaccine products
  - Safety and efficacy of a mixed series has not been evaluated

- Persons initiating series with Pfizer-BioNTech COVID-19 vaccine should complete series with same product

- If two doses of different mRNA COVID-19 vaccine products inadvertently administered, no additional doses of either vaccine recommended at this time
  - Recommendations may be updated as further information becomes available or additional vaccine types authorized

Coadministration with other vaccines

- Pfizer-BioNTech COVID-19 vaccine should be administered alone with a minimum interval of 14 days before or after administration with any other vaccines
  - Due to lack of data on safety and efficacy of the vaccine administered simultaneously with other vaccines

- If Pfizer-BioNTech COVID-19 vaccine is inadvertently administered within 14 days of another vaccine, doses do not need to be repeated for either vaccine

Vaccination of persons with prior SARS-CoV-2 infection or exposure

Persons with a history of SARS-CoV-2 infection

- Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection
  - Data from phase 2/3 clinical trials suggest vaccination safe and likely efficacious in these persons

- Viral or serologic testing for acute or prior infection, respectively, is not recommended for the purpose of vaccine decision-making

Persons with known current SARS-CoV-2 infection

- Vaccination should be deferred until recovery from acute illness (if person had symptoms) *and* criteria have been met to discontinue isolation

- No minimal interval between infection and vaccination

- However, current evidence suggests reinfection uncommon in the 90 days after initial infection and thus persons with documented acute infection in the preceding 90 days may defer vaccination until the end of this period, if desired

https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

Persons who previously received passive antibody therapy for COVID-19

- Currently no data on safety or efficacy of COVID-19 vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment

- Vaccination should be deferred for at least 90 days to avoid interference of the treatment with vaccine-induced immune responses
  - Based on estimated half-life of therapies and evidence suggesting reinfection is uncommon within 90 days of initial infection

Persons with a known SARS-CoV-2 exposure

- **Community or outpatient setting:**
  - Defer vaccination until quarantine period has ended to avoid exposing healthcare personnel (HCP) or other persons during vaccination visit

- **Residents of congregate healthcare settings (e.g., long-term care facilities):**
  - May be vaccinated, as likely would not result in additional exposures. HCP are already in close contact with residents and should employ appropriate infection prevention and control procedures

- **Residents of other congregate settings (e.g., correctional facilities, homeless shelters)**
  - May be vaccinated, in order to avoid delays and missed opportunities for vaccination
  - Where feasible, precautions should be taken to limit mixing of these individuals with other residents or non-essential staff

https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html
https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html

Vaccination of special populations

Persons with underlying medical conditions

- Vaccine may be administered to persons with underlying medical conditions who have no contraindications to vaccination

- Phase 2/3 clinical trials demonstrate similar safety and efficacy profiles in persons with underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Immunocompromised persons

- Persons with HIV infection, other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19

- Data not currently available to establish safety and efficacy of vaccine in these groups

- These individuals may still receive COVID-19 vaccine unless otherwise contraindicated

- Individuals should be counseled about:
  - Unknown vaccine safety and efficacy profiles in immunocompromised persons
  - Potential for reduced immune responses
  - Need to continue to follow all current guidance to protect themselves against COVID-19

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Pregnant women

- There are no data on the safety of COVID-19 vaccines in pregnant women
  - Animal developmental and reproductive toxicity (DART) studies are ongoing
  - Studies in humans are ongoing and more planned

- mRNA vaccines and pregnancy
  - Not live vaccines
  - They are degraded quickly by normal cellular processes and don't enter the nucleus of the cell

- COVID-19 and pregnancy
  - Increased risk of severe illness (ICU admission, mechanical ventilation and death)
  - Might be an increased risk of adverse pregnancy outcomes, such as preterm birth

- If a woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine and is pregnant, she may choose to be vaccinated. A discussion with her healthcare provider can help her make an informed decision.

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html

Pregnant women

- Considerations for vaccination:
  - level of COVID-19 community transmission, (risk of acquisition)
  - her personal risk of contracting COVID-19, (by occupation or other activities)
  - the risks of COVID-19 to her and potential risks to the fetus
  - the efficacy of the vaccine
  - the known side effects of the vaccine
  - the lack of data about the vaccine during pregnancy

- Pregnant women who experience fever following vaccination should be counseled to take acetaminophen as fever has been associated with adverse pregnancy outcomes

- Routine testing for pregnancy prior to receipt of a COVID-19 vaccine is not recommended.

Breastfeeding/Lactating women

- There are no data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or milk production/excretion

- mRNA vaccines are not considered live virus vaccines and are not thought to be a risk to the breastfeeding infant

- If a lactating woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine, she may choose to be vaccinated

Patient vaccine counseling

Reactogenicity

- Before vaccination, providers should counsel vaccine recipients about expected local and systemic post-vaccination symptoms

- Unless a person develops a contraindication to vaccination, they should be encouraged to complete the series even if they develop post-vaccination symptoms in order to optimize protection against COVID-19

- Antipyretic or analgesic medications may be taken for treatment of post-vaccination symptoms
  - Routine prophylaxis for the purposes of preventing symptoms is not recommended at this time, due to lack of information on impact of use on vaccine-induced antibody responses

Vaccine efficacy

- Two doses required to achieve high efficacy
  - Efficacy after 2nd dose: 95.0% (95% CI: 90.3%, 97.6%)

- Patients should be counseled on importance of completing the 2-dose series in order to optimize protection

Public health recommendations for vaccinated persons

- Protection from vaccine is not immediate; vaccine is a 2-dose series and will take 1 to 2 weeks following the second dose to be considered fully vaccinated

- No vaccine is 100% effective

- Given the currently limited information on how well the vaccine works in the general population; how much it may reduce disease, severity, or transmission; and how long protection lasts, vaccinated persons should continue to follow all current guidance to protect themselves and others, including:
  - Wearing a mask
  - Staying at least 6 feet away from others
  - Avoiding crowds
  - Washing hands often
  - Following CDC travel guidance
  - Following quarantine guidance after an exposure to someone with COVID-19
  - Following any applicable workplace or school guidance

https://www.cdc.gov/coronavirus/2019-ncov/index.html

Contraindications and precautions

Contraindications and precautions

- Package insert:
  - Severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 vaccine is a contraindication to vaccination
  - Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of the vaccine

- Because of reports of anaphylactic reactions vaccinated outside of clinical trials, the additional following guidance is proposed:
  - Persons who have had a severe allergic reaction to any vaccine or injectable therapy (intramuscular, intravenous, or subcutaneous) should not receive the Pfizer-BioNTech vaccine at this time
  - Vaccine providers should observe patients after vaccination to monitor for the occurrence of immediate adverse reactions:
    - Persons with a history of anaphylaxis: 30 minutes
    - All other persons: 15 mins

Interpretation of SARS-CoV-2 test results in vaccinated person

SARS-CoV-2 tests

- **Viral tests:** Prior receipt of the Pfizer-BioNTech COVID-19 vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests

- **Antibody tests:**
  - Currently available antibody tests for SARS-CoV-2 assess IgM and/or IgG to spike or nucleocapsid proteins
  - Pfizer-BioNTech COVID-19 vaccine contains mRNA that encodes the spike protein; thus, a positive test for spike protein IgM/IgG could indicate either prior infection or vaccination
  - To evaluate for evidence of prior infection in an individual with a history of Pfizer-BioNTech COVID-19 vaccination, a test specifically evaluating IgM/IgG to the nucleocapsid protein should be used

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/eua-authorized-serology-test-performance

Discussion

Discussion

- Does ACIP agree with the guidance around use in:
  - Immunocompromised persons
  - Pregnant or lactating women

- Does ACIP agree with the proposed contraindications to vaccination?

- Are there any other sections of the clinical considerations that ACIP would like to discuss?

Proposed Edits to 2021 Immunization Schedules

COVID-19 Vaccine

- Addendum to Recommended Adult Immunization Schedule, United States, 2021
- Addendum to Recommended Child/Adolescent Immunization Schedule, United States, 2021

Notes

For vaccine recommendations for persons 18 years of age or younger, see the Recommended Child/Adolescent Immunization Schedule.

Additional Information

COVID-19 Vaccination
ACIP recommends use of COVID-19 vaccines within the scope of the Emergency Use Authorization or Biologics License Application for the particular vaccine. Interim ACIP recommendations for the use of COVID-19 vaccines can be found at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html

***Haemophilus influenzae* type B vaccination**

- **At risk for hepatitis A virus infection**: 2-dose series HepA or 3-dose series HepA-HepB as above
  - **Chronic liver disease** (e.g., persons with hepatitis B, hepatitis C, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal)
  - **HIV infection**
  - **Men who have sex with men**
  - **Injection or noninjection drug use**
  - **Persons experiencing homelessness**
  - **Work with hepatitis A virus** in research laboratory or with nonhuman primates with hepatitis A virus infection
  - **Travel in countries with high or intermediate endemic hepatitis A** (HepA-HepB [Twinrix] may be administered on an accelerated weeks apart] or 3-dose series Engerix-B or Recombivax HB at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 weeks / dose 2 to dose 3: 8 weeks / dose 1 to dose 3: 16 weeks]) or 3-dose series HepA-HepB (Twinrix at 0, 1, 6 months [minimum intervals: dose 1 to dose 2: 4 weeks / 5 dose 2 to dose 3: 5 months])

Special situations

- **At risk for hepatitis B virus infection**: 2-dose (Heplisav-B) or 3-dose (Engerix-B, Recombivax HB) series or 3-dose series HepA-HepB (Twinrix) as above
  - **Chronic liver disease** (e.g., persons with hepatitis C, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice upper limit of normal)
  - **HIV infection**

Notes Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2021

For vaccine recommendations for persons 19 years of age or older, see the Recommended Adult Immunization Schedule.

Additional information

COVID-19 Vaccination

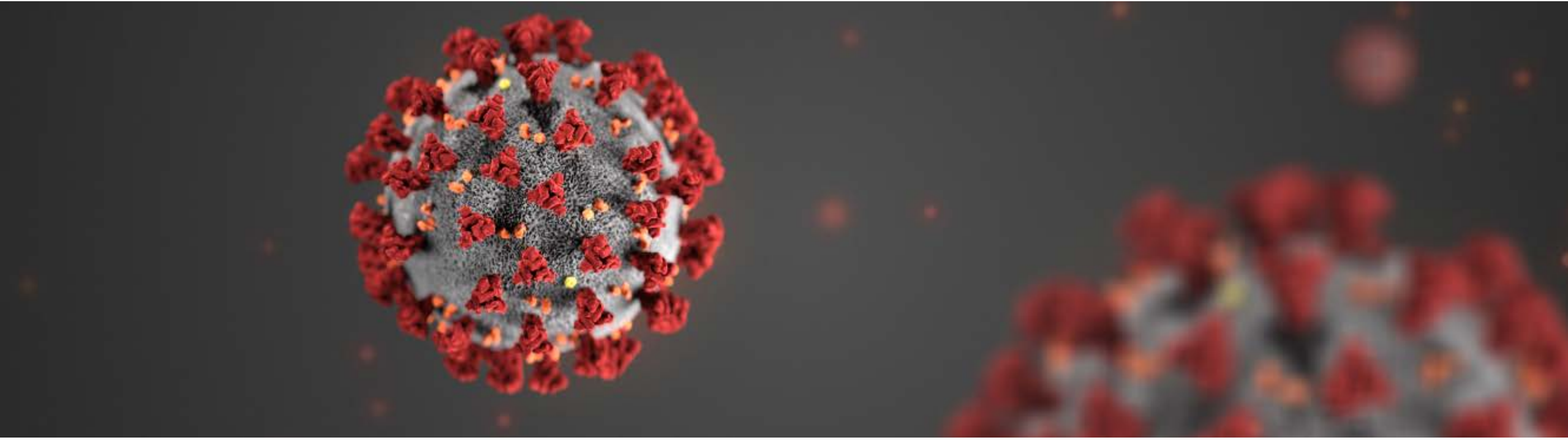
ACIP recommends use of COVID-19 vaccines within the scope of the Emergency Use Authorization or Biologics License Application for the particular vaccine. Interim ACIP recommendations for the use of COVID-19 vaccines can be found at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-

- Consult relevant ACIP statements for detailed recommendations at www.cdc.gov/vaccines/hcp/acip-recs/index.html.

The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see Table 3-1, Recommended and minimum ages and intervals between vaccine doses, in *General Best Practice Guidelines for Immunization* at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html.

- Information on travel vaccine requirements and recommendations is available at http://www.cdc.gov/travel/.

- For vaccination of persons with immunodeficiencies, see Table 8-1, Vaccination of persons with primary and secondary immunodeficiencies, in *General Best Practice Guidelines for Immunization* at https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html, and "Immunization in Special Clinical Circumstances" (In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee*



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Federal allocation program: Special Projects for Equitable and Efficient Distribution (SPEED)

On Monday, December 14th, the Chief Medical Officer of the Office of the Assistant Secretary for Preparedness and Response at HHS (HHS/ASPR), sent a communication to all State and Territorial Health Officials concerning their oversight of the allocation and distribution of COVID-19 therapeutics administered under Emergency Use Authorization. In support of this responsibility and to assist states and territories with their allocation and distribution efforts, HHS/ASPR is implementing a new federal allocation program called the Special Projects for Equitable and Efficient Distribution (SPEED).

The goal of SPEED is to assist states and territories with identifying and allocating monoclonal antibodies (mAbs) to non-hospital facilities that serve priority populations, including nursing homes and federally qualified health centers (FQHCs). **It should be noted that SPEED is separate and complementary to the state-based mAb allocation system.**

SPEED will be conducted in partnership with national organizations and associations that will assist with educating members (and non-members) and identifying those who are able and willing to administer these infusions. Membership in participating associations is not required for participation as a SPEED facility.

The first two SPEED initiatives will be launched this week and include:

1. **Home infusion in nursing homes and assisted living facilities**
    a. *Description:* Home infusion providers in 46 states and the District of Columbia will dispense and provide nursing support for administration of mAbs to residents of nursing homes and assisted living facilities
    b. *Patient courses (initial):* 560
    c. *Launch date:* 12/12/20
    d. *Partner:* National Home Infusion Association
2. **Direct allocation to long-term care pharmacies**
    a. *Description:* mAbs will be pre-positioned with long-term care pharmacies for ready deployment when cases occur in nursing homes and assisted living communities served by each pharmacy
    b. *Patient courses:* TBD
    c. *Launch date:* Week of 12/14/20
    d. *Partners:* **American Society of Consultant Pharmacists (ASCP)**; AMDA – The Society for Post-Acute and Long-Term Care Medicine

Additional SPEED initiatives are being explored for FQHCs, state/local correctional facilities, dialysis centers, and other settings. Treatment courses allocated through SPEED will be communicated with states for tracking and coordinating purposes.

ASCP Process in Process

Pharmacies interested in participating this this federal allocation need to submit information to ASCP including name of individual location, address, contact person and email address. Request initial allocation which is based on pharmacy size: >5000 SNF beds serviced – 50 doses, 2500 – 5000 SNF beds serviced – 30, <2000 SNF beds serviced – 20. It is critical that does aren't wasted or that the product isn't placed into environments that cannot manage the administration.

If the location is already an Amerisource Bergan customer, please **include your customer ID**.
If location is not an Amerisource Bergan customer, **please include pharmacy license number** for that location. HHS will work to expediate a relationship with Amerisource Bergan Specialty so you may receive the product.

ASCP will keep this information confidential and only be used to communicate to HHS for this program.

ASCP is finalizing the process with HHS but is recommending an initial supply of product to be sent to each pharmacy and then ordering new product **weekly** based on utilization and demand. This will be updated as needed.

Name	Phone	Website	Contact Name	Contact Email
Alabama Pharmacy Association	(334) 271-4222	http://www.aparx.org/	Louise Jones	ljones@aparx.org
Alaska Pharmacists	(907) 563-8880	http://www.alaskapharmacy.org/	Molly Gray	akphrmcy@alaska.net
Arizona Pharmacy	(480) 838-3385	http://www.azpharmacy.org/	Kelly Fine	kelly@azpharmacy.org
Arkansas Pharmacists Association	(501) 372-5250	http://www.arrx.org/	John Vinson, Pharm.D.	john@arrx.org
California Pharmacists Association	(916) 779-1400 ext. 400	http://www.cpha.com/	Susan Bonilla	sbonilla@cpha.com
Colegio de Farmaceuticos de Puerto Rico	(787) 753-7157	http://www.colegiodefarmaceuticospr.org/	Milagros Morales, R.Ph.	cfpradministracion@cfpr.org
Colorado Pharmacists Society	(720) 250-9585	http://www.copharm.org/	Emily Zadvorny, PharmD, BCPS	EMILY.ZADVORNY@CUANSCHUTZ.EDU
Connecticut Pharmacists Association	(860) 563-4619	http://www.ctpharmacists.org/	Nathan Tinker	ntinker@ctpharmacists.org
Delaware Pharmacists	(302) 659-3088	http://www.dpsrx.org/	Kim Robbins	rxistkim@gmail.com
Florida Pharmacy	(850) 222-2400	http://www.pharmview.com/	Michael Jackson,	jackson@pharmview.com
Georgia Pharmacy	(404) 231-5074	http://www.gpha.org/	Bob Coleman	bcoleman@gpha.org
Hawaii Pharmacists		http://www.hipharm.org/	Marcella Chock,	msetochock@gmail.com
Idaho State Pharmacy Association	(208) 342-0010	http://www.idahopharmacists.com/	Pam Eaton	ispa@idahopharmacists.com
Illinois Pharmacists	(217) 522-7300	http://www.ipha.org/	Garth K.	greynolds@ipha.org
Indiana Pharmacists Association	(317) 634-4968	http://www.indianapharmacists.org/	Darren Covington	Darren@indianapharmacists.org
Iowa Pharmacy Association	(515) 270-0713	http://www.iarx.org/	Kate Gainer	kgainer@iarx.org
Kansas Pharmacists Association	(785) 228-2327	http://www.ksrx.org/	Aaron Dunkel	aaron@ksrx.org
Kentucky Pharmacists Association	(502) 227-2303	http://www.kphanet.org/	Mark Glasper	mglasper@kphanet.org
Louisiana Pharmacists Association	(225) 346-6883	http://www.louisianapharmacists.com/	Julie Fuselier	julie.fuselier@amstrategies.co
Maine Pharmacy Association	(207) 502-0825	http://www.mparx.com/	Amy Downing	amy@mainepharmacy.org
Maryland Pharmacists Association	(443) 583-8000	http://www.marylandpharmacist.org/	Aliyah Horton	Aliyah.horton@mdpha.com
Massachusetts Pharmacists Association	(781) 933-1107	http://www.masspharmacists.org/	Lindsay DeSantis	ldesantis@masspharmacists.org

Michigan Pharmacists Association	(517) 484-1466	http://www.michiganpharmacists.org/	Larry Wagenknecht,	larry@michiganpharmacists.org
Minnesota Pharmacists Association	(651) 697-1771	http://www.mpha.org/	Sarah Derr, PharmD	sarahd@mpha.org
Mississippi Pharmacists Association	(601) 981-0416	http://www.mspharm.org/	Beau Cox	beau@mspharm.org
Missouri Pharmacy Association	(573) 636-7522	http://www.morx.com/	Ron Fitzwater, C.A.E. MBA	ron@morx.com
Montana Pharmacy	(406) 449-3843	http://www.rxmt.org/	Stuart Doggett	stuart@montana.com
Nebraska Pharmacists Association	(402) 420-1500	http://www.npharm.org/	Marcia Mueting	marcia@npharm.org
Nevada Pharmacy Alliance	702-714-1931	https://nevadapharmacyalliance.com/	Ken Kunke,	info@nevadapharmacyalliance.com
New Hampshire Pharmacists Association		http://www.nhpharmacists.net/	Robert Stout	rjstoutrph@comcast.net
New Jersey Pharmacists Association	(609) 275-4246	http://www.njpharmacists.org/	Elise M. Barry	ebarry@njpharma.org
New Mexico Pharmacists Association	(800) 464-8729	http://www.nmpharmacy.org	R. Dale Tinker	dtinker@nmpharmacy.org
North Carolina Association of Pharmacists	(984) 439-1646	http://www.ncpharmacists.org/	Penny Shelton	penny@ncpharmacists.org
North Dakota Pharmacists Association	(701) 258-4922	http://www.nodakpharmacy.net/	Michael Schwab	mschwab@nodakpharmacy.net
Ohio Pharmacists	(614) 389-3236	http://www.ohiopharmacists.org/	Ernest Boyd,	eboyd@ohiopharmacists.org
Oklahoma Pharmacists Association	(405) 557-5772	http://www.opha.com/	Debra Billingsley	dbillingsley@opha.com
Oregon State Pharmacy Association	(503) 582-9055	http://www.oregonpharmacy.org/	Brian Mayo	brian@oregonpharmacy.org
Pennsylvania Pharmacists Association	(717) 234-6151	http://www.papharmacists.com/	Patricia Epple	pepple@papharmacists.com
Pharmacists Society of the State of New York	(518) 869-6595	http://www.pssny.org/	Deanna Ennello-Butler	ed@pssny.org
Pharmacy Society of Wisconsin	(608) 827-9200	http://www.pswi.org/	Sarah Sorum	sarahs@pswi.org
Rhode Island Pharmacists Association	(401) 684-1874	http://www.ripharmacists.org/	Kenny Correia, PharmD	ripharmacistsassociation@gmail.com
South Carolina Pharmacy Association	(803) 354-9977	http://www.scrx.org/	Craig Burridge, M.S., C.A.E.	craig@scrx.org

South Dakota Pharmacists Association	(605) 224-2338	http://www.sdpha.org/	Amanda Bacon	amanda@sdpha.org
Tennessee Pharmacists Association	(615) 256-3023	http://www.tnpharm.org/	Micah Cost	micah@tnpharm.org
Texas Pharmacy Association	(512) 615-9170	https://www.texaspharmacy.org	Debbie Garza,	DGarza@texaspharmacy.org
Utah Pharmacy Association		http://www.upha.com/	Adam Jones	ajones@associationsutah.com
Vermont Pharmacists Association	(877) 483-2646	http://www.vtpharmacists.com/	James Marmar	vpamanager@gmail.com
Virginia Pharmacists	(804) 285-4145	http://www.virginiapharmacists.org/	Christina Barrille	christina@virginiapharmacists.org
Washington D.C. Pharmacy Association	(202) 437-7536	https://wdcpha.org/	Yolanda McKoy-Beach	wdcpha@gmail.com
Washington State Pharmacy Association	(425) 228-7171	http://www.wsparx.org/	Jeff Rochon	jeff@wsparx.org
West Virginia Pharmacists Association	(304) 344-5302	http://www.wvpharmacy.org/	Richard Stevens	wvrds@aol.com
Wyoming Pharmacy Association	(307) 331-0371	https://wypha.org/	Craig Frederick, PharmD	director@wpha.net

FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF BAMLANIVIMAB

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Bamlanivimab is not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Bamlanivimab has been authorized by FDA for the emergency uses described above. Bamlanivimab is not FDA-approved for these uses.

Bamlanivimab is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of bamlanivimab under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

This EUA is for the use of the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age

- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Bamlanivimab must be administered by intravenous (IV) infusion.

Bamlanivimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to bamlanivimab. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

- The authorized dosage for bamlanivimab is a single intravenous (IV) infusion of 700 mg administered as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.
- Bamlanivimab is available as concentrated solution and must be diluted prior to administration.
- Administer bamlanivimab 700 mg via IV infusion over at least 60 minutes via pump or gravity.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

The authorized dosage may be updated as additional data from clinical trials becomes available.

For information on clinical trials that are testing the use of bamlanivimab in COVID-19, please see www.clinicaltrials.gov.

Contraindications
None.

Dosing
Patient Selection and Treatment Initiation
This section provides essential information on the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Dosage
The dosage of bamlanivimab in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is:

- bamlanivimab 700 mg.

Administer bamlanivimab as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Bamlanivimab must be diluted and administered as a single IV infusion over at least 60 minutes.

Dosage Adjustment in Specific Populations
No dosage adjustment is recommended based on age, sex, race, body weight, renal or mild hepatic impairment, during pregnancy or while lactating, or for disease severity or inflammation *[see Full EUA Prescribing Information, Use in Specific Populations (11)]*.

Preparation and Administration
Preparation

Bamlanivimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

- Remove one bamlanivimab vial (700 mg/20 mL) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vial.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
    - Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
- Withdraw 20 mL bamlanivimab from one 20 mL vial and inject into an infusion bag containing 250 mL prefilled 0.9% Sodium Chloride Injection (see **Table 1**).
- Discard any product remaining in the vial.
- Gently invert IV bag by hand approximately 10 times to mix. **Do not shake.**
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab

Drug	Number of Vials	Volume of Bamlanivimab	Volume of 0.9% Sodium Chloride	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Bamlanivimab (700 mg/20 mL)	1 Vial	20 mL	250 mL	270 mL	270 mL/hr	60 minutes

Administration

Bamlanivimab infusion solution should be administered by a qualified healthcare professional.

- Gather the materials for infusion:
    - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC infusion set
    - Use of an in-line or add-on 0.20/0.22 micron polyethersulfone (PES) filter is strongly recommended.
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the entire infusion solution in the bag via pump or gravity over at least 60 minutes (see **Table 1**).
- Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- If the infusion must be discontinued due to an infusion reaction, discard any unused product.
- The use of closed system transfer devices (CSTDs), elastomeric pumps, and pneumatic transport with bamlanivimab has not been studied.

Storage
Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze, shake, or expose to direct light.

Warnings
There are limited clinical data available for bamlanivimab. Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions
There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of bamlanivimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

Infusion-related reactions have been observed with administration of bamlanivimab.

Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19
Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, bamlanivimab is not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Side Effects
Adverse events have been reported with bamlanivimab *[see Full EUA Prescribing Information, Clinical Trials Experience (6.1)]*.

Additional adverse events associated with the drug may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTHCARE PROVIDERS
As the healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” (and provide a copy of the Fact Sheet) prior to the patient receiving bamlanivimab, including:

- FDA has authorized the emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral

testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.
- The patient or parent/caregiver has the option to accept or refuse bamlanivimab.
- The significant known and potential risks and benefits of bamlanivimab, and the extent to which such potential risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.

For information on clinical trials that are testing the use of bamlanivimab for COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR BAMLANIVIMAB ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION:
In order to mitigate the risks of using this unapproved product under the EUA and to optimize the potential benefit of bamlanivimab, the following items are required. Use of bamlanivimab under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.
2. As the healthcare provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to the patient receiving bamlanivimab. Healthcare providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
    a. Given the "Fact Sheet for Patients, Parents and Caregivers",
    b. Informed of alternatives to receiving authorized bamlanivimab, and
    c. Informed that bamlanivimab is an unapproved drug that is authorized for use under this Emergency Use Authorization.
3. Patients with known hypersensitivity to any ingredient of bamlanivimab must not receive bamlanivimab.
4. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to bamlanivimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Bamlanivimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.

    - Submit adverse event reports to FDA MedWatch using one of the following methods:
        - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or

- By using a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form
- Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the statement "Bamlanivimab treatment under Emergency Use Authorization (EUA)"

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

5. The prescribing health care provider and/or the provider's designee are/is to provide mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of bamlanivimab.
6. OTHER REPORTING REQUIREMENTS
   In addition, please provide a copy of all FDA MedWatch forms to:
   Eli Lilly and Company, Global Patient Safety
   Fax: 1-317-277-0853
   E-mail: mailindata_gsmtindy@lilly.com
   Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved and available alternative to bamlanivimab for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html. The health care provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Eli Lilly and Company for the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at

high risk for progressing to severe COVID-19 and/or hospitalization.[1] As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that bamlanivimab may be effective for the treatment of mild to moderate COVID-19 in certain high-risk patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for bamlanivimab will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

CONTACT INFORMATION
For additional information visit
www.bamlanivimab.com

If you have questions, please contact
1-855-LillyC19 (1-855-545-5921)

END SHORT VERSION FACT SHEET
Long Version Begins on Next Page

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[1] The health care provider should visit clinicaltrials.gov to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

FULL EUA PRESCRIBING INFORMATION

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

1 AUTHORIZED USE

Bamlanivimab is authorized for use under an EUA for treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Bamlanivimab is not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation *[see Warnings and Precautions (5.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Bamlanivimab should be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset in adults and pediatric patients (12

years of age and older weighing at least 40 kg), who are at high risk for progressing to severe COVID-19 and/or hospitalization.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

2.2 Dosage

The dosage of bamlanivimab in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is:

- bamlanivimab 700 mg.

Administer bamlanivimab as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Bamlanivimab must be diluted and administered as a single IV infusion over at least 60 minutes.

2.3 Dosage Adjustment in Specific Populations

Pregnancy or Lactation
No dosage adjustment is recommended in pregnant or lactating women *[see Use in Specific Populations (11.1, 11.2)]*.

Pediatric Use
No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg and are older than 12 years of age. Bamlanivimab is not authorized for patients weighing less than 40 kg or those less than 12 years of age *[see Use in Specific Populations (11.3)]*.

Geriatric Use

No dosage adjustment is recommended in geriatric patients *[see Use in Specific Populations (11.4)]*.

Renal Impairment
No dosage adjustment is recommended in patients with renal impairment *[see Use in Specific Populations (11.5)]*.

Hepatic Impairment
No dosage adjustment is recommended in patients with mild hepatic impairment. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment *[see Use in Specific Populations (11.6)]*.

2.4 Dose Preparation and Administration

Preparation
Bamlanivimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

- Remove one bamlanivimab vial (700 mg/20 mL) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vial.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
    - Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
- Withdraw 20 mL bamlanivimab from one 20 mL vial and inject into an infusion bag containing 250 mL prefilled 0.9% Sodium Chloride Injection (see **Table 1**).
- Discard any product remaining in the vial.
- Gently invert IV bag by hand approximately 10 times to mix. **Do not shake.**
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab

Drug	Number of Vials	Volume of Bamlanivimab	Volume of 0.9% Sodium Chloride	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Bamlanivimab (700 mg/20 mL)	1 Vial	20 mL	250 mL	270 mL	270 mL/hr	60 minutes

Administration
Bamlanivimab infusion solution should be administered by a qualified healthcare professional.

- Gather the materials for infusion:
    - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC infusion set
    - Use of an in-line or add-on 0.20/0.22 micron polyethersulfone (PES) filter is strongly recommended.

- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the entire infusion solution in the bag via pump or gravity over at least 60 minutes (see **Table 1**).
- Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- If the infusion must be discontinued due to an infusion reaction, discard any unused product.
- The use of closed system transfer devices (CSTDs), elastomeric pumps, and pneumatic transport with bamlanivimab has not been studied.

Storage
This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.

3 DOSAGE FORMS AND STRENGTHS

Bamlanivimab is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow to slightly brown solution available as:

- Injection: 700 mg/20 mL (35 mg/mL) in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

There are limited clinical data available for bamlanivimab. Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab use.

5.1 Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of bamlanivimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of bamlanivimab. Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

5.2 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, bamlanivimab is not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

6 OVERALL SAFETY SUMMARY

Over 1350 subjects have been exposed to bamlanivimab in clinical trials in both hospitalized and non-hospitalized patients.

6.1 Clinical Trials Experience

The safety of bamlanivimab is based on interim data from one Phase 2 trial of 465 ambulatory (non-hospitalized) subjects with COVID-19.

BLAZE-1 is a randomized, double-blind, placebo-controlled clinical trial in ambulatory adults with mild to moderate COVID-19 symptoms who had sample collection for the first positive SARS-CoV-2 viral infection determination within 3 days prior to the start of the infusion. Subjects were treated with a single infusion of bamlanivimab at doses of 700 mg (N=101), 2,800 mg (N=107), or 7,000 mg (N=101) or placebo (N=156).

Based on data from 309 bamlanivimab-treated subjects followed for at least 28 days after treatment, adverse events occurred in 23% bamlanivimab-treated subjects and 26% of placebo-treated subjects. Serious adverse events occurred in 1 placebo-treated subject (1%) and in no bamlanivimab-treated subjects.

The most commonly reported adverse event was nausea. Table 2 shows adverse events reported in at least 1% of patients in any treatment group. Bamlanivimab is not authorized at doses of 2,800 mg or 7,000 mg.

Table 2: Treatment-emergent Adverse Events Reported in at Least 1% of All Subjects in BLAZE-1

Preferred term	Placebo N=156 %	Bamlanivimab			
		700 mg N=101 %	2,800 mg N=107 %	7,000 mg N=101 %	Total N=309 %
Nausea	4%	3%	4%	5%	4%
Diarrhea	5%	1%	2%	7%	3%
Dizziness	2%	3%	3%	3%	3%
Headache	2%	3%	2%	0%	2%
Pruritus	1%	2%	3%	0%	2%
Vomiting	3%	1%	3%	1%	2%

Hypersensitivity Including Anaphylaxis and Infusion-related Reactions:
Across ongoing, blinded clinical trials, a case of anaphylaxis and other cases of serious infusion-related reactions were reported with infusion of bamlanivimab. The infusions were stopped. All reactions required treatment, one required epinephrine. All events resolved.

Immediate non-serious hypersensitivity events were noted for 2% of bamlanivimab-treated subjects and 1% of placebo-treated subjects in BLAZE-1. Reported events of pruritus, flushing and hypersensitivity were mild with one case of face swelling which was moderate. All events resolved *[see Warnings and Precautions (5.1)]*.

7 PATIENT MONITORING RECOMMENDATIONS

Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete *[see Warnings and Precautions (5.1) and Clinical Trials Experience (6.1)]*.

8 ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS AND INSTRUCTIONS

Clinical trials evaluating the safety of bamlanivimab are ongoing *[see Overall Safety Summary (6)]*.

Completion of FDA MedWatch Form to report all medication errors and serious adverse events is mandatory. The prescribing healthcare provider and/or the provider's designee are/is responsible for the mandatory reporting of all medication errors and the following serious adverse events occurring during bamlanivimab use and considered to be potentially related to bamlanivimab. These adverse events must be reported within 7 calendar days from the onset of the event:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

If a serious and unexpected adverse event occurs and appears to be associated with the use of bamlanivimab, the prescribing healthcare provider and/or the provider's designee should complete and submit a MedWatch form to FDA using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Use a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA- 0178), or
- Call 1-800-FDA-1088 to request a reporting form

IMPORTANT: When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient initials, date of birth)
- Pertinent medical history
- Pertinent details regarding adverse events and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of bamlanivimab
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

- In section A, box 1, provide the patient's initials in the Patient Identifier
- In section A, box 2, provide the patient's date of birth
- In section B, box 5, description of the event:
    - Write "Bamlanivimab treatment under Emergency Use Authorization (EUA)" as the first line
    - Provide a detailed report of medication error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved drug. Please see information to include listed above.
- In section G, box 1, name and address:
    - Provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    - Provide the address of the treating institution (NOT the healthcare provider's office address).

9 OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:
Eli Lilly and Company, Global Patient Safety
Fax: 1-317-277-0853
E-mail: mailindata_gsmtindy@lilly.com

Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

10 DRUG INTERACTIONS

Bamlanivimab is not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Bamlanivimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Nonclinical reproductive toxicity studies have not been performed with bamlanivimab. In a tissue cross reactivity study with bamlanivimab using human fetal tissues, no binding of clinical concern was detected. Human immunoglobulin G1 (IgG1) antibodies are known to cross the placental barrier; therefore, bamlanivimab has the potential to be transferred from the mother to the developing fetus. It is unknown whether the potential transfer of bamlanivimab provides any treatment benefit or risk to the developing fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

11.2 Lactation

Risk Summary

There are no available data on the presence of bamlanivimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for bamlanivimab and any potential adverse effects on the breastfed child from bamlanivimab or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

11.3 Pediatric Use

The safety and effectiveness of bamlanivimab have not been assessed in pediatric patients. The recommended dosing regimen is expected to result in comparable serum exposures of bamlanivimab in patients 12 years of age and older and weighing at least 40 kg as observed in adults, based on a pharmacokinetic (PK) modeling approach which

accounted for effect of body weight changes associated with age on clearance and volume of distribution.

11.4 Geriatric Use

Of the 309 patients receiving bamlanivimab in BLAZE-1, 11% were 65 years of age and older and 3% were 75 years of age and older. Based on population PK analyses, there is no difference in PK in geriatric patients compared to younger patients.

11.5 Renal Impairment

Bamlanivimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab.

11.6 Hepatic Impairment

Based on population PK analysis, there is no significant difference in PK of bamlanivimab in patients with mild hepatic impairment compared to patients with normal hepatic function. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment.

11.7 Other Specific Populations

Based on population PK analysis, the PK of bamlanivimab was not affected by sex, race, or disease severity. Body weight had no clinically relevant effect on the PK of bamlanivimab in adults with COVID-19 over the body weight range of 41 kg to 173 kg.

12 OVERDOSAGE

Doses up to 7,000 mg (10 times the recommended dose) have been administered in clinical trials without dose-limiting toxicity. Treatment of overdose with bamlanivimab should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with bamlanivimab.

13 DESCRIPTION

Bamlanivimab is a human immunoglobulin G-1 (IgG1 variant) monoclonal antibody consisting of 2 identical light chain polypeptides composed of 214 amino acids each and 2 identical heavy chain polypeptides composed of 455 amino acids produced by a Chinese Hamster Ovary (CHO) cell line and molecular weight of 146 kDa.

Bamlanivimab injection is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow to slightly brown solution in a single-dose vial for intravenous infusion after dilution.

Each mL contains 35 mg of bamlanivimab, and L-histidine (0.4 mg), L-histidine hydrochloride monohydrate (0.6 mg), sodium chloride (2.9 mg), sucrose (60 mg), polysorbate 80 (0.5 mg), and Water for Injection. The bamlanivimab solution has a pH range of 5.5-6.5.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

Bamlanivimab is a recombinant neutralizing human IgG1κ monoclonal antibody (mAb) to the spike protein of SARS-CoV-2, and is unmodified in the Fc region. Bamlanivimab binds to spike protein with a dissociation constant K_D = 0.071 nM and blocks spike protein attachment to the human ACE2 receptor with an IC_{50} value of 0.025 µg/mL.

14.2 Pharmacodynamics

A Phase 2 trial evaluated bamlanivimab over a dose range of 1 to 10 times the recommended dose (700 to 7000 mg) of bamlanivimab in patients with mild to moderate COVID-19. A flat exposure-response relationship for efficacy was identified for bamlanivimab within this dose range, based on viral load and clinical outcomes.

14.3 Pharmacokinetics

The pharmacokinetic profile of bamlanivimab is linear and dose-proportional between 700 mg and 7000 mg following a single IV administration. There were no differences in PK of bamlanivimab between severe/moderate participants who were hospitalized and mild/moderate ambulatory participants.

Absorption
The mean maximum concentration (Cmax) of 700 mg bamlanivimab was 196 µg/mL (90% CI: 102 to 378 µg/mL) following approximately 1 hour 700 mg IV infusion.

Distribution
Bamlanivimab mean volume of distribution (V) was 2.87 L and 2.71 L for the central and peripheral compartments, respectively. The between subject variability was 23.2% CV.

Metabolism
Bamlanivimab is expected to be degraded into small peptides and component amino acids via catabolic pathways in the same manner as endogenous IgG antibodies.

Elimination
Bamlanivimab clearance (CL) was 0.27 L/hr (between subject variability 22.3% CV) and the mean apparent terminal elimination half-life was 17.6 days (between subject variability 15.8% CV). Following a single 700 mg IV dose, bamlanivimab was quantifiable for at least 29 days. The mean concentration was 22 µg/mL (90% CI: 10.7 to 41.6 µg/mL) on Day 29.

Special Populations:
The PK profile of bamlanivimab was not affected by age, sex, race, or disease severity based on a population PK analysis. Body weight had no clinically relevant effect on the PK of bamlanivimab in adults with COVID-19 over the body weight range of 41 kg to 173 kg *[see Use in Specific Populations (11.4, 11.7)]*.

Pediatric population
The PK of bamlanivimab in pediatric patients have not been evaluated.

Using modeling and simulation, the recommended dosing regimen is expected to result in comparable plasma exposures of bamlanivimab in pediatric patients ages 12 years of age or older who weigh at least 40 kg as observed in adult patients *[see Use in Specific Populations (11.3)]*.

Patients with renal impairment
Bamlanivimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab *[see Use in Specific Populations (11.5)]*.

Patients with hepatic impairment
Based on population PK analysis, there is no significant difference in PK of bamlanivimab in patients with mild hepatic impairment compared to patients with normal hepatic function. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment *[see Use in Specific Populations (11.6)]*.

Drug interactions:
Bamlanivimab is not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

15 MICROBIOLOGY/RESISTANCE INFORMATION

Antiviral Activity
The cell culture neutralization activity of bamlanivimab against SARS-CoV-2 was measured in a dose-response model using cultured Vero E6 cells. Bamlanivimab neutralized SARS-CoV-2 with an estimated EC_{50} value = 0.03 µg/mL and an estimated EC_{90} value = 0.09 µg/mL.

Bamlanivimab demonstrated antibody-dependent cell-mediated cytotoxicity on reporter Jurkat cells expressing FcγRIIIa following engagement with target cells expressing spike protein. Bamlanivimab did not elicit complement-dependent cytotoxicity activity in cell-based assays.

Antibody Dependent Enhancement (ADE) of Infection
The risk that bamlanivimab could mediate viral uptake and replication by immune cells was studied in THP-1 and Raji cell lines and primary human macrophages. This experiment did not demonstrate productive viral infection in immune cells exposed to SARS CoV-2 at concentrations of bamlanivimab down to 100-fold below the EC_{50} value.

Antiviral Resistance
There is a potential risk of treatment failure due to the development of viral variants that are resistant to bamlanivimab.

Non-clinical studies using serial passage of SARS-CoV-2 and directed evolution of the spike protein identified E484K, F490S, Q493R and S494P, amino acid substitutions in the spike protein receptor binding domain, that had reduced susceptibility to bamlanivimab as determined in neutralization assays using SARS-CoV-2 (F490S and S494P: >485-fold and >71-fold reduction, respectively) and/or vesicular stomatitis virus-based pseudovirus (all variants >100-fold reduction).

Genotypic and phenotypic testing are ongoing to monitor for potential bamlanivimab-resistance-associated spike variations in clinical trials. Known bamlanivimab-resistant variants at baseline were observed at a frequency of 0.27% (1/375) in Part A of clinical trial BLAZE-1. In the same trial, treatment-emergent variants were detected at spike protein amino acid positions E484, F490 and S494, and included E484A/D/G/K/Q/V, F490L/S/V and S494L/P; only E484K/Q, F490S and S494P have been assessed phenotypically to date. Considering all variants detected at positions E484, F490 and S494, 9.2% (9/98) and 6.1% (6/98) of participants in the 700 mg bamlanivimab arm harbored such a variant post-baseline at ≥15% and ≥50% allele fractions, respectively, compared with 8.2% (8/97) and 4.1% (4/97), respectively, of participants in the placebo arm. Most of these variants were first detected on Day 7 following treatment initiation and many were detected only at a single time point (700 mg arm: 5/9 and 2/6 at ≥15% and ≥50% allele fractions, respectively; placebo arm: 8/8 and 4/4, respectively). For the 700 mg bamlanivimab arm, these variants were detected more frequently in high-risk participants (14.0% [6/43] and 9.3% [4/43] at ≥15% and ≥50% allele fractions, respectively, vs 2.4% [1/41] and 0% [0/41], respectively, in the placebo arm). The clinical relevance of these findings is not known.

It is possible that bamlanivimab resistance-associated variants could have cross-resistance to other mAbs targeting the receptor binding domain of SARS-CoV-2. The clinical impact is not known.

Immune Response Attenuation
There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to re-infection.

16 NONCLINICAL TOXICOLOGY

Carcinogenesis, mutagenesis, and reproductive toxicology studies with bamlanivimab have not been conducted.

In toxicology studies in rats, bamlanivimab had no adverse effects when administered intravenously. Non-adverse increases in neutrophils were observed.

In tissue cross reactivity studies using human adult and fetal tissues, no binding of clinical concern was detected.

17 ANIMAL PHARMACOLOGIC AND EFFICACY DATA

In Vivo Efficacy Pharmacology
Prophylactic administration of bamlanivimab to female Rhesus macaques (n=3 or 4 per group) resulted in 1 to 4 $\log_{10}$ decreases in viral load (genomic RNA) and viral replication (sub-genomic RNA) in bronchoalveolar lavage samples relative to control animals, but less of an impact on viral RNA in throat and nasal swabs following SARS-CoV-2 inoculation. The applicability of these findings to a prophylaxis or treatment setting is not known.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Mild to Moderate COVID-19 (BLAZE-1)

The data supporting this EUA are based on an interim analysis from Part A of BLAZE-1 that occurred after all enrolled subjects completed at least Day 29 of the trial. BLAZE-1 Part A is a randomized, double-blind, placebo-controlled clinical trial studying bamlanivimab for the treatment of subjects with mild to moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized). BLAZE-1 enrolled adult patients who were not hospitalized and had at least 1 or more COVID-19 symptoms that were at least mild in severity. Treatment was initiated within 3 days of obtaining the clinical sample for the first positive SARS-CoV-2 viral infection determination. Subjects were treated with a single infusion of bamlanivimab (at doses of 700 mg [N=101], 2,800 mg [N=107], or 7,000 mg [N=101]) or placebo (N=156).

At baseline, median age was 45 years (with 12% of subjects aged 65 or older); 55% of subjects were female, 88% were White, 44% were Hispanic or Latino, and 6% were Black; 44% of subjects were considered high risk (as defined in Section 2). Subjects had mild (76%) to moderate COVID-19 (24%); the mean duration of symptoms was 5 days; mean viral load by cycle threshold (CT) was 24 at baseline. The baseline demographics and disease characteristics were well balanced across bamlanivimab and placebo treatment groups.

The pre-specified primary endpoint in this Phase 2 trial was change in viral load from baseline to Day 11 for bamlanivimab versus placebo. Most subjects, including those receiving placebo, effectively cleared virus by Day 11 (Figure 1).

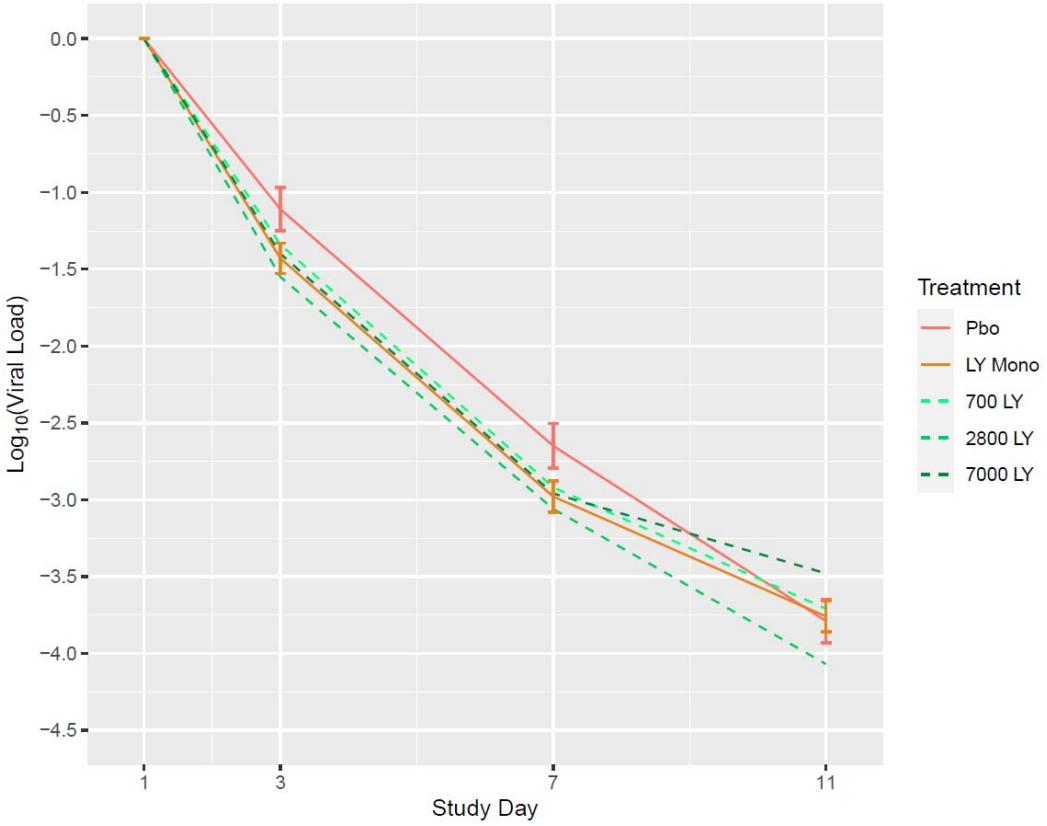


Figure 1: SARS-CoV-2 viral load change from baseline by visit.

While viral load was used to define the primary endpoint in this Phase 2 trial, the most important evidence that bamlanivimab may be effective came from the predefined secondary endpoint of COVID-19-related hospitalizations or emergency room visits within 28 days after treatment. A lower proportion of bamlanivimab-treated subjects progressed to COVID-19-related hospitalization or emergency room visits compared to placebo-treated subjects (Table 3). Results for this endpoint were suggestive of a relatively flat dose-response relationship.

Table 3: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits within 28 Days After Treatment

Treatment	N[a]	Events	Proportion of Subjects %
Placebo	156	9	6%
bamlanivimab 700 mg	101	1	1%
bamlanivimab 2800 mg	107	2	2%
bamlanivimab 7000 mg	101	2	2%
All bamlanivimab doses	309	5	2%

[a] N = number of treated patients in analysis.

The absolute risk reduction for bamlanivimab compared to placebo is greater in subjects at higher risk of hospitalization according to the high risk criteria (Table 4).

Table 4: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits for Subjects at Higher Risk of Hospitalization

Treatment	N[a]	Events	Proportion of Subjects %
Placebo	69	7	10%
bamlanivimab 700 mg	46	1	2%
bamlanivimab 2800 mg	46	1	2%
bamlanivimab 7000 mg	44	2	5%
All bamlanivimab doses	136	4	3%

[a] N = number of treated patients in analysis.

The median time to symptom improvement as recorded in a trial specific daily symptom diary was 6 days for bamlanivimab-treated subjects, as compared with 8 days for placebo-treated subjects. Symptoms assessed were cough, shortness of breath, feeling feverish, fatigue, body aches and pains, sore throat, chills, and headache. Symptom improvement was defined as symptoms scored as moderate or severe at baseline being scored as mild or absent, and symptoms scored as mild or absent at baseline being scored as absent.

19 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Bamlanivimab injection is a sterile, preservative-free clear to opalescent and colorless to slightly yellow to slightly brown solution supplied in a single-dose vial.

Bamlanivimab is supplied as:

Antibody	Concentration	Package Size	NDC
Bamlanivimab	700 mg/20 mL (35 mg/mL)	one vial per carton	0002-7910-01

Storage and Handling
Bamlanivimab is preservative-free. Discard unused portion.

Store unopened vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE, SHAKE, OR EXPOSE TO DIRECT LIGHT.

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted bamlanivimab infusion solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours and at room temperature (20°C to 25°C [68°F to 77°F]) for up to 7 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature prior to administration.

20 PATIENT COUNSELING INFORMATION

Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines. Also see Fact Sheet for Patients, Parents and Caregivers.

21 CONTACT INFORMATION

For additional information visit:
www.bamlanivimab.com

If you have questions, please contact:
1-855-LillyC19 (1-855-545-5921)

Literature revised December 2020

Eli Lilly and Company, Indianapolis, IN 46285, USA

BAM-0004-EUA HCP-20201211

FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab and imdevimab to be administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

Casirivimab and imdevimab have been authorized by FDA for the emergency uses described above.

Casirivimab and imdevimab are not FDA-approved for these uses.

Casirivimab and imdevimab are authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of casirivimab and imdevimab under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

This EUA is for the use of the unapproved products, casirivimab and imdevimab, to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease

- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to casirivimab and imdevimab. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

- The authorized dosage is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous (IV) infusion as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.
- Casirivimab and imdevimab solutions must be diluted prior to administration.
- Administer 1,200 mg of casirivimab and 1,200 mg of imdevimab together as a single IV infusion over at least 60 minutes via pump or gravity.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

The authorized dosage may be updated as additional data from clinical trials becomes available.

For information on clinical trials that are testing the use of casirivimab and imdevimab in COVID-19, please see www.clinicaltrials.gov.

Contraindications

None.

Dosing

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved products, casirivimab and imdevimab, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Dosage

The dosage in adults and in pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion over at least 60 minutes. Casirivimab and imdevimab solutions must be diluted prior to administration. Casirivimab and imdevimab should be given together as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Dosage Adjustment in Specific Populations

No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment *[see Full EUA Prescribing Information, Use in Specific Populations (11)]*.

Preparation and Administration

Preparation

Casirivimab and imdevimab are each supplied in individual single-dose vials. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials**.
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared.
   - The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.
3. Obtain an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab solutions according to **Table 1**.
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the infusion bag containing 0.9% Sodium Chloride Injection, see **Table 1**. Discard any product remaining in the vial.
5. Gently invert infusion bag by hand approximately 10 times to mix. **Do not shake**. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

Table 1: Recommended Dilution Instructions for Casirivimab and Imdevimab for IV Infusion

Casirivimab and Imdevimab 2,400 mg Dose[a]	Antibody Dose	Volume to Withdraw from Vial	Number of Vials Needed[b]	Volume of 0.9% Sodium Chloride to Discard from a	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time

				250 mL Infusion Bag			
	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL				

NOTE: casirivimab = REGN10933; imdevimab = REGN10987

[a] 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

[b] One 11.1 mL vial of one antibody may be prepared with four 2.5 mL vials of the other antibody to create one treatment course.

Administration

Casirivimab and imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), Polyethylene (PE)-lined PVC, or Polyurethane (PU) infusion set
  - In-line or add-on 0.2 micron polyethersulfone (PES) filter
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see **Table 1**).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.
- After infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

Storage

Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the individual original carton to protect from light. Do NOT freeze, shake, or expose to direct light.

Warnings

There are limited clinical data available for casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

Infusion-related reactions have been observed with administration of casirivimab and imdevimab.

Signs and symptoms of infusion-related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab are not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Side Effects

Adverse events have been reported with casirivimab and imdevimab [*see Full EUA Prescribing Information, Clinical Trials Experience (6.1)*].

Additional adverse events associated with casirivimab and imdevimab, some of which may be serious, may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the health care provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving casirivimab and imdevimab, including:

- FDA has authorized the emergency use of casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

- The patient or parent/caregiver has the option to accept or refuse casirivimab and imdevimab.
- The significant known and potential risks and benefits of casirivimab and imdevimab, and the extent to which such risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.

For information on clinical trials that are testing the use of casirivimab and imdevimab related to COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR CASIRIVIMAB AND IMDEVIMAB UNDER EMERGENCY USE AUTHORIZATION:

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of casirivimab and imdevimab to be administered together, the following items are required. Use of casirivimab and imdevimab under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.
2. As the health care provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to the patient receiving casirivimab and imdevimab. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
    a. Given the "Fact Sheet for Patients, Parents and Caregivers",
    b. Informed of alternatives to receiving casirivimab and imdevimab, and
    c. Informed that casirivimab and imdevimab are unapproved drugs that are authorized for use under this Emergency Use Authorization.
3. Patients with known hypersensitivity to any ingredient of casirivimab and imdevimab must not receive casirivimab and imdevimab.
4. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of casirivimab and imdevimab.
5. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to casirivimab and imdevimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.

- Submit adverse event reports to FDA MedWatch using one of the following methods:
    - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
    - By using a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
    - Call 1-800-FDA-1088 to request a reporting form
    - Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)."

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

6. OTHER REPORTING REQUIREMENTS
   In addition, please provide a copy of all FDA MedWatch forms to:
   Regeneron Pharmaceuticals, Inc
   Fax: 1-888-876-2736
   E-mail: medical.information@regeneron.com
   Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved and available alternatives to casirivimab and imdevimab to be administered together for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html. The health care provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Regeneron Pharmaceuticals, Inc. for the unapproved products, casirivimab and imdevimab, to be administered together, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral

testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. [1] As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that casirivimab and imdevimab, administered together, may be effective for the treatment of COVID-19 in patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for casirivimab and imdevimab will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

CONTACT INFORMATION

For additional information visit www.REGENCOV2.com
If you have questions, please contact Regeneron at 1-844-734-6643.

END SHORT VERSION FACT SHEET
Long Version Begins on Next Page

[1] The health care provider should visit https://clinicaltrials.gov/ to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

FULL EUA PRESCRIBING INFORMATION

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

1 AUTHORIZED USE

Casirivimab and imdevimab are authorized to be administered together for use under an EUA for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19 *[see Warnings and Precautions (5.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

The optimal dosing regimen for treatment of COVID-19 has not yet been established.
The recommended dosing regimen may be updated as data from clinical trials become available.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved products, casirivimab and imdevimab, to be administered together, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization *[see Limitations of Authorized Use]*.

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

2.2 Dosage

The dosage in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab should be given as soon as possible after a positive viral test for SARS-CoV-2 and within 10 days of symptom onset.

2.3 Dose Adjustment in Specific Populations

Pregnancy or Lactation

No dosage adjustment is recommended in pregnant or lactating women *[see Use in Specific Populations (11.1, 11.2)]*.

Pediatric Use

No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg and are older than 12 years of age. Casirivimab and imdevimab are not recommended for pediatric patients weighing less than 40 kg or those less than 12 years of age *[see Use in Specific Populations (11.3)]*.

Renal Impairment

No dosage adjustment is recommended in patients with renal impairment *[see Use in Specific Populations (11.5)]*.

2.4 Dose Preparation and Administration

Preparation

Casirivimab and imdevimab are each supplied in individual single-dose vials. Casirivimab and imdevimab solutions must be diluted prior to administration.

Casirivimab and imdevimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique:

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials.**
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.
3. Obtain an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab according to **Table 2**.
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the infusion bag containing 0.9% Sodium Chloride Injection, see **Table 2**. Discard any product remaining in the vial.
5. Gently invert infusion bag by hand approximately 10 times. **Do not shake.**
   This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C

(36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Table 2: Recommended Dilution Instructions for Casirivimab and Imdevimab for IV Infusion

Casirivimab and Imdevimab 2,400 mg Dose[a]	**Antibody Dose**	**Volume to Withdraw from Vial**	**Number of Vials Needed[b]**	**Volume of 0.9% Sodium Chloride to Discard from a 250 mL Infusion Bag**	**Total Volume for Infusion**	**Maximum Infusion Rate**	**Minimum Infusion Time**
	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL **OR** 4 vials of 2.5 mL				

NOTE: casirivimab = REGN10933; imdevimab = REGN10987

[a] 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

[b] One 11.1 mL vial of one antibody may be prepared with four 2.5 mL vials of the other antibody to create one treatment course.

Administration

Casirivimab and imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), Polyethylene (PE)-lined PVC, or Polyurethane (PU) infusion set
  - In-line or add-on 0.2 micron polyethersulfone (PES) filter
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see **Table 2**).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.

- After infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

Storage

This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

3 DOSAGE FORMS AND STRENGTHS

Casirivimab is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution available as:

- Injection: 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) in a single-dose vial

Imdevimab is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution available as:

- Injection: 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) in a single-dose vial

Casirivimab and **imdevimab** carton and vial labels may instead be labeled **REGN10933** and **REGN10987** respectively.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

There are limited clinical data available for casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

5.1 Hypersensitivity including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reactions, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant

hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of casirivimab and imdevimab.

Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

5.2 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab are not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

6 OVERALL SAFETY SUMMARY

Overall more than 2,100 subjects have been exposed to IV casirivimab and imdevimab in clinical trials in both hospitalized and non-hospitalized patients.

6.1 Clinical Trials Experience

The safety of casirivimab and imdevimab is based on analysis from one phase 1/2 trial of 799 ambulatory (non-hospitalized) subjects with COVID-19.

R10933-10987-COV-2067 is a randomized, double-blind, placebo-controlled clinical trial in ambulatory adults with mild to moderate COVID-19 symptoms who had a sample collected for the first positive SARS-CoV-2 viral infection determination within 3 days prior to the start of the infusion. Subjects were treated with a single infusion of 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) (N=258) or 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) (N=260), or placebo (n=262). The adverse events collected were infusion-related reactions and hypersensitivity reactions of moderate severity or higher through day 29, all serious adverse events (SAEs); and in phase 1 only, all grade 3 and 4 treatment-emergent adverse events.

Serious adverse events were reported in 4 subjects (1.6%) in the casirivimab and imdevimab 2,400 mg group, 2 subjects (0.8%) in the casirivimab and imdevimab 8,000 mg group, and 6 subjects (2.3%) in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg casirivimab and imdevimab), intestinal obstruction and dyspnea (8,000 mg casirivimab and imdevimab) and COVID-19, pneumonia and hypoxia (placebo). Casirivimab and imdevimab are not authorized at the 8,000 mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).

Hypersensitivity Including Anaphylaxis and Infusion-related Reactions

One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and include pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm and none were reported in the 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm.

In two subjects receiving the 8,000 mg dose of casirivimab and imdevimab, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved [*see Warnings and Precautions (5.1)*].

7 PATIENT MONITORING RECOMMENDATIONS

Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete *[see Warnings and Precautions (5.1) and Clinical Trials Experience (6.1)]*.

8 ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS AND INSTRUCTIONS

Clinical trials evaluating the safety of casirivimab and imdevimab are ongoing *[see Overall Safety Summary (6)]*.

Completion of FDA MedWatch Form to report all medication errors and serious adverse events* occurring during casirivimab and imdevimab use and considered to be potentially related to casirivimab and imdevimab is mandatory and must be done by the prescribing healthcare provider and/or the provider's designee. These adverse events must be reported within 7 calendar days from the onset of the event:

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;

- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

If a serious and unexpected adverse event occurs and appears to be associated with the use of casirivimab and imdevimab, the prescribing health care provider and/or the provider's designee should complete and submit a MedWatch form to FDA using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Use a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form

IMPORTANT: When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient initials, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of casirivimab and imdevimab
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In section A, box 1, provide the patient's initials in the Patient Identifier
2. In section A, box 2, provide the patient's date of birth or age
3. In section B, box 5, description of the event:
    a. Write "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)" as the first line
    b. Provide a detailed report of medication error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved drug. Please see information to include listed above.
4. In section G, box 1, name and address:
    a. Provide the name and contact information of the prescribing health care provider or institutional designee who is responsible for the report
    b. Provide the address of the treating institution (NOT the health care provider's office address).

9 OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:
Regeneron Pharmaceuticals, Inc
Fax: 1-888-876-2736
E-mail: medical.information@regeneron.com
Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

10 DRUG INTERACTIONS

Casirivimab and imdevimab are 2 monoclonal antibodies (mAbs) which are not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Casirivimab and imdevimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Nonclinical reproductive toxicity studies have not been conducted with casirivimab and imdevimab. In a tissue cross-reactivity study with casirivimab and imdevimab using human fetal tissues, no binding of clinical concern was detected. Human immunoglobulin G1 (IgG1) antibodies are known to cross the placental barrier; therefore, casirivimab and imdevimab have the potential to be transferred from the mother to the developing fetus. It is unknown whether the potential transfer of casirivimab and imdevimab provides any treatment benefit or risk to the developing fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

11.2 Nursing Mothers

Risk Summary

There are no available data on the presence of casirivimab and/or imdevimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of

breastfeeding should be considered along with the mother's clinical need for casirivimab and imdevimab and any potential adverse effects on the breastfed child from casirivimab and imdevimab or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

11.3 Pediatric Use

The safety and effectiveness of casirivimab and imdevimab have not been assessed in pediatric patients. The recommended dosing regimen is expected to result in comparable serum exposures of casirivimab and imdevimab in patients 12 years of age and older and weighing at least 40 kg as observed in adults, since adults with similar body weight have been included in Trial R10933-10987-COV-2067.

11.4 Geriatric Use

Of the 799 patients with SARS-CoV-2 infection randomized in Trial R10933-10987-COV-2067, 7% were 65 years or older, and 2% were 75 years of age or older. The difference in PK of casirivimab and imdevimab in geriatric patients compared to younger patients is unknown.

11.5 Renal Impairment

Casirivimab and imdevimab are not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of casirivimab and imdevimab.

11.6 Hepatic Impairment

The effect of hepatic impairment on PK of casirivimab and imdevimab is unknown.

11.7 Other Specific Populations

The effect of other covariates (e.g., sex, race, body weight, disease severity) on PK of casirivimab and imdevimab is unknown.

12 OVERDOSAGE

Doses up to 8,000 mg (4,000 mg each of casirivimab and imdevimab, greater than 3 times the recommended dose) have been administered in clinical trials without dose-limiting toxicity. Treatment of overdose should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with casirivimab and imdevimab.

13 PRODUCT DESCRIPTION

Casirivimab, a human immunoglobulin G-1 (IgG1) monoclonal antibody (mAb), is a covalent heterotetramer consisting of 2 heavy chains and 2 light chains produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture and has an approximate molecular weight of 145.23 kDa.

Casirivimab injection is a sterile, preservative-free, clear to slightly opalescent and colorless to pale yellow solution in a single-dose vial for intravenous infusion after dilution available as a 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) solution and must be administered with imdevimab.

- Casirivimab: Each 2.5 mL of solution contains 300 mg of casirivimab, L-histidine (1.9 mg), L-histidine monohydrochloride monohydrate (2.7 mg), polysorbate 80 (2.5 mg), sucrose (200 mg), and Water for Injection, USP. The pH is 6.0.

- Casirivimab: Each 11.1 mL of solution contains 1,332 mg of casirivimab, L-histidine (8.3 mg), L-histidine monohydrochloride monohydrate (12.1 mg), polysorbate 80 (11.1 mg), sucrose (888 mg), and Water for Injection, USP. The pH is 6.0.

Imdevimab, a human IgG1 mAb, is a covalent heterotetramer consisting of 2 heavy chains and 2 light chains produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture and has an approximate molecular weight of 144.14 kDa.

Imdevimab injection is a sterile, preservative-free, clear to slightly opalescent and colorless to pale yellow solution in a single-dose vial for intravenous infusion after dilution available as a 300 mg/2.5 mL (120 mg/mL) or 1,332 mg/11.1 mL (120 mg/mL) solution and must be administered with casirivimab.

- Imdevimab: Each 2.5 mL of solution contains 300 mg of imdevimab, L-histidine (1.9 mg), L-histidine monohydrochloride monohydrate (2.7 mg), polysorbate 80 (2.5 mg), sucrose (200 mg), and Water for Injection, USP. The pH is 6.0.

- Imdevimab: Each 11.1 mL of solution contains 1,332 mg of imdevimab, L-histidine (8.3 mg), L-histidine monohydrochloride monohydrate (12.1 mg), polysorbate 80 (11.1 mg), sucrose (888 mg), and Water for Injection, USP. The pH is 6.0.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

Casirivimab (IgG1κ) and imdevimab (IgG1λ) are two recombinant human mAbs which are unmodified in the Fc regions. Casirivimab and imdevimab bind to non-overlapping epitopes of the spike protein receptor binding domain (RBD) of SARS-CoV-2 with dissociation constants K_D = 45.8 pM and 46.7 pM, respectively. Casirivimab, imdevimab and the casirivimab + imdevimab combination blocked RBD binding to the human ACE2 receptor with IC_{50} values of 56.4 pM, 165 pM and 81.8 pM, respectively [*see Microbiology/Resistance Information (15)*].

14.2 Pharmacodynamics

Trial R10933-10987-COV-2067 evaluated casirivimab and imdevimab with doses of 1 and 3.33 times the recommended doses (1,200 mg casirivimab and 1,200 mg imdevimab; 4,000 mg casirivimab and 4,000 mg imdevimab) in ambulatory patients with COVID-19. A flat dose-response relationship for efficacy was identified for casirivimab and imdevimab at those two doses, based on viral load and clinical outcomes.

14.3 Pharmacokinetics

Pharmacokinetic profiles of casirivimab and imdevimab are expected to be consistent with the profile of other IgG1 mAbs.

Specific Populations

The effect of different covariates (e.g., age, sex, race, body weight, disease severity, hepatic impairment) on the PK of casirivimab and imdevimab is unknown. Renal impairment is not expected to impact the PK of casirivimab and imdevimab, since mAbs with molecular weight >69 kDa are known not to undergo renal elimination. Similarly, dialysis is not expected to impact the PK of casirivimab and imdevimab.

Drug-Drug Interactions

Casirivimab and imdevimab are mAbs which are not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely *[see Drug Interactions (10)]*.

15 MICROBIOLOGY/RESISTANCE INFORMATION

Antiviral Activity

In a SARS-CoV-2 virus neutralization assay in Vero E6 cells, casirivimab, imdevimab, and the casirivimab + imdevimab combination neutralized SARS-CoV-2 (USA-WA1/2020 isolate) with EC_{50} values of 37.4 pM (0.006 μg/mL), 42.1 pM (0.006 μg/mL), and 31.0 pM (0.005 μg/mL) respectively.

Antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) were assessed using Jurkat target cells expressing SARS-CoV-2 spike protein. Casirivimab, imdevimab and the casirivimab + imdevimab combination mediated ADCC with human natural killer (NK) effector cells. Casirivimab, imdevimab and the casirivimab + imdevimab combination mediated ADCP with human macrophages. Casirivimab, imdevimab and the casirivimab + imdevimab combination did not mediate complement-dependent cytotoxicity in cell-based assays.

Antibody Dependent Enhancement (ADE) of Infection

The potential of casirivimab and of imdevimab to mediate viral entry was assessed in immune cell lines co-incubated with recombinant vesicular stomatitis virus (VSV) pseudoparticles expressing SARS-CoV-2 spike protein at concentrations of mAb(s) down to approximately 10-fold below the respective neutralization EC_{50} values. The casirivimab + imdevimab combination and imdevimab alone, but not casirivimab alone, mediated entry of pseudoparticles into $Fc\gamma R2^+$ Raji and $Fc\gamma R1^+/Fc\gamma R2^+$ THP1 cells (maximum infection in total cells of 1.34% and 0.24%, respectively, for imdevimab; 0.69% and 0.06%, respectively for the casirivimab + imdevimab combination), but not any other cell lines tested (IM9, K562, Ramos and U937 cells).

Antiviral Resistance

There is a potential risk of treatment failure due to the development of viral variants that are resistant to the casirivimab + imdevimab combination.

Escape variants were identified following passage in cell culture of recombinant VSV encoding SARS-CoV-2 spike protein in the presence of casirivimab or imdevimab individually, but not following passage in the presence of the casirivimab + imdevimab combination. Variants which showed reduced susceptibility to casirivimab included spike protein amino acid substitutions K417E, Y453F, L455F, F486V and Q493K, and variants which showed reduced susceptibility to imdevimab included K444Q and V445A substitutions. Each variant showing reduced susceptibility to one mAb retained susceptibility to the other, and all variants retained susceptibility to the casirivimab + imdevimab combination.

In neutralization assays using VSV pseudotyped with 37 different receptor binding domain (RBD) variants identified as the most common RBD variations in circulation as of late March 2020, and D614G, D614N spike protein variants, casirivimab had reduced susceptibility (4.5-fold) to G476S and S494P variants, and imdevimab had reduced susceptibility (463-fold) to the N439K variant. The casirivimab + imdevimab combination retained activity against all variants tested.

In clinical trial R10933-10987-COV-2067, interim data indicated only one variant (G446V) occurring at an allele fraction ≥15%, which was detected in 3/66 subjects who had nucleotide sequencing data, each at a single time point (two at baseline in subjects from placebo and 2,400 mg casirivimab + imdevimab combination groups, and one at Day 25 in a subject from the 8,000 mg casirivimab + imdevimab combination group). The G446V variant had reduced susceptibility to imdevimab of 135-fold compared to wild-type in a VSV pseudoparticle neutralization assay but retained susceptibility to casirivimab and the casirivimab + imdevimab combination.

It is possible that resistance-associated variants to the casirivimab + imdevimab combination could have cross-resistance to other mAbs targeting the receptor binding domain of SARS-CoV-2. The clinical impact is not known.

Immune Response Attenuation

There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to re-infection.

16 NONCLINICAL TOXICOLOGY

Carcinogenicity, genotoxicity, and reproductive toxicology studies have not been conducted with casirivimab and imdevimab.

In a toxicology study in cynomolgus monkeys, casirivimab and imdevimab had no adverse effects when administered intravenously. Non-adverse liver findings (minor transient increases in AST and ALT) were observed.

In tissue cross-reactivity studies with casirivimab and imdevimab using human adult and fetal tissues, no binding of clinical concern was detected.

17 ANIMAL PHARMACOLOGIC AND EFFICACY DATA

The casirivimab + imdevimab combination has been assessed in rhesus macaque and Syrian golden hamster treatment models of SARS-CoV-2 infection. Therapeutic administration of the casirivimab + imdevimab combination at 25 mg/kg or 150 mg/kg into rhesus macaques (n=4 for each dosing group) 1-day post infection resulted in approximately 1-2 $\log_{10}$ reductions in genomic and sub-genomic viral RNA in nasopharyngeal swabs and oral swabs at Day 4 post-challenge in most animals, and reduced lung pathology relative to placebo-treated animals. Therapeutic administration of the casirivimab + imdevimab combination at 5 mg/kg and 50 mg/kg doses to hamsters 1-day post infection resulted in reduced weight loss relative to placebo treated animals, but had no clear effects on viral load in lung tissue. The applicability of these findings to a clinical setting is not known.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Mild to Moderate COVID-19 (R10933-10987-COV-2067)

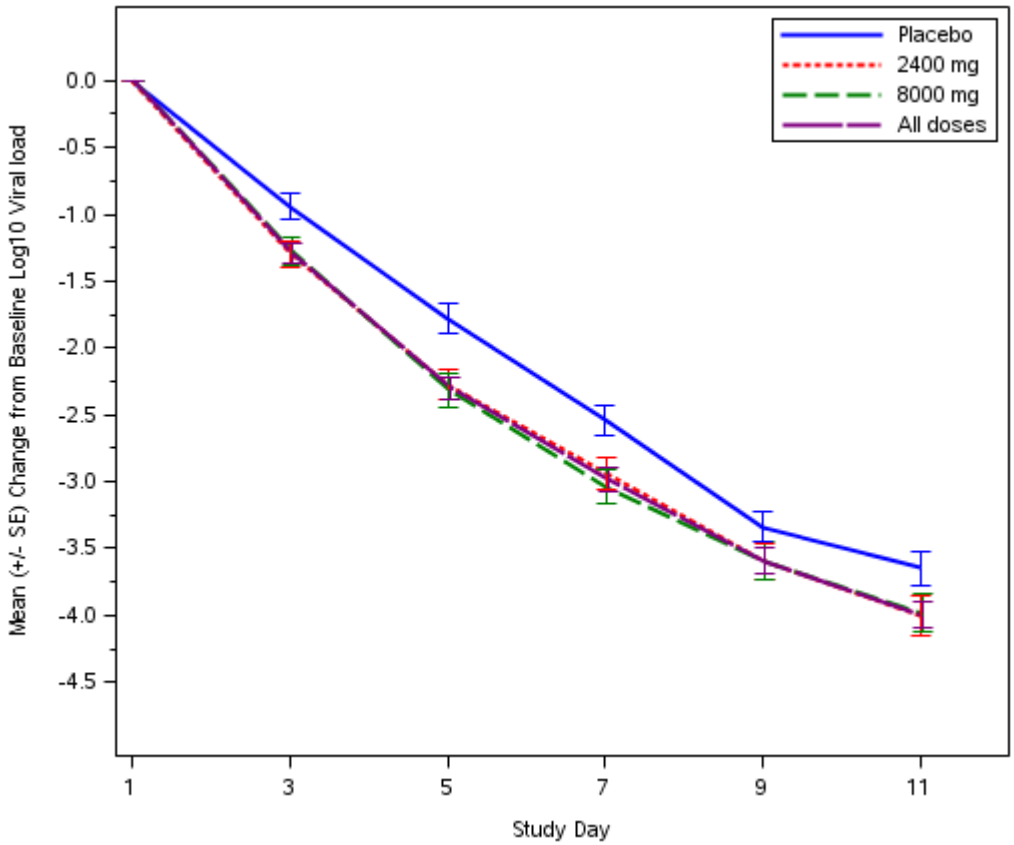
The data supporting this EUA are based on the analysis of Phase 1/2 from trial R10933-10987-COV-2067, that occurred after 799 enrolled subjects had completed at least 28 days of study duration. R10933-10987-COV-2067 is a randomized, double-blinded, placebo-controlled clinical trial studying casirivimab and imdevimab for the treatment of adult subjects with mild to moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized). The trial enrolled adult subjects who were not hospitalized and had at least 1 or more COVID-19 symptoms that were at least mild in severity. Treatment was initiated within 3 days of obtaining a positive SARS-CoV-2 viral infection determination. Subjects were randomized in a 1:1:1 manner to receive a single intravenous (IV) infusion of 2,400 mg of casirivimab and imdevimab (1,200 mg of each) (n=266), or 8,000 mg of casirivimab and imdevimab (4,000 mg of each) (n=267), or placebo (n=266).

At baseline, the median age was 42 years (with 7% of subjects ages 65 years or older), 53% of the subjects were female, 85% were White, 50% were Hispanic or Latino, and 9% were Black;

34% were considered high risk (as defined in Section 2). Approximately 31% of subjects reported at least 1 severe symptom at baseline, 36% reported at least 1 moderate symptom and no severe symptoms, and 13% reported only mild symptoms. The median duration of symptoms was 3 days; mean viral load was 5.8 $\log_{10}$ copies/mL at baseline. The baseline demographics and disease characteristics were well balanced across the casirivimab and imdevimab and placebo treatment groups.

The pre-specified primary endpoint in Phase 1/2 of trial R10933-10987-COV-2067 was the time weighted average (TWA) change from baseline in viral load ($\log_{10}$ copies/mL), as measured by RT-qPCR in nasopharyngeal swab samples, in subjects with a positive baseline RT-qPCR value, i.e., the modified full analysis set (mFAS). In the mFAS for the Phase 1/2 analysis, the difference in TWA from Day 1 through Day 7 for the pooled doses of casirivimab and imdevimab compared with placebo (n=665) was -0.36 $\log_{10}$ copies/mL ($p<0.0001$). The largest reductions in viral load relative to placebo occurred in patients with high viral load (-0.78 $\log_{10}$ copies/mL) or who were seronegative (-0.69 $\log_{10}$ copies/mL) at baseline. Reductions occurring from Day 1 through Day 11 were similar to those for Day 1 through Day 7. **Figure 1** shows the mean change from baseline in SARS-COV-2 viral load over time.

Figure 1. Mean Change from Baseline in SARS-COV-2 Viral Load Over Time



While viral load was used to define the primary endpoint in the Phase 1/2 analysis, clinical evidence demonstrating that casirivimab and imdevimab may be effective came from the predefined secondary endpoint, medically attended visits (MAV) related to COVID-19.

Medically attended visits comprised hospitalizations, emergency room visits, urgent care visits, or physician office/telemedicine visits for COVID-19. A lower proportion of subjects treated with casirivimab and imdevimab had COVID-19 related MAVs (2.8% for combined treatment arms vs 6.5% placebo). In post-hoc analyses, a lower proportion of subjects treated with casirivimab and imdevimab had COVID-19-related hospitalizations or emergency room visits compared to placebo, see Table 3. Results for this endpoint were suggestive of a relatively flat dose-response relationship. The absolute risk reduction for casirivimab and imdevimab compared to placebo was greater in subjects at high risk for progression to severe COVID-19 and/or hospitalization, according to the criteria outlined in section 2 (Table 4).

Table 3: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment[a]

Treatment	N[b]	Events	Proportion of subjects
Placebo	231	10	4%
2,400 mg[c] casirivimab and imdevimab	215	4	2%
8,000 mg[d] casirivimab and imdevimab	219	4	2%
All doses casirivimab and imdevimab	434	8	2%

[a] Hospitalization and emergency room visits were a subset of a key secondary endpoint, Medically-Attended Visits, which also included urgent care visits, physician's office visits and telemedicine visits.
[b] N = number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization
[c] 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab)
[d] 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab)

Table 4: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment for Subjects at Higher Risk of Hospitalization[a]

Treatment	N[b]	Events	Proportion of subjects
Placebo	78	7	9%
2,400 mg[c] casirivimab and imdevimab	70	2	3%
8,000 mg[d] casirivimab and imdevimab	81	2	2%
All doses casirivimab and imdevimab	151	4	3%

[a] Hospitalization and emergency room visits were a subset of a key secondary endpoint, Medically-Attended Visits, which also included urgent care visits, physician's office visits and telemedicine visits.
[b] N = number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization
[c] 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab)
[d] 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab)

The median time to symptom improvement, as recorded in a trial-specific daily symptom diary, was 5 days for casirivimab and imdevimab-treated subjects, as compared with 6 days for placebo-treated subjects. Symptoms assessed were shortness of breath or difficulty breathing, chills, feverish, sore throat, cough, nausea, vomiting, diarrhea, headache, red or watery eyes, body and muscle aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum/phlegm, runny nose. Symptom improvement was defined as symptoms scored as moderate or severe at baseline being scored as mild or absent, and symptoms scored as mild or absent at baseline being scored as absent.

19 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Casirivimab injection is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution supplied in a single-dose vial. Refer to Table 5.

Imdevimab injection is a sterile, preservative-free, clear to slightly opalescent, colorless to pale yellow solution supplied in a single-dose vial. Refer to Table 5.

CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER.

Table 5: How Casirivimab and Imdevimab are Supplied

Antibody	Concentration	Package Size	NDC Number
Casirivimab REGN 10933	1332 mg/11.1 mL (120 mg/mL)	1 vial per pack	61755-024-01
	300 mg/2.5 mL (120 mg/mL)	1 vial per pack	61755-026-01
Imdevimab REGN10987	1332 mg/11.1 mL (120 mg/mL)	1 vial per pack	61755-025-01
	300 mg/2.5 mL (120 mg/mL)	1 vial per pack	61755-027-01

Storage and Handling

Casirivimab is preservative-free. Discard any unused portion.
Imdevimab is preservative-free. Discard any unused portion.

Store unopened casirivimab and imdevimab vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE. DO NOT SHAKE. DO NOT EXPOSE TO DIRECT LIGHT.

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted casirivimab and imdevimab solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for no more

than 36 hours and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

20 PATIENT COUNSELING INFORMATION

Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines. Also see Fact Sheet for Patients, Parents and Caregivers.

21 CONTACT INFORMATION

For additional information visit www.REGENCOV2.com
If you have questions, please contact Regeneron at 1-844-734-6643.

REGENERON

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Authorized: 11/2020

THE SOCIETY FOR POST-ACUTE AND LONG-TERM CARE MEDICINE
amda

Readiness Document for Clinicians for Use of Monoclonal Antibody Infusions for Treatment of COVID-19

MONOCLONAL ANTIBODY ELIGIBILITY CRITERIA CHECKLIST

Several monoclonal antibodies have received emergency use authorization from the FDA for the treatment of mild to moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Resident Name: _____ Room: _____ Date: _____

Inclusion Criteria ***(Must Meet All 3 Criteria)***	**Yes**	**No**
Mild to moderately symptomatic COVID-19[1]		
Within 10 days of symptom onset, preferably in the first 3 days		
Positive direct test for SARS-CoV-2 *(either A or B)* A) If no outbreak present in the building, PCR positive B) If outbreak is present in the building, PCR or antigen positive		

High Risk Criteria for Adults ***(Must Have 1 of the Following)***	**Yes**	**No**
Body mass index ≥ 35		
Age ≥ 65		
Chronic kidney disease		
Diabetes		
Immunosuppressive disease or currently receiving immunosuppressive treatment		
≥ 55 years of age AND have: • cardiovascular disease, OR • hypertension, OR • chronic obstructive pulmonary disease/other chronic respiratory disease		

Exclusion Criteria ***(May Not Have Any of the Following)***	**Yes**	**No**
Patient is hospitalized or meets hospitalization criteria[2]		
Patient requires oxygen due to COVID-19 (Pulse ox ≤ 93% on room air)		
If on chronic oxygen, patient requires an increase in oxygen therapy due to COVID-19		
Patient is on hospice, is hospice eligible, had a palliative care/hospice consult within the prior 6 months, or has a life expectancy less than 6 months (clinician judgement or MDS J1400), inclusions of these residents can be decided on a case by case basis		

DEFINITIONS

[1]**Mild to Moderate Symptoms (1 or more of the following)**	[2]**Hospitalization Criteria Definition (1 or more of the following)**

• Fever (99.0 or greater) • New cough • Sore throat • Malaise • Headaches • Muscle pain/aches • Gastrointestinal symptoms • Shortness of breath with exertion • Loss of smell and taste	• RR≥30 • HR ≥ 130 • SBP < 90 despite fluid resuscitation

Infusion-related reactions have been observed and there is potential for severe reactions, including anaphylaxis. Monoclonal antibody treatment may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS).

Post-acute and long-term care settings with access to such expertise and resources may be able to administer monoclonal antibody in their own facilities.

Administration of monoclonal antibody treatment requires documentation of:

1. Patient has been given FDA Fact sheet for patients
2. Patient has been informed of alternatives to receiving monoclonal antibody treatment
3. Patient has been informed that this is an unapproved drug that is authorized for use under the FDA Emergency Use Authorization (EUA)
4. Reporting of adverse events to FDA MedWatch, following the requirements under Emergency Use Authorizations (see last page for details)

Fact sheets for patients:

https://www.fda.gov/media/143604/download (bamlavinimab)

https://www.fda.gov/media/143893/download (casirivimab plus imdevimab)

Resources for clinicians:

Further information for healthcare providers including instructions on preparation of infusions and side effects are available in the following factsheets

https://www.fda.gov/media/143603/download (bamlavinimab)

https://www.fda.gov/media/143892/download (casirivimab plus imdevimab)

https://asap.nebraskamed.com/monoclonal-antibody-project/

COVID-19 OUTPATIENT MONOCLONAL ANTIBODY INFUSION ORDERS

- ✓ **Place peripheral IV**

- ✓ **Monoclonal Antibody Infusion Orders**
  - bamlanivimab 700 mg IV over 1 hour once
  - casirivimab – imdevimab 2400 mg IV over 1 hour once

- ✓ **Hypersensitivity Reaction Management**
  - ✓ For ALL Reactions:
    - Provide supplemental oxygen via nasal cannula to keep O2 saturation >94%
    - Obtain vital signs and O2 saturation every 10 minutes
    - Refer to orders below for symptomatic management
    - Contact physician
    - Complete FDA Medwatch Event Report

  - ✓ For fever or chills:
    - acetaminophen 1000 mg PO once

  - ✓ For itching, rash, hives or flushing:
    - diphenhydramine 25 mg IV once
    - famotidine 20 mg IV once
    - If patient desires to complete infusion, decrease monoclonal antibody infusion rate by half
      - Change bamlanivimab infusion rate to 100 mL/hour until bag complete
      - Change casirivimab – imdevimab infusion rate to 125 mL/hour until bag complete

  - ✓ For shortness of breath, wheezing, or chest tightness:
    - Discontinue monoclonal antibody infusion
    - diphenhydramine 50 mg IV once
    - albuterol neb 2.5 mg INH once
    - methylprednisolone 125mg IVP once

  - ✓ For stridor, severe bronchospasm, sensation of throat closure or choking, or SBP <90
    - Discontinue monoclonal antibody infusion
    - Evaluate airway
    - epinephrine 0.3 mg IM once into anterolateral thigh
    - Place patient into recumbent position with lower extremities elevated
    - 0.9% sodium chloride 500 mL IV bolus once
    - Call “Condition” / Call 911

Monitoring for nurses and prescribers

- Patients treated with monoclonal antibody treatment should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.
- **Clinically monitor patients, including vital signs during administration and observe patients for at least 1 hour after infusion is complete.**
- There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of monoclonal antibody treatment. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration, and initiate appropriate medications and/or supportive care.

Suggested medications to be available in Nursing home infusion site: E-Box for MAb infusions:

Medication	**Number of doses**
epinephrine 0.3 mg IM	
methylprednisolone 125mg	
albuterol neb 2.5 mg INH	
diphenhydramine 50 mg IV	
famotidine 20 mg IV	
Albuterol syr 2 mg PO	
Diphenhydramine 25mg PO	

December 17, 2020

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ascp
American Society of Consultant Pharmacists

Memorandum: Vaccine Distribution Liability Under PREP Act

Background

On March 10, 2020, the Secretary of Health and Human Services (Secretary) issued a Declaration under the Public Readiness and Emergency Preparedness Act (PREP Act), effective February 4, 2020, for certain medical products to be used against COVID-19.[1] The PREP Act authorizes the Secretary to issue a declaration to provide liability immunity to certain individuals and entities against any claim of loss caused by, arising out of, relating to, or resulting from the manufacture, *distribution*, administration, or use of [vaccines] (referred to as covered countermeasures). It is ASCP's view that these declarations under the PREP Act cover various activities related to the distribution of a future Food and Drug Administration (FDA) approved COVID-19 vaccine in long-term care facilities (LTCF) and assisted living facilities (ALF).

PREP Act Covered Entities

It is the intent of congress to ensure that all individuals acting in good faith and taking "reasonable steps" to help treat COVID-19 are extended immunity under the PREP Act. A "covered-person" under the PREP Act means:

> B) a person or entity that is—
>
> (i) a manufacturer of such countermeasure;
> (ii) a distributor of such countermeasure;
> (iii) a program planner of such countermeasure;
> (iv) a qualified person who prescribed, administered, or dispensed such countermeasure; or
> (v) an official, agent, or employee of a person or entity described in clause (i), (ii), (iii), or (iv).[2]

The PREP Act offers broad immunity to all individuals who are engaged in the COVID-19 vaccination effort, but the PREP Act does not replace the need for individual contracts and agreements to be put in place when working to manufacture, distribute, or administer a COVID-19 vaccine. It is important to note that individuals provided immunity under the PREP Act may still be sued for equitable relief related to personal injury or damage to property and the federal government still has the ability to bring enforcement actions against individuals who are covered entities under PREP Act immunity. It is our view, however, that any individual involved in the manufacturing, distribution, or administration of a COVID-19 vaccine that participates with the federal government (an Authority Having Jurisdiction) as part of a federal government provider authorization is a covered entity afforded immunity under the PREP Act.

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[1] See 85 Fed. Reg. 15, 198, 15, 202 (March 17, 2020); see also Pub. L. No. 109-148, Public Health Service Act § 319F-3, 42 U.S.C. § 247d-6d and 42 U.S.C. § 247d-6e.
[2] 42 U.S.C. § 247d-6d(I)(2).

MEDICARE ENROLLMENT APPLICATION

Clinics/Group Practices and Certain Other Suppliers

CMS-855B

SEE PAGE 1 TO DETERMINE IF YOU ARE COMPLETING THE CORRECT APPLICATION.

SEE PAGE 2 FOR INFORMATION ON WHERE TO MAIL THIS APPLICATION.

SEE PAGE 35 TO FIND A LIST OF THE SUPPORTING DOCUMENTATION THAT MUST BE SUBMITTED WITH THIS APPLICATION.

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

Form Approved
OMB NO. 0938-0685
Expires: 08/19

WHO SHOULD SUBMIT THIS APPLICATION

Clinics and group practices can apply for enrollment in the Medicare program or make a change in their enrollment information using either:

- The Internet-based Provider Enrollment, Chain and Ownership System (PECOS), or
- The paper enrollment application process (e.g., CMS 855B).

For additional information regarding the Medicare enrollment process, including Internet-based PECOS, go to *http://www.cms.gov/MedicareProviderSupEnroll*.

Clinics and group practices who are enrolled in the Medicare program, but have not submitted the CMS 855B since 2003, are required to submit a Medicare enrollment application (i.e., Internet-based PECOS or the CMS 855B) as an initial application when reporting a change for the first time.

The following suppliers must complete this application to initiate the enrollment process:

- Ambulance Service Supplier
- Ambulatory Surgical Center
- Clinic/Group Practice
- Independent Clinical Laboratory
- Independent Diagnostic Testing Facility (IDTF)
- Intensive Cardiac Rehabilitation Supplier
- Mammography Center
- Mass Immunization (Roster Biller Only)
- Part B Drug Vendor
- Portable X-ray Supplier
- Radiation Therapy Center

If your supplier type is not listed above, contact your designated fee-for-service contractor before you submit this application.

Complete and submit this application if you are an organization/group that plans to bill Medicare and you are:

- A **medical practice or clinic that will bill for Medicare Part B services** (e.g., group practices, clinics, independent laboratories, portable x-ray suppliers).
- A **hospital or other medical practice or clinic** that may bill for Medicare Part A services but will also bill for Medicare Part B practitioner services or provide purchased laboratory tests to other entities that bill Medicare Part B.
- **Currently enrolled with a Medicare fee-for-service contractor but need to enroll in another fee-for-service contractor's jurisdiction** (e.g., you have opened a practice location in a geographic territory serviced by another Medicare fee-for-service contractor).
- **Currently enrolled in Medicare and need to make changes to your enrollment data** (e.g., you have added or changed a practice location). Changes must be reported in accordance with the timeframes established in 42 C.F.R. § 424.516(d). (IDTF changes of information must be reported in accordance with 42 C.F.R. § 410.33.)

BILLING NUMBER INFORMATION

The National Provider Identifier (NPI) is the standard unique health identifier for health care providers and is assigned by the National Plan and Provider Enumeration System (NPPES). **As a Medicare health supplier, you must obtain an NPI prior to enrolling in Medicare or before submitting a change for your existing Medicare enrollment information.** Applying for an NPI is a process separate from Medicare enrollment. As a supplier, it is your responsibility to determine if you have "subparts." A subpart is a component of an organization (supplier) that furnishes healthcare and is not itself a legal entity. If you do have subparts, you must determine if they should obtain their own unique NPIs. Before you complete this enrollment application, you need to make those determinations and obtain NPI(s) accordingly.

Important: For NPI purposes, sole proprietors and sole proprietorships are considered to be "Type 1" providers. Organizations (e.g., corporations, partnerships) are treated as "Type 2" entities. When reporting the NPI of a sole proprietor on this application, therefore, the individual's Type 1 NPI should be reported; for organizations, the Type 2 NPI should be furnished.

To obtain an NPI, you may apply online at *https://NPPES.cms.hhs.gov*. For more information about subparts, visit *www.cms.gov/NationalProvIdentStand* to view the "Medicare Expectations Subparts Paper."

The Medicare Identification Number, often referred to as a Provider Transaction Access Number (PTAN) or Medicare "legacy" number, is a generic term for any number other than the NPI that is used to identify a Medicare supplier.

INSTRUCTIONS FOR COMPLETING AND SUBMITTING THIS APPLICATION

- Type or print all information so that it is legible. Do not use pencil.
- Report additional information within a section by copying and completing that section for each additional entry.
- Attach all required supporting documentation.
- Keep a copy of your completed Medicare enrollment package for your records.
- Send the completed application with original signatures and all required documentation to your designated Medicare fee-for-service contractor.

AVOID DELAYS IN YOUR ENROLLMENT

To avoid delays in the enrollment process, you should:

- Complete all required sections.
- Ensure that the legal business name shown in Section 2 matches the name on the tax documents.
- Ensure that the correspondence address shown in Section 2 is the supplier's address.
- Enter your NPI in the applicable sections.
- Enter all applicable dates.
- Ensure that the correct person signs the application.
- Send your application and all supporting documentation to the designated fee-for-service contractor.

ADDITIONAL INFORMATION

For additional information regarding the Medicare enrollment process, visit *www.cms.gov/MedicareProviderSupEnroll*.

The fee-for-service contractor may request, at any time during the enrollment process, documentation to support and validate information reported on the application. You are responsible for providing this documentation in a timely manner.

Certain information you provide on this application is considered to be protected under 5 U.S.C. Section 552(b)(4) and/or (b)(6), respectively. For more information, see the last page of this application for the Privacy Act Statement.

MAIL YOUR APPLICATION

The Medicare fee-for-service contractor (also referred to as a carrier or a Medicare administrative contractor) that services your State is responsible for processing your enrollment application. To locate the mailing address for your fee-for-service contractor, go to *www.cms.gov/MedicareProviderSupEnroll*.

NEW ENROLLEES AND THOSE WITH A NEW TAX ID NUMBER

If you are:

- Enrolling in the Medicare program for the first time with this Medicare fee-for-service contractor under this tax identification number.
- Already enrolled with a Medicare fee-for-service contractor but are establishing a practice location in another fee-for-service contractor's jurisdiction.
- Enrolled with a Medicare fee-for-service contractor but have a new tax identification number. If you are reporting a change to your tax identification number, you must complete a new application.
- A hospital or an individual hospital department that is enrolling with a fee-for-service contractor to bill for Part B services.

The following actions apply to Medicare suppliers already enrolled in the program:

ENROLLED MEDICARE SUPPLIERS

Reactivation

To reactivate your Medicare billing privileges, submit this enrollment application. In addition, prior to being reactivated, you must be able to submit a valid claim and meet all current requirements for your supplier type before reactivation may occur.

Voluntary Termination

A supplier should voluntarily terminate its Medicare enrollment when it:

- Will no longer be rendering services to Medicare patients, or
- Is planning to cease (or has ceased) operations.

Change of Ownership

If a hospital, ambulatory surgical center, or portable X-ray supplier is undergoing a change of ownership (CHOW) in accordance with the principles outlined in 42 C.F.R. 489.18, the entity must submit a new application for the new ownership.

Change of Information

A change of information should be submitted if you are changing, adding or deleting information under your current tax identification number.

Changes in your existing enrollment data must be reported to the fee-for-service contractor in accordance with 42 C.F.R. § 424.516 (Physician and Non Physician Practitioner Organizations). (IDTF changes of information must comply with the provisions found at 42 C.F.R. § 410.33.)

If you are already enrolled in Medicare and are not receiving Medicare payments via EFT, any change to your enrollment information will require you to submit a CMS-588 form. All future payments will then be made via EFT.

Revalidation

CMS may require you to submit or update your enrollment information. The fee-for-service contractor will notify you when it is time for you to revalidate your enrollment information. Do not submit a revalidation application until you have been contacted by the fee-for-service contractor.

SECTION 1: BASIC INFORMATION
ALL APPLICANTS MUST COMPLETE THIS SECTION *(See instructions for details.)*

A. Check one box and complete the required sections.

REASON FOR APPLICATION	BILLING NUMBER INFORMATION	REQUIRED SECTIONS
☐ You are a **new enrollee** in Medicare	Enter your Medicare Identification Number *(if issued)* and the NPI you would like to link to this number in Section 4.	**Complete all applicable sections** **Ambulance suppliers** must complete **Attachment 1** **IDTF suppliers** must complete **Attachment 2**
☐ You are **enrolling in another fee-for-service contractor's jurisdiction**	Enter your Medicare Identification Number *(if issued)* and the NPI you would like to link to this number in Section 4.	**Complete all applicable sections** **Ambulance suppliers** must complete **Attachment 1** **IDTF suppliers** must complete **Attachment 2**
☐ You are **reactivating** your Medicare enrollment	Enter your Medicare Identification Number *(if issued)* and the NPI you would like to link to this number in Section 4. Medicare Identification Number(s) *(if issued):* National Provider Identifier *(if issued):*	**Complete all applicable sections** **Ambulance suppliers** must complete **Attachment 1** **IDTF suppliers** must complete **Attachment 2**
☐ You are **voluntarily terminating** your Medicare enrollment. (This is not the same as "opting out" of the program)	Effective Date of Termination: Medicare Identification Number(s) to Terminate *(if issued):* National Provider Identifier *(if issued):*	Sections **1, 2B1, 13,** and either **15 or 16** If you are terminating an employment arrangement with a physician assistant, complete Sections **1A, 2G, 13,** and either **15 or 16**

SECTION 1: BASIC INFORMATION *(Continued)*
ALL APPLICANTS MUST COMPLETE THIS SECTION *(See instructions for details.)*

A. Check one box and complete the required sections.

REASON FOR APPLICATION	BILLING NUMBER INFORMATION	REQUIRED SECTIONS
☐ You are **changing** your Medicare information	Medicare Identification Number: National Provider Identifier *(if issued):*	Go to Section 1B
☐ You are **revalidating** your Medicare enrollment	Enter your Medicare Identification Number *(if issued)* and the NPI you would like to link to this number in Section 4.	**Complete all applicable sections** **Ambulance suppliers** must complete **Attachment 1** **IDTF suppliers** must complete **Attachment 2**

SECTION 1: BASIC INFORMATION *(Continued)*

B. Check all that apply and complete the required sections:

	REQUIRED SECTIONS
☐ Identifying Information	**1, 2** (complete only those sections that are changing)**, 3, 13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Final Adverse Actions/Convictions	**1, 2B1, 3, 13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Practice Location Information, Payment Address & Medical Record Storage Information	**1, 2B1, 3, 4** (complete only those sections that are changing), **13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Change of Ownership (Hospitals, Portable X-Ray Suppliers & Ambulatory Surgical Centers Only)	**Complete all sections and provide a copy of the sales agreement**
☐ Ownership Interest and/or Managing Control Information (Organizations)	**1, 2B1, 3, 5, 13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Ownership Interest and/or Managing Control Information (Individuals)	**1, 2B1, 3, 6, 13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Billing Agency Information	**1, 2B1, 3, 8** (complete only those sections that are changing), **13,** and either **15** (if you are an authorized official) **or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Authorized Official(s)	**1, 2B1, 3, 13, 15 or 16** (if you are a delegated official), and **6** for the signer if that authorized or delegated official has not been established for this supplier
☐ Delegated Official(s) (Optional)	**1, 2B1, 3, 13, 15, 16,** and **6** for the signer if that delegated official has not been established for this supplier.

ATTACHMENT 1: AMBULANCE SERVICE SUPPLIERS (ONLY)	REQUIRED SECTIONS
☐ Geographic Area	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 1(A)**
☐ State License Information	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 1(B)**
☐ Paramedic Intercept Services Information	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 1(C)**
☐ Vehicle Information	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 1(D)**
ATTACHMENT 2: INDEPENDENT DIAGNOSTIC TESTING FACILITIES (ONLY)	**REQUIRED SECTIONS**
☐ CPT-4 and HCPCS Codes	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 2(B)**
☐ Interpreting Physician Information	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 2(C)**
☐ Personnel (Technicians) Who Perform Tests	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 2(D)**
☐ Supervising Physician(s)	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 2(E)**
☐ Liability Insurance Information	**1, 2B1, 3, 13, and 15** if you are the authorized official **or 16** if you are the delegated official **Attachment 2(F)**

SECTION 2: IDENTIFYING INFORMATION

A. Type of Supplier

Check the appropriate box to identify the type of supplier you are enrolling as with Medicare. If you are more than one type of supplier, submit a separate application for each type. If you change the type of service that you provide (i.e., become a different supplier type), submit a new application.

Your organization must meet all Federal and State requirements for the type of supplier checked below.

TYPE OF SUPPLIER: ***(Check one only)***

- ☐ Ambulance Service Supplier
- ☐ Ambulatory Surgical Center
- ☐ Clinic/Group Practice
- ☐ Hospital Department(s)
- ☐ Independent Clinical Laboratory
- ☐ Independent Diagnostic Testing Facility
- ☐ Intensive Cardiac Rehabilitation
- ☐ Mammography Center
- ☐ Mass Immunization (Roster Biller Only)
- ☐ Pharmacy
- ☐ Physical/Occupational Therapy Group in Private Practice
- ☐ Portable X-ray Supplier
- ☐ Radiation Therapy Center
- ☐ Other *(Specify)*: _____

B. Supplier Identification Information

1. BUSINESS INFORMATION

Legal Business Name (not the "Doing Business As" name) as reported to the Internal Revenue Service

Tax Identification Number

Other Name	Type of Other Name
	☐ Former Legal Business Name ☐ Doing Business As Name ☐ Other *(Specify)*: _____

Identify how your business is registered with the IRS. (**NOTE:** If your business is a Federal and/or State government provider or supplier, indicate "Non-Profit" below.)

☐ Proprietary ☐ Non-Profit

NOTE: If a checkbox indicating Proprietary or non-profit status is not completed, the provider/supplier will be defaulted to "Proprietary."

Identify the type of organizational structure of this provider/supplier *(Check one)*

☐ Corporation ☐ Limited Liability Company ☐ Partnership
☐ Sole Proprietor ☐ Other *(Specify)*: _____

Incorporation Date *(mm/dd/yyyy) (if applicable)*	State Where Incorporated *(if applicable)*

Is this supplier an Indian Health Facility enrolling with the designated Indian Health Service (IHS) Medicare Administrative Contractor (MAC)?

☐ Yes ☐ No

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

2. STATE LICENSE INFORMATION/CERTIFICATION INFORMATION

Provide the following information if the supplier has a State license/certification to operate as the supplier type for which you are enrolling.

☐ State License Not Applicable

License Number	State Where Issued
Effective Date *(mm/dd/yyyy)*	Expiration/Renewal Date *(mm/dd/yyyy)*

Certification Information

☐ Certification Not Applicable

Certification Number	State Where Issued
Effective Date *(mm/dd/yyyy)*	Expiration/Renewal Date *(mm/dd/yyyy)*

3. CORRESPONDENCE ADDRESS

Provide contact information for the entity or person listed in Question 1 of this section. Once enrolled, the information provided below will be used by the fee-for-service contractor if it needs to contact you directly. This address cannot be a billing agency's address.

Mailing Address Line 1 *(Street Name and Number)*
Mailing Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

C. Hospitals Only

This section should only be completed by hospitals that are currently enrolled or enrolling with a fee-for-service contractor (the Part A Medicare contractor), and will be billing a fee-for-service contractor for Medicare Part B services, as follows:

- Hospitals that need departmental billing numbers to bill for Part B practitioner services.
- Hospitals requiring a Part B billing number to provide pathology services.
- Hospitals requiring a Medicare Part B billing number to provide purchased tests to other Medicare Part B billers.
- If the hospital requires more than one departmental Part B billing number, list each department needing a number.

If your organization is not a hospital, and believes it will need a Part B billing number, contact the designated fee-for-service contractor to determine if this form should be submitted.

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

C. Hospitals Only *(Continued)*

NOTE: If your hospital is enrolling a clinic that is not provider-based, do not complete this section.

Check ☐ "Clinic/Group Practice" in Section 2A and complete this entire application for the clinic.

1. Are you going to:
   ☐ bill for the entire hospital with one billing number? (If yes, continue to Section 2D.)
   ☐ separately bill for each hospital department? (If yes, answer Question 2.)
2. List the hospital departments for which you plan to bill separately:

DEPARTMENT	MEDICARE IDENTIFICATION NUMBER	NPI

D. Comments/Special Circumstances

Explain any unique circumstances concerning your practice location, the method by which you render health care services, etc.

E. Physical Therapy (PT) and Occupational Therapy (OT) Groups Only

1. Are all of the group's PT/OT services rendered in patients' homes or in the group's private office space? ☐ YES ☐ NO
2. Does this group maintain private office space? ☐ YES ☐ NO
3. Does this group own, lease, or rent its private office space? ☐ YES ☐ NO
4. Is this private office space used exclusively for the group's private practice? ☐ YES ☐ NO
5. Does this group provide PT/OT services outside of its office and/or patients' homes? ☐ YES ☐ NO

If you responded YES to any of the questions 2–5 above, submit a copy of the lease agreement that gives the group exclusive use of the facilities for PT/OT services.

F. Accreditation for Ambulatory Surgical Centers (ASCs) Only

NOTE: Copy and complete this section if more than one accreditation needs to be reported.

Check one of the following and furnish any additional information as requested:

☐ The enrolling ASC supplier is accredited.

☐ The enrolling ASC supplier is not accredited (includes exempt providers).

Name of Accrediting Organization

Effective Date of Current Accreditation *(mm/dd/yyyy)*	Expiration of Current Accreditation *(mm/dd/yyyy)*

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

G. Termination of Physician Assistants *(Only)*

Complete this section to delete employed physician assistants from your group or clinic.

EFFECTIVE DATE OF DEPARTURE	PHYSICIAN ASSISTANT'S NAME	PHYSICIAN ASSISTANT'S MEDICARE IDENTIFICATION NUMBER	PHYSICIAN ASSISTANT'S NPI

H. Advanced Diagnostic Imaging (ADI) Suppliers Only

This section must be completed by all suppliers that also furnish and will bill Medicare for ADI services. All suppliers furnishing ADI services MUST be accredited in each ADI Modality checked below to qualify to bill Medicare for those services.

Check each ADI modality this supplier will furnish and the name of the Accrediting Organization that accredited that ADI Modality for this supplier.

☐ **Magnetic Resonance Imaging (MRI)**

Name of Accrediting Organization for MRI

Effective Date of Current Accreditation *(mm/dd/yyyy)*	Expiration Date of Current Accreditation *(mm/dd/yyyy)*

☐ **Computed Tomography (CT)**

Name of Accrediting Organization for CT

Effective Date of Current Accreditation *(mm/dd/yyyy)*	Expiration Date of Current Accreditation *(mm/dd/yyyy)*

☐ **Nuclear Medicine (NM)**

Name of Accrediting Organization for NM

Effective Date of Current Accreditation *(mm/dd/yyyy)*	Expiration Date of Current Accreditation *(mm/dd/yyyy)*

☐ **Positron Emission Tomography (PET)**

Name of Accrediting Organization for PET

Effective Date of Current Accreditation *(mm/dd/yyyy)*	Expiration Date of Current Accreditation *(mm/dd/yyyy)*

SECTION 3: FINAL ADVERSE LEGAL ACTIONS/CONVICTIONS

This section captures information on final adverse legal actions, such as convictions, exclusions, revocations, and suspensions. All applicable final adverse legal actions must be reported, regardless of whether any records were expunged or any appeals are pending.

Convictions

1. The provider, supplier, or any owner of the provider or supplier was, within the last 10 years preceding enrollment or revalidation of enrollment, convicted of a Federal or State felony offense that CMS has determined to be detrimental to the best interests of the program and its beneficiaries. Offenses include:

   Felony crimes against persons and other similar crimes for which the individual was convicted, including guilty pleas and adjudicated pre-trial diversions; financial crimes, such as extortion, embezzlement, income tax evasion, insurance fraud and other similar crimes for which the individual was convicted, including guilty pleas and adjudicated pre-trial diversions; any felony that placed the Medicare program or its beneficiaries at immediate risk (such as a malpractice suit that results in a conviction of criminal neglect or misconduct); and any felonies that would result in a mandatory exclusion under Section 1128(a) of the Act.

2. Any misdemeanor conviction, under Federal or State law, related to: (a) the delivery of an item or service under Medicare or a State health care program, or (b) the abuse or neglect of a patient in connection with the delivery of a health care item or service.
3. Any misdemeanor conviction, under Federal or State law, related to theft, fraud, embezzlement, breach of fiduciary duty, or other financial misconduct in connection with the delivery of a health care item or service.
4. Any felony or misdemeanor conviction, under Federal or State law, relating to the interference with or obstruction of any investigation into any criminal offense described in 42 C.F.R. Section 1001.101 or 1001.201.
5. Any felony or misdemeanor conviction, under Federal or State law, relating to the unlawful manufacture, distribution, prescription, or dispensing of a controlled substance.

Exclusions, Revocations, or Suspensions

1. Any revocation or suspension of a license to provide health care by any State licensing authority. This includes the surrender of such a license while a formal disciplinary proceeding was pending before a State licensing authority.
2. Any revocation or suspension of accreditation.
3. Any suspension or exclusion from participation in, or any sanction imposed by, a Federal or State health care program, or any debarment from participation in any Federal Executive Branch procurement or non-procurement program.
4. Any current Medicare payment suspension under any Medicare billing number.
5. Any Medicare revocation of any Medicare billing number.

SECTION 3: FINAL ADVERSE ACTIONS/CONVICTIONS *(Continued)*

FINAL ADVERSE HISTORY

1. Has your organization, under any current or former name or business identity, ever had any of the final adverse actions listed on page 13 of this application imposed against it?

   ☐ YES–Continue Below ☐ NO–Skip to Section 4

2. If yes, report each final adverse action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse action documentation and resolution.

FINAL ADVERSE ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 4: PRACTICE LOCATION INFORMATION

INSTRUCTIONS

This section captures information about the physical location(s) where you currently provide health care services. If you operate a mobile facility or portable unit, provide the address for the "Base of Operations," as well as vehicle information and the geographic area serviced by these facilities or units.

Only report those practice locations within the jurisdiction of the Medicare fee-for-service contractor to which you will submit this application. If you have practice locations in another Medicare fee-for-service contractor's jurisdiction, complete a separate enrollment application (CMS-855B) for those practice locations and submit it to the Medicare fee-for-service contractor that has jurisdiction over those locations.

Provide the specific street address as recorded by the United States Postal Service. Do not provide a P.O. Box. If you provide services in a hospital and/or other health care facility for which you bill Medicare directly for the services rendered at that facility, provide the name and address of the hospital or facility.

MOBILE FACILITY AND/OR PORTABLE UNIT

A "mobile facility" is generally a mobile home, trailer, or other large vehicle that has been converted, equipped, and licensed to render health care services. These vehicles usually travel to local shopping centers or community centers to see and treat patients inside the vehicle.

A "portable unit" is when the supplier transports medical equipment to a fixed location (e.g., physician's office, nursing home) to render services to the patient.

The most common types of mobile facilities/portable units are mobile IDTFs, portable X-ray suppliers, portable mammography, and mobile clinics. Physicians and non-physician practitioners (e.g., nurse practitioners, physician assistants) who perform services at multiple locations (e.g., house calls, assisted living facilities) are not considered to be mobile facilities/portable units.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

A. Practice Location Information

If you see patients in more than one practice location, copy and complete Section 4A for each location.

To ensure that CMS establishes the correct association between your Medicare legacy number and your NPI, providers and suppliers must list a Medicare legacy number—NPI combination for each practice location. If you have multiple NPIs associated with both a single legacy number and a single practice location, please list below all NPIs and associated legacy numbers for that practice location.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

If you are enrolling for the first time, or if you are adding a new practice location, the date you provide should be the date you saw your first Medicare patient at this location.

Practice Location Name *("Doing Business As" name if different from Legal Business Name)*

Practice Location Street Address Line 1 *(Street Name and Number – NOT a P.O. Box)*

Practice Location Street Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

Date you saw your first Medicare patient at this practice location *(mm/dd/yyyy)*

Medicare Identification Number *(if issued)*	National Provider Identifier
Medicare Identification Number *(if issued)*	National Provider Identifier
Medicare Identification Number *(if issued)*	National Provider Identifier
Medicare Identification Number *(if issued)*	National Provider Identifier
Medicare Identification Number *(if issued)*	National Provider Identifier

Is this practice location a:

☐ Group practice office/clinic
☐ Hospital
☐ Retirement/assisted living community
☐ Skilled Nursing Facility and/or Nursing Facility
☐ Other health care facility
*(Specify):*_____

CLIA Number for this location *(if applicable)*

Attach a copy of the most current CLIA certifications for each of the practice locations reported on this application

FDA/Radiology (Mammography) Certification Number for this location *(if issued)*

Attach a copy of the most current FDA certifications for each of the practice locations reported on this application.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

B. Where do you want remittance notices or special payments sent?
If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Medicare will issue payments via electronic funds transfer (EFT). Since payments will be made by EFT, the "Special Payments" address should indicate where all other payment information (e.g., remittance notices, special payments) should be sent.

☐ "Special Payments" address is the same as the practice location (only one address is listed in Section 4A). Skip to Section 4C.

☐ "Special Payments" address is different than that listed in Section 4A, or multiple locations are listed. Provide address below.

"Special Payments" Address Line 1 *(PO Box or Street Name and Number)*

"Special Payments" Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

C. Where do you keep patients' medical records?
If you store patients' medical records (current and/or former patients) at a location other than the location in Section 4A or 4E, complete this section with the address of the storage location.

Post Office boxes and drop boxes are not acceptable as physical addresses where patients' records are maintained. For IDTFs and mobile facilities/portable units, the patients' medical records must be under the supplier's control. The records must be the supplier's records, not the records of another supplier. If this section is not completed, you are indicating that all records are stored at the practice locations reported in Section 4A or 4E.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

First Medical Record Storage Facility (for current and former patients)

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Storage Facility Address Line 1 *(Street Name and Number)*

Storage Facility Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Second Medical Record Storage Facility (for current and former patients)

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Storage Facility Address Line 1 *(Street Name and Number)*

Storage Facility Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

D. Rendering Services in Patients' Homes

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Furnish the city/town, State and ZIP code for all locations where health care services are rendered in patients' homes. If you provide health care services in more than one State and those States are serviced by different Medicare fee-for-service contractors, complete a separate CMS-855B enrollment application for each Medicare fee-for-service contractor's jurisdiction.

If you are adding or deleting an entire State, it is not necessary to report each city/town. Simply check the box below and specify the State.

☐ Entire State of _____

If you are providing services in selected cities/towns, furnish the locations below. Only list ZIP codes if you are not servicing the entire city/town.

CITY/TOWN	STATE	ZIP CODE

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

E. Base of Operations Address for Mobile or Portable Suppliers (Location of Business Office or Dispatcher/Scheduler)

The base of operations is the location from where personnel are dispatched, where mobile/portable equipment is stored, and when applicable, where vehicles are parked when not in use.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Check here ☐ and skip to Section 4F if the "Base of Operations" address is the same as the "Practice Location" listed in Section 4A.

Street Address Line 1 *(Street Name and Number)*

Street Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

F. Vehicle Information

If the mobile health care services are rendered inside a vehicle, such as a mobile home or trailer, furnish the following vehicle information. Do not provide information about vehicles that are used only to transport medical equipment (e.g., when the equipment is transported in a van but is used in a fixed setting, such as a doctor's office) or ambulance vehicles. If more than two vehicles are used, copy and complete this section as needed.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE FOR EACH VEHICLE	TYPE OF VEHICLE *(van, mobile home, trailer, etc.)*	VEHICLE IDENTIFICATION NUMBER
☐ CHANGE ☐ ADD ☐ DELETE		
Effective Date:		
☐ CHANGE ☐ ADD ☐ DELETE		
Effective Date:		

For each vehicle, submit a copy of all health care related permits/licenses/registrations.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

G. Geographic Location for Mobile Or Portable Suppliers Where the Base of Operations and/or Vehicle Renders Services

Provide the city/town, State, and ZIP Code for all locations where mobile and/or portable services are rendered.

NOTE: If you provide mobile or portable health care services in more than one State and those States are serviced by different Medicare fee-for-service contractors, complete a separate enrollment application (CMS-855B) for each Medicare fee-for-service contractor's jurisdiction.

INITIAL REPORTING AND/OR ADDITIONS

If you are reporting or adding an entire State, it is not necessary to report each city/town. Simply check the box below and specify the State.

☐ Entire State of _____

If services are provided in selected cities/towns, provide the locations below. Only list ZIP codes if you are not servicing the entire city/town.

CITY/TOWN	STATE	ZIP CODE

DELETIONS

If you are deleting an entire State, it is not necessary to report each city/town. Simply check the box below and specify the State.

☐ Entire State of _____

If services you are deleting are furnished in selected cities/towns, provide the locations below. Only list ZIP codes if you are not servicing the entire city/town.

CITY/TOWN	STATE	ZIP CODE

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS)

NOTE: Only report organizations in this section. Individuals must be reported in Section 6.

Complete this section with information about all organizations that have 5 percent or more (direct or indirect) ownership interest of, any partnership interest in, and/or managing control of, the supplier identified in Section 2, as well as information on any adverse legal actions that have been imposed against that organization. For examples of organizations that should be reported here, visit our Web site: *www.cms.hhs.gov/MedicareProviderSupEnroll*. If there is more than one organization that should be reported, copy and complete this section for each.

MANAGING CONTROL (ORGANIZATIONS)

Any organization that exercises operational or managerial control over the supplier, or conducts the day-to-day operations of the supplier, is a managing organization and must be reported. The organization need not have an ownership interest in the supplier in order to qualify as a managing organization. For instance, it could be a management services organization under contract with the supplier to furnish management services for the business.

SPECIAL TYPES OF ORGANIZATIONS

Governmental/Tribal Organizations

If a Federal, State, county, city or other level of government, or an Indian tribe, will be legally and financially responsible for Medicare payments received (including any potential overpayments), the name of that government or Indian tribe should be reported as an owner. The supplier must submit a letter on the letterhead of the responsible government (e.g., government agency) or tribal organization that attests that the government or tribal organization will be legally and financially responsible in the event that there is any outstanding debt owed to CMS. This letter must be signed by an appointed or elected official of the government or tribal organization who has the authority to legally and financially bind the government or tribal organization to the laws, regulations, and program instructions of the Medicare program.

Non-Profit, Charitable and Religious Organizations

Many non-profit organizations are charitable or religious in nature, and are operated and/or managed by a board of trustees or other governing body. The actual name of the board of trustees or other governing body should be reported in this section. While the organization should be listed in Section 5, individual board members should be listed in Section 6. Each non-profit organization should submit a copy of a 501(c)(3) document verifying its non-profit status.

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

All organizations that have any of the following must be reported in Section 5:

- 5 percent or more ownership of the supplier,
- Managing control of the supplier, or
- A partnership interest in the supplier, regardless of the percentage of ownership the partner has.

Owning/Managing organizations are generally one of the following types:

- Corporations (including non-profit corporations)
- Partnerships and Limited Partnerships (as indicated above)
- Limited Liability Companies
- Charitable and/or Religious organizations
- Governmental and/or Tribal organizations

A. Organization with Ownership Interest and/or Managing Control—Identification Information

☐ Not Applicable

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Check all that apply:

☐ 5 Percent or More Ownership Interest ☐ Partner ☐ Managing Control

Legal Business Name as Reported to the Internal Revenue Service

"Doing Business As" Name *(if applicable)*

Address Line 1 *(Street Name and Number)*

Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

NPI *(if issued)*	Tax Identification Number *(Required)*	Medicare Identification Number(s) *(if issued)*

What is the effective date this owner acquired ownership of the provider identified in Section 2B1 of this application? *(mm/dd/yyyy)* _____

What is the effective date this organization acquired managing control of the provider identified in Section 2B1 of this application? *(mm/dd/yyyy)* _____

NOTE: Furnish both dates if applicable.

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

B. Final Adverse Legal Action History

If reporting a change to existing information, check "Change," provide the effective date of the change, and complete the appropriate fields in this section.

☐ Change
Effective Date:_____

1. Has this individual in Section 5A above, under any current or former name or business identity, ever had a final adverse legal action listed on page 13 of this application imposed against him/her?

   ☐ YES–Continue Below ☐ NO–Skip to Section 6

2. If YES, report each final adverse legal action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse legal action documentation and resolution.

FINAL ADVERSE LEGAL ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS)

NOTE: Only Individuals should be reported in Section 6. Organizations must be reported in Section 5. For more information on "direct" and "indirect" owners, go to *www.cms.hhs.gov/MedicareProviderSupEnroll*.

The supplier MUST have at least ONE owner and/or managing employee.

The following individuals must be reported in Section 6A:

- All persons who have a 5 percent or greater direct or indirect ownership interest in the supplier;
- If (and only if) the supplier is a corporation (whether for-profit or non-profit), all officers and directors of the supplier;
- All managing employees of the supplier;
- All individuals with a partnership interest in the supplier, regardless of the percentage of ownership the partner has; and
- Authorized and delegated officials.

Example: A supplier is 100 percent owned by Company C, which itself is 100 percent owned by Individual D. Assume that Company C is reported in Section 5A as an owner of the supplier. Assume further that Individual D, as an indirect owner of the supplier, is reported in Section 6A. Based on this example, the supplier would check the "5 percent or Greater Direct/Indirect Owner" box in Section 6A.

NOTE: All partners within a partnership must be reported on this application. This applies to both "General" and "Limited" partnerships. For instance, if a limited partnership has several limited partners and each of them only has a 1 percent interest in the supplier, each limited partner must be reported on this application, even though each owns less than 5 percent. The 5 percent threshold primarily applies to corporations and other organizations that are not partnerships.

Non-Profit, Charitable or Religious Organizations: If you are a non-profit charitable or religious organization that has no organizational or individual owners (only board members, directors or managers), you should submit with your application a 501(c)(3) document verifying non-profit status.

For purposes of this application, the terms "officer," "director," and "managing employee" are defined as follows:

Officer is any person whose position is listed as being that of an officer in the supplier's "articles of incorporation" or "corporate bylaws," or anyone who is appointed by the board of directors as an officer in accordance with the supplier's corporate bylaws.

Director is a member of the supplier's "board of directors." It does not necessarily include a person who may have the word "director" in his/her job title (e.g., departmental director, director of operations). Moreover, where a supplier has a governing body that does not use the term "board of directors," the members of that governing body will still be considered "directors." Thus, if the supplier has a governing body titled "board of trustees" (as opposed to "board of directors"), the individual trustees are considered "directors" for Medicare enrollment purposes.

Managing Employee means a general manager, business manager, administrator, director, or other individual who exercises operational or managerial control over, or who directly or indirectly conducts, the day-to-day operations of the supplier, either under contract or through some other arrangement, regardless of whether the individual is a W-2 employee of the supplier.

NOTE: If a governmental or tribal organization will be legally and financially responsible for Medicare payments received (per the instructions for Governmental/Tribal Organizations in Section 5), the supplier is only required to report its managing employees in Section 6. Owners, partners, officers, and directors do not need to be reported, except those who are listed as authorized or delegated officials on this application.

Any information on final adverse actions that have been imposed against the individuals reported in this section must be furnished. If there is more than one individual, copy and complete this section for each individual. Owners, Authorized Officials and/or Delegated Officials must complete this section.

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

A. Individuals with Ownership Interest and/or Managing Control—Identification Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

The name, date of birth, and social security number of each person listed in this Section must coincide with the individual's information as listed with the Social Security Administration.

First Name	Middle Initial	Last Name	Jr., Sr., etc.	Title

Date of Birth *(mm/dd/yyyy)*	Place of Birth *(State)*	Country of Birth

Social Security Number *(Required)*	Medicare Identification Number *(if issued)*	NPI *(if issued)*

What is the above individual's relationship with the supplier in Section 2B1? *(Check all that apply.)*

☐ 5 Percent or Greater Direct/Indirect Owner
☐ Authorized Official
☐ Delegated Official
☐ Partner
☐ Director/Officer
☐ Contracted Managing Employee
☐ Managing Employee (W-2)

What is the effective date this owner acquired ownership of the provider identified in Section 2B1 of this application? *(mm/dd/yyyy)* _____

What is the effective date this individual acquired managing control of the provider identified in Section 2B1 of this application? *(mm/dd/yyyy)* _____

NOTE: Furnish both dates if applicable.

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

B. Final Adverse Legal Action History

Complete this section for the individual reported in Section 6A above. If reporting a change to existing information, check "change," provide the effective date of the change and complete the appropriate fields in this section.

☐ Change
Effective Date:_____

1. Has this individual in Section 6A above, under any current or former name or business identity, ever had a final adverse legal action listed on page 13 of this application imposed against him/her?

   ☐ YES–Continue Below ☐ NO–Skip to Section 8

2. If YES, report each final adverse legal action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse legal action documentation and resolution.

FINAL ADVERSE LEGAL ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 7: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 8: BILLING AGENCY INFORMATION

A billing agency is a company or individual that you contract with to prepare and submit your claims. If you use a billing agency, you are responsible for the claims submitted on your behalf.

☐ **Check here if this section does not apply and skip to Section 13.**

BILLING AGENCY NAME AND ADDRESS

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Legal Business/Individual Name as Reported to the Social Security Administration or the Internal Revenue Service	If Individual, Billing Agent Date of Birth *(mm/dd/yyyy)*
"Doing Business As" Name *(if applicable)*	Tax Identification/Social Security Number *(required)*
Billing Agency Street Address Line 1 *(Street Name and Number)*	
Billing Agency Street Address Line 2 *(Suite, Room, etc.)*	

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

SECTION 9: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 10: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 11: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 12: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 13: CONTACT PERSON

If questions arise during the processing of this application, the fee-for-service contractor will contact the individual shown below. If the contact person is either an authorized or delegated official, check the appropriate box below.

☐ Contact an Authorized Official listed in Section 15.

☐ Contact a Delegated Official listed in Section 16.

First Name	Middle Initial	Last Name	Jr., Sr., etc.

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

Address Line 1 *(Street Name and Number)*

Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

SECTION 14: PENALTIES FOR FALSIFYING INFORMATION

This section explains the penalties for deliberately falsifying information in this application to gain or maintain enrollment in the Medicare program.

1. 18 U.S.C. § 1001 authorizes criminal penalties against an individual who, in any matter within the jurisdiction of any department or agency of the United States, knowingly and willfully falsifies, conceals or covers up by any trick, scheme or device a material fact, or makes any false, fictitious or fraudulent statements or representations, or makes any false writing or document knowing the same to contain any false, fictitious or fraudulent statement or entry.

   Individual offenders are subject to fines of up to $250,000 and imprisonment for up to five years. Offenders that are organizations are subject to fines of up to $500,000 (18 U.S.C. § 3571). Section 3571(d) also authorizes fines of up to twice the gross gain derived by the offender if it is greater than the amount specifically authorized by the sentencing statute.

2. Section 1128B(a)(1) of the Social Security Act authorizes criminal penalties against any individual who, "knowingly and willfully," makes or causes to be made any false statement or representation of a material fact in any application for any benefit or payment under a Federal health care program.

   The offender is subject to fines of up to $25,000 and/or imprisonment for up to five years.

3. The Civil False Claims Act, 31 U.S.C. § 3729, imposes civil liability, in part, on any person who:

   a) knowingly presents, or causes to be presented, to an officer or any employee of the United States Government a false or fraudulent claim for payment or approval;

   b) knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Government; or

   c) conspires to defraud the Government by getting a false or fraudulent claim allowed or paid.

   The Act imposes a civil penalty of $5,000 to $10,000 per violation, plus three times the amount of damages sustained by the Government.

SECTION 14: PENALTIES FOR FALSIFYING INFORMATION *(Continued)*

4. Section 1128A(a)(1) of the Social Security Act imposes civil liability, in part, on any person (including an organization, agency or other entity) that knowingly presents or causes to be presented to an officer, employee, or agent of the United States, or of any department or agency thereof, or of any State agency…a claim…that the Secretary determines is for a medical or other item or service that the person knows or should know:

   a) was not provided as claimed; and/or

   b) the claim is false or fraudulent.

   This provision authorizes a civil monetary penalty of up to $10,000 for each item or service, an assessment of up to three times the amount claimed, and exclusion from participation in the Medicare program and State health care programs.

5. 18 U.S.C. 1035 authorizes criminal penalties against individuals in any matter involving a health care benefit program who knowingly and willfully falsifies, conceals or covers up by any trick, scheme, or device a material fact; or makes any materially false, fictitious, or fraudulent statements or representations, or makes or uses any materially false fictitious, or fraudulent statement or entry, in connection with the delivery of or payment for health care benefits, items or services. The individual shall be fined or imprisoned up to 5 years or both.

6. 18 U.S.C. 1347 authorizes criminal penalties against individuals who knowing and willfully execute, or attempt, to executive a scheme or artifice to defraud any health care benefit program, or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by or under the control of any, health care benefit program in connection with the delivery of or payment for health care benefits, items, or services. Individuals shall be fined or imprisoned up to 10 years or both. If the violation results in serious bodily injury, an individual will be fined or imprisoned up to 20 years, or both. If the violation results in death, the individual shall be fined or imprisoned for any term of years or for life, or both.

7. The government may assert common law claims such as “common law fraud,” “money paid by mistake,” and “unjust enrichment.”

   Remedies include compensatory and punitive damages, restitution, and recovery of the amount of the unjust profit.

SECTION 15: CERTIFICATION STATEMENT

An **AUTHORIZED OFFICIAL** means an appointed official (for example, chief executive officer, chief financial officer, general partner, chairman of the board, or direct owner) to whom the organization has granted the legal authority to enroll it in the Medicare program, to make changes or updates to the organization's status in the Medicare program, and to commit the organization to fully abide by the statutes, regulations, and program instructions of the Medicare program.

A **DELEGATED OFFICIAL** means an individual who is delegated by an authorized official the authority to report changes and updates to the supplier's enrollment record. A delegated official must be an individual with an "ownership or control interest" in (as that term is defined in Section 1124(a)(3) of the Social Security Act), or be a W-2 managing employee of, the supplier.

Delegated officials may not delegate their authority to any other individual. Only an authorized official may delegate the authority to make changes and/or updates to the supplier's Medicare status. Even when delegated officials are reported in this application, an authorized official retains the authority to make any such changes and/or updates by providing his or her printed name, signature, and date of signature as required in Section 15B.

NOTE: Authorized officials and delegated officials must be reported in Section 6, either on this application or on a previous application to this same Medicare fee-for-service contractor. **If this is the first time an authorized and/or delegated official has been reported on the CMS-855B, you must complete Section 6 for that individual.**

By his/her signature(s), an authorized official binds the supplier to all of the requirements listed in the Certification Statement and acknowledges that the supplier may be denied entry to or revoked from the Medicare program if any requirements are not met. All signatures must be original and in ink. Faxed, photocopied, or stamped signatures will not be accepted.

Only an authorized official has the authority to sign (1) the initial enrollment application on behalf of the supplier or (2) the enrollment application that must be submitted as part of the periodic revalidation process. A delegated official does not have this authority.

By signing this application, an authorized official agrees to immediately notify the Medicare fee-for-service contractor if any information furnished on the application is not true, correct, or complete. In addition, an authorized official, by his/her signature, agrees to notify the Medicare fee-for-service contractor of any future changes to the information contained in this form, after the supplier is enrolled in Medicare, in accordance with the timeframes established in 42 C.F.R. 424.516. (IDTF changes of information must be reported in accordance with 42 C.F.R. 410.33.)

The supplier can have as many authorized officials as it wants. If the supplier has more than two authorized officials, it should copy and complete this section as needed.

EACH AUTHORIZED AND DELEGATED OFFICIAL MUST HAVE AND DISCLOSE HIS/HER SOCIAL SECURITY NUMBER.

SECTION 15: CERTIFICATION STATEMENT *(Continued)*

A. Additional Requirements for Medicare Enrollment

These are additional requirements that the supplier must meet and maintain in order to bill the Medicare program. Read these requirements carefully. By signing, the supplier is attesting to having read the requirements and understanding them.

By his/her signature(s), the authorized official(s) named below and the delegated official(s) named in Section 16 agree to adhere to the following requirements stated in this Certification Statement:

1. I authorize the Medicare contractor to verify the information contained herein. I agree to notify the Medicare contractor of any future changes to the information contained in this application in accordance with the timeframes established in 42 C.F.R. § 424.516. I understand that any change in the business structure of this supplier may require the submission of a new application.
2. I have read and understand the Penalties for Falsifying Information, as printed in this application. I understand that any deliberate omission, misrepresentation, or falsification of any information contained in this application or contained in any communication supplying information to Medicare, or any deliberate alteration of any text on this application form, may be punished by criminal, civil, or administrative penalties including, but not limited to, the denial or revocation of Medicare billing privileges, and/or the imposition of fines, civil damages, and/or imprisonment.
3. I agree to abide by the Medicare laws, regulations and program instructions that apply to this supplier. The Medicare laws, regulations, and program instructions are available through the Medicare contractor. I understand that payment of a claim by Medicare is conditioned upon the claim and the underlying transaction complying with such laws, regulations, and program instructions (including, but not limited to, the Federal anti-kickback statute and the Stark law), and on the supplier's compliance with all applicable conditions of participation in Medicare.
4. Neither this supplier, nor any five percent or greater owner, partner, officer, director, managing employee, authorized official, or delegated official thereof is currently sanctioned, suspended, debarred, or excluded by the Medicare or State Health Care Program, e.g., Medicaid program, or any other Federal program, or is otherwise prohibited from supplying services to Medicare or other Federal program beneficiaries.
5. I agree that any existing or future overpayment made to the supplier by the Medicare program may be recouped by Medicare through the withholding of future payments.
6. I will not knowingly present or cause to be presented a false or fraudulent claim for payment by Medicare, and I will not submit claims with deliberate ignorance or reckless disregard of their truth or falsity.
7. I authorize any national accrediting body whose standards are recognized by the Secretary as meeting the Medicare program participation requirements, to release to any authorized representative, employee, or agent of the Centers for Medicare & Medicaid Services (CMS) a copy of my most recent accreditation survey, together with any information related to the survey that CMS may require (including corrective action plans).

SECTION 15: CERTIFICATION STATEMENT *(Continued)*

B. 1ST Authorized Official Signature

I have read the contents of this application. My signature legally and financially binds this supplier to the laws, regulations, and program instructions of the Medicare program. By my signature, I certify that the information contained herein is true, correct, and complete and I authorize the Medicare fee-for-service contractor to verify this information. If I become aware that any information in this application is not true, correct, or complete, I agree to notify the Medicare fee-for-service contractor of this fact in accordance with the time frames established in 42 CFR § 424.516.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Authorized Official's Information and Signature

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*
Telephone Number	Title/Position		
Authorized Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*			Date Signed *(mm/dd/yyyy)*

(blue ink preferred)

C. 2ND Authorized Official Signature

I have read the contents of this application. My signature legally and financially binds this supplier to the laws, regulations, and program instructions of the Medicare program. By my signature, I certify that the information contained herein is true, correct, and complete and I authorize the Medicare fee-for-service contractor to verify this information. If I become aware that any information in this application is not true, correct, or complete, I agree to notify the Medicare fee-for-service contractor of this fact in accordance with the time frames established in 42 CFR § 424.516.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Authorized Official's Information and Signature

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*
Telephone Number	Title/Position		
Authorized Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*			Date Signed *(mm/dd/yyyy)*

All signatures must be original and signed in ink (blue ink preferred). Applications with signatures deemed not original will not be processed. Stamped, faxed or copied signatures will not be accepted.

SECTION 16: DELEGATED OFFICIAL (OPTIONAL)

- You are not required to have a delegated official. However, if no delegated official is assigned, the authorized official(s) will be the only person(s) who can make changes and/or updates to the supplier's status in the Medicare program.
- The signature of a delegated official shall have the same force and effect as that of an authorized official, and shall legally and financially bind the supplier to the laws, regulations, and program instructions of the Medicare program. By his or her signature, the delegated official certifies that he or she has read the Certification Statement in Section 15 and agrees to adhere to all of the stated requirements. A delegated official also certifies that he/she meets the definition of a delegated official. When making changes and/or updates to the supplier's enrollment information maintained by the Medicare program, a delegated official certifies that the information provided is true, correct, and complete.
- Delegated officials being deleted do not have to sign or date this application.
- Independent contractors are not considered "employed" by the supplier, and therefore cannot be delegated officials.
- The signature(s) of an authorized official in Section 16 constitutes a legal delegation of authority to all delegated official(s) assigned in Section 16.
- If there are more than two individuals, copy and complete this section for each individual.

A. 1ST Delegated Official Signature

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Delegated Official First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Delegated Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

☐ Check here if Delegated Official is a W-2 Employee	Telephone Number

Authorized Official's Signature Assigning this Delegation *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

(blue ink preferred)

SECTION 16: DELEGATED OFFICIAL (OPTIONAL)

B. 2ND Delegated Official Signature

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Delegated Official First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Delegated Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

☐ Check here if Delegated Official is a W-2 Employee	Telephone Number

Authorized Official's Signature Assigning this Delegation *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

(blue ink preferred)

All signatures must be original and signed in ink (blue ink preferred). Applications with signatures deemed not original will not be processed. Stamped, faxed or copied signatures will not be accepted.

SECTION 17: SUPPORTING DOCUMENTS

This section lists the documents that, if applicable, must be submitted with this enrollment application. If you are newly enrolling, or are reactivating or revalidating your enrollment, you must provide all applicable documents. For changes, only submit documents that are applicable to that change.

The fee-for-service contractor may request, at any time during the enrollment process, documentation to support or validate information reported on the application. The Medicare fee-for-service contractor may also request documents from you, other than those identified in this Section 17, as are necessary to bill Medicare.

MANDATORY FOR ALL PROVIDER/SUPPLIER TYPES

- ☐ Written confirmation from the IRS confirming your Tax Identification Number with the Legal Business Name (e.g., IRS form CP 575) provided in Section 2.
  (**NOTE:** This information is needed if the applicant is enrolling their professional corporation, professional association, or limited liability corporation with this application or enrolling as a sole proprietor using an Employer Identification Number.)"
- ☐ Completed Form CMS-588, for Electronic Funds Transfer Authorization Agreement.
  (**NOTE:** If a supplier already receives payments electronically and is not making a change to its banking information, the CMS-588 is not required.)

MANDATORY FOR SELECTED PROVIDER/SUPPLIER TYPES

- ☐ Copy(s) of all documentation verifying IDTF Supervisory Physician(s) proficiency and/or State licenses or certification for IDTF non-physician personnel.
- ☐ Copy(s) of all documentation verifying the State licenses or certifications of the laboratory Director or non-physician practitioner personnel of an independent clinical laboratory.

MANDATORY, IF APPLICABLE

- ☐ Copy of IRS Determination Letter, if supplier is registered with the IRS as non-profit.
- ☐ Written confirmation from the IRS confirming your Limited Liability Company (LLC) is automatically classified as a Disregarded Entity. (e.g., Form 8832).
  (**NOTE:** A disregarded entity is an eligible entity that is treated as an entity not separate from its single owner for income tax purposes.
- ☐ Statement in writing from the bank. If Medicare payment due a supplier of services is being sent to a bank (or similar financial institution) with whom the supplier has a lending relationship (that is, any type of loan), then the supplier must provide a statement in writing from the bank (which must be in the loan agreement) that the bank has agreed to waive its right of offset for Medicare receivables.
- ☐ Copy(s) of all final adverse action documentation (e.g., notifications, resolutions, and reinstatement letters).
- ☐ Completed Form(s) CMS 855R, Reassignment of Medicare Benefits.
- ☐ Completed Form CMS-460, Medicare Participating Physician or Supplier Agreement.
- ☐ Copy of an attestation for government entities and tribal organizations.
- ☐ Copy of FAA 135 certificate (air ambulance suppliers).
- ☐ Copy(s) of comprehensive liability insurance policy (IDTFs only).

ATTACHMENT 1: AMBULANCE SERVICE SUPPLIERS

All ambulance service suppliers enrolling in the Medicare program must complete this attachment.

A. Geographic Area

This section is to be completed with information about the geographic area in which this company provides ambulance services. If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

Provide the city/town, State, and ZIP code for all locations where this ambulance company renders services.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

NOTE: If the ambulance company has vehicles garaged within a different Medicare contractor's jurisdiction, a separate CMS-855B enrollment application must be submitted to that fee-for-service contractor.

1. INITIAL REPORTING AND/OR ADDITIONS

If services are provided in selected cities/towns, provide the locations below. List ZIP codes only if they are not within the entire city/town.

CITY/TOWN	STATE	ZIP CODE

2. DELETIONS

If services are no longer provided in selected cities/towns, provide the locations below. List ZIP codes only if they are not within the entire city/town.

CITY/TOWN	STATE	ZIP CODE

B. State License Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

Crew members must complete continuing education requirements in accordance with State and local licensing laws. Evidence of re-certification must be retained with the employer in case it is required by the Medicare fee-for-service contractor.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Is this ambulance company licensed in the State where services are rendered and billed for? ☐ YES ☐ NO

If **NO**, explain why:

If **YES**, provide the license information for the State where this ambulance service supplier will be rendering services and billing Medicare. Attach a copy of the current State license.

License Number	Issuing State *(if applicable)*	Issuing City/Town *(if applicable)*

Effective Date *(mm/dd/yyyy)*	Expiration Date *(mm/dd/yyyy)*

C. Paramedic Intercept Services Information

Paramedic Intercept Services involve an arrangement between a Basic Life Support (BLS) ambulance company and an Advanced Life Support (ALS) ambulance company whereby the latter provides the ALS services and the BLS ambulance company provides the transportation component. If such an arrangement exists between the enrolling ambulance company and another ambulance company, the enrolling ambulance company must attach a copy of the signed contract. For more information, see 42 C.F.R. 410.40.

If reporting a change to information about a previously reported agreement/contract, check "Change" and provide the effective date of the change.

☐ Change
Effective Date:_____

Does this ambulance company currently participate in a paramedic intercept services arrangement?

☐ YES ☐ NO

D. Vehicle Information

Complete this section with information about the vehicles used by this ambulance company and the services they provide. If there is more than one vehicle, copy and complete this section as needed. Attach a copy of each vehicle registration.

To qualify as an air ambulance supplier, the following is required:

- A written statement, signed by the President, Chief Executive Officer or Chief Operating Officer of the airport from where the aircraft is hangared that gives the name and address of the facility, and
- Proof that the enrolling ambulance company, or the company leasing the air ambulance vehicle to the enrolling ambulance company, possesses a valid charter flight license (FAA 135 Certificate) for the aircraft being used as an air ambulance. If the enrolling ambulance company owns the aircraft, the owner's name on the FAA 135 Certificate must be the same as the enrolling ambulance company's name (or the ambulance company owner as reported in Sections 5 or 6) in this application. If the enrolling ambulance company leases the aircraft from another company, a copy of the lease agreement must accompany this enrollment application.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Type *(automobile, aircraft, boat, etc.)*	Vehicle Identification Number

Make *(e.g., Ford)*	Model *(e.g., 350T)*	Year *(yyyy)*

Does this vehicle provide:

Advanced life support (Level 1)	☐ YES	☐ NO	Specialty care transport	☐ YES	☐ NO
Advanced life support (Level 2)	☐ YES	☐ NO	Land ambulance	☐ YES	☐ NO
Basic life support	☐ YES	☐ NO	Air ambulance–fixed wing	☐ YES	☐ NO
Emergency runs	☐ YES	☐ NO	Air ambulance–rotary wing	☐ YES	☐ NO
Non-emergency runs	☐ YES	☐ NO	Marine ambulance	☐ YES	☐ NO

ATTACHMENT 2: INDEPENDENT DIAGNOSTIC TESTING FACILITIES

INDEPENDENT DIAGNOSTIC TESTING FACILITY (IDTF) PERFORMANCE STANDARDS

Below is a list of the performance standards that an IDTF must meet in order to obtain or maintain their Medicare billing privileges. These standards, in their entirety, can be found in 42 C.F.R section 410.33(g).

1. Operate its business in compliance with all applicable Federal and State licensure and regulatory requirements for the health and safety of patients.
2. Provides complete and accurate information on its enrollment application. Changes in ownership, changes of location, changes in general supervision, and adverse legal actions must be reported to the Medicare fee-for-service contractor on the Medicare enrollment application within 30 calendar days of the change. All other changes to the enrollment application must be reported within 90 calendar days.
3. Maintain a physical facility on an appropriate site. For the purposes of this standard, a post office box, commercial mail box, hotel or motel is not considered an appropriate site.
   (i) The physical facility, including mobile units, must contain space for equipment appropriate to the services designated on the enrollment application, facilities for hand washing, adequate patient privacy accommodations, and the storage of both business records and current medical records within the office setting of the IDTF, or IDTF home office, not within the actual mobile unit.
   (ii) IDTF suppliers that provide services remotely and do not see beneficiaries at their practice location are exempt from providing hand washing and adequate patient privacy accommodations.
4. Have all applicable diagnostic testing equipment available at the physical site excluding portable diagnostic testing equipment. A catalog of portable diagnostic equipment, including diagnostic testing equipment serial numbers, must be maintained at the physical site. In addition, portable diagnostic testing equipment must be available for inspection within two business days of a CMS inspection request. The IDTF must maintain a current inventory of the diagnostic testing equipment, including serial and registration numbers, provide this information to the designated fee-for-service contractor upon request, and notify the contractor of any changes in equipment within 90 days.
5. Maintain a primary business phone under the name of the designated business. The primary business phone must be located at the designated site of the business, or within the home office of the mobile IDTF units. The telephone number or toll free numbers must be available in a local directory and through directory assistance.
6. Have a comprehensive liability insurance policy of at least $300,000 per location that covers both the place of business and all customers and employees of the IDTF. The policy must be carried by a non-relative owned company. Failure to maintain required insurance at all times will result in revocation of the IDTF's billing privileges retroactive to the date the insurance lapsed. IDTF suppliers are responsible for providing the contact information for the issuing insurance agent and the underwriter. In addition, the IDTF must:
   (i) Ensure that the insurance policy must remain in force at all times and provide coverage of at least $300,000 per incident; and
   (ii) Notify the CMS designated contractor in writing of any policy changes or cancellations.
7. Agree not to directly solicit patients, which include, but is not limited to, a prohibition on telephone, computer, or in-person contacts. The IDTF must accept only those patients referred for diagnostic testing by an attending physician, who is furnishing a consultation or treating a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem. Nonphysician practitioners may order tests as set forth in §410.32(a)(3).

8. Answer, document, and maintain documentation of a beneficiary's written clinical complaint at the physical site of the IDTF (For mobile IDTFs, this documentation would be stored at their home office.) This includes, but is not limited to, the following:
   (i) The name, address, telephone number, and health insurance claim number of the beneficiary.
   (ii) The date the complaint was received; the name of the person receiving the complaint; and a summary of actions taken to resolve the complaint.
   (iii) If an investigation was not conducted, the name of the person making the decision and the reason for the decision.
9. Openly post these standards for review by patients and the public.
10. Disclose to the government any person having ownership, financial, or control interest or any other legal interest in the supplier at the time of enrollment or within 30 days of a change.
11. Have its testing equipment calibrated and maintained per equipment instructions and in compliance with applicable manufacturers suggested maintenance and calibration standards.
12. Have technical staff on duty with the appropriate credentials to perform tests. The IDTF must be able to produce the applicable Federal or State licenses or certifications of the individuals performing these services.
13. Have proper medical record storage and be able to retrieve medical records upon request from CMS or its fee-for-service contractor within 2 business days.
14. Permit CMS, including its agents, or its designated fee-for-service contractors, to conduct unannounced, on-site inspections to confirm the IDTF's compliance with these standards. The IDTF must be accessible during regular business hours to CMS and beneficiaries and must maintain a visible sign posting the normal business hours of the IDTF.
15. With the exception of hospital-based and mobile IDTFs, a fixed base IDTF does not include the following:
   (i) Sharing a practice location with another Medicare-enrolled individual or organization.
   (ii) Leasing or subleasing its operations or its practice location to another Medicare enrolled individual or organization.
   (iii) Sharing diagnostic testing equipment using in the initial diagnostic test with another Medicare-enrolled individual or organization.
16. Enrolls in Medicare for any diagnostic testing services that it furnishes to a Medicare beneficiary, regardless of whether the service is furnished in a mobile or fixed base location.
17. Bills for all mobile diagnostic services that are furnished to a Medicare beneficiary, unless the mobile diagnostic service is part of a service provided under arrangement as described in section 1861(w)(1) of the Act.

Instructions

If you perform diagnostic tests, other than clinical laboratory or pathology tests, and are required to enroll as an IDTF, you must complete this attachment. CMS requires the information in this attachment to determine whether the enrolling supplier meets all IDTF standards including, but not limited to, those listed on page 40 of this application. Not all suppliers that perform diagnostic tests are required to enroll as an IDTF.

Diagnostic Radiology

Many diagnostic tests are radiological procedures that require the professional services of a radiologist. A radiologist's practice is generally different from those of other physicians because radiologists usually do not bill E&M codes or treat a patient's medical condition on an ongoing basis. A radiologist or group practice of radiologists is not necessarily required to enroll as an IDTF. If enrolling as a diagnostic radiology group practice or clinic and billing for the technical component of diagnostic radiological tests without enrolling as an IDTF (if the entity is a free standing diagnostic facility), it should contact the carrier to determine that it does not need to enroll as an IDTF.

A mobile IDTF that provides X-ray services is not classified as a portable X-ray supplier.

Regulations governing IDTFs can be found at 42 C.F.R. 410.33.

CPT-4 and HCPCS Codes—Report all CPT-4 and HCPCS codes for which this IDTF will bill Medicare. Include the following:

- Provide the CPT-4 or HCPCS codes for which this IDTF intends to bill Medicare,
- The name and type of equipment used to perform the reported procedure, and
- The model number of the reported equipment.

The IDTF should report all Current Procedural Terminology, Version 4 (CPT-4) codes, Healthcare Common Procedural Coding System codes (HCPCS), and types of equipment (including the model number), for which it will perform tests, supervise, interpret, and/or bill. All codes reported must be for diagnostic tests that an IDTF is allowed to perform. Diagnostic tests that are clearly surgical in nature, which must be performed in a hospital or ambulatory surgical center, should not be reported.

Consistent with IDTF supplier standard 6 on page 40 of this application, all IDTFs enrolling in Medicare must have a comprehensive liability insurance policy of at least $300,000 per location, that covers both the place of business and all customers and employees of the IDTF. The policy must be carried by a non-relative owned company. Failure to maintain the required insurance at all times will result in revocation of the Medicare supplier billing number, retroactive to the date the insurance lapsed. Malpractice insurance policies do not demonstrate compliance with this requirement.

All IDTFs must submit a complete copy of the aforementioned liability insurance policy with this application.

ATTACHMENT 2: INDEPENDENT DIAGNOSTIC TESTING FACILITIES *(Continued)*

A. Standards Qualifications

Provide the date this Independent Diagnostic Testing Facility met all current CMS standards *(mm/dd/yyyy)*

B. CPT-4 and HCPCS Codes

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

All codes reported here must be for diagnostic tests that an IDTF is allowed to perform. Diagnostic tests that are clearly surgical in nature, which must be performed in a hospital or ambulatory surgical center, should not be reported. Clinical laboratory and pathology codes should not be reported. This page may be copied for additional codes or equipment.

	CPT–4 OR HCPCS CODE	EQUIPMENT	MODEL NUMBER *(Required)*
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			
11.			
12.			
13.			
14.			
15.			

C. Interpreting Physician Information

Check here ☐ if this section does not apply because the interpreting physician will bill separate from the IDTF.

All physicians whose interpretations will be billed by this IDTF with the technical component (TC) of the test (i.e., global billing) must be listed in this section. If there are more than three physicians, copy and complete this section as needed. All interpreting physicians must be currently enrolled in the Medicare program.

If you are billing for interpretations as an individual reassigning benefits, the interpreting physician must complete the Reassignment of Benefits Form (CMS 855R). Note: Both the IDTF and individual physician must be enrolled with the fee-for-service contractor where the IDTF is located.

If you are billing for purchased interpretations, all requirements for purchased interpretations must be met.

When a mobile unit of the IDTF performs a technical component of a diagnostic test and the interpretive physician is the same physician who ordered the test, the IDTF cannot bill for the interpretation. Therefore, these interpreting physicians should not be reported since the interpretive physician must submit his/her own claims for these tests.

1ST Interpreting Physician Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*
Medicare Identification Number *(if issued)*	**NPI**

2ND Interpreting Physician Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*
Medicare Identification Number *(if issued)*	**NPI**

3RD Interpreting Physician Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*
Medicare Identification Number *(if issued)*	**NPI**

D. Personnel (Technicians) Who Perform Tests

Complete this section with information about all non-physician personnel who perform tests for this IDTF. Notarized or certified true copies of the State license or certificate should be attached.

1ST PERSONNEL (TECHNICIAN) INFORMATION

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*

Is this technician State licensed or State certified? *(see instructions for clarification)* ☐ YES ☐ NO

License/Certification Number *(if applicable)*	License/Certification Issue Date *(mm/dd/yyyy) (if applicable)*

Is this technician certified by a national credentialing organization? ☐ YES ☐ NO

Name of credentialing organization *(if applicable)*	Type of Credentials *(if applicable)*

Is this technician employed by a hospital? ☐ YES ☐ NO

If **YES**, provide the name of the hospital here: _____

2ND Personnel (Technician) Information

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*

Is this technician State licensed or State certified? *(see instructions for clarification)* ☐ YES ☐ NO

License/Certification Number *(if applicable)*	License/Certification Issue Date *(mm/dd/yyyy) (if applicable)*

Is this technician certified by a national credentialing organization? ☐ YES ☐ NO

Name of credentialing organization *(if applicable)*	Type of Credentials *(if applicable)*

Is this technician employed by a hospital? ☐ YES ☐ NO

If **YES**, provide the name of the hospital here: _____

E. Supervising Physicians

Complete this section with identifying information about the physician(s) who supervise the operation of the IDTF and who provides the personal, direct, or general supervision per 42 C.F.R. 410.32(b)(3). The supervising physician must also attest to his/her supervising responsibilities for the enrolling IDTF.

Information concerning the type of supervision (personal, direct, or general) required for performance of specific IDTF tests can be obtained from your Medicare fee-for-service contractor. All IDTFs must report at least one supervisory physician, and at least one supervising physician must perform the supervision requirements stated in 42 C.F.R. 410.32(b)(3). All supervisory physician(s) must be currently enrolled in Medicare.

The type of supervision being performed by each physician who signs the attestation on page 47 of this application should be listed in this section.

Definitions of the types of supervision are as follows:

- **Personal Supervision** means a physician must be in attendance in the room during the performance of the procedure.
- **Direct Supervision** means the physician must be present in the office suite and immediately available to provide assistance and direction throughout the performance of the procedure. It does not mean that the physician must be present in the room when the procedure is performed.
- **General Supervision** means the procedure is provided under the physician's overall direction and control, but the physician's presence is not required during the performance of the procedure. General supervision also includes the responsibility that the non-physician personnel who perform the tests are qualified and properly trained and that the equipment is operated properly, maintained, calibrated and that necessary supplies are available.

E. Supervising Physicians *(Continued)*

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy) (Required)*

Medicare Identification Number *(if issued)*	NPI

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

TYPE OF SUPERVISION PROVIDED

Check the appropriate box below indicating the type of supervision provided by the physician reported above for the tests performed by the IDTF in accordance with 42 C.F.R. 410.32 (b)(3) (See instructions for definitions).

☐ Personal Supervision ☐ Direct Supervision ☐ General Supervision

For each physician performing General Supervision, at least one of the three functions listed here must be checked. However, to meet the General Supervision requirement, in accordance with 42 C.F.R. 410.33(b), the enrolling IDTF must have at least one supervisory physician for each of the three functions. For example, two physicians may be responsible for function 1, a third physician may be responsible for function 2, and a fourth physician may be responsible for function 3. All four supervisory physicians must complete and sign the supervisory physician section of this application. Each physician should only check the function(s) he/she actually performs.

☐ Assumes responsibility for the overall direction and control of the quality of testing performed.

☐ Assumes responsibility for assuring that the non-physician personnel who actually perform the diagnostic procedures are properly trained and meet required qualifications.

☐ Assumes responsibility for the proper maintenance and calibration of the equipment and supplies necessary to perform the diagnostic procedures.

OTHER SUPERVISION SITES

Does this supervising physician provide supervision at any other IDTF? ☐ YES ☐ NO

If yes, list all other IDTFs for which this physician provides supervision. For more than five, copy this sheet.

	NAME OF FACILITY	ADDRESS	TAX IDENTIFICATION NUMBER	LEVEL OF SUPERVISION
1.				
2.				
3.				
4.				
5.				

E. Supervising Physicians *(Continued)*

ATTESTATION STATEMENT FOR SUPERVISING PHYSICIANS

All Supervising Physician(s) rendering supervisory services for this IDTF must sign and date this section. All signatures must be original.

1. I hereby acknowledge that I have agreed to provide (IDTF Name)_____ with the Supervisory Physician services checked above for all CPT-4 and HCPCS codes reported in this Attachment. (See number 2 below if all reported CPT-4 and HCPCS codes do not apply). I also hereby certify that I have the required proficiency in the performance and interpretation of each type of diagnostic procedure, as reported by CPT-4 or HCPCS code in this Attachment (except for those CPT-4 or HCPCS codes identified in number 2 below). I have read and understand the Penalties for Falsifying Information on this Enrollment Application, as stated in Section 14 of this application. I am aware that falsifying information may result in fines and/or imprisonment. If I undertake supervisory responsibility at any additional IDTFs, I understand that it is my responsibility to notify this IDTF at that time.
2. I am not acting as a Supervising Physician for the following CPT-4 and/or HCPCS codes reported in this Attachment.

CPT–4 OR HCPCS CODE	CPT–4 OR HCPCS CODE	CPT–4 OR HCPCS CODE

3. Signature of Supervising Physician *(First, Middle, Last, Jr., Sr., M.D., D.O., etc.)*	Date *(mm/dd/yyyy)*

All signatures must be original and signed and dated in ink (blue ink preferred). Applications with signatures deemed not original will not be processed. Stamped, faxed or copied signatures will not be accepted.

MEDICARE SUPPLIER ENROLLMENT APPLICATION PRIVACY ACT STATEMENT

The Centers for Medicare & Medicaid Services (CMS) is authorized to collect the information requested on this form by sections 1124(a)(1), 1124A(a)(3), 1128, 1814, 1815, 1833(e), and 1842(r) of the Social Security Act [42 U.S.C. §§ 1320a-3(a)(1), 1320a-7, 1395f, 1395g, 1395(l)(e), and 1395u(r)] and section 31001(1) of the Debt Collection Improvement Act [31 U.S.C. § 7701(c)].

The purpose of collecting this information is to determine or verify the eligibility of individuals and organizations to enroll in the Medicare program as suppliers of goods and services to Medicare beneficiaries and to assist in the administration of the Medicare program. This information will also be used to ensure that no payments will be made to providers who are excluded from participation in the Medicare program. All information on this form is required, with the exception of those sections marked as "optional" on the form. Without this information, the ability to make payments will be delayed or denied.

The information collected will be entered into the Provider Enrollment, Chain and Ownership System (PECOS). The information in this application will be disclosed according to the routine uses described below.

Information from these systems may be disclosed under specific circumstances to:

1. CMS contractors to carry out Medicare functions, collating or analyzing data, or to detect fraud or abuse;
2. A congressional office from the record of an individual health care provider in response to an inquiry from the congressional office at the written request of that individual health care practitioner;
3. The Railroad Retirement Board to administer provisions of the Railroad Retirement or Social Security Acts;
4. Peer Review Organizations in connection with the review of claims, or in connection with studies or other review activities, conducted pursuant to Part B of Title XVIII of the Social Security Act;
5. To the Department of Justice or an adjudicative body when the agency, an agency employee, or the United States Government is a party to litigation and the use of the information is compatible with the purpose for which the agency collected the information;
6. To the Department of Justice for investigating and prosecuting violations of the Social Security Act, to which criminal penalties are attached;
7. To the American Medical Association (AMA), for the purpose of attempting to identify medical doctors when the National Plan and Provider Enumeration System is unable to establish identity after matching contractor submitted data to the data extract provided by the AMA;
8. An individual or organization for a research, evaluation, or epidemiological project related to the prevention of disease or disability, or to the restoration or maintenance of health;
9. Other Federal agencies that administer a Federal health care benefit program to enumerate/enroll providers of medical services or to detect fraud or abuse;
10. State Licensing Boards for review of unethical practices or non-professional conduct;
11. States for the purpose of administration of health care programs; and/or
12. Insurance companies, self insurers, health maintenance organizations, multiple employer trusts, and other health care groups providing health care claims processing, when a link to Medicare or Medicaid claims is established, and data are used solely to process supplier's health care claims.

The supplier should be aware that the Computer Matching and Privacy Protection Act of 1988 (P.L. 100-503) amended the Privacy Act, 5 U.S.C. § 552a, to permit the government to verify information through computer matching.

Protection of Proprietary Information

Privileged or confidential commercial or financial information collected in this form is protected from public disclosure by Federal law 5 U.S.C. § 552(b)(4) and Executive Order 12600.

Protection of Confidential Commercial and/or Sensitive Personal Information

If any information within this application (or attachments thereto) constitutes a trade secret or privileged or confidential information (as such terms are interpreted under the Freedom of Information Act and applicable case law), or is of a highly sensitive personal nature such that disclosure would constitute a clearly unwarranted invasion of the personal privacy of one or more persons, then such information will be protected from release by CMS under 5 U.S.C. §§ 552(b)(4) and/or (b)(6), respectively.

AGREEMENT TO PROVIDE CONTRACT NURSING SERVICE
(FOR VACCINE OR MONCLONAL ANTIBODY ADMINISTRATION)

FACILITY: _____ Phone_____

(Facility) Name

_____

Administrator or Owner

_____

Street Address

_____

City, State Zip

PHARMACY: (legal name and address)

1. The **PHARMACY**, being duly registered and licensed in this state, agrees to provide, and supply Medicare Part-B covered vaccines, monoclonal antibody, safety syringes and needles pursuant to a prescription, chart order, physician-pharmacy protocol, state-approved vaccine protocol or Federal CDC vaccine/monoclonal antibody administration guideline.

2. The **PHARMACY** and the **FACILITY** agree to comply with all applicable State and Federal laws and regulations.

3. Personal protective equipment and syringe disposal will follow guidelines established by the **FACILITY** Policy and Procedure Manual and will be in accordance with State and Federal regulations.

4. The **FACILITY** agrees to obtain signed patient/responsible party consent for each vaccine/monoclonal antibody and document the required billing information. A copy of this consent form will stay in the patient medical record in the facility and a copy returned to the **PHARMACY**.

5. The **FACILITY** agrees to have a licensed nurse, qualified to administer a vaccine or monoclonal antibody (mAB), perform a contract service of administering the vaccine/mAB to eligible patients who have consented to receive the vaccine/mAB.

6. The **PHARMACY** will perform the billing of the vaccine/mAB to Medicare Part-B for the vaccine/mAB and the administration fee. The **FACILITY** will receive a per vaccine payment of $_____ for the time and labor of having their nurse administering each vaccine and a fee of $_____ for the time and labor of their nurse infusing the monoclonal antibody.

BY _____ **Date**_____

PHARMACY Representative

PRINTED NAME: _____

BY: _____ **Date** _____

FACILITY Representative

PRINTED NAME: _____

Proposed Data Fields for LTC/Home Infusion Pilot

Resident/Facility Contact Information:

- First and Last name
- External Identifier (could be a Pilot generated number or MRN)
- MRN-Optional
- Race and Ethnicity- required but has a choice of in dropdown to not provide a selection
- Biological Sex (Male/Female) –
- Facility name, address, phone
    - If a nursing home, Federal provider number, also known as CCN
    - Facility point of contact:_____
    - Resident's healthcare proxy (if applicable):_____
    - Alternative methods to reach resident or healthcare proxy (private phone, email) (optional)

Eligibility for mAb

- Age:
- Height:
- Weight:
- COVID-19 Symptom Onset Date:_____
    - List current COVID-19 symptoms (if available):
- Date of SARS-CoV-2 positive test for current infection:
- Does the resident currently require oxygen? (Y/N)
    - If yes, is this a new or increased oxygen requirement? (Y/N)
- Does the resident have any pre-existing COVID-19 related high-risk conditions?
    - Select all that apply
        - *Chronic kidney disease*
        - *Diabetes*
        - *Immunosuppressive disease*
        - *Cardiovascular disease*
        - *Hypertension*
        - *Chronic obstructive pulmonary disease/ other chronic respiratory disease*
        - *Neurologic conditions*

- Is the resident taking any immunosuppressive medications or biologic agents? (Y/N)
    - If yes, list medications:
- Had the resident had COVID-19 or positive SARS-CoV-2 tests prior to this illness? (Y/N)
    - If yes, estimated date of previous infection:
- Has the resident received any doses of a COVID-19 vaccine? (Y/N)
- Has the resident previously received mAb infusion? (Y/N)
- Is the resident currently participating in a clinical trial? (Y/N)
    - If yes, please provide details [free text box]

Infusion Details

- Infusion company, address/phone,
    - Point of contact:
- Product name:
- Product lot number
- Product expiration date/time
- Infusion start Date and time
- Infusion end date and time
- Was the infusion completed? (Y/N)
    - If no, provide details [free text box]:
- Infusion Pause Events – may track multiple
    - Date and time of infusion pause
    - Date and time of infusion restart
    - Reason for infusion pause [free text box]
- Adverse Events
    - Did the resident experience any of the following new symptoms during or within 1 hour of the infusion: (Y/N)
        - If yes, please indicate which symptoms occurred (select all that apply)
            - *Nausea*
            - *Diarrhea*
            - *Dizziness*
            - *Headache*
            - *Pruritis (Itching)*
            - *Vomiting*
            - *Flushing*
            - *Face Swelling*
            - *Uritcaria (Hives)*
            - *Fever*
            - *Chills*
            - *Hypotension*
            - *Hypertension*
            - *Tachycardia*
            - *Bradycardia*
            - *Other*
        - If yes:
            - How long after the infusion started did the symptoms start
            - Did the adverse event result in an emergency department visit?
            - Did the resident require hospitalization?
            - What category was the adverse event? (list categories)
                - Link to MedWatch Form
                - Record MedWatch Report ID
                - Record MedWatch Report Date

Post-infusion Follow-up (to be collected in coordination with the nursing home)

- Did the resident experience any new symptoms within 24 hours of the infusion: Y/N
  - If yes:
    - List symptoms:
    - How long after the infusion did the symptoms start (in hours)
    - Did the symptoms result in an emergency department visit?
    - Did the resident require hospitalization?

- During the 28 days following the infusion
  - Did the resident's clinical status improve/remain stable/worsen (select one)
  - Did the resident's COVID-19 symptoms resolve? Y/N
    - If yes, what was the total duration of illness (in days)?
  - Did the resident recover from COVID-19 (return to baseline health)? Y/N
  - Did the resident require any emergency department visit? Y/N
    - If yes, what was the reason?
  - Was the resident hospitalized? Y/N
    - If yes, what was the reason for hospitalization?
  - Did the resident die? Y/N
    - If yes, what was the cause of death (if known)?

Casirivimab (a.k.a. REGN10933) Injection (120 mg/ml)

MUST ADMINISTER WITH IMDEVIMAB

Manufacturer: Regeneron Pharmaceuticals, Inc.

Distributor: AmerisourceBergen (a.k.a. ABC); c19therapies@amerisourcebergen.com

Product: Component of 2-drug monoclonal antibody cocktail for outpatient infusion

Emergency Use Authorization (EUA): 11/21/20

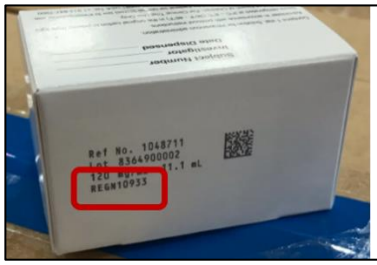
Units: Supplied in 2 volumes

- 1332 mg/11.1 ml single-dose vial in carton (10 ml from 1 vial needed for patient course)
- 300 mg/2.5 ml single-dose vials in cartons (10 ml; 2.5 ml from each of 4 vials needed for patient course)

Note: Some cartons and vials of casirivimab may be instead labeled REGN10933

Example: 1332 mg/11.1 ml carton

Example: 300 mg/2.5 ml carton



Example: Manufacturer's label for case of 11.1 ml vials (REGN10933)

Example: 2.5 ml & 11.1 ml vials

Storage: Keep in carton until use. Unopened vials must be stored at refrigerated temperature (2°C–8°C / 36°F–46°F) until use. Do not freeze, shake, or expose to direct light.

Earliest Expiration Date of Units Shipped: 06/2022

Single Vial w/ Carton Dimensions: 1.7"(d) x 1.8"(w) x 2.8"(h)
Single Vial w/ Carton Weight: 1.5 oz. for 1332 mg/11.1 ml vial; 0.9 oz. for 300 mg/2.5 ml vial

Case: A full case contains 24 vials in cartons
Case Dimensions: 9.6"(d) x 7.4"(w) x 4.6"(h)
Case Weight: 2.7 lb. for 1332mg/11.1 ml vials; 1.8 lb. for 300 mg/2.5 ml vials

Administration: (For detailed guidelines, click here)

1. Remove 20 ml from 250-ml normal saline IV bag
2. Inject 10 ml (1200 mg) casirivimab
3. Inject 10 ml (1200 mg) imdevimab
4. Infuse final volume (250 ml) containing cocktail of 2 monoclonal antibodies over at least 60 min

Note: If immediate patient infusion is not possible, store the diluted cocktail solution at refrigerated temperature (2°C–8°C / 36°F–46°F) for no more than 36 hours and at room temperature for no more than 4 hours, including infusion time.

Resources/Links:

- Regeneron webpage, including:
  - FDA Letter of Authorization
  - Fact Sheet for Healthcare Providers
  - Fact Sheet for Patients and Caregivers (English)
  - Fact Sheet for Patients and Caregivers (Spanish)
- FDA Frequently Asked Questions on the EUA for Casirivimab + Imdevimab
- FAQ: Allocation, Distribution, and Administration of Casirivimab + Imdevimab

Imdevimab (a.k.a. REGN10987) Injection (120 mg/ml)

MUST ADMINISTER WITH CASIRIVIMAB

Manufacturer: Regeneron Pharmaceuticals, Inc.

Distributor: AmerisourceBergen (a.k.a. ABC); c19therapies@amerisourcebergen.com

Product: Component of 2-drug monoclonal antibody cocktail for outpatient infusion

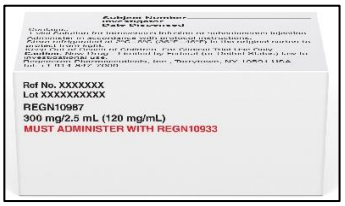
Emergency Use Authorization (EUA): 11/21/20

Units: Supplied in 2 volumes

- 1332 mg/11.1 ml single-dose vial in carton (10 ml from 1 vial needed for patient course)
- 300 mg/2.5 ml single-dose vials in cartons (10 ml; 2.5 ml each from 4 vials needed for patient course)

Note: Some cartons and vials of imdevimab may be instead labeled REGN10987

Example: 1332 mg/11.1 ml carton



Example: 300 mg/2.5 ml carton

Example: Manufacturer's label for case of 11.1 ml vials (REGN10987)

Example: 2.5 ml & 11.1 ml vials

Storage: Keep in carton until use. Unopened vials must be stored at refrigerated temperature (2°C–8°C / 36°F–46°F) until use. Do not freeze, shake, or expose to direct light.

Earliest Expiration Date of Units Shipped: 06/2022

Single Vial w/ Carton Dimensions: 1.7"(d) x 1.8"(w) x 2.8"(h)
Single Vial w/ Carton Weight: 1.5 oz. for 1332 mg/11.1 ml vial; 0.9 oz. for 300 mg/2.5 ml vial

Case: A full case contains 24 vials in cartons
Case Dimensions: 9.6"(d) x 7.4"(w) x 4.6"(h)
Case Weight: 2.7 lb. for 1332mg/11.1 ml vials; 1.8 lb. for 300 mg/2.5 ml vials

Administration: (For detailed guidelines, click here)

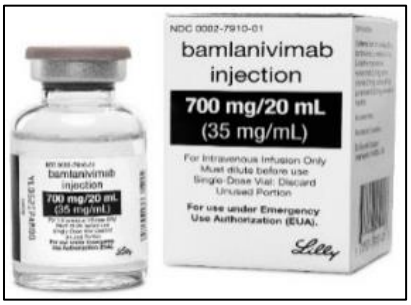
5. Remove 20 ml from 250-ml normal saline IV bag
6. Inject 10 ml (1200 mg) casirivimab
7. Inject 10 ml (1200 mg) imdevimab
8. Infuse final volume (250 ml) containing cocktail of 2 monoclonal antibodies over at least 60 min

Note: If immediate patient infusion is not possible, store the diluted cocktail solution at refrigerated temperature (2°C–8°C / 36°F–46°F) for no more than 36 hours and at room temperature for no more than 4 hours, including infusion time.

Resources/Links:

- Regeneron webpage, including:
  - FDA Letter of Authorization
  - Fact Sheet for Healthcare Providers
  - Fact Sheet for Patients and Caregivers (English)
  - Fact Sheet for Patients and Caregivers (Spanish)
- FDA Frequently Asked Questions on the EUA for Casirivimab + Imdevimab
- FAQ: Allocation, Distribution, and Administration of Casirivimab + Imdevimab

Bamlanivimab Injection (700 mg/20 ml)



Manufacturer: Eli Lilly and Company

Distributor: AmerisourceBergen (a.k.a. ABC); c19therapies@amerisourcebergen.com

Product: Single monoclonal antibody for outpatient infusion

Emergency Use Authorization (EUA): 11/9/2020

Unit: Supplied as one single-dose 20-ml vial per carton

Storage: Keep in carton until use. Unopened vials must be stored at refrigerated temperature (2°C–8°C / 36°F–46°F) until use. Do not freeze, shake, or expose to direct light.

Earliest Expiration Date of Units Shipped: 9/9/2021

Single Vial w/Carton Dimensions: 1.7”(d) x 1.8”(w) x 2.7”(h)
Single Vial w/Carton Weight: 2.1 oz.

Case: A full case contains 100 vials in cartons
Case Dimensions: 9.3”(d) x 18.9”(w) x 6.3”(h)
Case Weight: 13.3 lb.

Administration: (For detailed guidelines, click here)

1. Remove 70 ml from 250-ml normal saline IV bag
2. Inject 20 ml bamlanivimab
3. Infuse final volume (200 ml) containing bamlanivimab over at least 60 min

Note: If immediate patient infusion is not possible, store the diluted bamlanivimab solution at refrigerated temperature (2°C–8°C / 36°F–46°F) for no more than 24 hours and at room temperature for no more than 7 hours, including infusion time.

Resources/Links:

- Lilly Bamlanivimab webpage, including:
  - FDA Letter of Authorization
  - Fact Sheet for Healthcare Providers
  - Fact Sheet for Patients and Caregivers (English)
  - Fact Sheet for Patients and Caregivers (Spanish)
  - Lilly Bamlanivimab Antibody Playbook
- FDA Frequently Asked Questions on the EUA for Bamlanivimab
- FAQ: Allocation, Distribution, and Administration of Bamlanivimab

BAMLANIVIMAB INFUSION TREATMENT CONSENT

The facility will keep this record in your medical file. They will record that SARS COV-2 monoclonal antibody therapy (Bamlanivimab) was administered, when it was given, and the signature and title of the person who administered the infusion.

I have received the **Bamlanivimab** or **Casirivimab/Imdevimab** Emergency Use Authorization Information and/or fact sheet for Patients, Parents and Caregivers. I have read or had explained to me the information about the monoclonal antibody being administered to me. I have been informed of alternatives to receiving bamlanivimab. I understand that bamlanivimab is an unapproved drug that is authorized for use under a FDA Emergency Use Authorization. I understand that this treatment may have significant side effects and that some of the side effects can be life threatening. The risks associated with this therapy may include, but not limited to: nausea, diarrhea, dizziness, headache, pruritus, vomiting and hypersensitivity including anaphylaxis. There can also be infusion-related reactions. I understand the benefits and risks of the antibody and ask that it be administered to me or to the person named below for whom I am authorized to make this request.

Information about resident to receive Bamlanivimab (Please print).				
Facility Name:				
Resident's Medicare Number (required for Part-B billing of the therapy):				
Resident/Employee SSN Number:				
Name: Last First Middle Initial			**Birth Date**	**Age**
Address: Street	**City**	**State**	**Zip**	
Cell Phone Number:				
Signature of person to receive therapy or person authorized to make the request (relative or guardian): **X**_____ **Date:** _____				

MONOCLONAL ANTIBODY DOCUMENTATION

Antibody Maker	Therapy Name	Date Administered	Time of Infusion	Injection Site	Signature of Infusion Administrator	Title
Eli Lilly	**Balanivimab**					
Regeneron	**Casirivimab and imdevimab**					

File completed consent form in the patient's medical record.
(Form-Bamlanivimab-Consent: Version 12/04/2020)

BAMLANIVIMAB INFUSION TREATMENT CONSENT

Fact Sheet for Patients, Parents and Caregivers
Emergency Use Authorization (EUA) of Bamlanivimab for Coronavirus Disease 2019 (COVID-19)

You are being given a medicine called **bamlanivimab** for the treatment of coronavirus disease 2019 (COVID-19). This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking bamlanivimab, which you may receive.

Receiving bamlanivimab may benefit certain people with COVID-19.

Read this Fact Sheet for information about bamlanivimab. Talk to your healthcare provider if you have questions. It is your choice to receive bamlanivimab or stop it at any time.

What is COVID-19?
COVID-19 is caused by a virus called a coronavirus. People can get COVID-19 through contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. People of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

What are the symptoms of COVID-19?
The symptoms of COVID-19 include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure. Serious illness including breathing problems can occur and may cause your other medical conditions to become worse.

What is bamlanivimab?
Bamlanivimab is an investigational medicine used for the treatment of COVID-19 in non-hospitalized adults and adolescents 12 years of age and older with mild to moderate symptoms who weigh 88 pounds (40 kg) or more, and who are at high risk for developing severe COVID-19 symptoms or the need for hospitalization. Bamlanivimab is investigational because it is still being studied. There is limited information known about the safety or effectiveness of using bamlanivimab to treat people with COVID-19.

The FDA has authorized the emergency use of bamlanivimab for the treatment of COVID-19 under an Emergency Use Authorization (EUA). For more information on EUA, see the section "**What is an Emergency Use Authorization (EUA)?**" at the end of this Fact Sheet.

What should I tell my healthcare provider before I receive bamlanivimab?
Tell your healthcare provider about all of your medical conditions, including if you:
- Have any allergies
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illnesses
- Are taking any medications (prescription, over-the-counter, vitamins, and herbal products)

How will I receive bamlanivimab?
- Bamlanivimab is given to you through a vein (intravenous or IV) for at least 1 hour.
- You will receive one dose of bamlanivimab by IV infusion.

What are the important possible side effects of bamlanivimab?
Possible side effects of bamlanivimab are:
- Allergic reactions. Allergic reactions can happen during and after infusion with bamlanivimab. Tell your healthcare provider right away if you get any of the following signs and symptoms of allergic reactions: fever,

chills, nausea, headache, shortness of breath, low blood pressure, wheezing, swelling of your lips, face, or throat, rash including hives, itching, muscle aches, and dizziness.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

These are not all the possible side effects of bamlanivimab. Not a lot of people have been given bamlanivimab. Serious and unexpected side effects may happen. Bamlanivimab is still being studied so it is possible that all of the risks are not known at this time.

It is possible that bamlanivimab could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, bamlanivimab may reduce your body's immune response to a vaccine for SARS-CoV-2. Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

What other treatment choices are there?
Like bamlanivimab, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to https://www.covid19treatmentguidelines.nih.gov/ for information on the emergency use of other medicines that are not approved by FDA to treat people with COVID-19. Your healthcare provider may talk with you about clinical trials you may be eligible for.

It is your choice to be treated or not to be treated with bamlanivimab. Should you decide not to receive bamlanivimab or stop it at any time, it will not change your standard medical care.

What if I am pregnant or breastfeeding?
There is limited experience treating pregnant women or breastfeeding mothers with bamlanivimab. For a mother and unborn baby, the benefit of receiving bamlanivimab may be greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

How do I report side effects with bamlanivimab?
Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch, call 1-800-FDA-1088, or contact Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921).

How can I learn more?

- Ask your healthcare provider
- Visit www.bamlanivimab.com
- Visit https://www.covid19treatmentguidelines.nih.gov/
- Contact your local or state public health department

What is an Emergency Use Authorization (EUA)?
The United States FDA has made bamlanivimab available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Bamlanivimab has not undergone the same type of review as an FDA-approved or cleared product. The FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is reasonable to believe that the product meets certain criteria for safety, performance, and labeling and may be effective in treatment of patients during the COVID-19 pandemic. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for bamlanivimab is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the product may no longer be used).

Literature issued November 2020

Eli Lilly and Company, Indianapolis, IN 46285, USA

BAM-0001-EUA PAT-20201109

FACT SHEET FOR PATIENTS, PARENTS AND CAREGIVERS
EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB
FOR CORONAVIRUS DISEASE 2019
(COVID-19)

You are being given a medicine called **casirivimab** and **imdevimab** for the treatment of coronavirus disease 2019 (COVID-19). This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking casirivimab and imdevimab, which you may receive.

Receiving casirivimab and imdevimab may benefit certain people with COVID-19.

Read this Fact Sheet for information about casirivimab and imdevimab. Talk to your healthcare provider if you have questions. It is your choice to receive casirivimab and imdevimab or stop at any time.

WHAT IS COVID-19?

COVID-19 is caused by a virus called a coronavirus. People can get COVID-19 through contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can occur and may cause some of your other medical conditions to become worse. People of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

WHAT ARE THE SYMPTOMS OF COVID-19?

The symptoms of COVID-19 include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure. Serious illness including breathing problems can occur and may cause your other medical conditions to become worse.

WHAT IS CASIRIVIMAB AND IMDEVIMAB?

Casirivimab and imdevimab are investigational medicines used to treat mild to moderate symptoms of COVID-19 in non-hospitalized adults and adolescents (12 years of age and older who weigh at least 88 pounds (40 kg)), and who are at high risk for developing severe COVID-19 symptoms or the need for hospitalization. Casirivimab and imdevimab are investigational because they are still being studied. There is limited information known about the safety and effectiveness of using casirivimab and imdevimab to treat people with COVID-19.

The FDA has authorized the emergency use of casirivimab and imdevimab for the treatment of COVID-19 under an Emergency Use Authorization (EUA). For more information on EUA, see the **"What is an Emergency Use Authorization (EUA)?"** section at the end of this Fact Sheet.

WHAT SHOULD I TELL MY HEALTH CARE PROVIDER BEFORE I RECEIVE CASIRIVIMAB AND IMDEVIMAB?

Tell your healthcare provider about all of your medical conditions, including if you:

- Have any allergies
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illnesses
- Are taking any medications (prescription, over-the-counter, vitamins, and herbal products)

HOW WILL I RECEIVE CASIRIVIMAB AND IMDEVIMAB?

- Casirivimab and imdevimab are two investigational medicines given together as a single intravenous infusion (through a vein) for at least 1 hour.
- You will receive one dose of casirivimab and imdevimab by intravenous infusion.

WHAT ARE THE IMPORTANT POSSIBLE SIDE EFFECTS OF CASIRIVIMAB AND IMDEVIMAB?

Possible side effects of casirivimab and imdevimab are:

- Allergic reactions. Allergic reactions can happen during and after infusion with casirivimab and imdevimab. Tell your healthcare provider or nurse, or get medical help right away if you get any of the following signs and symptoms of allergic reactions: fever, chills, low blood pressure, changes in your heartbeat, shortness of breath, wheezing, swelling of your lips, face, or throat, rash including hives, itching, headache, nausea, vomiting, sweating, muscle aches, dizziness and shivering.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

These are not all the possible side effects of casirivimab and imdevimab. Not a lot of people have been given casirivimab and imdevimab. Serious and unexpected side effects may happen. Casirivimab and imdevimab are still being studied so it is possible that all of the risks are not known at this time.

It is possible that casirivimab and imdevimab could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, casirivimab and imdevimab may reduce your body’s immune response to a vaccine for SARS-CoV-2. Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

WHAT OTHER TREATMENT CHOICES ARE THERE?

Like casirivimab and imdevimab, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to https://www.covid19treatmentguidelines.nih.gov/ for information on other medicines used to treat people with COVID-19.

It is your choice to be treated or not to be treated with casirivimab and imdevimab. Should you decide not to receive casirivimab and imdevimab or stop it at any time, it will not change your standard medical care.

WHAT IF I AM PREGNANT OR BREASTFEEDING?
There is limited experience treating pregnant women or breastfeeding mothers with casirivimab and imdevimab. For a mother and unborn baby, the benefit of receiving casirivimab and imdevimab may be greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

HOW DO I REPORT SIDE EFFECTS WITH CASIRIVIMAB AND IMDEVIMAB?
Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch or call 1-800-FDA-1088 or call 1-844-734-6643.

HOW CAN I LEARN MORE?

- Ask your health care provider.
- Visit www.REGENCOV2.com
- Visit https://www.covid19treatmentguidelines.nih.gov/
- Contact your local or state public health department.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?
The United States FDA has made casirivimab and imdevimab available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Casirivimab and imdevimab have not undergone the same type of review as an FDA-approved or cleared product. The FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is reasonable to believe that the product meets certain criteria for safety, performance, and labeling and may be effective in treatment of patients during the COVID-19 pandemic. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for casirivimab and imdevimab is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

REGENERON

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

Authorized: 11/2020

Reset Form

U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH

For VOLUNTARY reporting of adverse events, product problems and product use/medication errors

Form Approved: OMB No. 0910-0291, Expires: 11-30-2021
See PRA statement on reverse.

FDA USE ONLY
Triage unit sequence #
FDA Rec. Date

FORM FDA 3500 (2/19)
The FDA Safety Information and Adverse Event Reporting Program

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2018.

A. PATIENT INFORMATION

1. **Patient Identifier**
In Confidence

2. **Age**
☐ Year(s) ☐ Month(s) ☐ Week(s) ☐ Day(s)
or Date of Birth *(e.g., 08 Feb 1925)*

3. **Gender** *(check one)*
☐ Female ☐ Male ☐ Intersex ☐ Transgender ☐ Prefer not to disclose

4. **Weight**
☐ lb ☐ kg

5. **Ethnicity** *(check one)*
☐ Hispanic/Latino ☐ Not Hispanic/Latino

6. **Race** *(check all that apply)*
☐ Asian ☐ American Indian or Alaskan Native ☐ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

1. **Type of Report** *(check all that apply)*
☐ Adverse Event ☐ Product Problem *(e.g., defects/malfunctions)*
☐ Product Use/ Medication Error ☐ Problem with Different Manufacturer of Same Medicine

2. **Outcome Attributed to Adverse Event** *(check all that apply)*
☐ Death *Date of death (dd-mmm-yyyy):*
☐ Life-threatening ☐ Disability or Permanent Damage
☐ Hospitalization (initial or prolonged) ☐ Congenital Anomaly/Birth Defects
☐ Other Serious or Important Medical Events
☐ Required Intervention to Prevent Permanent Impairment/Damage

3. **Date of Event** *(dd-mmm-yyyy)*

4. **Date of this Report** *(dd-mmm-yyyy)*

5. **Describe Event, Problem or Product Use/Medication Error**

(Continue on page 2)

6. **Relevant Tests/Laboratory Data** **Date** *(dd-mmm-yyyy)*

(Continue on page 2)

7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

(Continue on page 2)

C. PRODUCT AVAILABILITY

1. **Product Available for Evaluation?** *(Do not send product to FDA)*
☐ Yes ☐ No ☐ Returned to Manufacturer on *(dd-mmm-yyyy)*

2. **Do you have a picture of the product?** *(check yes if you are including a picture)* ☐ Yes

D. SUSPECT PRODUCTS

1. **Name, Strength, Manufacturer/Compounder** *(from product label).*
Does this report involve cosmetic, dietary supplement or food/medical food? **#1** ☐ Yes **#2** ☐ Yes

#1 – Name and Strength	#1 – NDC # or Unique ID
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
#2 – Manufacturer/Compounder	#2 – Lot #

2. **Dose or Amount** | **Frequency** | **Route**
#1
#2

3. **Treatment Dates/Therapy Dates** *(give best estimate of length of treatment (start/stop) or duration.)*
#1 Start
#1 Stop
Is therapy still on-going? ☐ Yes ☐ No
#2 Start
#2 Stop
Is therapy still on-going? ☐ Yes ☐ No

4. **Diagnosis for Use** *(Indication)*
#1
#2

5. **Product Type** *(check all that apply)*
#1 ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar
#2 ☐ OTC ☐ Compounded ☐ Generic ☐ Biosimilar

6. **Expiration Date** *(dd-mmm-yyyy)*
#1
#2

7. **Event Abated After Use Stopped or Dose Reduced?**
#1 ☐ Yes ☐ No ☐ Doesn't apply
#2 ☐ Yes ☐ No ☐ Doesn't apply

8. **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☐ Doesn't apply
#2 ☐ Yes ☐ No ☐ Doesn't apply

E. SUSPECT MEDICAL DEVICE

1. **Brand Name**

2a. **Common Device Name** | 2b. **Procode**

3. **Manufacturer Name, City and State**

4. **Model #** | **Lot #** | 5. **Operator of Device** ☐ Health Professional ☐ Patient/Consumer ☐ Other
Catalog # | **Expiration Date** *(dd-mmm-yyyy)*
Serial # | **Unique Identifier** *(UDI) #*

6a. **If Implanted, Give Date** *(dd-mmm-yyyy)* | 6b. **If Explanted, Give Date** *(dd-mmm-yyyy)*

7a. **Is this a single-use device that was reprocessed and reused on a patient?** ☐ Yes ☐ No

7b. **If Yes to Item 7a, Enter Name and Address of Reprocessor**

8. **Was this device serviced by a third party servicer?** ☐ Yes ☐ No ☐ Unknown

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

1. **Product names and therapy dates** *(Exclude treatment of event)*

(Continue on page 2)

G. REPORTER *(See confidentiality section on back)*

1. **Name and Address**
Last Name: | First Name:
Address:
City: | State/Province/Region:
ZIP/Postal Code: | Country:
Phone #: | Email:

2. **Health Professional?** ☐ Yes ☐ No

3. **Occupation**

4. **Also Reported to:** ☐ Manufacturer/ Compounder ☐ User Facility ☐ Distributor/Importer

5. **If you do NOT want your identity disclosed to the manufacturer, please mark this box:** ☐

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.
* Please see instructions

Reset Form

U.S. Department of Health and Human Services
Food and Drug Administration
MEDWATCH

FORM FDA 3500 (2/19) *(continued)*
The FDA Safety Information and Adverse Event Reporting Program

(CONTINUATION PAGE)
For VOLUNTARY reporting of adverse events, product problems and product use/medication errors

B.5. **Describe Event or Problem** *(continued)*

Back to Item B.5

B.6. **Relevant Tests/Laboratory Data** *(continued)*

Date *(dd-mmm-yyyy)*	**Relevant Tests/Laboratory Data**	**Date** *(dd-mmm-yyyy)*

Additional comments

Back to Item B.6

B.7. **Other Relevant History** *(continued)*

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F.1. **Concomitant Medical Products and Therapy Dates** *(Exclude treatment of event) (continued)*

Back to Item F.1

ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: **http://www.fda.gov/medwatch/report/consumer/instruct.htm**

Report adverse events, product problems or product use errors with:

- Medications (drugs or biologics)
- Medical devices (including diabetes glucose-test kit, hearing aids, breast pumps, and many more)
- Combination products (medication & medical devices)
- Blood transfusions, gene therapies, and human cells and tissue transplants (for example, tendons, bone, and corneas)
- Special nutritional products (dietary supplements, medical foods, infant formulas)
- Cosmetics (such as moisturizers, makeup, shampoos and conditioners, face and body washes, deodorants, nail care products, hair dyes and relaxers, and tattoos)
- Food (including beverages and ingredients added to foods)

Report product problems – quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details
- Just fill in the sections that apply to your report

How to report:

- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer (or both)

How to submit report:

- To report by phone, call toll-free: 1-800-FDA (332)-1088
- To fax report: 1-800-FDA(332)-0178
- To report online: www.fda.gov/medwatch/report.htm

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

If your report involves an adverse event with a vaccine, go to http://vaers.hhs.gov to report or call 1-800-822-7967.

Confidentiality:

The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

The information in this box applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information has been estimated to average 40 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed, and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

Please DO NOT RETURN this form to the PRA Staff e-mail above.

OMB statement:

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration