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New Drugs 2017 PART 2

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This article reviews seven drugs recently approved by the FDA, including:

- two highly effective antiviral treatments for hepatitis C virus infection.
- a treatment for gout with a unique mechanism of action.
- a fast-acting drug to reverse the muscle relaxant effects of vecuronium and rocuronium.

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.; 2017.

Nursing2017 Drug Handbook. Philadelphia, PA: Lippincott Williams & Wilkins; 2017.

Physician's Desk Reference. 70th ed. Montvale, NJ: Medical Economics; 2017.

The author and planners have disclosed no potential conflicts of interest, financial or otherwise.

ANTIDIABETIC DRUG

Lixisenatide

Fifth GLP-1 receptor agonist marketed in U.S.

Glucagon-like peptide-1 (GLP-1) is a peptide hormone released soon after a meal is eaten. It's been shown to suppress glucagon secretion from pancreatic alpha cells, stimulate glucose-dependent insulin secretion by pancreatic beta cells, slow gastric emptying, and promote satiety. Lixisenatide (*Adlyxin*, Sanofi; marketed as Lyxumia in many other countries) is the fifth GLP-1 receptor agonist to be marketed in the United States, joining exenatide and extended-release exenatide, liraglutide, albiglutide, and dulaglutide.

Lixisenatide is administered once a day. Like the other drugs in this class, it's administered subcutaneously and is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Its effectiveness was evaluated in 10 clinical trials that enrolled 5,400 patients with type 2 diabetes. The new drug was studied as monotherapy and in combination with other antidiabetic agents, including metformin, sulfonylureas, pioglitazone, and a basal insulin. Lixisenatide provided reductions in hemoglobin A1c and fasting plasma glucose concentrations.

As with the other GLP-1 receptor agonists, lixisenatide isn't recommended as first-line therapy for patients whose diabetes is inadequately controlled with diet and exercise. Metformin is the usual initial treatment of choice in patients with type 2 diabetes who don't have risk factors that would preclude its use, such as severe renal impairment, known hypersensitivity to metformin, or acute or chronic metabolic acidosis. A GLP-1 receptor agonist may be added to the treatment regimen for patients with diabetes who don't experience adequate glycemic control with metformin alone. The limitations of use for lixisenatide are generally similar to limitations for the other GLP-1 receptor agonists.

Lixisenatide has been evaluated in a placebo-controlled cardiovascular outcomes trial in more than 6,000 patients with type 2 diabetes after a recent acute coronary syndromes event. The primary composite endpoint was the time to the first occurrence of a major adverse cardiovascular event, such as cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina. Use of lixisenatide didn't increase or decrease the risk of such events.

Many patients with diabetes are overweight. Numerous patients treated with a GLP-1 receptor agonist have experienced weight loss; in most of the studies of lixisenatide, patients experienced a small loss in weight.

Lixisenatide isn't likely to cause hypoglycemia, but the risk of hypoglycemia increases if a GLP-1 receptor agonist is used in combination with insulin or an insulin secretagogue such as a sulfonylurea. A dosage reduction of the latter agent may be necessary.

Precautions: (1) Not indicated for patients with type 1 diabetes or patients with diabetic ketoacidosis. (2) Not recommended for patients with gastroparesis because the GLP-1 receptor angonists delay gastric emptying. (3) Immediately discontinue use if pancreatitis develops or is suspected. Acute pancreatitis has been infrequently reported with GLP-1 receptor agonists. Other antidiabetic agents should be considered for patients with a history of pancreatitis. (4) Use caution in patients who've experienced a hypersensitivity reaction to another GLP-1 receptor agonist. Serious hypersensitivity reactions including anaphylaxis have been infrequently experienced by patients taking other drugs in this class. (5) Lixisenatide isn't recommended in patients with end-stage renal disease. (6) Acute kidney injury and worsening of chronic renal failure have occurred in a small number of patients treated with a GLP-1 receptor agonist. Most of these events have been reported in patients who experienced severe gastrointestinal (GI) adverse reactions. Closely monitor renal function when initiating treatment or increasing the dosage of lixisenatide in patients with renal impairment and in patients who have experienced serious GI reactions. (7) Because GLP-1 receptor agonists delay gastric emptying, they may reduce the rate at which orally administered medications are absorbed. Oral medications that have a narrow therapeutic index such as warfarin or that otherwise require close monitoring must be used with caution in patients taking lixisenatide.

Adverse reactions: nausea, vomiting, headache, hypoglycemia, diarrhea, dizziness

Supplied as: single-patient-use pens containing 3 mL of solution. The green starter pen used for initiating treatment contains the drug in a concentration of 50 mcg/mL and delivers 14 doses of 10 mcg. The burgundy pen to be used for maintenance treatment contains lixisenatide in a concentration of 100 mcg/mL, and delivers 14 doses of 20 mcg.

Dosage: initially, 10 mcg administered subcutaneously once a day via the green starter pen within 1 hour before the first meal of the day for 14 days. On Day 15, the dosage should be increased to 20 mcg once a day administered via the burgundy maintenance dosage pen.

Nursing considerations: (1) Teach patients to administer lixisenatide by subcutaneous injection in the abdomen, thigh, or upper arm. Review the instructions for use and ensure that patients know how to initiate therapy with the starter pen and maintain therapy with the maintenance pen. Reinforce that a new needle must be attached to the pen for each injection. (2) Instruct patients to administer each dose of the drug within 1 hour of the first meal of the day. (3) Advise patients who must take an oral medication with food to take the oral medication with a meal or snack other than the first meal of the day (that is, not at the same time they administer lixisenatide). Oral medications such as antibiotics that are particularly dependent on threshold concentrations for efficacy and medications such as acetaminophen for which a delay in the onset of action is undesirable should be administered at least 1 hour before lixisenatide. (4) Teach patients to recognize and report signs and symptoms of pancreatitis, such as vomiting and/or persistent severe abdominal pain, which may radiate to the back. (5) Advise women taking an oral contraceptive to take it at least 1 hour before or at least 11 hours after each lixisenatide dose because lixisenatide may interfere with an oral contraceptive's effectiveness. (6) If a dose of lixisenatide is missed, tell patients to administer a dose within 1 hour before the next meal. (7) Tell patients to store pens in a refrigerator prior to the first use. Pens in use may be stored at room temperature and should be protected from light. Pens should be discarded 14 days after first use.

REFERENCE

Adlyxin (lixisenatide) injection, for subcutaneous use. Prescribing information. www.accessdata.fda.gov/drugsatfda_docs/label/2016/208471Orig1s000lbl.pdf.

ANTIVIRAL DRUGS FOR HCV

Two new combination antiviral formulations for treating chronic hepatitis C virus (HCV) infection were recently marketed. Elbasvir/grazoprevir (*Zepatier*, Merck) is approved to treat adults with chronic HCV genotypes 1 or 4 infection. Sofosbuvir/velpatasvir (*Epclusa*, Gilead) is approved to treat adults with chronic HCV genotypes 1, 2, 3, 4, 5, or 6 infection.

The antiviral agents that have been approved for the treatment of chronic HCV infection inhibit enzymes/proteins that are essential for the replication of HCV. Elbasvir and velpatasvir are HCV NS5A inhibitors with properties that are most similar to those of ledipasvir, ombitasvir, and daclatasvir. Grazoprevir is an HCV NS3/4A protease inhibitor with properties that are most similar to those of simeprevir and paritaprevir. Sofosbuvir is a nucleotide analogue NS5B polymerase inhibitor.

Some of the recommended treatment regimens of the new combination products, as well as some other treatment regimens for chronic HCV infection, also include ribavirin. In that case, clinicians must also take into account the risks and warnings associated with ribavirin.

Of particular importance is the potential for ribavirin to cause teratogenic and/or embryocidal effects, so it's contraindicated in women who are pregnant and in the male partners of women who are pregnant. Ribavirin has a long half-life and may not be completely eliminated for as long as 6 months. Pregnancy must be avoided during treatment and for 6 months following completion of treatment, and at least two reliable forms of effective contraception must be used during this period.

The elbasvir/grazoprevir and sofosbuvir/velpatasvir combinations are considered on an individual basis in the following discussions.

Elbasvir/grazoprevir

Highly successful for patients with HCV genotypes 1 or 4

A fixed-dose combination product, elbasvir/grazoprevir (*Zepatier*, Merck) is indicated to treat adults with chronic HCV genotypes 1 or 4 infection. For some patients, ribavirin is also included in the treatment regimen. The effectiveness of elbasvir/grazoprevir was evaluated in two placebo-controlled trials and four uncontrolled trials in which sustained virologic response (SVR) was the primary endpoint. The overall SVR rates ranged from 94% to 97% in patients with genotype 1 infection and from 97% to 100% in patients with genotype 4 infection.

Precautions: (1) Contraindicated in patients with moderate or severe hepatic impairment because of the expected significantly increased grazoprevir plasma concentration and an increased risk of alanine aminotransferase (ALT) elevations. Hepatic lab testing should be conducted before and during treatment. In patients receiving a 12-week course of treatment, hepatic lab testing should be performed before the start of therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, additional hepatic lab testing should be performed at treatment week 12. (2) Discontinuation of treatment should be considered if ALT concentrations remain persistently greater than 10 times the upper limit of normal. Treatment should be discontinued if the ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalized ratio. (3) Patients with genotype 1a infection should be tested before initiation of treatment for the presence of virus with NS5A resistance-associated polymorphisms because this is a factor in determining if ribavirin should be included in the regimen, as well as the dosage and

duration of treatment. (4) Both drugs in this medication are metabolized primarily via the CYP3A pathway, so plasma concentrations and antiviral action of elbasvir/grazoprevir may be significantly reduced by strong CYP3A inducers (such as carbamazepine, phenytoin, rifampin, and St. John's wort) and increased by CYP3A inhibitors such as ketoconazole and certain combination products for HIV infection. Concurrent use with these drugs is contraindicated. (5) The concentrations of atorvastatin and rosuvastatin may be increased by the concurrent use of elbasvir/grazoprevir. Daily doses of these lipid-regulating drugs shouldn't exceed 20 mg and 10 mg, respectively. (6) Consult the prescribing information for precautions about potential interactions between elbasvir/grazoprevir and many other drugs, including efavirenz, tacrolimus, and organic anion transporting polypeptides 1B1/3 inhibitors such as cyclosporine.

Adverse reactions: fatigue, headache, nausea. *In patients who were also treated with ribavirin for a longer period:* anemia, headache

Supplied as: tablets containing 50 mg of elbasvir and 100 mg of grazoprevir, packaged in a carton containing 28 tablets in two 14-count child-resistant dose packs

Dosage: one tablet once a day with or without food. Consult the prescribing information for the recommended duration of treatment based on factors such as HCV genotype and patient history.

Nursing considerations: (1) Inform patients that elbasvir/grazoprevir may be taken without regard to food. (2) Teach patients to report early warning signs of liver inflammation such as fatigue, weakness, anorexia, nausea, and vomiting, and later signs such as jaundice and discolored stools. (3) Tell patients to keep tablets in the original blister package until use to protect them from moisture.

REFERENCE

Zepatier (elbasvir and grazoprevir) tablets, for oral use. Prescribing information. https://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf.

Sofosbuvir/velpatasvir

First treatment approved to treat all six major HCV genotypes

Also a fixed-dose combination product, sofosbuvir/velpatasvir (*Epclusa*, Gilead) is indicated to treat adults with chronic HCV genotypes 1, 2, 3, 4, 5, or 6 infection. It's the first product to be approved for the treatment of all six major HCV genotypes. It's indicated for patients without cirrhosis or with compensated cirrhosis. It should be used in combination with ribavirin in patients with decompensated cirrhosis (moderate-to-severe cirrhosis).

The effectiveness of sofosbuvir/velpatasvir was evaluated in three clinical trials in treatment-naive and treatment-experienced patients without cirrhosis or with compensated cirrhosis (mild cirrhosis). One study included patients with HCV genotypes 1, 2, 4, 5, or 6 infection, another study included patients with genotype 2 infection, and the third study included patients with genotype 3 infection. The SVR rates were 95-99% at 12 weeks following the completion of a 12-week course of treatment. In another study, patients with HCV infection of all six genotypes and with decompensated cirrhosis were treated with sofosbuvir/velpatasvir and ribavirin. The SVR rate was 94% at 12 weeks following the completion of a 12-week course of treatment.

The effectiveness of sofosbuvir/velpatasvir in treating patients with chronic HCV infections of all six genotypes is of particular importance in patients with genotype 2 or 3 infection, in whom previous treatment options were limited and/or even more costly. In addition, performing genotype testing may not be necessary if resources aren't readily available.

The duration of treatment with sofosbuvir/velpatasvir, with or without ribavirin, is 12 weeks, which is an advantage compared with some regimens for other medications that are 16 weeks, 24 weeks, or longer for certain HCV infections.

Precautions: (1) Symptomatic bradycardia has been reported in patients taking amiodarone concurrently with a sofosbuvir-containing regimen, and some have required cardiac pacing. Patients also taking beta-blockers, or those with underlying cardiac comorbidities and/or advanced liver disease, may be at increased risk for this response when amiodarone is administered concurrently with sofosbuvir/velpatasvir. Concurrent therapy isn't recommended; however, if no other viable treatment option is available, the drugs may be used concomitantly with cardiac monitoring in an in-patient setting for the first 48 hours of coadministration, after which outpatient or self-monitoring of the heart rate should occur daily through at least the first 2 weeks of treatment. Because amiodarone has a long half-life, patients discontinuing this drug before initiation of treatment with sofosbuvir/velpatasvir should undergo similar cardiac monitoring. (2) Drugs that are inducers of P-glycoprotein and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4 (such as carbamazepine, rifampin, St. John's wort, and efavirenz) may reduce the therapeutic benefit of sofosbuvir/velpatasvir, and concurrent use isn't recommended. (3) The activity of sofosbuvir/velpatasvir may also be reduced by tipranavir/ritonavir, and concomitant use isn't recommended. (4) Sofosbuvir/velpatasvir has been reported to increase the concentrations of topotecan, digoxin, tenofovir, rosuvastatin, and atorvastatin. Concurrent use with topotecan isn't recommended and patients using

the other agents concurrently should be closely monitored for adverse events. The daily dosage of rosuvastatin shouldn't exceed 10 mg when used concurrently with sofosbuvir/velpatasvir. (5) Because the solubility of velpatasvir decreases as pH increases, drugs that increase gastric pH may decrease its concentration and activity. Administration of sofosbuvir/velpatasvir and an antacid should be separated by an interval of at least 4 hours. An H_2-receptor antagonist may be administered simultaneously with or 12 hours apart from sofosbuvir/velpatasvir at a dose that doesn't exceed doses comparable to 40 mg of famotidine twice daily. (6) The concurrent use of the proton pump inhibitor omeprazole isn't recommended, but if using both agents is medically necessary, sofosbuvir/velpatasvir should be administered with food and taken 4 hours before omeprazole in a dose of 20 mg. The use of sofosbuvir/velpatasvir with other proton pump inhibitors hasn't been studied.

Adverse reactions: *In patients without cirrhosis or with compensated cirrhosis:* headache, fatigue, nausea. *In patients with decompensated cirrhosis who were also treated with ribavirin:* fatigue, anemia, nausea, headache, insomnia, diarrhea

Supplied as: tablets containing 100 mg of velpatasvir and 400 mg of sofosbuvir. Each bottle contains 28 tablets that should be dispensed in the original container.

Dosage: one tablet once a day with or without food. In patients with chronic HCV infection with decompensated cirrhosis, ribavirin should also be included in the treatment regimen.

Nursing considerations: (1) Tell patients they can take each dose without regard to food. (2) Teach patients to immediately seek medical attention if they experience signs or symptoms of bradycardia, such as dizziness, lightheadedness, syncope, weakness, and shortness of breath. (3) Tell patients to store tablets at room temperature and keep them in the original container.

REFERENCE

Epclusa (sofosbuvir and valpatasvir) tablets, for oral use. Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208341s000lbl.pdf.

DRUG FOR GOUT

Lesinurad

Unique mechanism of action lowers uric acid levels

Hyperuricemia is characterized by elevated uric acid concentrations in the blood. Although most people with hyperuricemia don't experience gout, some experience concentrations of uric acid that exceed its solubility, resulting in the precipitation of crystals in the joints and other tissues, inflammation, and acute pain.

Lesinurad (*Zurampic*, Ironwood) has a unique mechanism of action in inhibiting the function of transporter proteins involved in uric acid reabsorption in the kidneys. Uric acid transporter 1 (URAT1) is responsible for most reabsorption of filtered uric acid from the renal tubular lumen, and organic anion transporter 4 (OAT4) is a uric acid transporter associated with diuretic-induced hyperuricemia. Lesinurad inhibits the action of URAT1 and OAT4, thereby increasing renal clearance and excretion of uric acid and reducing serum uric acid concentrations.

Lesinurad is used in combination with a xanthine oxidase inhibitor such as allopurinol or febuxostat. These drugs inhibit xanthine oxidase, which catalyzes the breakdown of purines to form uric acid.

Lesinurad is indicated to treat hyperuricemia associated with gout in patients who haven't achieved target serum uric acid concentrations with a xanthine oxidase inhibitor alone. It was evaluated in combination with a xanthine oxidase inhibitor in three 12-month long, placebo-controlled studies involving more than 1,500 participants. Patients received prophylaxis for gout flares with colchicine or a nonsteroidal anti-inflammatory drug during the first 5 months of lesinurad treatment. Studies 1 and 2 included patients who were on a stable daily dose of allopurinol of at least 300 mg (or 200 mg in patients with moderate renal impairment), had a serum uric acid concentration greater than 6.5 mg/dL, and had reported at least two gout flares in the prior 12 months. The combination of allopurinol and lesinurad (200 mg once a day) lowered serum uric acid to the target concentration of less than 6 mg/dL in approximately 55% of patients at 6 months, compared with approximately 25% of patients receiving allopurinol plus placebo.

In Study 3, lesinurad was used in combination with febuxostat. The average decrease in serum uric acid concentrations was similar to that reported in Studies 1 and 2.

Because changing serum uric acid concentrations result in mobilization of urate from tissue deposits, gout flares may occur following initiation of urate-lowering therapy and gout flare prophylaxis is recommended. If a gout flare occurs during treatment with lesinurad, it can be managed without discontinuing treatment.

Precautions: (1) Not indicated for use as monotherapy due to the risk of acute renal failure, the subject of a boxed warning in its labeling. A higher incidence of renal adverse reactions has been observed in patients who were treated with lesinurad as monotherapy and in patients treated with a daily dose of 400 mg of the drug. Lesinurad should always be used with a xanthine oxidase inhibitor and the daily dosage shouldn't exceed 200 mg. If treatment with the xanthine oxidase inhibitor is interrupted, the use of lesinurad should also be interrupted. (2) Contraindicated in patients with

severe renal impairment, end-stage renal disease, or on dialysis, and in patients who've received a kidney transplant. (3) Contraindicated in patients with tumor lysis syndrome associated with a rapid breakdown of cancer cells and high uric acid concentrations, and in patients with Lesch-Nyhan syndrome, a rare inherited disorder characterized by high blood uric acid concentrations. (4) Not recommended for patients with asymptomatic hyperuricemia, or for those taking daily doses of allopurinol less than 300 mg (or less than 200 mg in patients with an estimated creatinine clearance less than 60 mL/min). (5) Treatment shouldn't be initiated in patients with an estimated creatinine clearance less than 45 mL/min. Renal function should be monitored periodically during treatment, and more frequently in patients with a creatinine clearance less than 60 mL/min or with serum creatinine elevations 1.5 to 2 times the pretreatment value. Treatment should be interrupted if serum creatinine is elevated to greater than 2 times the pretreatment value. (6) Use of lesinurad increases the risk of acute uric acid nephropathy. Treatment should be interrupted and the serum creatinine concentration determined if a patient experiences symptoms such as flank pain, nausea, or vomiting. (7) Lesinurad's activity may be increased in patients who are CYP2C9 poor metabolizers and in those also being treated with a CYP2C9 inhibitor such as fluconazole or amiodarone. Conversely, its activity may be decreased in patients being treated with a CYP2C9 inducer such as carbamazepine or rifampin. (8) Inhibitors of epoxide hydrolase such as valproic acid may interfere with the metabolism of lesinurad; concurrent use should be avoided. (9) The use of aspirin in doses higher than 325 mg a day may reduce the efficacy of lesinurad in combination with allopurinol. However, doses of aspirin of 325 mg or less per day for cardiovascular protection don't decrease the efficacy of lesinurad and can be used concurrently. (10) Lesinurad has been reported to reduce the plasma concentrations of sildenafil and amlodipine, which are CYP3A substrates. Concurrent use with these and other medications that are substrates for this metabolic pathway should be closely monitored.

Adverse reactions: headache, influenza, gastroesophageal reflux disease

Supplied as: 200 mg tablets

Dosage: 200 mg once a day in the morning

Nursing considerations: (1) Tell patients to take each dose with food and water at the same time as the morning dose of allopurinol or febuxostat. Because the body's production of urine is lower at night, administration of the drug in the morning may lower the possibility of patients developing renal calculi. (2) Instruct patients with gout to stay well hydrated by drinking at least 2 L (68 oz) of liquid daily. (3) Hormonal contraceptives may not be reliable when lesinurad is used concurrently. Advise women to use additional methods of contraception and not to rely on hormonal contraception alone.

REFERENCE

Zurampic (lesinurad) tablets, for oral use. Prescribing information. http://irwdpi.com/zurampic/zurampic.pdf#page=1.

DRUG FOR PSORIASIS

Ixekizumab

Another option for moderate-to-severe plaque psoriasis

Psoriasis is a chronic immune-mediated disease characterized by thick and extensive skin lesions (plaques) that can cause pruritus, scaling, and pain. Mild and limited lesions can often be effectively treated with topically applied medications such as corticosteroids or calcipotriene, a vitamin D analogue. Options for treating more widespread and/or severe lesions, as well as lesions that don't respond adequately to topical treatment, include phototherapy with UV light, or systemic therapy with an orally administered medication (such as methotrexate or apremilast) or a parenterally administered medication such as a tumor necrosis factor inhibitor (for example, adalimumab or etanercept).

Certain naturally occurring interleukins have been identified as having a role in the occurrence and worsening of psoriasis. Interleukin-17A (IL-17A) is one interleukin that's present in elevated concentrations in psoriatic plaques. Ixekizumab (*Taltz*, Lilly) is a monoclonal antibody that inhibits IL-17A. Like secukinumab, a previously approved IL-17A antagonist, it's administered subcutaneously. Ixekizumab and secukinumab are both indicated to treat moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy; secukinumab is also approved to treat psoriatic arthritis and ankylosing spondylitis. Although ixekizumab and secukinumab haven't been directly compared in clinical research, studies on the individual drugs suggest that injection site reactions are more likely with ixekizumab.

As with other medications that suppress immune function, ixekizumab increases the risk of infection, with upper respiratory tract infection being one of the most common. Oral candidiasis, conjunctivitis, and tinea infections also occurred more frequently in patients treated with ixekizumab than in those treated with placebo.

Precautions: (1) Contraindicated in patients with known serious hypersensitivity to ixekizumab. The drug should be discontinued immediately in patients who experience serious hypersensitivity reactions, including angioedema and urticaria. (2) If a patient develops a serious infection during treatment, ixekizumab should be discontinued until the

infection resolves. (3) Patients treated with ixekizumab shouldn't receive live vaccines. (4) Patients should be evaluated for tuberculosis infection before starting treatment with ixekizumab. In patients with a history of latent or active tuberculosis in whom an adequate course of antitubercular therapy can't be confirmed, such treatment should be considered before initiating treatment with ixekizumab. (5) Patients should be monitored for the onset or exacerbation of inflammatory bowel disease; in clinical trials, a few cases of Crohn disease and ulcerative colitis, including exacerbations, were reported.

Adverse reactions: upper respiratory tract infections, injection site reactions, nausea, tinea infections

Supplied as: single-dose prefilled syringes and single-dose prefilled autoinjectors containing 80 mg of the drug in 1 mL of solution

Dosage: 160 mg (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2,4,6,8,10, and 12; then 80 mg every 4 weeks

Nursing considerations: (1) Advise patients to discuss their vaccination status with their healthcare provider; all age-appropriate vaccinations should be given before treatment starts. (2) Educate patients and caregivers about proper subcutaneous injection technique and teach them how to use the autoinjector or prefilled syringes correctly. Review the *Medication Guide and Instructions for Use* provided with the medication and advise patients to review it each time their prescription is renewed because the information may change. (3) Inform patients about the increased risk for infection and instruct them to contact the healthcare provider immediately if they develop signs and symptoms of infection. (4) Teach patients to recognize signs and symptoms of a hypersensitivity reaction including anaphylaxis, angioedema, and urticaria, and to seek emergency medical care for serious reactions. (5) Tell patients to store the medication in a refrigerator and to let it warm to room temperature for about 30 minutes before administration.

REFERENCE

Taltz (ixekizumab) injection, for subcutaneous use. Prescribing information. https://pi.lilly.com/us/taltz-uspi.pdf.

DRUG FOR DRY EYE DISEASE

Lifitegrast

A new alternative to artificial tears

Dry eye disease is estimated to affect about 5% of adults ages 30 to 40 and 10% to 15% of adults over age 65. It's more common in women than men.[1] When severe and untreated, it can lead to pain and corneal ulceration.

Dry eye disease is typically associated with reduced production of tears and/or altered composition of tears. Causative or contributing factors include environmental conditions, diseases such as Sjögren syndrome, and the use of medications such as those with anticholinergic activity.

Usually a chronic disorder, dry eye disease is characterized by inflammation of the ocular surface. Besides eye dryness, signs and symptoms may include eye stinging, burning, or other discomfort, a gritty feeling, blurred vision, and sensitivity to bright light and other environmental factors such as wind.

Dry eye disease is often initially treated with artificial tears but many patients don't respond adequately to these products even when administered frequently. Other agents that have been used in ophthalmic formulations include corticosteroids, hydroxypropyl cellulose, and cyclosporine.

Lifitegrast (*Xiidra*, Shire), a lymphocyte function-associated antigen 1 (LFA-1) antagonist, is the first in this new class of drugs to be approved by the FDA to treat signs and symptoms of dry eye disease.[2] The inflammation associated with dry eye disease is thought to be primarily mediated by T cells and associated cytokines. This process may be initiated by the increased expression of intercellular adhesion molecule-1 (ICAM-1) in corneal and conjunctival tissues. ICAM-1 interacts with LFA-1, a cell surface protein found on leukocytes. Lifitegrast binds to integrin LFA-1 and blocks its interaction with ICAM-1. This action is thought to inhibit T-cell adhesion to ICAM-1 and reduce secretion of inflammatory cytokines.

The effectiveness of lifitegrast was evaluated in four 12-week studies that included more than 2,000 patients who received lifitegrast. In all four studies, patients using lifitegrast experienced a larger reduction in patient-reported Eye Dryness Score (EDS). In two of the four studies, an improvement in EDS was observed in 2 weeks following initiation of treatment, which may provide an advantage over cyclosporine ophthalmic emulsion, which may not be fully effective for several months. However, lifitegrast and cyclosporine have not been directly compared in clinical studies.

Precaution: Contact lenses should be removed before medication instillation. They can be reinserted 15 minutes later.

Adverse reactions: instillation site irritation, altered taste sensation, reduced visual acuity

Supplied as: ophthalmic solution containing the drug in a 5% concentration (50 mg/mL) in single-use containers in cartons with 60 containers

Dosage: one drop in each eye twice a day approximately 12 hours apart

Nursing considerations: (1) Teach patients how to instill eye drops properly, without touching the container tip to the eye or any other surface. (2) Tell patients to use solution from each single-use con-

tainer immediately after opening it. It can be used to dose both eyes. The container and any remaining contents should be discarded immediately after use. (3) Tell patients to store containers in their original foil package until ready for use.

REFERENCES

1. FDA approves new medication for dry eye disease. Food and Drug Administration. News release. July 12, 2016.

2. Xiidra (lifitegrast ophthalmic solution) 5%, for topical ophthalmic use. Prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208073s000lbl.pdf.

DRUG FOR MUSCLE RELAXANT REVERSAL

Sugammadex sodium

Fast action to reverse rocuronium and vecuronium

Neuromuscular blocking drugs are often used as an adjunct to general anesthesia to facilitate tracheal intubation, promote skeletal muscle relaxation to prevent patients from moving during surgery, and prevent spontaneous breathing during mechanical ventilation. Nondepolarizing neuromuscular blockers, including rocuronium, vecuronium, pancuronium, and atracurium, reduce the action of acetylcholine. Although these agents have a slower onset and longer duration of action than the depolarizing neuromuscular blocker succinylcholine, they're less likely to cause serious adverse reactions.

Neuromuscular blockade may extend for a longer period than the duration of surgery. Drugs that reverse the effects of muscle relaxants may restore normal muscle function and spontaneous breathing sooner following surgery. The acetylcholinesterase inhibitor neostigmine has been used to reverse the action of the nondepolarizing neuromuscular blocking agents, but its onset and intensity of activity may be inconsistent and it's associated with cardiovascular and gastrointestinal adverse events.

Sugammadex sodium (*Bridion*, Merck) has been approved for the reversal of neuromuscular blockade induced by the nondepolarizing neuromuscular blockers rocuronium and vecuronium in adults undergoing surgery. Administered via I.V. bolus injection, this modified gamma cyclodextrin forms a complex with rocuronium and vecuronium, reducing the binding of these drugs to the nicotinic cholinergic receptors in the neuromuscular junction. Reversal of muscle relaxation induced by rocuronium and vecuronium occurs quickly, providing greater flexibility in inducing and maintaining the level of muscle relaxation necessary throughout surgery. In addition, the muscle relaxant's effect can be reversed quickly if necessary.

Sugammadex's effectiveness was evaluated in a study in which it was compared with neostigmine in patients with moderate neuromuscular blockade induced by rocuronium or vecuronium. The median recovery times with sugammadex (2 mg/kg) in patients treated with rocuronium and vecuronium were 1.4 minutes and 2.1 minutes, respectively, compared with median recovery times with neostigmine (50 mcg/kg) of 21.5 and 29 minutes, respectively. In a second study in patients with deep neuromuscular blockade induced by rocuronium or vecuronium, the median recovery times following administration with sugammadex (4 mg/kg) were 2.7 minutes, and 3.3 minutes, respectively.

In another study, a higher dosage of sugammadex (16 mg/kg) was evaluated to assess its action in reversing the neuromuscular blockade induced by a dose of rocuronium (1.2 mg/kg) administered 3 minutes earlier. The median recovery time from the start of administration of rocuronium was 4.2 minutes.

Sugammadex is specifically indicated to reverse the action of rocuronium and vecuronium in adults. In studies, it was generally well tolerated at lower doses (2 mg/kg-4 mg/kg). However, at a dosage of 16 mg/kg, 13% of patients experienced hypotension and 9% experienced hypertension.

Sugammadex should be administered only by healthcare providers who are familiar with the use, actions, characteristics, and complications of neuromuscular blocking agents and reversal agents. The dose and timing of administration of sugammadex should be based on monitoring for twitch responses and the extent of spontaneous recovery that has occurred. The recommended dose doesn't depend on the anesthetic regimen.

Precautions: (1) Sugammadex is indicated for use only to reverse blockade induced by rocuronium or vecuronium, which are classified as steroidal nondepolarizing neuromuscular blockers. It's not indicated to reverse the effects of any other steroidal neuromuscular blocker (such as pancuronium), or to reverse nonsteroidal neuromuscular blocking agents that include nondepolarizing benzylisoquinolinium derivatives (for example, atracurium) or the depolarizing agent succinylcholine. (2) Sugammadex is contraindicated in patients with a known hypersensitivity to sugammadex or any of its components. A few patients have experienced hypersensitivity reactions to sugammadex including anaphylaxis, and appropriate precautions must be observed. (3) Marked bradycardia has been infrequently reported. An anticholinergic agent such as atropine should be administered if the patient develops clinically significant bradycardia. (4) Sugammadex isn't recommended in patients with severe renal impairment, as the drug hasn't been adequately studied in this population. (5) Toremifene, an estrogen agonist/antagonist indicated for certain patients with metastatic breast cancer, has been reported to have a high binding affinity for sugammadex; its use on the day of surgery might reduce the binding of the new drug to rocuronium or vecuronium and delay the reversal of the neuromuscular blockade. (6) Sugammadex has been

reported to increase activated partial thromboplastin time, prothrombin time, and international normalized ratio for up to 1 hour in healthy volunteers. When it's administered in a dosage of 16 mg/kg, coagulation parameters should be closely monitored in patients with known coagulopathies and in those receiving therapeutic anticoagulation with thromboprophylaxis drugs other than heparin or low-molecular-weight heparin, with which no problems were observed in clinical studies, or thromboprophylaxis drugs when sugammadex will be administered in a dosage of 16 mg/kg.

Adverse reactions: pain, nausea, vomiting, headache, hypotension

Supplied as: single-use vials in an amount equivalent to a concentration of sugammadex of 100 mg/ml. Vials contain 200 mg/2 mL and 500 mg/5 mL.

Dosage: a single I.V. bolus injection is administered over 10 seconds into an I.V. line running an infusion of a compatible solution such as 0.9% Sodium Chloride or 5% Dextrose. The recommended dosage is 2 mg/kg in patients with moderate blockade induced by rocuronium or vecuronium, or 4 mg/kg in patients with deep blockade induced by these drugs. A higher dose of 16 mg/kg is recommended if there is a clinical need to reverse rocuronium-induced neuromuscular blockade quickly (within 3 minutes) after administration of a single dose of 1.2 mg/kg of rocuronium.

Nursing considerations: (1) Sugammadex may bind to estrogen and progestogen, diminishing the effectiveness of hormonal contraceptives. Advise patients who take an oral contraceptive on the same day that sugammadex is administered to use an additional nonhormonal contraceptive method (such as condoms) for the next 7 days. This recommendation also applies to non-oral hormonal contraceptives. (2) Consult the product labeling for recommendations regarding the monitoring of patients, the risk of recurrence of neuromuscular blockade, and the readministration of neuromuscular blocking agents for intubation following reversal with sugammadex.

REFERENCE

Bridion (sugammadex) injection, for intravenous use. Prescribing information. https://www.merck.com/product/usa/pi_circulars/b/bridion/bridion_pi.pdf.

DOI-10.1097/01.NURSE.0000520502.21675.94