

Association of British Neurologists Guidance on COVID-19 for people with neurological conditions, their doctors and carers

Prepared by The ABN Executive in association with subspecialist Advisory groups.

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The ABN recognises that this is a rapidly changing field. We will update our advice as we learn more. What follows below should be considered general advice. There are many neurological conditions and treatments, and treatment decisions should be tailored to the needs of the individual.

Some people have expressed concern that being identified at increased risk would reduce their priority should hospital treatment be required. These guidelines should not be used in triaging patients for treatment. Although some neurological conditions or treatments increase the risk of complicated COVID-19, most patients in these groups will overcome the infection.

General Introduction

COVID-19 is a disease caused by a new coronavirus that affects the lungs and airways. It is related to viruses that cause the common cold. Unlike the common cold, this virus is new, so nobody has immunity to it. The entire population is therefore at risk of catching it. It is estimated that as many as 80% of people who catch the virus may experience relatively mild or no symptoms but are able to pass on the infection to others. People who do develop symptoms are at risk of passing it on to others for up around 7 days before symptoms emerge. The commonest symptoms are high fever, cough, or shortness of breath.

People aged over 70, with long-term conditions or a weakened immune system are at risk of developing complications of the infection, including secondary lung infections or damaging excess activity of the immune system ([https://doi.org/10.1016/S0140-6736\(20\)30628-0](https://doi.org/10.1016/S0140-6736(20)30628-0))

Some patients with particular neurological conditions, who receive certain treatments for neurological conditions, or who also have other non-neurological condition are at increased risk of complications of COVID-19.

Social distancing reduces the risk of catching COVID-19, but self-isolation is the most effective means of avoiding infection. Public Health England has published guidance on minimising the risk of catching or passing on COVID-19:
<https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people>

Assessment of risk

Experts in neurological subspecialties have attempted to estimate the risk associated with COVID-19 from each neurological condition or its treatment. It is difficult to accurately assess risk for every condition. The **risk has been subdivided into three levels; low, moderate, and high:**

We recommend social distancing for all people with any neurological condition, their carers and family.

We recommend self-isolation only for people in the high risk category.

People with a neurological condition with low or moderate risk might be considered high risk if they have additional risk associated with other conditions affecting the lungs, heart, kidneys etc.

Frailty is a risk factor for a poor response to treatment for COVID-19. People with neurological conditions resulting in frailty, or who are frail as a result of age or other conditions are at increased risk from COVID-19.

It is important to emphasise that we do not expect most patients in the high-risk groups to suffer severe complications of the virus. Treatments for complex COVID-19 are under development; however, the best advice for all people, and particularly for those at increased risk of complications, is to reduce or avoid the risk of catching the virus.

Information is available from the NHS: <https://www.nhs.uk/conditions/coronavirus-covid-19>

Patients who think they may have the virus should use the 111 coronavirus service on-line: <https://111.nhs.uk/covid-19>

The NHS recommends calling 111 only if advice is not available on-line.

Risk arising from treatment for COVID-19

A number of drugs are being trialled for COVID-19 treatment, including Atazanavir, Lopinavir/ritonavir, Remdesivir, Favipiravir, Chloroquine Hydroxychloroquine Nitazoxanide Ribavirin and Tocilizumab. There are potential interactions between drugs and standard neurology drugs. The Liverpool Drug Interactions Group has published very clear tables describing the risks for each class of medication, including anticonvulsants, analgesics, immunosuppressants and others (<http://www.covid19-druginteractions.org/>). The table for anticonvulsants is attached to these guidelines [section

Preliminary experience suggests that there is a possible benefit from hydroxychloroquine and azithromycin treatment in COVID-19 infection, however both may lead to a deterioration in myasthenia gravis. Doctors will have to balance the risks from myasthenia and COVID-19 on a case-by-case basis.

Which conditions are unlikely to increase the risk from COVID-19?

Patients with conditions that do not affect their swallowing or breathing muscles and in whom the immune system is working normally are not considered to be at increased risk from COVID-19.

Milder or moderate forms of many of the commoner neurological disorders, such as Parkinson's disease, multiple sclerosis, epilepsy are not currently considered to confer increased risk, so long as the breathing and swallowing muscles are functioning well.

How do neurological conditions increase the risk from COVID-19?

Neurological conditions and their treatment affect susceptibility to COVID-19 in a number of different ways. The guidance in this document divides up neurological conditions by the area of the nervous system affected; brain or spinal cord, nerve, neuromuscular junction and muscle.

Conditions can also be divided up by the way in which the nervous system is affected by a disease or treatment. Most of the conditions or treatments that increase susceptibility to COVID-19 suppress the immune system.

Additionally, since COVID-19 is a disease of the lungs and airways, any condition that has affected swallowing or breathing might increase the severity of COVID-19 infection.

A combination of risk factors will increase the chance of experiencing a severe form of COVID-19 infection.

The greater the risk of experiencing a severe form of COVID-19, the more strongly we recommend social distancing. For individuals at the highest overall risk, we recommend self-isolation.

General comments on immune disorders of the nervous system

Neurological immune conditions such as multiple sclerosis and some peripheral nerve diseases may affect the nervous system in people who are otherwise healthy. They may also occur in elderly people with other non-neurological conditions (known as co-morbidities). The neurological disease may be part of a multi-system disorder, such as pulmonary and neurological sarcoidosis, or systemic vasculitis, which increase the risks of a more severe COVID-19 infection. Overall risk is increased when more than one risk factor is present

Some neurological conditions are associated with weakness of the swallowing mechanism (bulbar weakness), weakness of respiratory muscles or cardiac function (such as motor neurone disease and some myopathies). These factors increase risk of more severe infection.

Many people with neuro-immunological conditions receive immunotherapies. Some of these immunotherapies might increase the severity of a COVID-19 infection. The additional risk from these treatments is not known but it should be emphasised that the risk of stopping therapy for some patients is high and the consequences of doing so may be devastating.

General advice related to immunosuppression in neurology patients in individuals without symptoms of COVID-19 infection

1. People with neurological conditions should **not** stop or alter their medication without prior discussion with their neurology team.
2. Individuals taking **azathioprine, mycophenolate mofetil, methotrexate** with or without **prednisolone** should continue to take their tablets as normal. Evidence is limited, but these medications may increase the risk of COVID-19 infection and its complications. However, in almost all cases this risk is outweighed by the benefits of the medication in reducing the chance of a relapse of the neurological condition.
3. **For those taking an immunosuppressive drug (azathioprine, mycophenolate mofetil or methotrexate) combined with prednisolone, there is an increased risk. The level of risk is uncertain, however any of these drugs combined with a daily prednisolone dose of 10mg or above is considered high risk, and self-isolation is recommended. Combining prednisone up to 9 mg with an immunosuppressive agent increases the risk to medium. Steroids increase risk of diabetes, hypertension and high BMI, which are associated with poor outcomes after COVID-19.**
3. **Infliximab/Rituximab/Ocrelizumab.** These infusions moderately increase the risk of viral infections, so individuals may be more prone to COVID-19 and its complications. In many patients this risk is outweighed by the benefits of rituximab in suppressing otherwise progressive or

severe neurological disease, and the treatment should continue as normal. In all cases the consultant should review the timing of re-treatment and delay treatment if possible or consider alternative options.

4. **Multiple sclerosis disease-modifying therapies** present distinct challenges and are dealt with in detail elsewhere [https://cdn.ymaws.com/www.theabn.org/resource/collection/6750BAE6-4CBC-4DDB-A684-116E03BFE634/ABN Guidance on DMTs for MS and COVID19 APPROVED 11 March.pdf](https://cdn.ymaws.com/www.theabn.org/resource/collection/6750BAE6-4CBC-4DDB-A684-116E03BFE634/ABN_Guidance_on_DMTs_for_MS_and_COVID19_APPROVED_11_March.pdf)
5. Some immunomodulatory drugs (for example tocilizumab) are in trial to treat the complications of COVID-19 infection. This fact alone does not mean their use as disease modifying therapies is safe. Each case will need to be considered individually with specialist medical oversight.
6. Some immunotherapies require frequent attendance at hospitals, for instance monthly infusions of natalizumab for multiple sclerosis. As this would be incompatible with social distancing, the administration of such therapies may not be feasible at the height of the epidemic. Individual neurology departments will advise on local arrangements for service delivery.

Advice for Carers

Some patients with neurological diseases require day-to-day care. Carers should be aware both of their own ability to spread COVID-19 through touch or respiratory droplets and should follow the advice on general hygiene here and prevention of spread here .

Users of high flow non-invasive ventilation devices will aerosolise infectious particles extensively to the local environment. Appropriate measures should be utilised to prevent unintended spread to people in the vicinity.

Advice for doctors

Concern has been raised about the potential for COVID-19 transmission through procedures that bring healthcare staff in close proximity with the nose, mouth and eyes of patients including fundoscopy and other parts of the cranial nerve examination. There are emerging reports of anosmia and dysgeusia in individuals with COVID-19, suggesting the potential for nasal carriage of the virus, which remain as yet unverified.

There is insufficient evidence at present to make a firm recommendation on practice, however, we feel it is important to bring this issue to the attention of neurologists who are examining patients during the current COVID-19 pandemic. At the present time, the ABN suggests

members are aware of this issue and only perform these procedures where there is a specific clinical need. **Local advice on the use of personal protection equipment and clinical examination should be followed at all times.** If an examination is felt necessary, but deferred for any reason, a note should be made of this for follow-up.

The ABN will update members if further information becomes available on this issue.

Specific Neurological Disease Groups

A. Multiple sclerosis

Patients with multiple sclerosis are not significantly at risk from COVID-19, unless they have advanced disability with swallowing or breathing difficulties, or they are receiving selected immunotherapies. Very early unpublished data from China suggests that multiple sclerosis patients may not be at significantly increased risk if they are on Disease Modifying Therapies.

We do **not** recommend that patients stop injectable or oral therapies or natalizumab, as the risk of a relapse of multiple sclerosis exceeds the risk of the medication itself.

The risks of COVID-19 infection and its complications are moderately increased with ocrelizumab, so we recommend caution in starting this treatment, and delaying re-treatments, during the epidemic.

We **advise against** autologous haematopoietic stem cell transplantation, as well as alemtuzumab or cladribine treatments and re-treatments, as these represent the highest risk to patients.

Patients with serious COVID-19 complications and multiple sclerosis may safely stop their immunotherapy for up to four weeks, but only after consultation with their MS team.

Detailed guidance on each drug used to treat MS is contained in this document:

https://cdn.ymaws.com/www.theabn.org/resource/collection/6750BAE6-4CBC-4DDB-A684-116E03BFE634/ABN_Guidance_on_DMTs_for_MS_and_COVID19_APPROVED_11_March.pdf

Multiple Sclerosis	Risk from COVID-19: High (H), Moderate (M) or Low (L)	Additional comments
Multiple Sclerosis	M/H	Risk conferred by immunosuppression: within three months of alemtuzumab or cladribine Those who have had AHSCT (within a time period that remains to be resolved) Those with bulbar failure [i.e. have a PEG] or with respiratory failure [very unusual]

B. Muscle disease

Patients with muscle disease may be significantly at risk from COVID-19.

Specific diseases with risk are mentioned in the table below.

Patients with muscular weakness of the chest or diaphragm, resulting in lung volumes less than 60% predicted (FVC<60%) are at significant risk, regardless of the underlying diagnosis. Patients with kyphoscoliosis are at additional risk.

Patients with cardiac involvement (and/or on medication for heart involvement) are at high risk. The British Society of Cardiovascular Medicine does **not** recommend stopping ACE inhibitors or Beta blockers in myopathy patients with cardiac involvement.

Patients with active inflammatory disease (myositis) who are on immunosuppression are at additional risk from the medication (see medication table).

We do not recommend that patients with treated active disease routinely stop their medication as the risk of a flare exceeds the risk of the medication itself. Patients on steroids should not stop steroids. Some patients actually may need higher steroid doses during acute infection. We would not recommend stopping steroids in Duchenne Muscular Dystrophy patients.

Note that a prednisolone dose of 10mg per day or above is considered an additional risk factor. A patient with a condition with a moderate risk would rise to the high risk group if taking 10 mg prednisolone or above. Steroids increase risk of diabetes, hypertension and high BMI, which are associated with poor outcomes after COVID-19.

Patients with acute COVID-19 infection should suspend their immunosuppression but **not** steroids (see immunosuppression table) and restart once recovered.

Muscle Diseases	Risk from coronavirus: High (H), Moderate (M) or low (L)	Additional comments
Myositis, polymyositis	H/M	If disease active – increased risk due to respiratory muscle weakness as well as co-existing interstitial lung disease which is common in these patients and other overlap connective tissue disorders May be on immunosuppression, do not stop steroids
X-linked Muscular dystrophies (Duchenne/Becker)	H	High risk: FVC<60%, non-invasive ventilation, weak cough or cardiomyopathy. Ensure Duchenne patients have sufficient supply of steroids and cardiac medications. Do not stop steroids, ACE Inhibitors or beta blockers. If moderately unwell (more than a simple cold) double the steroid dose for 3 days and then taper back to original dose over 5 days. For severe illness give systemic steroids.
Limb girdle muscular dystrophies	H/M	High risk: FVC<60%, NIV, weak cough, cardiomyopathy Ensure patients have supply of cardiac medications, do not stop ACE inhibitors or beta blockers.
Myotonic dystrophy	H/M	High risk: FVC<60%, Poor cough, risk of chest infection, risk of choking with coughing.

Congenital muscular dystrophy	H	High risk: patients with FVC<60%, those NIV and with weak cough. Patients with cardiomyopathy. Ensure patients have supply of cardiac medications, do not stop ACE inhibitors or beta blockers.
Spinal Muscular Atrophy	H/M	Type 2 SMA high risk Type 3 high risk if FVC<60% or using BiPAP (usually non-ambulant)
Congenital Myopathy	H/M	High risk: patients with FVC<60%, those NIV and with weak cough.
Fatty acid oxidation disorder	H	Risk of acute rhabdomyolysis with fever, infection, fasting. Ensure emergency regimen is in place see BIMDG website for details. May need IV dextrose
Mitochondrial disease	H/M	Risk of decompensation during infection, risk of cardiomyopathy Patients with diabetes at high risk Patients immunosuppressed for organ transplantation at high risk Aggressively treat seizure activity during episodes of decompensation or stroke like episodes
Glycogen Storage Diseases	H/M/L	Patients with Pompe disease with FVC<60% or on BiPAP at risk of respiratory decompensation Patients with glycolytic disorders (GSDV, VII, XIII) should take care to avoid disease related rhabdomyolysis Patients with secondary diabetes and ischaemic heart disease at high risk

C. Nerve disease

Most patients with peripheral neuropathies alone are not at additional risk from COVID-19, except in some special categories. Specific diseases with increased risk are mentioned in the table below.

Patients with active disease who are on immunosuppression are at additional risk from the medication (see medication table).

We do not recommend that patients with active disease on medication should routinely stop their medication, as the risk of a flare exceeds the risk of the medication itself. Patients on steroids should not stop steroids. Some patients may need higher doses during acute infection. A Prednisolone dose of 10mg per day or above should be considered an independent risk factor in increasing a patient risk category. A prednisolone dose of 10-19 mg is a moderate risk. An immunosuppressive combined with prednisolone 10-19 mg is high risk and the patient should self-isolate. A prednisolone dose of 20 mg or greater is high risk.

Patients with acute COVID-19 infection should suspend their immunosuppression but **not** steroids (see immunosuppression table) and restart once recovered.

Nerve Diseases	Risk from coronavirus: High (H), Moderate (M) or low (L)	Additional comments
Guillain-Barre Syndrome	M	Likely only to be at risk if acutely ventilated and whilst there is neuromuscular respiratory weakness. No additional risk of causation or recurrence known. No usual immunosuppressant.
Vasculitis (any)	H/M	Risk conferred by immunosuppression Lung/renal involvement further increases risk
Chronic Inflammatory Demyelinating Polyneuropathy	M/L	Except in exceptional cases with respiratory/diaphragmatic involvement, no additional risk from COVID-19 infection. Risk conferred by immunosuppression agents

Nerve Diseases	Risk from coronavirus: High (H), Moderate (M) or low (L)	Additional comments
POEMS syndrome	H/M	<p>Acute disease patients with reduced transfer factors secondary to alveolar fluid.</p> <p>Risk conferred by immunosuppression from lenalidomide/dexamethasone or autografting.</p> <p>Some patients with neuromuscular weakness from diaphragm weakness.</p>
Paraproteinaemic neuropathies	H/L	<p>No additional risk from COVID-19 if untreated</p> <p>Risk conferred by immunosuppression, such as rituximab</p>
Multifocal motor neuropathy	H/L	Intravenous immunoglobulin probably does not increase risk. Cyclophosphamide high risk.
Idiopathic neuropathies	None	
Inherited neuropathies	None/H	<p>No risk to uncomplicated Charcot-Marie-Tooth.</p> <p>Patients with kyphoscoliosis and/or neuromuscular chest/diaphragm weakness may be at high risk.</p>
Amyloid neuropathy	H/M	<p>Moderate risk with Autonomic neuropathy</p> <p>High risk with cardiac involvement</p>
Autonomic neuropathy	H/M	Increased risk of blood pressure instability. Other comorbidities might increase risk category [e.g. bulbar weakness in atypical Parkinsonian syndromes]

D. Motor neurone disease

Patients with more advanced motor neurone disease are at higher risk from the complications of COVID-19 infection.

This is particularly the case for patients with bulbar or respiratory muscle weakness. Patients with muscular weakness of the chest or diaphragm, resulting in lung volumes less than 60% predicted (FVC<60%) are at significant risk as are patients with ventilator support.

Motor Neurone Diseases	Risk from coronavirus: High (H), Moderate (M) or Low (L)	Additional comments
Motor neurone disease	H	Patients on NIV are at higher risk from COVID-19 infection than those with no ventilator support.

E. Neuromuscular Junction Diseases

Patients with Neuromuscular Junction (NMJ) Diseases may be significantly at risk from COVID-19.

Patients with NMJ-related weakness of the chest or diaphragm, resulting in lung volumes less than 60% predicted (FVC<60%), are at high risk.

Immunosuppressant medication may further increase the risk from coronavirus (see medication table). A Prednisolone dose of 20mg per day or above should be considered an independent risk factor increasing a patient from a moderate to a high risk category.

We do **not** recommend that patients with active disease on medication routinely stop their medication as the risk of a flare exceeds the risk of the medication itself. Patients on steroids should **not** stop steroids and may need higher doses during acute infection. Care may be needed in increasing doses of prednisolone too rapidly in myasthenia gravis which can increase muscle weakness. Specialist advice should be sought.

Patients with acute coronavirus infection and myasthenia gravis should NOT suspend their immunosuppression but should seek advice from their medical team.

Colleagues are reminded that there are a number of drugs that may result in a deterioration in myasthenia symptoms. For a list, check <https://www.myaware.org/drugs-to-avoid>. Preliminary experience suggests that there is a possible benefit from hydroxychloroquine and azithromycin treatment in COVID-19 infection, however both may lead to a deterioration in myasthenia gravis. Doctors will have to balance the risks from myasthenia and COVID-19 on a case-by-case basis.

Neuromuscular Junction Diseases	Risk from coronavirus: High (H), Moderate (M) or Low (L)	Additional comments
Myasthenia Gravis (AChR and MuSK antibody positive and negative)	H/M	Well controlled MG (M); Myasthenia gravis on immunosuppression and/or with respiratory involvement is at a greater risk from COVID-19 infection (H)
Lambert Eaton myasthenic syndrome	H/M	
Fast channel congenital myasthenic syndrome or Congenital myasthenic syndrome with respiratory crises that needing hospital admission within the last 10 years	H/M	
Congenital myasthenia with previous respiratory involvement or needing nocturnal ventilation	H	
Ocular myasthenia or well controlled adult congenital myasthenia without respiratory involvement in last 10 years and normal sleep studies	L	

F. A. Inflammatory or autoimmune diseases of the central nervous system (excluding multiple sclerosis)

Patients with inflammatory or autoimmune diseases of the CNS are not significantly at risk from COVID-19, except if the condition leads to swallowing or respiratory weakness, such as neuromyelitis optica or cerebral vasculitis.

Immunosuppressant medication may further increase the risk from coronavirus (see medication table). A Prednisolone dose of 20mg per day or above should be considered an independent risk factor placing a patient in the high risk category.

We do not recommend that patients with CNS inflammatory conditions stop immunotherapy because the risks of a relapse are usually greater than the risk of infection. For patients on rituximab, the neurology team may consider delaying re-treatment, except in patients where the risk of relapse may be very high, for instance in neuromyelitis optica spectrum disorders (NMOSD) (see below).

Patients with serious COVID-19 infection complications should stop their immunotherapy in consultation with their neurology team. In conditions where relapses may be sudden and life-threatening, such as neuromyelitis optica, it may be reasonable to replace immunosuppressive treatments with corticosteroids during a coronavirus infection or, in some rare cases, continue on their immunotherapy where the risk of relapse is high.

B. Advice related to immunosuppression in NMOSD in individuals without symptoms of COVID-19 infection

1. People with NMOSD should **not** stop or alter their medication without prior discussion with their NMOSD neurology team, because of the risk of relapse.
2. Individuals taking azathioprine, mycophenolate mofetil, methotrexate, with or without regular prednisolone, should continue to take their tablets as normal. Evidence is limited but these medications might increase the risk of COVID-19 infection and its complications. However, in almost all cases this risk is outweighed by the benefits of the medication in reducing the chance of an NMOSD relapse. For those patients taking an immunosuppressive drug (azathioprine, mycophenolate mofetil or methotrexate) combined with prednisolone, there is an increased risk. **The level of risk is uncertain; however any of these drugs combined with a daily prednisolone dose of 10mg or above is considered high risk, and self-isolation is recommended.**
3. **Rituximab** infusions moderately increase the risk of viral infections, so individuals may be more prone to COVID-19 and its complications. In most NMOSD patients this risk is outweighed by the effectiveness of rituximab in suppressing relapses, and the treatment will continue as normal. In occasional cases the NMOSD consultant may review the timing of re-treatment and consider alternative options e.g. if people with NMOSD have additional risk factors or are negative for AQP4 antibodies.

Advice for people with NMOSD on immunosuppression who have COVID-19

- Caution is required as some treatments being trialled for COVID-19, such as beta interferon or fingolimod are known to cause deterioration in NMOSD.
- Please inform your NMOSD team by telephone if you have contracted COVID-19 and they will advise further.
- For mild cases of COVID-19, we do not recommend stopping your treatment.
- During severe infection, in discussion with your neurologist, your immunosuppressant might be temporarily discontinued, often covered by higher dose prednisolone, depending on your antibody status.
- This advice is likely to differ on a case by case basis, as will decisions about optimal timing of restarting immunosuppression.

Advice for patients with NMO can be obtained from the National NMOSD Service: <http://www.nmouk.nhs.uk/>

Inflammatory or autoimmune diseases of the central nervous system	Risk from coronavirus: High (H), Moderate (M) or low (L)	Additional comments
Neuromyelitis optica spectrum disorder	H/M	Risk conferred by immunosuppression Occasional patients may have bulbar or respiratory weakness that confers additional risk.
Autoimmune encephalitis	H/M	Risk conferred by immunosuppression
Cerebral vasculitis	H/M	Risk conferred by immunosuppression and also by any co-morbidities [e.g. renal or lung disease] Occasional patients may have bulbar or respiratory weakness that confers additional risk.
Anti-MOG disease	H/M	Risk conferred by immunosuppression
Neurosarcoidosis	H/M	Risk conferred by immunosuppression and also by any co-morbidities [e.g. lung disease]

G. Non-inflammatory disorders of the central nervous system

These conditions do not in themselves render the patient susceptible to infection, however disability, especially bulbar and respiratory failure, or the presence of co-morbidities increase the risk from COVID-19.

Non-inflammatory diseases of the central nervous system	Risk from coronavirus: High (H), Moderate (M) or Low (L)	Additional comments
Any disorder affecting swallowing or respiratory function	H/M/L	See specific disorders below
Stroke	H/M/L	Depending on disability and comorbidities, including cardiac disease and diabetes Risk factors for stroke also might influence infection risk (diabetes, hypertension, other cardiovascular disease).
Genetic Degenerative/Ataxic Syndromes	M	If associated with bulbar weakness
Cognitive Disorders	H/M/L	More advanced forms of dementia at higher risk, especially with reduced mobility/frailty. Increased risk particularly with bulbar difficulties (e.g. FTD/MND)
Learning Disabilities	L	Additional neuromuscular comorbidities might increase risk
Hereditary spastic paraparesis	M/L	
Cerebral Palsy	L	Depending on disability
Complex Epilepsy	L	Risk associated with: Significant bulbar or respiratory muscle weakness

And see table below for interactions between anticonvulsants and experimental COVID-19 therapies		Those with respiratory compromise associated with kyphoscoliosis or impaired mobility. Fever-sensitive epilepsies (e.g. Dravet Syndrome) Rasmussen's encephalitis on immunosuppressive medication.
Idiopathic Intracranial Hypertension	L	BMI>40 places patients in 'increased risk of severe illness from coronavirus' category. This applies to many IIH patients
Traumatic Brain Injury	M/L	Patients with significantly impaired bulbar function
Movement Disorders (for example, Parkinson's disease, so-called atypical parkinsonism, dystonia)	H/M/L	Patients in care homes Patients with significantly impaired bulbar or respiratory function Patients with additional cognitive impairment which may limit their ability to understand and follow healthcare advice
Ataxia	H/M/L	Ataxia may be a feature of complex syndromes. Risk rises in patients with comorbidities or related risks: bulbar weakness, cardiomyopathy or diabetes, immunosuppressive treatments. Patients in care homes or with significantly reduced mobility/ wheelchair bound.

Epilepsy Medication interaction with experimental COVID19 Therapies taken from <http://www.covid19-druginteractions.org>.

Interactions with Experimental COVID-19 Therapies

Charts updated 20 March 2020

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Please check www.covid19-druginteractions.org for updates.

Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister. No recommendation to use experimental therapy for COVID-19 is made. Drug interaction data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers.

Anticonvulsants

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV	TCZ
Carbamazepine	↑↓	↑↓	↓	↔	↓	↓	↔	↔	↓
Clonazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Eslicarbazepine	↓▼	↓▼	↓	↔	↓	↓	↔	↔	↔
Ethosuximide	↑	↑	↔	↔	↔	↔	↔	↔	↔
Gabapentin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Lacosamide	↔▼	↔▼	↔	↔	↔	↔	↔	↔	↔
Lamotrigine	↔	↓ 50%	↔	↔	↔	↔	↔	↔	↔
Levetiracetam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Oxcarbazepine	↓	↓	↓	↔	↓	↓	↔	↔	↔
Perampanel	↑	↑	↔	↔	↔	↔	↔	↔	↔
Phenobarbital (Phenobarbitone)	↓	↓	↓	↔	↓	↓	↔	↔	↓
Phenytoin	↓	↓	↓	↔	↓	↓	↑	↔	↓
Pregabalin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Primidone	↓	↓↓	↓	↔	↓	↓	↔	↔	↓
Retigabine	↔	↔	↔	↔	↔	↔	↔	↔	↔
Rufinamide	↓	↓	↓	↔	↓	↓	↔	↔	↔
Sultiame	↑	↑	↔	↔	↔	↔	↔	↔	↔
Tiagabine	↑	↑	↔	↔	↔	↔	↔	↔	↔
Topiramate	↔	↔	↔	↔	↔	↔	↔	↔	↔
Valproate (Divalproex)	↔	↑ 38%	↔	↔	↔	↔	↔	↔	↔
Vigabatrin	↔	↔	↔	↔	↔	↔	↔	↔	↔
Zonisamide	↔	↔	↔	↔	↔	↔	↔	↔	↔

Text Legend

- ↑ Potential increased exposure of the comedication
- ↓ Potential decreased exposure of the comedication
- ↑ Potential increased exposure of COVID drug
- ↓ Potential decreased exposure of COVID drug
- ↔ No significant effect

▼ One or both drugs may cause QT and/or PR prolongation. ECG monitoring is advised if coadministered.

Numbers refer to increase or decrease in AUC as observed in drug-drug interaction studies.

Notes:

Valproate + LPV/r

Case report of a 48% decrease in valproate concentration in previously stable patient who developed exacerbated mania on starting lopinavir/ritonavir; dose increase of valproate was required.

Table 2: List of immunosuppressant medications that could put patients at risk

For those taking an immunosuppressive drug (azathioprine, mycophenolate mofetil or methotrexate) combined with prednisolone, there is an increased risk. **The level of risk is uncertain; however any of these drugs combined with a daily prednisolone dose of 10mg or above is considered high risk, and self-isolation is recommended.**

Immunosuppressant or indicative medications

The risks for a patient are often more defined by their immunotherapy than the underlying individual disease.

Many patients are on more than one drug, thus increasing their overall risk.

All of the drugs listed below would put an individual at an increased risk. The presence of additional risk factors would put them at a moderate or high risk.

These risk factors include:

- high doses of immunotherapy
- use of multiple immunotherapies (not necessarily currently)
- active disease
- swallowing or respiratory muscle weakness
- most importantly, the presence of other co-morbidities, such as interstitial lung disease/pulmonary fibrosis, pulmonary hypertension/pulmonary arterial hypertension, glomerulonephritis/renal impairment (any cause), neutropaenia, lymphopenia, liver disease, diabetes mellitus, ischaemic heart disease, other underlying lung disease (such as asthma, chronic obstructive pulmonary disease; COPD), pregnancy and older age.

Some patients with very active disease, e.g. newly diagnosed and on IV cyclophosphamide, or who have received antibody depleting therapies, particularly those causing hypogammaglobulinemias

(rituximab/ocrelizumab) or alemtuzemab (Campath) may be at high risk.

The following examples illustrate this:

- female aged 35, myasthenia gravis, no co-morbidity on azathioprine – low risk
- female aged 35, myasthenia gravis, no co-morbidity, rituximab <12 months ago – moderate risk
- female aged 35, myasthenia gravis, no co-morbidity, rituximab <12 months ago and hypogammaglobulinemia –high risk
- female aged 75, myasthenia gravis, COPD and renal impairment on steroids –high risk.

Patients must not suddenly stop prednisolone and may actually require higher doses during infection.

Patients can continue hydroxychloroquine and sulfasalazine if they are infected with COVID-19

If a patient is infected with COVID-19, they should temporarily stop their conventional DMARD and biological therapy, unless they have myasthenia gravis or neuromyelitis optica (NMO) spectrum disorders. Any cessation should be reported to non-neurological health care professionals. Any questions about cessation in myasthenia or NMO should be discussed with the neurology team first.

Intravenous immunoglobulin probably does not increase risk.

Prednisolone monotherapy up to 10mg monotherapy: low risk. Add an immunosuppressive: medium risk

Prednisolone monotherapy 10-19mg: medium risk. Add an immunosuppressive agent: high risk

Prednisolone monotherapy 20 mg or greater: high risk

Methotrexate (M)

Leflunomide (M)

Azathioprine (H) and 6-mercaptopurine (M)

Mycophenolate mofetil (M/H)

Myfortic (M/H)

Cyclophosphamide IV or oral (H)
Ciclosporin (M)
Tacrolimus (M)
NOTE: the following biological therapies may or may not be on a primary care record/database as they are prescribed in secondary care but can be searched for on HES if given in a day-case unit, e.g. X92.1 includes rituximab, tocilizumab and infliximab. Subcutaneous drugs, e.g. adalimumab and etanercept, are supplied by homecare companies. The receipt of most biologics probably puts the patient in the moderate or high risk categories (there are some exceptions in the multiple sclerosis category).
Rituximab (Mabthera, Truxima, Rixathon), especially if given in last 12 months and/or with low CD19 and CD27 counts
All anti-TNF drugs: etanercept (e.g. Enbrel, Elrezi, Benepali), adalimumab (e.g. Humira, Amgevita), infliximab (e.g. Remicade, Inflectra), golimumab, certolizumab
Tocilizumab – unable to mount a CRP response, IV or s/c
Abatacept IV or SC
JAK inhibitors (e.g. baricitinib oral, tofacitinib oral)
Belimumab IV
Anakinra SCc
Secukinumab
Ixekizumab
Apremilast (L)

Sarilumab
Ustekinumab
Multiple sclerosis drugs- see link for details. Outline summarised below: https://cdn.ymaws.com/www.theabn.org/resource/collection/6750BAE6-4CBC-4DDB-A684-116E03BFE634/ABN_Guidance_on_DMTs_for_MS_and_COVID19_APPROVED_11_March.pdf
Beta interferons (Avonex, Betaferon, Extavia, Rebif, Plegridy) no increased risk
Glatiramer acetate (Copaxone, Brabio) no increased risk
Teriflunomide (Aubagio), Dimethylfumarate (Tecfedera) [L]
Fingolimod (Gilenya) [M]
Natalizumab (Tysabri) no increased risk
Ocrelizumab (Ocrevus) [M]
Cladribine (mavenclad) [M/H] VH for 3 months following treatment
Alemtuzumab (Lemtrada) [M/H] VH for 3 months following treatment
Other treatments not listed elsewhere with an increased risk:
Human stem cell transplant
Apheresis