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ZERBOR / SHUTTERSTOCK

PART 1

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Abstract: This article reviews seven drugs recently approved by the FDA, including indications, precautions, adverse reactions, and nursing considerations.

Keywords: istradefylline, omadacycline tosylate, pitolisant hydrochloride, prucalopride succinate, romosozumab-aqqg, sarecycline hydrochloride, solriamfetol hydrochloride

THIS ARTICLE reviews seven recently marketed drugs, including:

- two new-generation tetracyclines.
- an adjunctive treatment for managing "off" episodes in patients with Parkinson disease.
- the first in a new class of drugs indicated to treat osteoporosis in postmenopausal women at high risk for fracture.

Unless otherwise specified, the information in the following summaries applies to adults, not children. Consult a pharmacist or the package insert for information on drug safety during pregnancy and breastfeeding. Consult a pharmacist, the prescribing information, or a current and comprehensive drug reference for more details on precautions, drug interactions, and adverse reactions for all these drugs.

SELECTED REFERENCES

Drug Facts and Comparisons. St. Louis, MO: Facts and Comparisons, Inc.; 2020.

Nursing2020 Drug Handbook. Philadelphia, PA: Lippincott Williams & Wilkins; 2020.

Physician's Desk Reference. 72st ed. Montvale, NJ: Medical Economics; 2020.

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DRUG FOR CONSTIPATION

Prucalopride succinate

Relief for patients with chronic idiopathic constipation

Patients who experience persistent constipation for more than 6 months for which there is no apparent explanation (such as obstruction or use of medications such as opioids) are diagnosed with chronic idiopathic constipation (CIC). CIC is experienced most often by older adults and is more common in women than men. Standard treatments for constipation such as increased fiber and laxatives do not provide adequate relief for many patients with CIC.

Indicated to treat CIC in adults, prucalopride succinate (*Motegrity*, Shire) is a selective serotonin-4 (5-HT_4) receptor agonist that acts as a gastrointestinal prokinetic agent to stimulate colonic peristalsis.[1] Its effectiveness was evaluated in six placebo-controlled clinical trials in approximately 2,500 patients with onset of constipation symptoms more than 6 months before screening, and who had fewer than three complete spontaneous bowel movements (CSBMs) per week. For the primary efficacy endpoint, a responder was defined as a patient with an average of three or more CSBMs per week over a 12-week treatment period. In five of the six studies, the responder rate was significantly higher in the patients treated with prucalopride (responder rates ranging from 19% to 38% in the five studies), than in those receiving placebo (responder rates ranging from 10% to 18%). When results were based on an alternative efficacy endpoint, the responder rate in the same five studies was also significantly higher in the patients treated with prucalopride than in those receiving placebo.

Severe diarrhea occurred in 2% of those treated with the new drug, compared with 1% of those receiving placebo. Most patients who experienced diarrhea reported it in the first week of treatment, and it usually resolved within a few days.

Precautions: (1) Contraindicated in patients with intestinal perforation or obstruction due to structural or functional disorder of the gut wall, obstructive ileus, or severe inflammatory conditions of the intestinal tract such as Crohn disease, ulcerative colitis, and toxic megacolon/megarectum. (2) Suicides, suicide attempts, and suicidal ideation have been reported in the clinical studies of prucalopride, but a causal association between the drug and these events has not been established. Patients, caregivers, and family members should be counseled to report any unusual changes in mood or behavior. (3) The dosage of prucalopride should be reduced in patients with severe renal impairment.

Adverse reactions: headache, abdominal pain, nausea, diarrhea, abdominal distension, dizziness, vomiting, flatulence, fatigue

Supplied as: 1 mg and 2 mg tablets

Dosage: 2 mg once a day

Nursing considerations: (1) Tell patients they can take each dose without regard to food. (2) Warn patients and caregivers about the risk of depression and suicidal ideation and instruct them to report any unusual change in mood or behaviors. (3) Tell patients to keep the medication in its original container to protect it from moisture.

REFERENCE

1. Motegrity (prucalopride) tablets, for oral use. Prescribing information. www.mogrityhcp.com.

ANTIPARKINSON DRUG

Istradefylline

Unique action decreases "off" episodes

Approximately one million Americans have Parkinson disease (PD), and an estimated 50,000 people are diagnosed with this disorder each year. It is the second most common neurodegenerative disorder in the US after Alzheimer disease.[1]

PD is associated with a reduction in dopamine activity in the brain. Most medications used to treat PD are dopaminergic or dopamine agonist drugs, which increase the concentration and activity of this neurotransmitter. The combination of levodopa and carbidopa is the most effective treatment for PD's motor signs, but its effectiveness diminishes with long-term use. Over time, patients experience more and/or longer "off" episodes: periods during treatment in which PD motor signs such as tremor and difficulty walking increase.[1]

Istradefylline (*Nourianz*, Kyowa Kirin) is an adenosine receptor antagonist indicated as adjunctive treatment to levodopa/carbidopa in adults with PD experiencing "off" episodes. Its precise mechanism of action is not known but its benefit is thought to result from its antagonism of adenosine A_{2A} receptors. This action is unique among drugs used to treat PD.[2]

The effectiveness of istradefylline was evaluated in four placebo-controlled clinical trials in which the primary endpoint was the change from baseline in the daily awake percentage of "off" time. A secondary efficacy endpoint was a change from baseline in "on" time without troublesome dyskinesia. Compared with placebo, patients treated with istradefylline experienced a statistically significant decrease in the percentage of daily awake "off" time and an increase in "on" time without troublesome dyskinesia.

Some patients treated with certain antiparkinson agents, particularly the dopamine agonists, and levodopa to a lesser extent, have experienced impulse control disorders/compulsive behaviors, such as intense urges to gamble or spend money, binge or compulsive eating, and/or increased sexual urges, and the inability to

control these urges. One patient in the clinical studies who was treated with istradefylline at a dosage of 40 mg/day was reported to have impulse control disorder. No patients taking 20 mg/day or placebo experienced this adverse reaction.

Precautions: (1) Istradefylline may cause dyskinesia or exacerbate preexisting dyskinesia; in clinical trials, this was the most common reason for discontinuation of treatment. (2) Because of the potential for hallucinations and the risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with istradefylline. If a patient develops hallucinations or psychotic behaviors during treatment, a reduction of dosage or discontinuation of treatment should be considered. (3) If a patient experiences obsessive/compulsive behaviors during treatment with istradefylline, reducing the dosage or discontinuing treatment should be considered. (4) Women of reproductive potential should be advised to use effective contraception during treatment. (5) Istradefylline has not been studied in patients with severe hepatic impairment and use in these patients should be avoided. (6) Istradefylline's activity may be affected by concurrent use of strong CYP3A4 inducers (such as carbamazepine, rifampin, and St. John's wort), strong CYP3A4 inhibitors (such as clarithromycin and itraconazole), CYP3A4 substrates (such as midazolam and atorvastatin), and/or P-glycoprotein substrates such as digoxin. Consult the prescribing information for more information and recommended dosage adjustments.

Adverse reactions: dyskinesia, dizziness, constipation, nausea, hallucination, insomnia

Supplied as: 20 mg and 40 mg tablets

Dosage: 20 mg once a day. The dosage may be increased to a maximum of 40 mg once a day, based on the need of the patient and tolerability. Consult the prescribing information for recommended dosage adjustments for patients with hepatic impairment and those who smoke heavily.

Nursing considerations: (1) Tell patients they can take each dose without regard to food. (2) Teach patients and caregivers to monitor for potentially serious adverse reactions, such as dyskinesias, psychotic symptoms, or obsessive/compulsive behaviors, and to report worrisome signs and symptoms. (3) Tell patients to inform their healthcare provider about their smoking status and about all of the medications they are taking or plan to take, including over-the-counter and herbal products and dietary supplements.

REFERENCES

1. US Food and Drug Administration. FDA approves new add-on drug to treat off episodes in adults with Parkinson's disease. News release. August 27, 2019.

2. Nourianz (istradefylline) tablets, for oral use. Prescribing information. www.nourianzhcp.com.

DRUGS FOR EXCESSIVE SLEEPINESS

Solriamfetol hydrochloride

Indicated for patients with narcolepsy or OSA

Patients with narcolepsy and obstructive sleep apnea (OSA) often experience excessive daytime sleepiness. Solriamfetol hydrochloride (*Sunosi*, Jazz) is a dopamine and norepinephrine reuptake inhibitor indicated to improve wakefulness in adults with excessive daytime sleepiness associated with narcolepsy or OSA.[1] It is not indicated to treat the underlying airway obstruction in OSA. For patients with OSA, interventions such as continuous positive airway pressure (CPAP) should be employed for at least 1 month before initiating solriamfetol for excessive daytime sleepiness. The new drug should be used in addition to, and not as a substitute for, interventions such as CPAP.

The effectiveness of solriamfetol in patients with narcolepsy was evaluated in a placebo-controlled study in which patients were assessed using three validated tools for measuring excessive sleepiness. Compared with the placebo group, patients treated with solriamfetol at a dosage of 150 mg/day showed statistically significant improvements on all three tools.

In patients with OSA, solriamfetol was also evaluated in a placebo-controlled study that produced similar statistically significant results. In both studies, the effects were apparent at Week 1 and consistent with the results at Week 12.

The maintenance effect of solriamfetol was assessed in two studies in which some patients were continued on a stable dosage of the new drug while others were switched to placebo. Compared with the patients who remained on treatment with solriamfetol, those randomized to placebo experienced statistically significant worsening of sleepiness.

Solriamfetol has a potential for abuse and is included in Schedule IV. Data to assess the risk of using solriamfetol during pregnancy is insufficient. A pregnancy exposure registry is available to monitor pregnancy outcomes in women who use the drug during pregnancy. Patients may be enrolled by calling 1-877-283-6220.

Precautions: (1) Solriamfetol has not been evaluated in patients with psychosis or bipolar disorders. Patients with these disorders should be closely monitored for potential psychiatric adverse reactions, including anxiety or irritability. (2) Before treatment starts, the patient's BP should be assessed and preexisting hypertension controlled. Solriamfetol increases BP and heart rate in a dose-dependent manner. Regularly monitor BP throughout treatment. (3) Use caution in patients

who are being treated concurrently with other drugs that increase BP and heart rate, and/or that have a dopaminergic action. (4) Use of the new drug is not recommended in patients with unstable cardiovascular disease, serious dysrhythmias, or other serious cardiac problems. (5) Because of the risk of a hypertensive reaction, the use of solriamfetol is contraindicated in patients being treated with a monoamine oxidase inhibitor (MAOI), or within 14 days following the discontinuation of an MAOI. (6) A dosage reduction is recommended for patients with moderate or severe renal impairment because they may be at greater risk for adverse reactions. Solriamfetol is not recommended in patients with end-stage renal disease.

Adverse reactions: headache, nausea, anorexia, insomnia, anxiety

Supplied as: 75 mg (functionally scored) and 150 mg tablets

Dosage: *Starting dose for patients with narcolepsy:* 75 mg/day. *Starting dose for patients with OSA:* 37.5 mg/day. Doses may be increased at intervals of at least 3 days to a maximum dose of 150 mg/day. Consult the prescribing information for recommended dosage adjustments in patients with mild to moderate renal impairment.

Nursing considerations: (1) Teach patients to take solriamfetol once a day upon awakening. Warn them not to take a dose within 9 hours of planned bedtime because of the drug's potential to interfere with sleep if taken too late in the day. (2) For patients taking a 37.5 mg dose, the 75 mg tablet is functionally scored to be broken in half. (3) Inform patients that solriamfetol is a federally controlled substance because it has the potential to be abused. Advise them to keep their medication in a secure place and to dispose of unused medication as recommended in the Medication Guide provided with the drug. (4) Educate patients about potentially serious adverse reactions. Tell them to have their BP checked regularly as directed by the healthcare provider and to report any disturbing psychiatric adverse reactions, including anxiety, insomnia, irritability, agitation, and mood swings.

REFERENCE

1. Sunosi (solriamfetol) tablets, for oral use, CIV. Prescribing information. https://pp.jazzpharma.com/pi/sunosi.en.USPI.pdf.

Pitolisant hydrochloride

Indicated for patients with narcolepsy only

Pitolisant hydrochloride (*Wakix,* Harmony) joins solriamfetol as the second new drug to be marketed in 2019 to treat excessive daytime sleepiness in adult patients with narcolepsy. Although pitolisant's specific mechanism of action is unclear, its effectiveness is thought to be mediated through its activity as an antagonist/inverse agonist at histamine-3 (H3) receptors. Unlike solriamfetol, it is not indicated to treat excessive sleepiness in patients with OSA.[1]

Pitolisant was evaluated in two clinical studies in which it was compared with placebo and modafinil, a mild stimulant indicated to improve wakefulness in adults with excessive sleepiness associated with narcolepsy, OSA, and shift work disorder. The primary endpoint was a reduction in scores on the Epworth Sleepiness Scale (ESS). When compared with placebo, pitolisant provided a statistically significant reduction/improvement in ESS scores, but it was not determined to be noninferior to modafinil. However, unlike modafinil and other medications prescribed for excessive daytime sleepiness in patients with narcolepsy, pitolisant is not classified as a controlled substance.

The new drug's safety in pregnancy has not been studied. A pregnancy exposure registry has been established to monitor outcomes in women who use the drug during pregnancy. Patients can enroll by calling 1-800-833-7460.

Precautions: (1) Pitolisant may prolong the QT interval. Avoid its use in patients with a history of cardiac dysrhythmias or who have risk factors for dysrhythmias, including congenital prolongation of the QT interval, symptomatic bradycardia, hypokalemia, or hypomagnesemia. Its use should also be avoided in patients taking other medications known to prolong the QT interval, such as class Ia antiarrhythmic agents (quinidine, procainamide, or disopyramide), class III antiarrhythmic agents (amiodarone or sotalol), certain antipsychotic medications (ziprasidone, chlorpromazine, or thioridazine), and antibacterial drugs such as moxifloxacin. (2) Because pitolisant increases histamine concentrations in the brain, its activity may be reduced by the concurrent use of H1 receptor antagonists that cross the blood-brain barrier, such as the antihistamines diphenhydramine and promethazine, and certain tri- and tetracyclic antidepressants such as imipramine and mirtazapine. The concurrent use of such agents with opposing pharmacologic actions should be avoided. (3) The risk of prolongation of the QT interval is increased in patients with hepatic and/or renal impairment; closely monitor treatment in these patients. (4) Pitolisant is contraindicated in patients with severe hepatic impairment and the dosage should be reduced in patients with moderate hepatic impairment. Dosage should also be reduced in patients with moderate or severe renal impairment. It is not recommended for use in

patients with end-stage renal disease. (5) Pitolisant interacts with many drugs, including sensitive CYP3A4 substrates such as hormonal contraceptives. Consult the prescribing information for warnings and recommended dosage adjustments.

Adverse reactions: insomnia, nausea, anxiety

Supplied as: 4.45 mg and 17.8 mg film-coated tablets

Dosage: Initially, 8.9 mg (two 4.45 tablets) once a day during Week 1. In Week 2, the dosage is increased to 17.8 mg once a day. In Week 3 and thereafter, the dosage may be increased to 35.6 mg (two 17.8 mg tablets) once a day. Consult the prescribing information for dosage adjustments for patients with renal or hepatic impairment and those taking medications that may interact with pitolisant.

Nursing considerations: (1) Teach patients to take each daily dose in the morning upon awakening. Inform them that they may not achieve a clinical response for up to 8 weeks. (2) Tell patients to immediately contact the healthcare provider or seek emergency care if they feel faint, lose consciousness, or experience heart palpitations. (3) Because of the potential for drug interactions, instruct patients to inform the healthcare provider before they start using any new prescription or over-the-counter drugs or supplements. (4) Advise women using hormonal contraception to use an alternative nonhormonal contraceptive method during treatment with pitolisant and for at least 21 days following discontinuation of treatment. Encourage patients who become pregnant to enroll in the pregnancy registry by calling 1-800-833-7460.

REFERENCE

1. Wakix—pitolisant hydrochloride tablet, film coated. Prescribing information. https://wakix.com.

ANTIBACTERIAL DRUGS

Omadacycline tosylate

One of a new generation of tetracyclines designed to overcome drug resistance

The ability of many bacteria to develop mechanisms of resistance to antibacterial drugs is a growing concern. The CDC estimates that drug-resistant bacteria cause 2 million illnesses and approximately 23,000 deaths each year in the US. *Streptococcus pneumoniae*, the bacterium most often responsible for causing community-acquired bacterial pneumonia (CABP), causes 1.2 million infections and 7,000 deaths, and acute bacterial skin and skin structure infections (ABSSSI) result in more than 750,000 hospitalizations.[1] Although older antibacterial agents are still highly effective for many patients with these infections, drug-resistant strains of bacteria may cause serious and even fatal infections for which effective alternative treatments are limited or not available.

Omadacycline tosylate (*Nuzyra*, Paratek) is a broad-spectrum, semisynthetic tetracycline antibacterial drug that has been structurally modified to be effective against certain strains of bacteria resistant to older tetracyclines. It binds to the 30S ribosomal subunit and blocks bacterial protein synthesis and is generally bacteriostatic. Representing a new class of antibiotics called aminomethylcyclines, omadacycline was designed to overcome bacterial resistance to tetracyclines.[1,2]

Omadacycline is available in I.V. and oral formulations. It is indicated to treat adults with CABP and adults with ABSSSI caused by susceptible microorganisms, as identified in the prescribing information.

Other antibacterial agents are usually considered for first-line treatment of patients with either CABP or ABSSSI. However, for patients whose infections do not respond adequately or who have a history of hypersensitivity or other risks to the standard antibacterial regimens, omadacycline may be a highly effective alternative.

The effectiveness of omadacycline for treating CABP was evaluated in a study in which it was compared with moxifloxacin. Omadacycline was found to be noninferior to moxifloxacin, with a clinical response rate at the posttherapy evaluation visit (5 to 10 days after the last dose) of 88%, compared with 85% with moxifloxacin.

For treating patients with ABSSSI (cellulitis, major abscess, wound infection), two studies were conducted to compare omadacycline with linezolid. The new drug was noninferior to linezolid in both studies.

Precautions: (1) Contraindicated in patients with known hypersensitivity to any of the tetracyclines. (2) Monitor patients for development of *Clostridioides* (formerly *Clostridium*) *difficile*-associated diarrhea, which has been reported with the use of almost all systemic antibacterial drugs. (3) As with other tetracyclines, the labeling for omadacycline includes warnings regarding tooth discoloration and enamel hypoplasia, as well as inhibition of bone growth. These risks are related to exposure to tetracycline drugs during the last half of pregnancy, infancy, and childhood. The labeled indications for omadacycline are for adult patients, and the use of any of the tetracyclines in infants and children younger than 8 years or during the second or third trimester of pregnancy is not recommended. In addition, breastfeeding is not recommended during treatment and for 4 days after the last dose. (3) Omadacycline has the potential to cause other adverse reactions associated with tetracyclines, such as photosensitivity, pseudotumor cerebri, and antianabolic effects. (4) Tetracyclines may reduce plasma prothrombin activity. Patients who are taking an anticoagulant concurrently may require a lower

dosage of the anticoagulant. (5) Multivalent cations can reduce the antibacterial activity of tetracyclines. Omadacycline should not be administered through the same I.V. line with any solution containing cations such as calcium and magnesium. Following the oral administration of omadacycline, multivalent cation-containing products such as multivitamins, dairy products, and certain antacids should not be taken for 4 hours.

Adverse reactions: nausea, vomiting, infusion site reactions, hypertension, headache, diarrhea, insomnia, constipation, increased serum alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase

Supplied as: 150 mg capsules for oral administration. For I.V. administration, it is supplied as a lyophilized powder in single-dose vials in an amount equivalent to 100 mg of omadacycline. The contents of a vial should be reconstituted with 5 mL of Sterile Water for Injection, 0.9% Sodium Chloride Injection, or 5% Dextrose Injection. The resultant solution (or 10 mL if two vials are used to provide a dose of 200 mg) should be diluted within 1 hour to 100 mL with 0.9% Sodium Chloride Injection or 5% Dextrose Injection.

Dosage: In patients with CABP, the dosage on Day 1 is 200 mg by I.V. infusion over 60 minutes, or 100 mg by I.V. infusion over 30 minutes twice during Day 1. The maintenance dosage is 100 mg by I.V. infusion over 30 minutes once a day, or 300 mg orally once a day for 7 to 14 days. The same dosage regimen may be used in patients with ABSSSI. An alternative dosage regimen in patients with ABSSSI is to administer omadacycline orally in a loading dose of 450 mg once a day on Days 1 and 2, followed by a maintenance dosage of 300 mg once a day for 7 to 14 days.

Nursing considerations: (1) When reconstituting the medication, gently swirl the contents and let the vial stand until the cake has completely dissolved and any foam disperses. Do not shake the vial. (2) Ask patients about any previous hypersensitivity reactions to any class of antibacterials. Teach them that signs and symptoms of a serious allergic reaction require immediate treatment. (3) Warn women of childbearing potential about the risk of adverse developmental effects in infants and children and advise them to use effective contraception during treatment. (4) Food significantly reduces the rate and extent of omadacycline absorption. Tell patients to fast for at least 4 hours before taking an oral dose and take each dose with water. Following oral administration, they should not consume food or beverages (except water) for at least 2 hours. Antacids containing aluminum, magnesium, or calcium; iron preparations; bismuth subsalicylate; multivitamins; or dairy products should not be taken for 4 hours.

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1. Biospace.com. Paratek announces FDA approval of Nuzyra(tm) (omadacycline). Globe Newswire. October 2, 2018. www.biospace.com/article/paratek-announces-fda-approval-of-nuzyra-omadacycline-/.

2. Nuzyra (omadacycline) for injection, for intravenous use. Nuzyra (omadacycline) tablets, for oral use. Prescribing information. www.accessdata.fda.gov/drugsatfda_docs/label/2018/209816_209817lbl.pdf.

Sarecycline hydrochloride

Indicated to treat acne

Sarecycline hydrochloride (*Seysara*, Almirall) is the fifth tetracycline derivative to be approved for the oral treatment of acne vulgaris, joining doxycycline, minocycline, tetracycline, and demeclocycline. Unlike the other tetracyclines, which have a broad spectrum of antibacterial activity, sarecycline has a narrow spectrum of activity. Its spectrum of action includes *Cutibacterium acnes* (formerly *Propionibacterium acnes*), the bacterium most often implicated in acne, as well as certain staphylococci and streptococci.[1]

Sarecycline is indicated to treat inflammatory lesions of nonnodular moderate to severe acne vulgaris in patients age 9 years and older. The benefit of tetracyclines in treating acne is thought to result from their antibacterial and anti-inflammatory properties. Treating acne is this drug's only labeled indication.

Use of sarecycline has the potential to permit development of bacterial resistance to other tetracyclines. Accordingly, sarecycline and other oral antibacterial drugs should be reserved for use only in patients with acne who do not respond adequately to topical treatments such as benzoyl peroxide and topical retinoids. Sarecycline should not be used concurrently with oral retinoids.

Precautions: (1) Sarecycline is contraindicated in patients with a history of hypersensitivity to any of the tetracycline derivatives. (2) Like other antibiotics, sarecycline may promote the overgrowth of nonsusceptible organisms, leading to superinfection. Vulvovaginal mycotic infection and vulvovaginal candidiasis were experienced in 0.8% and 0.6%, respectively, of female patients in the clinical studies. (3) Monitor patients for *C. difficile*-associated diarrhea and discontinue the drug if this develops. (4) The risks and precautions associated with other drugs in the tetracycline class of medications also apply to sarecycline. For example, it may cause photosensitivity during treatment, adverse developmental effects if used in pregnant women, and permanent discoloration of the teeth if it is used during the second and third trimesters of pregnancy, infancy, childhood up to the age of 8 years, and in nursing mothers. Sarecycline should not be used by women attempting to conceive a child or by their male partners,

based on evidence of adversely affected spermatogenesis with high doses in animal studies. (5) Avoid concurrent use of sarecycline with isotretinoin, which is sometimes prescribed to treat severe acne. Intracranial hypertension, characterized by headache and visual disturbances, has been infrequently reported with the tetracyclines and isotretinoin, also has the potential to cause intracranial hypertension. (6) Because sarecycline may depress plasma prothrombin activity, patients being treated with an anticoagulant may require a reduced dosage of the anticoagulant. (7) Because tetracyclines may interfere with the bactericidal action of penicillin derivatives, the concurrent use of sarecycline should be avoided in patients being treated with a penicillin. (8) If used concurrently with a P-gp substrate such as digoxin, the dosage of the latter agent may have to be reduced.

Adverse reaction: nausea

Supplied as: 60 mg, 100 mg, and 150 mg tablets

Dosage: 60 mg/day in patients weighing between 33 and 54 kg, 100 mg/day in patients weighing between 55 and 84 kg, and 150 mg/day in those weighing between 85 and 136 kg

Nursing considerations: (1) Document the patient's allergy history and teach patients to recognize signs and symptoms of a hypersensitivity reaction. (2) Sarecycline may be taken without regard to food but tell patients to take each dose with plenty of fluid to reduce the possibility of esophageal irritation and ulceration. (3) Inform patients about the risk of photosensitivity. To prevent severe sunburn, advise them to avoid or minimize exposure to natural or artificial sunlight during treatment. (4) Some patients treated with tetracyclines have experienced central nervous system effects such as lightheadedness, dizziness, or vertigo. Warn patients not to drive or engage in other activities requiring their full attention until they learn how the medication affects them. (5) Inform patients that antacids and other products containing multivalent cations such as aluminum, magnesium, iron, and calcium may reduce the absorption and effectiveness of sarecycline. Tell them to separate administration of sarecycline and any of these products by several hours. (6) Teach patients to inform the healthcare provider if they develop diarrhea or watery stools during therapy. (7) Inform female patients that sarecycline may injure an unborn or nursing infant. Tell them to discontinue the drug and contact the healthcare provider if they become pregnant.

REFERENCE

1. Seysara (sarecycline) tablets for oral use. Prescribing information. www.accessdata.fda.gov/drugsatfda_docs/label/2018/209521s000lbl.pdf.

DRUG FOR OSTEOPOROSIS

Romosozumab-aqqg

The first sclerostin inhibitor stimulates osteoblastic activity

Osteoporosis, which is characterized by a reduction in bone mineral density and bone strength, is often asymptomatic until a fracture occurs. It is most common in women following menopause when a reduction in estrogen concentrations results in a bone remodeling imbalance in which bone loss (resorption) exceeds bone formation. In the US, an estimated 10 million people have osteoporosis.[1]

The glycoprotein sclerostin is a regulatory factor in bone metabolism that inhibits activation of osteoblast function and bone formation. Romosozumab-aqqg (*Evenity*, Amgen), classified as a humanized monoclonal antibody, is the first sclerostin inhibitor. By inhibiting sclerostin, it stimulates osteoblastic activity and increases bone formation and, to a lesser extent, decreases bone resorption. Its primary action is to stimulate bone formation, whereas most other prescription medications used for postmenopausal osteoporosis inhibit bone resorption.

Administered subcutaneously once a month, romosozumab is indicated to treat osteoporosis in postmenopausal women at high risk for fracture, defined as having a history of osteoporotic fracture or multiple risk factors for fracture; and for patients who have failed or are intolerant of other available osteoporosis therapy.[2]

The effectiveness of romosozumab was evaluated in two clinical trials that included more than 11,000 women with postmenopausal osteoporosis who also received calcium and vitamin D supplementation. In the first trial, either romosozumab or placebo was used for the first 12 months, then patients in both groups were treated with denosumab for the next 12 months. Classified as a RANK ligand inhibitor, denosumab binds to RANK ligand, a transmembrane or soluble protein essential for the formation and function of osteoclasts, and modulates calcium release from bone.[3] Romosozumab significantly reduced the occurrence of new vertebral fracture in the first 12 months of treatment compared with those receiving placebo. However, the difference in the occurrence of nonvertebral fractures such as the hip or wrist was not statistically significant.

All patients were treated with denosumab for the next 12-month period. At month 24, 0.6% of patients treated with romosozumab experienced a new vertebral fracture, compared with 2.5% of those receiving placebo followed by denosumab.

In the second trial, women were randomized to receive romosozumab or oral alendronate, a bisphosphonate, during the first 12 months, and all patients were treated with alendronate during the following 12-month period. Of the patients treated with

romosozumab followed with alendronate, 4.1% experienced a new vertebral fracture through month 24, compared with 8% of those who were treated with alendronate alone. Romosozumab followed by alendronate also significantly reduced the risk of nonvertebral fracture. In both clinical trials, romosozumab significantly increased bone mineral density as well.

The beneficial effect of romosozumab declines after 12 monthly doses, so its duration of use should be limited to 12 months. If osteoporosis treatment is still warranted, continued therapy with an antiresorptive agent should be considered.

Precautions: (1) Romosozumab may increase the risk of myocardial infarction, stroke, and cardiovascular death, and this is the subject of a boxed warning in its labeling. Treatment with romosozumab should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. If a patient experiences these events during therapy, treatment should be discontinued. (2) Romosozumab is contraindicated in patients with hypocalcemia. If present, hypocalcemia should be corrected before initiating treatment. (3) Patients with severe renal impairment or who are receiving dialysis are at greater risk for developing hypocalcemia. Serum calcium concentrations should be monitored in these patients, and adequate supplementation with calcium and vitamin D should be provided. (4) Romosozumab is contraindicated in patients with known hypersensitivity to it. (5) One patient in the clinical trials experienced osteonecrosis of the jaw, and one patient experienced an atypical femoral fracture. New or unusual thigh, hip, or groin pain should be evaluated to rule out an incomplete femur fracture.

Adverse reactions: arthralgia, headache

Supplied as: single-use prefilled syringes containing 105 mg of the drug in 1.17 mL of solution

Dosage: 210 mg once a month for 12 doses administered subcutaneously in the abdomen, thigh, or upper arm

Nursing considerations: (1) Romosozumab should be administered by a healthcare professional. Store syringes in a refrigerator but allow them to sit at room temperature for at least 30 minutes before injection. Two separate syringes are needed to provide the dose of 210 mg; these should be administered one after the other. (2) Ensure that patients are adequately supplemented with calcium and vitamin D during treatment. (3) Educate patients about possible adverse reactions, including cardiovascular events, hypocalcemia, atypical femoral fracture, and osteonecrosis of the jaw. Advise them to practice good oral hygiene during treatment and tell their dentist that they are taking romosozumab before undergoing any dental work. (4) Tell patients to seek immediate medical attention if they experience signs and symptoms of a hypersensitivity reaction such as angioedema, erythema multiforme, dermatitis, rash, and urticaria. ■

REFERENCES

1. US Food and Drug Administration. FDA approves new treatment for osteoporosis in postmenopausal women at high risk of fracture. News release. April 9, 2019.

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3. Xgeva (denosumab) injection, for subcutaneous use. Prescribing information. www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/xgeva/xgeva_pi.pdf.

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