New Drugs 2015 PART 2

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THIS ARTICLE reviews eight drugs recently approved by the FDA, including:

> three antibacterial drugs to treat skin and skin structure infections.

> two antidiabetic medications for patients with type 2 diabetes mellitus.

> the first drug approved to treat non-24, a sleep-wake disorder experienced by many people who are totally blind.

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 package insert, 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.; 2015.

Nursing2015 Drug Handbook. Philadelphia, PA: Lippincott Williams & Wilkins; 2015.

Physician's Desk Reference. 69th ed. Montvale, NJ: Medical Economics; 2015.

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DRUG FOR IBD

Vedolizumab

Relief from symptoms of GI inflammation

Ulcerative colitis and Crohn disease are the two main forms of chronic inflammatory bowel disease (IBD). Ulcerative colitis is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon, typically involving the rectum. Crohn disease is characterized by transmural inflammation and skip lesions; it can affect any part of the gastrointestinal (GI) tract but most often affects the ileum and proximal colon.[1] An estimated 1.6 million Americans currently have IBD.[2]

Vedolizumab (*Entyvio*, Takeda) is a humanized monoclonal antibody that acts as an integrin receptor antagonist by specifically binding to alpha-4 beta-7 integrin receptors. These receptors are expressed on the surface of a subset of memory T-lymphocytes that preferentially migrate into the GI tract. Vedolizumab inhibits the migration of memory T-lymphocytes across the endothelium into inflamed GI parenchymal tissue, reducing GI inflammation.

Administered as an I.V. infusion, vedolizumab is approved for adult patients with moderately to severely active ulcerative colitis or moderately to severely active Crohn disease who've had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor blocker or an immunomodulator such as methotrexate or cyclosporin; or who've had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. In patients with ulcerative colitis, the new drug is indicated for inducing and maintaining clinical response, inducing and maintaining clinical remission, improving the endoscopic appearance of the mucosa, and achieving corticosteroid-free remission. In patients with Crohn disease, it's indicated for achieving clinical response, achieving clinical remission, and achieving corticosteroid-free remission.[3]

The effectiveness of vedolizumab was demonstrated in placebo-controlled studies. The extent of the benefits of treatment and the percentage of patients who experienced improvement were greater in patients with ulcerative colitis than in those with Crohn disease.

Because vedolizumab affects immune function, it increases the risk of infection. Patients should be brought up to date with all immunizations according to current guidelines before initiating treatment. However, patients being treated with the drug may receive nonlive vaccines, such as influenza vaccine injection.

Use of the other integrin receptor antagonist, natalizumab, has been associated with an increased risk of progressive multifocal leukoencephalopathy (PML), a rare but often fatal opportunistic infection of the central nervous system. Because of the potential for a similar risk with other integrin receptor antagonists, patients in the clinical studies of vedolizumab were actively monitored for PML, but none developed this infection.

Precautions: (1) Contraindicated in patients with a history of a severe hypersensitivity reaction to the drug or any of the excipients in its formulation. A few hypersensitivity reactions were reported in the clinical studies, including one case of anaphylaxis. Treatment should be discontinued if serious allergic reactions occur. (2) Don't initiate treatment in patients with active, serious infections until the infections are controlled. In patients who develop a severe infection during treatment, withholding therapy should be considered. (3) Because of the risk of PML, monitor patients for any new onset or worsening of neurologic signs or symptoms, such as progressive paresis of the extremities, visual disturbances, confusion, memory deficit, and personality changes. If PML is suspected, the drug should be withheld and a neurologist consulted. If PML is confirmed, the drug should be permanently discontinued. (4) Patients may experience elevations of transaminase and/or bilirubin concentrations. The drug should be discontinued if a patient experiences jaundice or other evidence of significant liver injury.

Adverse reactions: nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough

Supplied as: vials containing 300 mg of the drug in lyophilized form

Dosage: 300 mg via I.V. infusion over 30 minutes at 0, 2, and 6 weeks; then every 8 weeks thereafter

Nursing considerations: (1) Reconstitute the vial contents with 4.8 mL of Sterile Water for Injection. Gently swirl the vial for at least 15 seconds to dissolve the powder. Don't vigorously shake or invert it. Withdraw 5 mL of the reconstituted solution and add it to 250 mL of 0.9% Sodium Chloride Injection. Consult the product labeling for full recommendations for reconstituting and diluting the medication. (2) Administer each dose I.V. over 30 minutes; never give I.V. push. (3) The drug should be administered by a healthcare professional who's prepared to manage hypersensitivity reactions if they occur. Patients should be observed during the infusion until the infusion is complete. (4) The drug should be discontinued if the patient experiences no therapeutic benefit by

week 14 of treatment. (5) Store vials in the refrigerator.

REFERENCES

1. Peppercorn MA, Cheifetz AS. Definition, epidemiology, and risk factors in inflammatory bowel disease. UpToDate; 2015. http://www.uptodate.com.

2. Crohn & Colitis Foundation of America. The facts about inflammatory bowel diseases. http://www.ccfa.org/assets/pdfs/updatedibdfactbook.pdf.

3. Prescribing information. Entyvio (vedolizumab) injection, for intravenous use. http://www.entyvio.com.

ANTIBACTERIAL DRUGS

Dalbavancin Tedizolid phosphate Oritavancin diphosphate

Skin and skin structure infections are most often caused by Gram-positive bacteria such as streptococci and staphylococci. The number of these infections that are caused by methicillin-resistant *Staphylococcus aureus* (MRSA) has rapidly increased in recent years in both community and hospital settings. Hospitalized patients with skin and skin structure infections caused by MRSA usually require, at least initially, treatment with an I.V. antibiotic.

In 2014, three new drugs discussed below were approved for treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible microorganisms. Based on the provisions of the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act, each of these antibiotics has been designated as a Qualified Infectious Disease Product (QIDP) because it's intended to treat a serious or life-threatening infection. Drugs receiving the QIDP designation are given an expedited review of their application and qualify for an additional 5 years of marketing exclusivity.

Dalbavancin

One-two punch

Dalbavancin (*Dalvance*, Durata) is a lipoglycopeptide that's a mixture of five closely related active homologs. It interferes with bacterial cell wall synthesis and exhibits a bactericidal action. Administered via I.V. infusion, dalbavancin is specifically indicated for treatment of adults with ABSSSI caused by susceptible isolates of the Gram-positive microorganisms *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant strains), *Streptococcus pyogenes, Streptococcus agalactiae*, and *Streptococcus anginosus* group (including *S. anginosus, S. intermedius,* and *S. constellatus*). To reduce the development of drug-resistant bacteria and maintain the effectiveness of this and other antibacterial drugs, it should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.[1]

The effectiveness of dalbavancin was demonstrated in two studies in which it was compared with a regimen of I.V. vancomycin with an option to switch to oral linezolid after 3 days. Study results indicated that the new drug was as effective as the vancomycin regimen.

Because dalbavancin has a long duration of action, patients need only two doses administered 1 week apart. Most of a dose is eliminated in the urine as unchanged drug and metabolites, so the dosage should be reduced in some patients with severe renal impairment (creatinine clearance less than 30 mL/min who aren't receiving regularly scheduled dialysis).

Precautions: (1) Contraindicated in patients who've experienced serious hypersensitivity reactions to dalbavancin, which occurred infrequently in clinical trials. Use caution in patients with a history of allergy to other glycopeptides, including vancomycin. (2) Monitor patients for reactions that resemble "red-man syndrome," such as flushing of the upper body, urticaria, pruritus, or rash, which may occur if the infusion is administered too rapidly. The infusion should be slowed or stopped until symptoms subside. To minimize this risk, the drug should be infused over 30 minutes. (4) Monitor patients for *Clostridium difficile*-associated diarrhea, which has been reported with the use of nearly all systemic antibacterial drugs, including dalbavancin.

Adverse reactions: nausea, headache, diarrhea

Supplied as: single-use vials containing 500 mg of the drug as a sterile powder

Dosage: 1,000 mg via I.V. infusion over 30 minutes, followed 1 week later with a dose of 500 mg. Consult the product insert for recommended dosage adjustments for patients with impaired renal function.

Nursing considerations: (1) Reconstitute the powder with 25 mL of Sterile Water for Injection, alternating between gentle swirling and inversion of the vial to avoid foaming. Transfer the required dose of reconstituted dalbavancin solution to an I.V. bag or bottle containing 5% Dextrose Injection. The diluted solution must have a final concentration of dalbavancin of 1 mg/mL to 5 mg/mL. (2) Infuse doses over 30 minutes; avoid rapid administration. (3) Dosage adjustment isn't necessary for patients receiving regularly scheduled hemodialysis.

REFERENCE

1. Prescribing information. Dalvance (dalbavancin) for injection. http://www.duratatherapeutics.com/products/dalvance.

Tedizolid phosphate

As effective as linezolid with less-frequent dosing

Tedizolid phosphate (*Sivextro*, Cubist) is a prodrug that's converted by phosphatases to tedizolid, its active form. It's classified as an oxazolidinone antibacterial drug and has properties that are most similar to those of linezolid.

Administered orally or as an I.V. infusion, it's specifically indicated for adult patients with ABSSSI caused by susceptible isolates of the Gram-positive microorganisms *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant isolates), *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus* group (including *S. anginosus, S. intermedius,* and *S. constellatus*), and *Enterococcus faecalis*. It should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.[1]

The effectiveness of tedizolid (200 mg once a day for 6 days) was demonstrated in two noninferiority studies in which it was compared with linezolid (600 mg every 12 hours for 10 days). With both drugs, the percentages of patients attaining the endpoints in the two studies were approximately 80% and 85%, respectively, and tedizolid was considered to be as effective as the linezolid regimen.

Because *Clostridium difficile*-associated diarrhea is associated with the use of nearly all systemic antibacterial drugs, this possibility should be considered in patients who experience watery diarrhea following use of tedizolid or any other antibacterial agent.

Precautions: (1) Due to the similarity of tedizolid and linezolid, other antimicrobial agents should be considered for use in patients taking a serotonergic agent or a monoamine oxidase inhibitor (MAOI). Although interaction between tedizolid and these drugs hasn't been specifically studied, linezolid is contraindicated in patients taking an MAOI or within 2 weeks of taking an MAOI. The labeling for linezolid also includes a warning regarding the risk of serotonin syndrome with the concurrent use of serotonergic agents such as selective serotonin reuptake inhibitors. (2) Linezolid has been associated with the occurrence of myelosuppression in some patients and weekly complete blood cell count monitoring is recommended. The effectiveness and safety of tedizolid in patients with neutropenia (neutrophil counts less than 1,000 cells/mm^3) have not been adequately evaluated; alternative therapies should be considered in patients with neutropenia and an ABSSSI.

Adverse reactions: nausea, headache, diarrhea

Supplied as: film-coated 200 mg tablets and single-use vials containing 200 mg of the drug as a lyophilized powder

Dosage: 200 mg once a day for 6 days

Nursing considerations: (1) Reconstitute the contents of a vial with 4 mL of Sterile Water for Injection. The reconstituted solution must be further diluted in 250 mL of 0.9% Sodium Chloride Injection. Tedizolid for injection is incompatible with solutions containing divalent cations such as calcium and magnesium, including products such as lactated Ringer injection. (2) Following reconstitution and dilution, administer tedizolid via I.V. infusion over a total time of 1 hour. (3) Tell patients taking oral tablets that doses can be taken without regard to food. (4) Instruct patients to take the full course of treatment as prescribed, even after they feel better, to prevent treatment failure and/or antibiotic resistance. (5) If patients miss a dose, they should take it as soon as possible up to 8 hours prior to the next scheduled dose. After 8 hours, they should wait to take the next scheduled dose. (6) Inform patients about the risk of watery diarrhea, which can develop months after taking the last prescribed dose of antibiotic. Tell them to report severe, prolonged, or bloody diarrhea to their healthcare provider.

REFERENCE

1. Prescribing information. Sivextro (tedizolid phosphate) for injection, for intravenous use; Sivextro (tedizolid phosphate) tablets, for oral use. http://sivextro.com/pdf/sivextro-prescribing-info.pdf.

Oritavancin diphosphate

Only a single dose required

Oritavancin diphosphate (*Orbactiv*, The Medicines Company) is a lipoglycopeptide antibacterial drug with properties that are most similar to those of dalbavancin and telavancin. It acts by inhibiting bacterial cell wall synthesis and disrupting bacterial membrane activity, and exhibits a bactericidal action. Administered I.V., it's indicated for adult patients with ABSSSI caused by susceptible isolates of the Gram-positive microorganisms *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant isolates), *Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus anginosus* group (including *S. anginosus, S. intermedius,* and *S. constellatus*), and *Enterococcus faecalis* (vancomycin-susceptible isolates only). It should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.[1]

The effectiveness of oritavancin (in a single dose of 1,200 mg) was demonstrated in two noninferiority studies in which it was compared with I.V. vancomycin (1 gram or 15 mg/kg every 12 hours for 7 to 10 days). In both studies, oritavancin was considered to be as effective as vancomycin.

Oritavancin has a terminal half-life of approximately 245 hours. Its long duration of action allows treatment for ABSSSI in just a single dose.

Because *Clostridium difficile*-associated diarrhea has been reported with the use of nearly all systemic antibacterial drugs including oritavancin, this possibility should be considered in patients who experience watery diarrhea following use of an antibacterial agent.

Precautions: (1) Contraindicated in patients who've experienced serious hypersensitivity reactions to oritavancin, which have occurred

infrequently. Use caution in patients with a history of allergy to other glycopeptides, including vancomycin. (2) Slow or interrupt the infusion if infusion-related reactions develop, such as pruritus, urticaria, and flushing. (3) In clinical trials, more patients treated with oritavancin experienced osteomyelitis compared with those treated with vancomycin. If osteomyelitis is suspected or confirmed, another antibacterial regimen should be used instead of oritavancin. (4) Closely monitor patients on warfarin for bleeding. Although oritavancin has no effect on the coagulation system, it may result in higher exposure of warfarin, increasing the risk of bleeding. (5) Be aware that monitoring the anticoagulant effect of warfarin is unreliable up to 24 hours after a dose of oritavancin, which has been shown to artificially prolong prothrombin time and international normalized ratio for up to 24 hours and activated partial thromboplastin time (aPTT) for 48 hours. (6) Use of I.V. unfractionated heparin sodium is contraindicated for 48 hours after oritavancin administration because aPTT test results may remain falsely elevated during this period. For patients who require aPTT monitoring within 48 hours of oritavancin administration, a nonphospholipid-dependent coagulation test such as a Factor Xa (chromogenic) assay or an alternative anticoagulant not requiring aPTT monitoring may be considered.

Adverse reactions: nausea, headache, vomiting, diarrhea, limb and subcutaneous abscesses

Supplied as: single-use vials containing a lyophilized powder with the equivalent of 400 mg of oritavancin

Dosage: 1,200 mg via I.V. infusion over 3 hours

Nursing considerations: (1) Three vials of the drug are used to provide the recommended dose of 1,200 mg. The contents of each vial should be reconstituted with 40 mL of Sterile Water for Injection. The reconstituted solution must then be diluted in 5% Dextrose in Sterile Water (D_5W). From a 1,000 mL bag of D_5W, withdraw and discard 120 mL of solution. Forty milliliters of solution should be withdrawn from each of the three vials containing the reconstituted drug and added to the D_5W I.V. bag to bring the bag volume to 1,000 mL. The resulting drug concentration is 1.2 mg/mL. (2) Administer the diluted solution within 6 hours when stored at room temperature, or within 12 hours when refrigerated. (3) Use only D_5W to dilute the reconstituted solution of oritavancin. Sodium Chloride Injection is incompatible with the drug and may cause precipitation.

REFERENCE

1. Prescribing information. Orbactiv (oritavancin) for injection. http://www.themedicinescompany.com/page/orbactiv/1.

ANTIPLATELET DRUG

Vorapaxar sulfate

Long half-life makes it effectively irreversible.

The inhibition of platelet aggregation has been demonstrated to reduce the occurrence of thrombotic cardiovascular events such as myocardial infarction (MI) and stroke in patients at risk. Protease-activated receptors (PARs), particularly PAR-1, are thought to facilitate the action of thrombin in the formation of thrombi. PAR-1 has a high affinity for thrombin and is found primarily on platelets, smooth muscle cells, and endothelial cells.

Vorapaxar sulfate (*Zontivity*, Merck) is classified as a selective, reversible antagonist of the PAR-1 expressed on platelets, but its long half-life makes it effectively irreversible. It inhibits thrombin-induced and thrombin receptor agonist peptide-induced platelet aggregation, and is the first drug with this mechanism of action. It's indicated for the reduction of thrombotic cardiovascular events in patients with a history of MI or with peripheral arterial disease. The new drug has been studied only in regimens that also include aspirin and/or clopidogrel, and experience with its use as a single agent, or with antiplatelet agents other than aspirin and clopidogrel, is very limited.[1]

The effectiveness of vorapaxar was demonstrated in a multicenter, placebo-controlled study (vorapaxar or placebo in addition to aspirin and/or clopidogrel) involving more than 26,000 patients. The primary endpoint was the composite of cardiovascular death, MI, stroke, and urgent coronary revascularization (UCR). A key secondary endpoint was these same events but not including UCR. In patients without a history of stroke or transient ischemic attack (TIA), the 3-year event rate for the primary efficacy endpoint was 10.1% in the patients treated with vorapaxar, compared with 11.8% in the placebo group. With respect to the secondary efficacy endpoint, the 3-year event rate was 7.9% in patients treated with vorapaxar, compared with 9.5% in the placebo group.

Bleeding, the most important risk associated with vorapaxar, was experienced by 25% of patients. Severe bleeding, defined as fatal bleeding, intracranial hemorrhage (ICH), or bleeding with hemodynamic compromise requiring intervention, occurred in 1% of patients. Bleeding risks are identified in a boxed warning in the drug's labeling.

Significant inhibition of platelet aggregation remains for approximately 4 weeks following discontinuation of the drug. No antidote or treatment is available to reverse the drug's antiplatelet effect.

Precautions: (1) Contraindicated in patients with a history of stroke, TIA, or ICH because of an increased risk of ICH. (2) Contraindicated in patients with active pathologic

bleeding such as ICH or peptic ulcer. (3) Discontinue vorapaxar in patients who experience a severe bleeding event during treatment. Withholding the drug for a short time won't manage an acute bleeding event because of the drug's long half-life. (4) Avoid concurrent use of warfarin or another anticoagulant with vorapaxar. Other medications that may increase the risk of bleeding include chronic nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, and serotonin norepinephrine reuptake inhibitors. (5) Vorapaxar isn't recommended for patients with severe hepatic impairment because of the inherent bleeding risks. Dosage adjustment isn't necessary in patients with renal impairment or in those with mild to moderate hepatic impairment. (6) Avoid concurrent use of vorapaxar with a strong CYP3A inhibitor (such as clarithromycin or itraconazole), or a strong CYP3A inducer (such as carbamazepine, rifampin, or St. John's wort).

Adverse reaction: bleeding

Supplied as: film-coated tablets containing 2.5 mg of the drug as the sulfate salt that represents 2.08 mg of vorapaxar

Dosage: one tablet once a day

Nursing considerations: (1) Tell patients that vorapaxar can be taken without regard to food. (2) Inform patients that they'll bleed and bruise more easily while taking this drug, and that the drug's effects will persist for about 4 weeks after they discontinue it. (3) Instruct patients to call 911 if they experience severe or uncontrolled bleeding, and to call their healthcare provider right away to report signs of occult bleeding, such as red, pink, or brown urine; "coffee-ground" vomit; or black tarry stools.

REFERENCE

1. Prescribing information. Zontivity (vorapaxar) tablets. http://www.zontivity.com.

DRUG FOR NON-24

Tasimelteon

First drug approved for this circadian rhythm disorder

Non-24-hour sleep-wake disorder (non-24) is a chronic circadian rhythm (body clock) disorder mostly experienced by people who are totally blind. Because they don't perceive light, they can't synchronize their body clock to the 24-hour light-dark cycle, causing insomnia or excessive sleepiness.[1]

Approximately 1.3 million Americans are legally blind and about 130,000 of them have no light perception. As many as 70% of those who can't perceive light suffer from non-24, which prevents them from establishing a normal sleep-wake schedule.[2] They may have difficulty falling asleep or staying asleep, wake up feeling as if they need more rest, and have difficulty establishing and following a normal daily schedule. Sleep patterns may even be reversed, with a perceived need to sleep during the day and be awake at night.[1,2]

Tasimelteon (*Hetlioz*, Vanda) is a melatonin receptor agonist at MT_1 and MT_2 receptors, the receptors that are thought to be involved in the control of circadian rhythms. Indicated for the treatment of non-24-hour sleep-wake disorder, it's the first medication demonstrated to be effective for treating this disorder.[3]

Tasimelteon was evaluated in two placebo-controlled studies in totally blind patients with non-24. Patients treated with the new drug experienced increased nighttime sleep (mean of 28 minutes longer than with placebo) and reduced daytime sleep duration (mean of 27 minutes shorter than with placebo).

Precautions: (1) Somnolence can occur with use of tasimelteon and it may impair the performance of activities requiring complete mental alertness. (2) Not recommended for use in patients with severe hepatic impairment. (3) Avoid concurrent use with fluvoxamine and other strong CYP1A2 inhibitors, which may significantly increase the exposure and activity of tasimelteon. Also avoid concurrent use with strong CYP3A4 inducers such as rifampin, which may significantly reduce the new drug's exposure and activity.

Adverse reactions: headache, nightmares/abnormal dreams, upper respiratory tract infection, urinary tract infection, increased alanine aminotransferase concentrations

Supplied as: 20 mg capsules

Dosage: 20 mg/day prior to bedtime at the same time every night and apart from food

Nursing considerations: (1) Teach patients to take the drug at bedtime and apart from meals because food may reduce the maximum serum concentration. They should swallow the capsule whole, take it at the same time each day, and limit activity afterward as they prepare for bed. (2) Inform patients who smoke that smoking may reduce the drug's effectiveness. (3) Warn patients that the drug may cause somnolence. Advise them to avoid activities requiring alertness until they determine how the drug affects them. (4) Inform them that the drug may not take effect for weeks or months due to individual differences in circadian rhythms.

REFERENCES

1. Judd BG, Sateia MJ. Classification of sleep disorders. UpToDate; 2014. http://www.uptodate.com.

2. Non-24: A Circadian Rhythm Disorder. http://www.non-24.com/about-non-24.php.

3. Prescribing information. Hetlioz (tasimelteon) capsules, for oral use. http://www.hetliozpro.com.

ANTIDIABETIC DRUGS

Albiglutide

Administered subcutaneously once a week

The third glucagon-like peptide-1 (GLP-1) receptor agonist to be

approved by the FDA, albiglutide (*Tanzeum*, GlaxoSmithKline) joins exenatide and liraglutide. These drugs augment glucose-dependent insulin secretion and also slow gastric emptying, resulting in lower fasting glucose and reduced postprandial glucose excursions in patients with type 2 diabetes. Like the other GLP-1 agonists, albiglutide is administered subcutaneously.

Albiglutide's longer half-life permits once-weekly dosing. Liraglutide is administered once a day and exenatide twice a day; however, the exenatide extended-release formulation is also administered once a week.

Albiglutide is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.[1] Its effectiveness was demonstrated in eight clinical trials that included more than 2,000 patients with type 2 diabetes. Albiglutide was evaluated as a stand-alone therapy, as well as in combination with other antidiabetic agents including metformin, glimepiride, pioglitazone, and/or insulin (but not prandial insulin). Its use resulted in an improvement (lowering) of A1c and fasting plasma glucose concentrations.

In a study in which albiglutide was compared with liraglutide, the new drug provided less of an A1c reduction (0.8%) than liraglutide (1.0%). The limitations of use, warnings, and other risks associated with albiglutide are generally similar to those for the other GLP-1 agonists.

Precautions: (1) Contraindicated for patients with type 1 diabetes and patients with diabetic ketoacidosis. (2) Contraindicated in patients with a personal or family history of medullary thyroid carcinoma and in patients with multiple endocrine neoplasia syndrome type 2; these risks are included in a boxed warning in the drug's labeling. (3) Not recommended as first-line therapy for patients whose blood glucose levels are inadequately controlled by diet changes and exercise. (4) Not recommended in patients with preexisting severe gastrointestinal disease, including severe gastroparesis. (5) Acute pancreatitis has been infrequently experienced with use of the GLP-1 agonists, including albiglutide. Promptly discontinue treatment if pancreatitis is suspected. Other antidiabetic agents should be considered in patients with a history of pancreatitis. (6) Discontinue treatment if a patient experiences a serious hypersensitivity reaction, which occurred in one patient in clinical trials. (7) Use caution when oral medications are used concurrently with albiglutide, particularly if their absorption is incomplete and/or not highly predictable when they're used alone. Because albiglutide delays gastric emptying, a potential exists for alteration of the absorption and activity of concomitantly administered oral medications. (8) Use caution when initiating treatment or increasing the dosage in patients with renal impairment because gastrointestinal adverse reactions to albiglutide have been reported to increase as renal function declines.

Adverse reactions: upper respiratory tract infection, diarrhea, nausea, injection site reaction

Supplied as: a lyophilized powder in 30 mg and 50 mg doses in single-dose pen injectors for reconstitution

Dosage: 30 mg once a week via subcutaneous injection; the dosage may be increased to 50 mg/week if the glycemic response isn't adequate

Nursing considerations: (1) Prior to dispensing, the pen injectors should be stored in the refrigerator. After they're dispensed, the pen injectors may be stored at room temperature for up to 4 weeks before use. (2) Consult the product labeling for information regarding reconstitution of the powder and administration of the injection, and educate patients accordingly. The diluent is supplied in the injector; turning the cartridge on the injector as directed permits mixing the diluent with the powder. Tell patients to administer the reconstituted solution via subcutaneous injection within 8 hours after preparation. (3) Teach patients to administer albiglutide by subcutaneous injection in the abdomen, thigh, or upper arm region on the same day each week. Doses may be administered at any time of the day without regard to meals. (4) If patients miss a dose, they should administer it as soon as possible within 3 days after the missed dose and thereafter on the usual day of administration. If more than 3 days pass after the missed dose, they should wait to administer the next regularly scheduled weekly dose. (5) Teach patients how to recognize and respond to signs and symptoms of hypoglycemia. When used as monotherapy, albiglutide isn't likely to cause hypoglycemia, but this response is a risk when it's used in combination with an insulin secretagogue (such as a sulfonylurea) or insulin. A reduction in dosage of the latter drugs may be necessary. (6) Tell patients to immediately report severe, acute abdominal pain, a possible symptom of pancreatitis.

REFERENCE

1. Prescribing information. Tanzeum (albiglutide) for injection, for subcutaneous use. http://www.tanzeum.com.

Empagliflozin

Third in its class

Empagliflozin (*Jardiance*, Boehringer-Ingelheim; Lilly) is the third drug in a new class of orally administered antidiabetic agents designated as sodium-glucose cotransporter 2 (SGLT2) inhibitors, joining canagliflozin and dapagliflozin. Expressed in the proximal renal tubules, SGLT2 is responsible for the reabsorption of most of the glucose filtered by the kidneys. By inhibiting SGLT2, empagliflozin and the other drugs in this class reduce the reabsorption of filtered glucose, increase urinary glucose excretion, and reduce blood glucose and A1c.

Like canagliflozin and dapagliflozin, empagliflozin is specifically indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.[1] Its effectiveness has been demonstrated in studies in which it was used as monotherapy, or in combination regimens with metformin, glimepiride, pioglitazone, or insulin. The use of empagliflozin resulted in reductions in A1c and fasting plasma glucose (FPG) concentrations and, in many patients, weight reduction. Patients treated with empagliflozin lost an average of approximately 3 kg of body weight, compared with an average loss of 0.4 kg in those receiving placebo. The reductions in A1c and FPG in patients treated with combination regimens that included empagliflozin, as well as the percentage of patients achieving an A1c of less than 7%, were generally similar to those attained with empagliflozin monotherapy.

Empagliflozin isn't recommended for the treatment of patients with type 1 diabetes mellitus or diabetic ketoacidosis.

Although empagliflozin isn't likely to cause hypoglycemia, it can increase the risk of hypoglycemia when used in combination with insulin or an insulin secretagogue such as a sulfonylurea. A lower dosage of the latter drug may be necessary when such combination regimens are used.

Precautions: (1) Contraindicated in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2) or end-stage renal disease, and in patients on dialysis. Renal function should be evaluated before initiating treatment and periodically thereafter. Treatment shouldn't be initiated in patients with an eGFR less than 45 mL/min/1.73 m^2; if the eGFR is persistently less than this value during treatment, the drug should be discontinued. (2) Before initiating therapy, assess and, if necessary, correct volume status in older adults, patients with impaired renal function or low systolic BP, and patients treated with a diuretic. The SGLT2 inhibitors cause intravascular volume contraction that may result in symptomatic hypotension.

Adverse reactions: urinary tract infection, female genital mycotic infection (such as vulvovaginal candidiasis), dyslipidemia, increased urination, male genital mycotic infection (such as balanitis), upper respiratory tract infection

Supplied as: 10 mg and 25 mg tablets

Dosage: 10 mg once a day in the morning; dosage may be increased to 25 mg/day in patients who need additional glycemic control

Nursing considerations: (1) Inform patients that empagliflozin may be administered without regard to food. (2) Tell patients not to use urine glucose tests to monitor glycemic control. Because the SGLT2 inhibitors increase urinary glucose excretion, positive urine glucose tests will result. (3) Teach patients how to recognize and respond to signs and symptoms of hypoglycemia. ■

REFERENCE

1. Prescribing information. Jardiance (empagloiflozin) tablets, for oral use. http://www.jardiance.com.

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