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The Contraceptive Equity Act and its Effect on Maryland Healthcare

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In May of 2016, the Contraceptive Equity Act was signed by Governor Hogan; the law went into effect on January 1, 2018.[1] This law provides benefits for many patients by decreasing costs and increasing access. Many co-payments for birth control were eliminated, men were given easier access to receive vasectomies, and female patients were allowed access to six months of birth control per visit to the pharmacy.[1] If you combine the Contraceptive Equity Act with a pharmacist's ability to prescribe certain oral contraception, total patient

burden is decreased while simultaneously increasing access to appropriate contraception. An outpatient pharmacy can be a "one stop shop" for patients.

On the surface, this seems to be primarily a topic for outpatient community pharmacies. However, there is also a role for pharmacists who work primarily within a healthcare system. Unintended pregnancies provide a financial cost to healthcare systems, governments, and patients. According to the Centers for Disease Control and Prevention, there were 71,000 unintended pregnancies in the state of Maryland in 2010.[2] In Maryland, the teen birth rate per 1,000 women was 17.8 in 2014.[2] Both of these statistics are above the national averages. While the cost to healthcare systems from unintended pregnancies have not been sufficiently recorded, there is data on government spending. In 2010, the Maryland state government spent $180.9 million on unintended pregnancies; the federal government spent $285.4 million that same year on unintended pregnancies in the state of Maryland.[3] According to the US Department of Agriculture, in 2015 it cost approximately $13,000 per year to raise a child.[4]

How can we help from an inpatient setting? Prior to discharge, discuss if the patient has any needs regarding her contraception. Clarify if she needs any prescriptions refilled and discuss if she has trouble affording her medications or if she has difficulty finding access to a pharmacy. Educate patients on both proper usage of contraception and the laws of the state. Educating patients on these topics can result in a decreased rate of unintended pregnancies, and will decrease financial burden on healthcare systems, the government, and patients.

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Medication Use Safety and Investigational Drugs

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In 1946, the first randomized controlled trial showed the effects of streptomycin on tuberculosis was significantly different from those of a placebo.[1] The framework for clinical trials has vastly evolved since, and advancements in ethical, regulatory and scientific exploration have improved the safety of clinical trials and investigational drugs. This includes ethical milestones including the Declaration of Helsinki and Belmont Report, as well as the regulatory framework for clinical trials that we use today.[1,2] Although these advancements show a commitment to protect patients and ensure medication safety in research, there are additional areas of improvement to be made when handling investigational drugs.

In 2018, the Institute for Safe Medication Practices (ISMP) published a two-part article that identified several potentially dangerous practices with investigational drugs. These practices include naming, drug labels, packaging, and expiration dating.[2,3] The American Society of Health-System Pharmacists (ASHP) and the

Hematology/Oncology Pharmacy Association (HOPA) have both published best practice standards for investigational drugs which recommend development of policies and standard operating procedures pertaining to investigational drug management, storage, temperature, and expiration date monitoring.[3,4] In addition, the Joint Commission's Medication Management Standards require hospitals to address review, approval, supervision, and monitoring.[2,4,5] These best practice standards should be followed by sponsors and pharmacies that handle investigational drugs.

Early phase trials, especially Phase I or II, use abbreviated drug names for the investigational drug that pose look-alike/sound-alike risks.[2,6] Labeling on investigational drugs may be inconsistent, lots or kits may not always have appropriate identification, and outside packaging may be overloaded with information in small font.[1-4] This presents the opportunity for potential errors in selection of an incorrect product in the dispensing to study participants. Any site that conducts a high volume of clinical trials should have an organization system using unique identifiers or protocol numbers to distinguish products.[2,7] The ISMP recommends ready-to-use unit dose packaging when available. Additionally, standardizing label requirements may be warranted in the future to guarantee accuracy, efficiency, and safety.[2]

Many investigational drugs do not utilize barcode scanning, which can be a safety mechanism to ensure the correct patient specific drug is administered. This is often because these products do not include barcodes on labels, and clinical sites would be required to add on their own barcode label.[1,2] Barcode scanning is a standard identified in both ASHP and HOPA best practice guidelines; and although the process is time-consuming it should be encouraged for use with all investigational drugs as it will provide an added layer of safety for research participants.[1-5]

Continued safety advancements in managing investigational drugs will require changes from all parties involved – sponsors, pharmacies, and regulatory bodies. Following best practice guidelines, ISMP recommendations and various regulatory requirements can promote standardization of processes involving investigational drugs such as developing operating procedures for protocol changes, having pharmacists involved with their Institutional Review Board, and creating reference sheets or a pharmacy manual for investigator initiated studies to summarize important protocol information. Advancing the safety of investigational drugs and clinical trials research will help reduce medication errors and improve care provided to research participants.

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Insourcing Compounding Services at the University of Maryland Medical Center

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At the University of Maryland Medical Center (UMMC), we serve as an academic flagship for Maryland. The UMMC Pharmacy Department's primary vision is to be a national leader in quality, service, and patient care. We live our mission by providing the medications needed to the patients at any given time. In order to achieve our dedication to superior clinical care, the pharmacy department must successfully manage inventory control.

Inventory control is the practice of governing inventory to satisfy customer demand. Drug shortages are one of the major challenges of inventory control that pharmacies all across the country face. Our access to medications can often become limited, which in turn causes the Pharmacy Department to reallocate supplies, purchase different products, provide alternatives, and limit the use of specific medications. Insourcing and outsourcing are two key strategies pharmacies must properly manage in order to combat major issues associated with inventory control.

Outsourcing is the process of partnering with an approved outsourcing facility to compound drugs in standard concentrations or packaging. At UMMC, the pharmacy clinical and operations committees decide on all products to be outsourced. Key factors that are considered when selecting a product includes formulary status/restrictions, demand, waste reduction, extended beyond use dating, cost savings, resource limitations, volume excess/workload, error risk, and regulatory compliance. Outsourcing has many advantages such as allowing staff to focus on core in-house activities, promoting efficiency, reducing labor cost, etc. However, there are times when outsourcing facilities are unable to provide us with the final compounded products as expected. Product delivery disruptions result in an increased workload, last minute workflow adjustments, potential patient care delays and an overall increased burden to the pharmacy team.

Insourcing provides a route of cost and inventory stabilization for the pharmacy when there are inconsistencies with outsourcing. Insourcing is the process of preparing standard medications in house versus receiving the products from an outside vendor. Insourcing requires drug product purchasing changes in addition to changes within a facility's infrastructure such as allocating resources to execute the workflow adjustment (i.e., staff additions). Although outsourcing reduces labor costs, insourcing can generate long-term cost savings and control over quality, safety, and inventory.

In May 2018, the Pharmacy Department opened its very own Central IV Lab compounding pharmacy. This new compounding pharmacy uses robotics to compound our fast-moving standard premix bags and syringes. This satellite currently produces a total of 15 medications with extended beyond use dates. Based on real time usage data, the par for each compounded item is determined, adjusted and prepared by the technicians using the robots. Once the prepared items are checked and labeled by the pharmacist, a sample of each batch is sent out for sterility and stability testing by a third party laboratory. The remainder of the batch is quarantined until the sterility results from the lab are received. This typically is a two week process. Product is released for patient use only if it passes sterility testing. We currently compound antibiotics, vasopressors, syringes utilized by anesthesia and specific bags used in specialized services like the operating suite and labor and delivery. We monitor total daily output and waste very little product.

The non-sterile compounding pharmacy is responsible for the preparation of non-sterile compounded oral liquids, topical creams, and ointments. Final dosage forms of oral syringes, unit dose cups, packaged tablets and capsules, and topical creams are also prepared by the non-sterile compounding pharmacy. Preparation is based on the non-commercial availability of the product or even a comparable product, manufacturer shortages or recalls. We are able to buy bulk containers and repack in clinically appropriate doses when they are not available in unit dose packaging. We utilize automatic dispensing cabinet data to adjust pars and plan the daily compounding tasks.

All staff are provided with proper training and must meet required competencies prior to participating in either non-sterile or sterile compounding. The corresponding manager will ensure staff remains up-to-date with current policies, protocols, guidelines, and competency completion. Technicians are responsible for following procedures precisely, seeking guidance from pharmacists, and properly documenting and preparing all compounded products for pharmacist's review. Pharmacists are responsible for reviewing product suitability, appropriate materials, procedure compliance, preparation accuracy, beyond-use dating appropriateness, documentation, and product testing when necessary. All preparations are made in accordance with USP chapters <795> Non-Sterile Compounding, <797> Sterile Compounding, and <800> Hazardous Drugs.

Overall, insourcing has allowed the Pharmacy Department at UMMC to maintain better control of inventory, promote significant cost savings and provide a more complete workflow that incorporates assistance needed with shortages, recalls, or delivery delays. We have significantly reduced the purchasing burden and decreased our dependency on outsourced products. We are able to evaluate needs in real time and adjust production to usage. Our inventory is used to the last possible date and waste has decreased. We no longer need to buy large quantities in fear of delivery problems. In addition, these changes reduce the need to reallocate resources and restrict medications, while still upholding high quality and safety standards. Higher staff satisfaction and a relative shift in expectation has been notable secondary to the implementation of insourcing. Most importantly, this implementation improved the focus of providing superior healthcare to our patients ensuring the pharmacy department consistently supports the University of Maryland Medical Center mission.

New Drug Update: Romosozumab (Evenity®)

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In April 2019, the Food and Drug Administration (FDA) approved romosozumab (Evenity®) for the treatment of osteoporosis in postmenopausal women who are at high risk for fracture (a history of osteoporotic fracture or multiple risk factors for fracture).[1] This subcutaneous injectable agent is a humanized monoclonal antibody (IgG2) developed by Amgen and UCB Pharma which is produced in a mammalian cell line (Chinese Hamster Ovary) via recombinant DNA technology.[1] The use of romosozumab should be limited to 12 months of therapy as the anabolic effects of this agent begin to decline after this time.[1,2]

Mechanism of action: Romosozumab binds to and inhibits sclerostin, a regulatory factor in bone metabolism.[1]

As a result of this inhibition it primarily increases bone formation and decreases bone resorption, to a lesser extent.[1]

Clinical Trial: The FDA approved romosozumab based on the results from two clinical trials that examined the safety and efficacy of this medication in treating postmenopausal women 55-90 years old with osteoporosis. The Fracture Study in Postmenopausal Women with Osteoporosis (FRAME) was an international, randomized, double-blind, placebo-controlled, parallel-group trial that examined the safety of romosozumab.[2] A total of 7180 patients were included in this trial with 3591 assigned to the placebo group and 3589 assigned to the romosozumab group. Patients received either placebo or romosozumab subcutaneously monthly for 12 months followed by 12 months of open-label denosumab given at a dose of 60 mg subcutaneously every 6 months. At 12 months romosozumab was found to have a 73% lower risk of new vertebral fractures and a 36% lower risk of clinical fractures compared to placebo. After transitioning to denosumab, patients in the romosozumab arm had a 75% lower risk of vertebral fracture at 24 months.

The Active-Controlled Fracture Study in Postmenopausal Women with Osteoporosis at High Risk (ARCH) was a randomized, multicenter, double-blind trial that compared the safety and efficacy of romosozumab versus alendronate.[3] A total of 4093 patients were enrolled in this study, with 2047 assigned to receive 70 mg alendronate orally once weekly and 2046 to receive 210 mg romosozumab subcutaneously one time monthly for 12 months. After 12 months, patients in both groups received open-label 70 mg oral alendronate one time weekly for an additional 12 months. At 24 months, patients treated with romosozumab followed by alendronate had a 48% lower risk of new vertebral fracture and a 27% lower risk of clinical fracture compared to treatment with alendronate alone. The safety results found that romosozumab was associated with an increase in serious cardiovascular adverse events and ischemic cardiac events, with 2.5% and 0.8% of patients reporting these events compared to 1.9% and 0.3% in the alendronate group.

Dosage: The recommended dose for romosozumab is 210 mg administered via the subcutaneous route monthly. The total duration of treatment is 12 months. No renal dose adjustment is required. Manufacturer's labeling does not provide dose adjustments for patients with hepatic impairment.

Available Products: Romosozumab is currently available as a solution for subcutaneous injection supplied in a prefilled single-use syringe containing 105 mg/1.17 mL. Two consecutive syringes are required to make a single dose.[1,4]

Adverse Reactions/Events: Common side effects associated with this agent that were observed in clinical trials include arthralgia and injection-site reaction.[1,4] Less common but potential side effects for which patients should be monitored include osteonecrosis of the jaw, hypersensitivity reactions, and atypical femoral fractures.[1] Patients should also be monitored for hypocalcemia.

Warnings and Precautions: The FDA issued a US boxed warning for romosozumab being associated with an increased risk of myocardial infarction, stroke, and cardiovascular death.[1,4] Hypocalcemia is possible with the use of this agent, especially in renal impairment. Therefore, patients require sufficient calcium and vitamin D while being treated with this agent.[1]

Drug-drug Interactions: There are currently no known drug interactions.

Cost: Romosozumab costs $935.90 per prefilled single-dose syringe.[4]

Place in therapy: The place in therapy for romosozumab is not yet known. This agent is used in clinical practice and therapeutic benefits are observed with its use. Some limitations include the duration of therapy for this agent being limited to 12 months and that the body's exposure to the drug decreases as body weight increases.

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New FDA Approval: Selinexor for Refractory Multiple Myeloma

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On Wednesday, July 3rd, 2019, the United States Food and Drug Administration (FDA) approved selinexor (Xpovio®) for relapsed refractory multiple myeloma treatment in combination with dexamethasone. Selinexor is indicated in patients that have received four or more prior therapies and are penta-refractory to standard of care medications for multiple myeloma.[1]

According to the National Cancer Institute, multiple myeloma accounts for 1.8% of all cancers, and has a 52.2% five-year survival .[2] Multiple myeloma is an incurable plasma cell malignancy that arises from genetic mutations in B cells inciting the creation and proliferation of monoclonal plasma cells, which secrete a monoclonal immunoglobulin (m-protein). Evolution of multiple myeloma is thought to start as monoclonal gammopathy (MGUS), develop into smoldering myeloma, and eventually progress to symptomatic myeloma.[3] Myeloma cancer cells may form masses throughout the bone marrow that can destroy surrounding bone, and cause a decreased creation of normal blood cells.

Combination therapies utilizing proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies targeting CD38 have revolutionized multiple myeloma management, and have led to significant improvements in patient survival.[5] Immunomodulatory agents such as lenalidomide, pomalidomide, and thalidomide inhibit angiogenesis, inhibit adhesion of myeloma cells to extracellular matrix proteins in the bone marrow, and enhance the host immune response against myeloma cells. Proteasome inhibitors such as bortezomib, carfilzomib, and ixazomib inhibit proteasomes causing accumulation of abnormal proteins in the myeloma cell, and eventually lead to myeloma cell death. Additionally, inhibition of proteasomes downregulate NF kb signaling, thereby downregulating angiogenesis factors, cytokine signaling, and cell adhesion in the microenvironment.[3] Daratumumab and elotuzumab are monoclonal antibodies that target transmembrane glycoproteins, CD-38 and SLAMF7, respectively. Expression of CD38 and SLAMF7 on normal lymphoid and myeloid cells is relatively low, but is highly expressed on myeloma cells. Binding of these targets stimulates the host immune system to increase anti-tumor activity.[5] Other medications that are also considered standard of care medications are dexamethasone and cyclophosphamide.[6] While these agents are highly effective and

have improved outcomes in the treatment of multiple myeloma, patients who relapse and become refractory to these medication classes have a poor prognosis and shorter overall survival.[7] This highlights the importance of the recent approval of selinexor as it can serve as another line of therapy for patients who have progressed on multiple other available treatment options.

Selinexor is the first oral selective inhibitor of nuclear export. It inhibits exportin 1 (XPO1), a major export factor in the nucleus that is overexpressed in cancer cells and correlated with increased bone disease and shorter survival. Selinexor modifies cysteine-528, an essential XPO1 cargo-binding site, that irreversibly inactivates XPO1-mediated nuclear export of cargo proteins like tumor suppressor proteins (TSPs). Trapped TSPs accumulate in the nucleus and ultimately leads to myeloma cell apoptosis. Therefore, this agent recovers endogenous tumor suppressing processes through selective inhibition of nuclear export to target and eradicate tumor cells, but avoid normal cells.[7-8]

The FDA approval of selinexor in combination with dexamethasone was based on the results from the STORM study. This was a phase 2b, multicenter, single arm, open label study that included 122 patients. The approval of selinexor was based on analysis of 83 patients that were penta-refractory to prior therapy with bortezomib, carflizomib, lenalidomide, pomalidomide, and daratumumab due to the greater benefit-risk profile of heavily pretreated patients versus the overall trial population. The population of those 83 patients in this study had a median age of 65, 51% were male, and 58% were white. In these patients the first median response time was four weeks with a range of one to ten weeks, a median response duration of 3.8 months, and an overall response rate (partial response or better) of 25.3%.[7] The National Comprehensive Cancer Network Guidelines for Multiple Myeloma provide different parameters to define a partial response, very good partial response, and complete response. A partial response is defined as a $\geq$50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by $\geq$90% or to <200 mg per 24 hours. A very good partial response is defined as a $\geq$ 90% reduction in serum M-protein and urine M-protein level <100 mg per 24 hours. A complete response is defined as disappearance of any soft tissue plasmacytomas, negative immunofixation on the serum and urine, and <5% plasma cells in bone marrow aspirates.[6]

Selinexor is indicated in patients with relapsed or refractory multiple myeloma in adults who have received four or more prior therapies, and are refractory to at least two proteasome inhibitors, two immunomodulatory agents, and an anti-CD38 monoclonal antibody. Selinexor comes in 20mg tablets, and administration is 80mg/dose twice weekly on days one and three each week for a total weekly dose of 160mg in combination with dexamethasone 20mg also on days 1 and 3. Patients should continue on the agent until unacceptable toxicity or disease progression.[9] Adverse reactions include thrombocytopenia, anemia, neutropenia, infections, gastrointestinal toxicity such as nausea, vomiting, diarrhea, anorexia, and weight loss, hyponatremia, neurological toxicity, and embryo fetal toxicity. Females of reproductive potential and males with a female partner of reproductive potential should be advised of the potential risk to the fetus and the use of effective contraception. Due to selinexor's emetogenic potential adequate antiemetic medications such as 5HT3 antagonists should be provided and patients should be counseled to take their dexamethasone dose before they take their selinexor.

While there are no dosing adjustments required for renal or hepatic impairment, dosing adjustments may be required for toxicities such as thrombocytopenia, neutropenia, anemia, fatigue, hyponatremia, and gastrointestinal toxicities. Overall management for most of these adverse reactions entails dose interruption,

reduction, and supportive care. Dose adjustments for adverse reactions entail decreasing the weekly dose. The first reduction is 100 mg once weekly, then 80 mg once weekly, and last 60 mg once weekly. Selinexor should be discontinued if further dose reduction below 60 mg once weekly is needed due to toxicity.[10] Recommended monitoring parameters for patients on selinexor are complete blood panels, blood chemistries, pregnancy status, body weight, hydration status, signs and symptoms of bleeding, infection, neurotoxicity, GI toxicity, and adherence.[9] While the FDA product label indicates that there have been no dedicated drug interaction studies, selinexor is metabolized by CYP3A4, so CYP3A4 inhibitors and inducers could potentially affect selinexor metabolism.[10]

Ongoing clinical trials with selinexor include the STOMP study and the Boston study.[11, 12, 13] The STOMP study is a phase 1b/2, randomized, open label, multicenter study evaluating the combination of selinexor and dexamethasone with backbone treatments such as lenalidomide, pomalidomide, bortezomib, carfilzomib, or daratumumab in patients with relapsed refractory multiple myeloma who have received more than 1 previous therapy. In 2018, a new arm of the study was added to evaluate selinexor and bortezomib combination in newly diagnosed patients.[11,12] The Boston study is a phase 3, randomized, two arm, active comparator controlled open-label multicenter study in patients with relapsed refractory multiple myeloma that have received 1-3 prior agents for multiple myeloma. It aims to assess the safety and compare the efficacy and health-related quality of life of selinexor/bortezomib/dexamethasone versus bortezomib and dexamethasone.[12,13]

Novel therapeutic agents are continuing to change the landscape of multiple myeloma management. While new treatment modalities are available or under investigation, there is still no cure for multiple myeloma. This highlights the importance of continued research and education about the available pharmacologic interventions in both newly diagnosed patients, and relapsed refractory patients with limited treatment options. The recent approval of selinexor, with a unique mechanism of action, is another step in the right direction toward longer-term management of multiple myeloma.

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Rifapentine for Latent *Mycobacterium tuberculosis* Infection

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Rifapentine is a rifamycin antimycobacterial agent. Like other rifamycins, rifapentine inhibits DNA-dependent RNA polymerase in susceptible strains of *Mycobacterium tuberculosis*. It was originally approved in 1998 for the treatment of active pulmonary tuberculosis (TB) in combination with one or more agents in patients ≥12 years of age; however, it was rarely used in clinical practice due to higher cost. In 2014, the FDA approved an additional indication for the treatment of latent TB in combination with isoniazid in patients ≥2 years of age at high risk of progression to TB disease (high risk patients including those in close contact with active TB patients, recent conversion to a positive tuberculin skin test, HIV-infected patients, or those with pulmonary fibrosis on an X-ray).

Rifapentine is only available as an oral formulation (150 mg tablets). Its bioavailability is 68% with maximum concentrations achieved 4-5 hours after oral administration. It should be administered with food as this has been shown to increase absorption by 40-50% as compared to fasting condition. Rifapentine distributes to many tissues but it does not cross the blood brain barrier. The drug is highly (98%) protein bound, primarily to albumin. Rifapentine is metabolized via hydrolysis to active metabolite 25-desacetyl rifapentine, which contributes to 38% of its clinical activity against *M. tuberculosis*. The drug is predominantly eliminated in the feces (70%) and to a lesser extent via the kidneys (17%), so it does not require renal or hepatic dose adjustment. The drug elimination half-life is approximately 17 hours and its post-antibiotic effect is 104 hours, allowing once weekly dosing.

It is a moderate CYP3A4 inducer and is therefore expected to decrease the levels of all CYP3A4 substrates to an extent. However, compared to rifampin, rifapentine is a significantly less potent inducer and can be used in HIV-positive patients with certain antiretrovirals. Two studies in HIV-positive patients have shown no clinically significant drug interactions when rifapentine was co-administered with raltegravir or efavirenz.[1,2] There is little data with other antiretroviral drugs that are metabolized via CYP3A4, but rifapentine is expected to decrease the levels of these drugs, considering it is a CYP3A4 inducer.[3] The most common adverse drug reactions include red-orange discoloration of bodily fluids, nausea, vomiting and headache. Adverse events were reported in about ~ 4% of patients in studies evaluating weekly rifapentine in combination with isoniazid for latent TB and included flu-like symptoms, fever, headache, dizziness, nausea, vomiting, muscle/bone pain, rash, itching, and red eyes.[4]

The Center for Disease Control and Prevention (CDC) currently recommends four treatment options for latent TB: 1) isoniazid/ rifapentine once weekly for 3 months for all adults and children ≥2 years of age, 2) rifampin daily for 4 months for both adults and children, 3) isoniazid daily or twice weekly for 6 months, though this is not recommended in children or 4) isoniazid daily or twice weekly for 9 months for both adults and children.[5] Historically, isoniazid has been used as the first line choice for latent TB. However, recently an alternative regimen has been gaining momentum. The combination of isoniazid and rifapentine allows for once weekly dosing, for a total of 12 weeks.[6] All regimens are equally safe and effective, but the CDC advocates for more convenient, shorter regimens (i.e. rifapentine/ isoniazid) to improve adherence.[5]

Initially, the CDC recommended rifapentine with isoniazid only in adult HIV-negative adult patients, based on the study conducted in 2011 by Sterling and colleagues with 8,053 subjects. Patients received once weekly

rifapentine (900 mg) plus isoniazid (900 mg) for 3 months or daily isoniazid (300 mg) for 9 months in subjects at a high risk for developing tuberculosis. Three months of the two-drug regimen was as effective as 9 months of isoniazid alone in preventing tuberculosis (0.19% combination therapy vs. 0.43% monotherapy), ultimately leading to the additional FDA approved indication for latent TB. The shorter regimen also had a higher completion rate of 82.1%, as compared to 69.0% (P<0.001), promoting higher rates of adherence.[7] The CDC expanded its recommendations in 2018 to include HIV-positive patients and children aged 2-17 based on a meta-analysis conducted by CDC Work Group which showed that this regimen is safe and effective in these patient populations.[6] Furthermore, rifapentine daily (300-600 mg depending on the weight) plus isoniazid daily (300 mg) for one month was compared to isoniazid daily (300 mg) for 9 months for preventing tuberculosis in HIV-infected patients in a recently published clinical trial by Swindell and colleagues. In contrast to prior studies that examined a 3-month regimen, this one-month regimen was modeled off a murine model which showed that daily treatment with rifapentine plus isoniazid for 1 month was as effective as 3 months of weekly rifapentine plus isoniazid and at least as effective as 6 months of isoniazid alone. The shorter two-drug regimen was non-inferior to the longer duration of isoniazid alone with a primary endpoint occurrence of 2% in both groups, with the primary endpoint being diagnosis of tuberculosis or death from tuberculosis or an unknown cause. This study also had a higher completion rate of 97% with shorter durations, as compared to 90% (P<0.001).[8]

The CDC has also revised their recommendations to allow patients ≥2 years of age to receive self-administered therapy (SAT) with weekly rifapentine/isoniazid. This was based on the randomized control trial conducted by Belknap and colleagues who found that self-administered once weekly isoniazid/rifapentine treatment of latent TB was noninferior to directly observed therapy (DOT) in adult patients. The completion rates in the USA were 77.9% in SAT and 85.4% in DOT group.[9] Rifapentine continues to gain attraction by clinicians for the treatment of latent TB due to shorter duration with improved adherence and potential to eliminate DOT.

Administration	Each dose should be taken with food (preferably a high fat meal) to increase absorption. Tablets may be crushed.	
Dose	**Latent tuberculosis:** Isoniazid orally 15 mg/kg (up to 900 mg) once weekly PLUS rifapentine orally once weekly; 600 mg (26-32 kg) or 750 mg (33-49 kg) or 900 mg (>50 kg) for 3 months.	
Dosage adjustments	No dose adjustments are needed.	
Drug Interactions	**Type of Interaction**	**Recommendation**
	Levels likely decreased by rifapentine: CYP3A4 substrates. Always check for potential drug interactions. Please note that list below is not a complete.	
	Warfarin, SSRIs, venlafaxine, antipsychotics, opioids, midazolam	Monitor carefully.
	Cyclosporine, statins, calcium channel blockers (oral)	Consider alternative therapy.
	Azole Antifungals	Consider alternative therapy; voriconazole is contraindicated.
	Macrolides	Consider alternative therapy or monitor carefully.
	Oral Contraceptives	Women should add or switched to barrier

		method of contraception.
	Anti-retroviral drugs Protease inhibitor NNRTI, except efavirenz CCR5 antagonist INSTI, except raltegravir NRTI	Consider alternative therapy. Do not co-administer. Do not co-administer or contraindicated. Do not co-administer. Do not co-administer. Co-administration is not recommended.
Side effects	Common: headache, dizziness, nausea, vomiting, muscle/bone pain, rash, itching, and red eyes Rare: hepatotoxicity, hypersensitivity	
Monitoring	Baseline liver enzymes (at least AST) in patients with latent TB and with the following: HIV, liver disorders, postpartum period (≤3 months after delivery), regular alcohol use, injection drug use, or use of medications with known possible interactions. Monitor liver enzymes at subsequent clinical visits in patients whose baseline testing is abnormal and for others at risk for liver disease.	

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