New Drugs part I

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IN THIS ARTICLE, you'll learn about 11 recently approved drugs, including:

> belimumab, the first drug approved to treat systemic lupus erythematosus since 1955.

> ceftaroline, the first cephalosporin approved to treat methicillin-resistant *Staphylococcus aureus*.

> boceprevir and telaprevir, two major advances in the treatment of hepatitis C infection.

Unless otherwise specified, the information in the following summaries applies to adults, not children. Consult a pharmacist or the package insert for information about each drug's safety during pregnancy and breastfeeding. Consult a pharmacist, the package insert, or a 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; 2012.

Nursing2012 Drug Handbook. Ambler, PA: Lippincott Willliams & Wilkins; 2012.

Physicians' Desk Reference. 66th ed. Montvale, NJ: Medical Economics; 2012.

*Common adverse reactions are italicized throughout this article.

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DRUG FOR SLE

Belimumab

First drug approved for SLE since 1955

More than 300,000 Americans suffer from systemic lupus erythematosus (SLE), a serious and potentially fatal autoimmune disease that attacks healthy tissues, including joints, skin, kidneys, lungs, heart, and brain.[1] Belimumab (*Benlysta*; Human Genome Sciences, GlaxoSmithKline) is the first drug approved to treat SLE since 1955.[2]

Belimumab is a human monoclonal antibody produced by recombinant DNA technology that's specific for soluble human B lymphocyte stimulator (BLyS) protein, a B cell survival factor. In SLE, abnormal B cells contribute to formation of autoantibodies and may be at least partially responsible for signs, symptoms, and complications associated with SLE. The new drug prevents soluble BLyS from binding to receptors on B cells, inhibiting B cell survival.

Administered I.V., belimumab is indicated for adults with active, autoantibody-positive SLE who are receiving therapy with standard SLE drugs, such as nonsteroidal anti-inflammatory drugs, corticosteroids, immunosuppressives, and antimalarials.[3] In clinical trials, some patients treated with belimumab had a reduced likelihood of severe disease flares, and some were able to reduce their corticosteroid dosage. But data were insufficient to establish these responses as definitive benefits of the new drug. Patients of African heritage who participated in the study didn't appear to benefit from belimumab treatment, but the number of these patients was too small to be definitive. The incidence of SLE in Black women is approximately three times higher than in White women.[2]

Precautions: (1) Belimumab may cause hypersensitivity or infusion reactions. It's contraindicated in patients with a history of anaphylaxis to the drug. (2) Belimumab increases the risk of serious infections. Treatment shouldn't be initiated in patients in treatment for a chronic infection. If an infection develops during therapy, discontinuing therapy should be considered. (3) Patients taking belimumab shouldn't receive live vaccines for 30 days before treatment starts or concurrently with belimumab treatment. (4) Belimumab isn't recommended for patients with active lupus nephritis or severe active central nervous system lupus, or for patients being treated with other biologic medications or I.V. cyclophosphamide. The drug's safety and effectiveness for these patients hasn't been studied.

Adverse reactions: *nausea, diarrhea, pyrexia, nasopharyngitis, bronchitis, insomnia, pain in extremity, depression, migraine, pharyngitis*

Supplied as: lyophilized powder in single-use vials containing 120 and 400 mg of the drug

Dosage: 10 mg/kg via I.V. infusion administered over 1 hour, given at 2-week intervals for the first three doses and at 4-week intervals thereafter.

Nursing considerations: (1) Belimumab lyophilized powder must be reconstituted with Sterile Water for Injection, and the reconstituted drug must be diluted in 0.9% Sodium Chloride Injection. Consult the product insert for detailed instructions. (2) Dextrose solutions are incompatible with belimumab and shouldn't be used for either reconstitution or dilution. (3) The total time from reconstitution to completion of the infusion shouldn't exceed 8 hours. (4) Administer the infusion slowly over 1 hour. Never give belimumab via I.V. bolus injection. (5) Closely monitor the patient for signs and symptoms of an infusion reaction (such as headache, nausea, or skin reactions) or a hypersensitivity reaction (such as hypotension, angioedema, urticaria or other rash, pruritus, or dyspnea). Immediately stop the infusion if the patient develops a serious hypersensitivity reaction. Data is insufficient to establish whether premedication diminishes the frequency or severity of infusion-related reactions. (6) Teach the patient to recognize and report signs and symptoms of infection to the healthcare provider. (7) Also tell the patient to report new or worsening depression, suicidal thoughts, or other mood changes. (8) Tell women of childbearing potential to use adequate contraception during treatment and for at least 4 months following the final treatment. Women who become pregnant during treatment are encouraged to enroll in the Pregnancy Registry (1-877-681-6296). (9) Store vials of belimumab in the refrigerator. Before a dose is prepared, remove the vial from the refrigerator and allow it to stand for 10 to 15 minutes to reach room temperature.

REFERENCES

1. American College of Rheumatology. Press Release: study finds changes in incidence of end-stage renal disease from lupus nephritis. 2011. http://www.rheumatology.org/about/newsroom/2011/2011_01_12.asp.

2. Food and Drug Administration. FDA news release: FDA approves Benlysta to treat lupus. 2011. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm246489.htm.

3. Benlysta [package insert]. Rockville, MD: Human Genome Sciences, Inc; 2011. http://www.hgsi.com/images/Benlysta/pdf/benlysta_pi.pdf.

ANTIBIOTIC

Ceftaroline fosamil

Important new weapon against MRSA

Classified as a cephalosporin, ceftaroline fosamil (*Teflaro*, Forest) inhibits penicillin-binding proteins and bacterial cell wall synthesis. Active against many Gram-positive and Gram-negative bacteria, it's the first cephalosporin approved to treat infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA). It's administered I.V. for treatment of acute bacterial skin and skin structure infections caused by MRSA and other susceptible bacteria, as well as for treatment of community-acquired bacterial pneumonia.

Precautions: (1) Contraindicated in patients with a history of serious hypersensitivity to any cephalosporin. Because of the potential for cross-sensitivity with other beta-lactam antibiotics, use caution in patients allergic to penicillin or carbapenem. (2) Like most systemic antibiotics, ceftaroline may cause *Clostridium difficile*-associated disease (CDAD), which ranges in severity from mild diarrhea to fatal colitis. (3) The dosage should be reduced for patients with moderate-to-severe renal impairment. See the package insert for recommendations.

Adverse reactions: *diarrhea, nausea,* rash and other hypersensitivity reactions

Supplied as: powder in single-use vials containing 400 and 600 mg of the drug

Dosage: 600 mg every 12 hours via I.V. infusion administered over a 1-hour period; duration of therapy is usually 5 to 7 days to treat community-acquired

pneumonia; 5 to 14 days to treat bacterial skin and skin structure infections

Nursing considerations: (1) Assess patients' allergy history before treatment begins. (2) Reconstitute the vial contents with 20 mL of Sterile Water for Injection; then further dilute the solution in a volume of at least 250 mL of 0.9% Sodium Chloride Injection, 0.45% Sodium Chloride Injection, 5% Dextrose Injection, 2.5% Dextrose Injection, or Lactated Ringer Injection. (3) Administer the diluted solution in the infusion bag within 6 hours when stored at room temperature or with 24 hours when refrigerated. (4) Closely monitor the patient for signs and symptoms of a hypersensitivity reaction, such as hypotension and respiratory distress. (5) Monitor patients for CDAD and tell them to report persistent or severe diarrhea. CDAD can develop 2 months or more after treatment ends. (6) For patients on dialysis, administer ceftaroline after hemodialysis on hemodialysis days. (7) Store drug vials in the refrigerator.

REFERENCE

Teflaro (ceftaroline fosamil) injection for intravenous (IV) use [package insert]. St. Louis, MO: Forest Pharmaceuticals, Inc; 2010. http://www.frx.com/pi/teflaro_pi.pdf.

ANTIPSYCHOTIC DRUG

Lurasidone hydrochloride

An atypical antipsychotic indicated to treat schizophrenia

Classified as a benzoisothiazol derivative, lurasidone hydrochloride (*Latuda*, Sunovion) is an atypical antipsychotic drug with properties similar to risperidone, paliperidone, iloperidone, and ziprasidone. At present, the new drug's only labeled indication is for treatment of schizophrenia.

As with other atypical antipsychotics, lurasidone's labeling contains a boxed warning about the risk of increased mortality in older adults with dementia-related psychosis, including the statement that these drugs aren't approved for treating older patients with dementia-related psychosis.

Compared with most of the other atypical antipsychotic drugs, lurasidone appears less likely to cause metabolic changes such as diabetes and weight gain, but may be more likely to cause somnolence/sedation. Unlike ziprasidone and iloperidone, lurasidone hasn't been associated with significant QT interval prolongation.

Precautions: (1) Like other atypical antipsychotic drugs, lurasidone has the potential for causing cerebrovascular adverse events such as stroke in older adults with dementia-related psychosis, neuroleptic malignant syndrome, tardive dyskinesia, hyperprolactinemia, hyperglycemia/diabetes mellitus, weight gain, orthostatic hypotension/syncope, seizures, cognitive and motor impairment, dysphagia, problems associated with body temperature regulation, leukopenia, neutropenia, and agranulocytosis. (2) Because lurasidone is metabolized primarily by CYP3A4, coadministration with other drugs using this pathway could significantly alter lurasidone's effects. Lurasidone is contraindicated for concurrent use with strong CYP3A4 inhibitors such as ketoconazole or strong CYP3A4 inducers such as rifampin. (3) Use caution in patients taking other central nervous system (CNS) depressants (including alcohol) because of the potential for additive depressant effects. (4) Closely monitor patients for suicidal thoughts and behavior. Although no suicide attempts were reported during clinical trials, the risk of suicide is inherent in psychotic illness.

Adverse reactions: *somnolence, akathisia, nausea, parkinsonism,* agitation, anxiety, dystonia

Supplied as: 40 and 80 mg tablets

Dosage: initially 40 mg/day; the maximum recommended dosage is 80 mg/day. Dosage shouldn't exceed 40 mg/day in patients with moderate or severe renal or hepatic impairment or in those also being treated with a moderate CYP3A4 inhibitor such as diltiazem.

Nursing considerations: (1) Tell patients to take each dose with food. (2) Warn patients to avoid alcohol during treatment to prevent excessive CNS depression. (3) Monitor patients for suicidal tendencies and encourage them to report suicidal thoughts or mood changes to the healthcare provider.

REFERENCE

Latuda (lurasidone HCl) tablets [package insert]. Marlborough, MASS: Sunovion Pharmaceuticals Inc; 2011. http://www.latuda.com/LatudaPrescribingInformation.pdf.

ANTIHYPERTENSIVE DRUG

Azilsartan medoxomil

Armed with another ARB to manage BP

Azilsartan medoxomil (*Edarbi*, Takeda) is the eighth angiotensin II receptor blocker (ARB) to be marketed in the United States, joining candesartan cilexetil, eprosartan, irbesartan, losartan, olmesartan medoxomil, telmisartan, and valsartan. The ARBs treat hypertension by preventing the potent vasoconstrictor angiotensin II from binding to its receptor sites. Like other ARBs, azilsartan is well tolerated and may be used alone or in combination with another antihypertensive drug, typically a diuretic.

Along with hypertension, some ARBs have been approved to treat other conditions, such as heart failure. However, hypertension is currently the only labeled indication for azilsartan. As with the other ARBs, azilsartan is less effective in lowering BP in Black patients than in White patients.

Precautions: (1) ARBs may cause neonatal morbidity and death if used in the second or third trimester of pregnancy. (2) Use caution in volume- or salt-depleted patients (such as those using a diuretic) to prevent symptomatic hypotension; use of a lower dosage should be considered in these patients. (3) ARBs can cause changes in renal function, so use caution in patients at risk; for example, those with preexisting renal impairment or renal artery stenosis. (4) Concurrent use of a nonsteroidal anti-inflammatory drug (NSAID) may cause renal function to deteriorate in patients at risk. NSAIDs may also reduce azilsartan's antihypertensive effects.

Adverse reaction: *diarrhea*

Supplied as: 40 and 80 mg tablets

Dosage: 80 mg once a day; treatment may be initiated at 40 mg/day in patients also being treated with a high diuretic dosage

Nursing considerations: (1) Warn women of childbearing potential to use reliable contraception during treatment. If a patient becomes pregnant during treatment, azilsartan therapy should be stopped as soon as possible. (2) Tell patients that azilsartan can be taken without regard to food. (3) Advise patients to avoid NSAIDs unless directed otherwise by their healthcare provider. (4) Tell patients to keep the drug in its original container to protect it from light and moisture.

REFERENCE

Edarbi (azilsartan medoxomil) tablet [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc; 2011. http://www.edarbi.com/Default.aspx.

ANTIVIRAL DRUGS

Boceprevir Telaprevir

Two important advances for treating chronic hepatitic C infection

Liver disease resulting from hepatitis C virus (HCV) infection is the most frequent reason for liver transplantation in the United States. More than 3 million Americans have chronic HCV infection, with genotype 1 infection being the most common form.[1] Standard treatment for chronic HCV infection is a combination regimen that includes peginterferon alfa-2a or peginterferon alfa-2b, plus ribavirin for 48 weeks. This treatment can produce a sustained virologic response (SVR), characterized by undetectable plasma HCV RNA 24 weeks after treatment ends; this is considered a cure. However, fewer than 50% of patients with HCV genotype 1 attain this response.[2]

Two similar antiviral agents newly approved and marketed represent an important advance in the treatment of chronic HCV infection. Classified as HCV protease inhibitors, boceprevir (*Victrelis*, Merck) and telaprevir (*Incivek*, Vertek) interfere with actions necessary for replication of the HCV virus.[3,4] Because of their similarities, they'll be discussed together first, followed by a discussion of points specific to each drug.

Both new drugs are administered orally. Boceprevir is indicated for the treatment of chronic HCV genotype 1 infection in combination with peginterferon alfa and ribavirin in adults age 18 and older with compensated liver disease, including cirrhosis, who are previously untreated or who've failed previous interferon and ribavirin therapy. The indication for telaprevir is similar.

Both drugs should always be used in combination with peginterferon alfa and ribavirin, never alone. Consequently, precautions and contraindications for these drugs apply to therapy with either new drug. For example, anemia has been reported with peginterferon alfa and ribavirin therapy. In clinical trials, the incidence of anemia was doubled when boceprevir or telaprevir was added to the regimen, so complete blood cell counts should be closely monitored.

In addition, because ribavirin can cause birth defects and fetal death, it's classified in pregnancy category X. Any regimen containing ribavirin is contraindicated in pregnant women and in men whose female partners are pregnant. Additional precautions include:

- Obtain a negative pregnancy test before therapy starts.
- Tell women of childbearing potential and men to use at least two forms of nonhormonal contraception (for example, barrier methods) during treatment and for at least 6 months afterward. Warn them that systemic hormonal contraceptives may not be effective when they're taking boceprevir or telaprevir.
- Perform monthly pregnancy testing throughout treatment and for 6 months afterward.

Both new drugs interact with numerous other medications and herbal preparations. The use of rifampin and St. John's wort with either boceprevir or telaprevir is contraindicated because of a likely reduction in the activity of the latter agents, resulting in a loss of virologic response. Other drugs contraindicated for use with one or both new drugs include carbamazepine, phenobarbital, phenytoin, drospirenone, and atorvastatin. Use with many other drugs, while not contraindicated, may require dosage adjustments and additional monitoring. For example, the activity of warfarin may increase or decrease when used concurrently with boceprevir or telaprevir, so the international normalized ratio should be even more closely monitored to ensure safe and effective treatment.

Consult each drug's product labeling for a complete list of contraindications, precautions, and dosage recommendations. Tell patients to check with the healthcare provider or pharmacist before taking any additional drugs, including over-the-counter preparations, and to inform all healthcare providers about their prescribed medications.

REFERENCES

1. Centers for Disease Control and Prevention. Hepatitis C FAQs for Health Professionals. http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm.

2. Ghany MG, Nelson DR, Strader DB, Thomas DL, Seeff LB. An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. *Hepatology.* 2011;54(4):1433-1444. Epub 2011 Sep 26.

3. Victrelis (boceprevir) capsules [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2011. http://www.merck.com/product/usa/pi_circulars/v/victrelis/victrelis_pi.pdf.

4. Incivek (telaprevir) film coated tablets [package insert]. Cambridge, MASS: Vertex Pharmaceuticals Inc; 2011. http://pi.vrtx.com/files/uspi_telaprevir.pdf.

BOCEPREVIR

In clinical studies, patients were initially treated with peginterferon alfa-2b and ribavirin for 4 weeks. Following this, some patients continued this two-drug regimen plus placebo for a total of 48 weeks, while other patients took the two-drug regimen plus boceprevir (for 24 to 44 weeks) for the same period. In a study of patients who'd not previously received antiviral therapy, 65% of those receiving boceprevir experienced SVR, compared with 38% of those who continued with the two-drug regimen plus placebo. Both regimens were less effective in Black patients compared to non-Black patients. Severe adverse events were reported in 11% of patients treated with the three-drug regimen and in 8% of those treated with the two-drug regimen.

Precautions: (1) Boceprevir must be given as part of a regimen that also includes peginterferon alfa and ribavirin, and must not be used without these drugs. Treatment is initiated with the latter two drugs for the first 4 weeks of therapy, then boceprevir is added to the regimen. (2) Obtain complete blood cell counts pretreatment and at treatment weeks 4, 8, and 12 and more often if appropriate. (3) If hemoglobin concentration is less than 10 g/dL, a decrease in dosage or interruption of ribavirin is recommended. If hemoglobin is less than 8.5 g/dL, discontinuation of ribavirin is recommended. (4) Neutropenia may require dosage reduction or discontinuation of the drug regimen.

Adverse reactions: *anemia*, *nausea*, *dysgeusia, fatigue*, *headache, chills, insomnia, neutropenia*

Supplied as: 200 mg capsules

Dosage: 800 mg (four capsules) three times daily (every 7 to 9 hours) with food. The duration of therapy varies depending on the patient's condition, treatment history, and response to treatment.

Nursing considerations: (1) Tell patients to take boceprevir with food or a snack. It can be taken 5 minutes before a meal, during the meal, or immediately after the meal. The type of food is unimportant. Inform them that taking the drug on an empty stomach may significantly reduce its effectiveness. (2) If patients miss a dose of boceprevir more than 2 hours before the next scheduled dose, they should take the missed dose with food. If a dose is missed less than 2 hours before the next dose, they should skip the missed dose.

REFERENCE

Victrelis (boceprevir) capsules [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2011. http://www.merck.com/product/usa/pi_circulars/v/victrelis/victrelis_pi.pdf.

TELAPREVIR

In clinical trials, the SVR rate for patients treated with telaprevir as part of a three-drug regimen, across all studies and across all patient groups, was between 20% and 45% higher than in patients treated with peginterferon alfa and ribavirin.

A small proportion (<1%) of patients treated with telaprevir developed serious skin reactions, including drug rash with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome. These patients required hospitalization, but all recovered. Serious adverse reactions occurred in 3% of patients treated with the three-drug regimen (peginterferon alfa, ribavirin, and telaprevir) versus none of the patients treated with the two-drug regimen.

Precautions: (1) Telaprevir must be administered as part of a regimen that also includes peginterferon alfa and ribavirin, not as monotherapy. (2) Monitor patients for development of a rash, a common adverse reaction. Treatment should stop immediately if a rash worsens or becomes severe, or if systemic symptoms develop. (3) Monitor hemoglobin before and at least every 4 weeks during telaprevir combination treatment. To manage anemia, a reduction in the ribavirin dosage should be considered. If this isn't adequate, discontinuing telaprevir may be indicated. (4) About 75% of patients experience elevated uric acid concentration during telaprevir treatment. Chemistry and hematology evaluations are recommended at weeks 2, 4, 8, and 12, or as clinically appropriate. (5) Telaprevir isn't recommended for patients with moderate or severe hepatic impairment.

Adverse reactions: *rash*, *fatigue*, *pruritus*, *nausea*, *anemia*, *diarrhea*, vomiting, hemorrhoids, anorectal discomfort, dysgeusia

Supplied as: 375 mg tablets

Dosage: 750 mg (two tablets) three times daily every 7 to 9 hours with food (not low fat). The duration of therapy depends on the patient's condition, treatment history, and response to treatment.

Nursing considerations: (1) Tell patients to take telaprevir with food (but not a low-fat meal). Taking it on an empty stomach significantly reduces the drug's effectiveness. (2) Tell patients to report a rash immediately to the healthcare provider. (3) If patients miss a dose of telaprevir and it's less than 4 hours after the scheduled time for the dose, they should take the dose with food as soon as possible. If more than 4 hours have elapsed from the time they'd usually take the dose, they should skip the dose.

REFERENCE

Incivek (telaprevir) film coated tablets [package insert]. Cambridge, MASS: Vertex Pharmaceuticals Inc; 2011. http://pi.vrtx.com/files/uspi_telaprevir.pdf.

PEDICULICIDE

Spinosad

Death to head lice

Head lice infestation is most commonly experienced by school-age children. Spinosad (*Natroba*, ParaPRO) is a pediculicide derived from fermentation of a soil bacterium, *Saccharopolyspora spinosa*. The drug causes neuronal excitation in insects; after periods of hyperexcitation, lice become paralyzed and die.

Spinosad is a topical medication indicated to treat head lice infestation in patients age 4 years and older. Currently, this is the only labeled indication for spinosad.

In two studies comparing spinosad with permethrin, a commonly used nonprescription pediculicide, spinosad was effective in 85% and 87% of patients, respectively, compared with 45% and 43% of patients treated with permethrin. Compared to the permethrin-treated patients, fewer patients treated with spinosad required two treatments. Spinosad therapy was well tolerated by patients.

Precautions: (1) Contraindicated in neonates and infants below age 6 months. The formulation contains benzyl alcohol, which can be absorbed systemically and has been associated with serious reactions and death in neonates and low birth-weight infants. Spinosad's safety and effectiveness hasn't been established in children under age 4 years. (2) Because benzyl alcohol could be absorbed through skin and enter breast milk, lactating women must use caution when applying spinosad. A lactating woman may choose to pump and discard breast milk for 8 hours after use to avoid infant ingestion of benzyl alcohol.

Spinosad suspension should be used as part of an overall lice management program.[1,2]

Adverse reactions: *application site erythema, ocular erythema,* application site irritation

Supplied as: topical suspension containing the drug in a 0.9% concentration in 120 mL bottles

Dosage: apply enough to cover the dry scalp and then apply to dry hair; up to 120 mL may be needed per application depending on the length of hair

Nursing considerations: (1) Shake the suspension well before use. (2) Cover the patient's face and eyes with a towel. Instruct the patient to keep eyes tightly closed during treatment. (3) Leave the medication in place for 10 minutes; then thoroughly rinse with warm water. (4) You may remove treated lice and nits from hair and scalp with a fine-tooth comb, but combing isn't required. (5) Teach patients and/or parents to assess for lice after treatment. If live lice are observed 7 days after the first treatment, a second treatment is indicated. (6) Educate patients and/or parents about removing lice from clothing, bedding, and personal care items.

REFERENCES

1. Natroba (spinosad) topical suspension 0.9% [package insert and patient information]. Carmel, IND: ParaPRO LLC; 2011. http://www.natroba.com/Full%20Prescribing%20Information.pdf.

2. Centers for Disease Control and Prevention. Parasites-lice-head lice. Prevention & control. http://www.cdc.gov/parasites/lice/head/prevent.html.

TREATMENT FOR COPD

Roflumilast

Reducing the risk of COPD exacerbations

Chronic obstructive pulmonary disease (COPD) is a progressive, irreversible lung disorder. Significant exacerbations of symptoms (such as breathlessness, cough, and excessive mucus production) may last for weeks and be severe enough to require hospitalization. The fourth leading cause of death in the United States, COPD is most often caused by cigarette smoking.[1]

Roflumilast (*Daliresp*, Forest) is a selective inhibitor of phosphodiesterase 4 (PDE4).[2] PDE4 is a major cyclic-3´,5´-adenosine monophosphate (cyclic AMP)-metabolizing enzyme in lung tissue. Inhibition of PDE4 allows cyclic AMP to accumulate in cells. Although the specific mechanism behind roflumilast's effect is unknown, increased intracellular cyclic AMP in lung cells may reduce inflammation and related symptoms.

Administered orally, roflumilast is indicated to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. It hasn't been evaluated for treatment of COPD associated with emphysema.

Precautions: (1) Roflumilast isn't a bronchodilator and isn't indicated for relief of acute bronchospasm. (2) Monitor patients for suicidal ideation and behavior, which have been reported in some patients taking roflumilast. (3) Roflumilast is contraindicated in patients with moderate-to-severe hepatic impairment; use with caution in patients with mild hepatic impairment. (4) Roflumilast is converted to its active metabolite primarily via the CYP1A2 and CYP3A4 pathways. The drug's activity may be increased by the concurrent use of a CYP3A4 inhibitor (such as ketoconazole or erythromycin) or dual CYP3A4/1A2 inhibitors such as fluvoxamine. Its activity may be decreased by concurrent use of CYP3A4 inducers such as rifampin and carbamazepine.

Adverse reactions: *diarrhea*, *nausea*, headache, back pain, insomnia, weight loss, influenza, dizziness, anorexia, anxiety, depression

Supplied as: 500 mcg tablets

Dosage: 500 mcg once a day

Nursing considerations: (1) Educate patients and families about the potential for suicidal ideation and behavior, and tell them to report the emergence or worsening of insomnia, anxiety, depression, or other mood changes to the healthcare provider. (2) Monitor patients' weight regularly during treatment. In studies of 1-year duration, 20% of patients taking roflumilast experienced moderate weight loss (between 5% and 10% of body weight). (3) Tell patients that roflumilast can be taken without regard to food.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Revised 2011. http://www.goldcopd.org/uploads/users/files/GOLD_Report_2011.pdf.

2. Daliresp (roflumilast) tablets [package insert]. St. Louis, MO: Forest Pharmaceuticals Inc; 2011. http://www.frx.com/pi/Daliresp_pi.pdf.

ANTIDEPRESSANT

Vilazodone hydrochloride

Another SSRI indicated for major depressive disorder

Classified as a selective serotonin reuptake inhibitor (SSRI), vilazodone hydrochloride (*Viibryd*, Forest) has properties similar to citalopram, escitalopram, fluoxetine, paroxetine, and sertraline. No data suggest that vilazodone is more effective than these other SSRIs, but it may be effective in some patients who haven't responded adequately to another SSRI.

Vilazodone is indicated to treat adults with major depressive disorder. The drug-related problems, warnings, and precautions associated with vilazodone are generally similar to those for the other SSRIs. The labeling for all of these drugs includes a boxed warning regarding the increased risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18 to 24).

In 8-week clinical trials, vilazodone wasn't linked to a significant change in body weight. However, long-term use of other SSRIs is associated with weight gain. The SSRIs have been associated with seizures, mania/hypomania, hyponatremia, and abnormal bleeding.

Vilazodone is extensively metabolized through CYP (primarily CYP3A4) and non-CYP pathways. The dosage of vilazodone should be reduced if used

concurrently with a strong CYP3A4 inhibitor such as clarithromycin or ketoconazole. Consult the product insert for complete information about potential drug interactions.

Precautions: (1) Contraindicated in patients being treated with a monoamine oxidase inhibitor (MAOI) and in those who've taken an MAOI within 14 days. In patients treated with vilazodone first, an interval of at least 14 days should elapse following discontinuation of vilazodone before starting treatment with an MAOI. (2) Potentially life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions have been reported with the use of SSRIs alone and in combination with other drugs that have serotonergic activity (such as serotonin-norepinephrine reuptake inhibitors) and antidopaminergic activity (such as antipsychotic drugs). If combination therapy with these drugs is clinically warranted, monitor patients closely, especially when treatment is initiated and when dosages are increased. Discontinue treatment immediately if the patient develops symptoms of serotonin syndrome or NMS, such as agitation, nausea and vomiting, hyperthermia, mental status changes including hallucinations, autonomic instability, fluctuating vital signs, and neuromuscular aberrations (such as muscle rigidity, hyperreflexia, and incoordination). (3) Because of the increased risk of serotonin syndrome or NMS-like reactions, the concurrent use of vilazodone with a serotonin precursor such as tryptophan isn't recommended. (4) Use caution in patients concurrently taking warfarin or another anticoagulant, aspirin, or any other nonsteroidal anti-inflammatory drug because of the increased bleeding risk.

Adverse reactions: *diarrhea, nausea, dizziness,* vomiting, insomnia, sexual dysfunction

Supplied as: 10, 20, and 40 mg immediate-release film-coated tablets

Dosage: initially, 10 mg once a day for 7 days, followed by 20 mg once a day for 7 days, then increased to the recommended maintenance dosage of 40 mg once a day. Consult the product insert for recommended dosage adjustments when the patient is taking other drugs concurrently.

Nursing considerations: (1) Monitor patients for suicidality and tell patients to report worsening depression and other mood changes. (2) Vilazodone may cause central nervous system (CNS) effects such as dizziness, so warn patients not to drive or engage in other activities requiring alertness until they determine how the medication affects them. (3) Warn patients to avoid other CNS-active substances, including alcoholic beverages, while taking vilazodone. (4) Tell patients to take the drug with food (a light meal or high-fat snack). Taking the drug without food may reduce its effectiveness. (5) Instruct patients to report troublesome adverse reactions and warn them not to discontinue the drug abruptly. If indicated, the healthcare provider will instruct them to taper the dosage gradually.

REFERENCE

Viibryd (vilazodone HCl) tablets for oral administration [package insert]. St. Louis, MO: Forest Pharmaceuticals Inc; 2011. http://www.frx.com/pi/viibryd_pi.pdf.

DRUG FOR ALLERGIC CONJUNCTIVITIS

Alcaftadine

Relief for itchy eyes

The most common type of ocular allergy, allergic conjunctivitis causes itching, redness, tearing, burning, and eyelid edema. Alcaftadine (*Lastacaft*, Allergan) is the sixth ophthalmic antihistamine that also has mast cell stabilizing activity to be approved, joining azelastine, bepotastine, epinastine, ketotifen, and olopatadine. Studies directly comparing alcaftadine with these drugs are very limited, and no data suggest that it's more effective than the other drugs. Most patients tolerate alcaftadine well.

Precaution: Alcaftadine ophthalmic solution contains benzalkonium chloride as a preservative, an agent that may be absorbed by soft contact lenses.

Adverse reactions: *eye irritation, burning and/or stinging upon instillation, eye redness, ocular pruritus*, nasopharyngitis, headache, influenza

Supplied as: an ophthalmic solution containing the drug in a concentration of 0.25%

Dosage: one drop in each eye once a day

Nursing considerations: (1) Teach patients how to administer eye drops correctly. (2) Tell patients who wear contact lenses to remove the lenses before instilling the medication. Lenses may be reinserted 10 minutes after instillation. (3) Advise patients not to wear contact lenses if their eyes are red, and inform them that alcaftadine shouldn't be used to treat contact lens-related eye irritation.

REFERENCE

Lastacaft (alcaftadine ophthalmic solution) 0.25%. Irvine, CALIF: Allergan; 2011. http://www.allergan.com/assets/pdf/lastacaft_pi.pdf.

ANTIDIABETIC DRUG

Linagliptin

Oral adjunct to diet and exercise

Incretin hormones are involved in the physiologic regulation of glucose homeostasis. Secreted at a low level throughout the day, they're normally produced in larger amounts in the presence of elevated glucose concentrations (for example, after a meal). Incretins are rapidly inactivated by the enzyme dipeptidyl peptidase-4 (DPP-4). The oral antidiabetic drugs sitagliptin and saxagliptin are DPP-4 inhibitors prescribed to help control blood glucose levels.

Linagliptin (*Tradjenta*, Boehringer Ingelheim, Lilly), the third DPP-4 inhibitor on the market, has properties similar to sitagliptin and saxagliptin. Like those drugs, linagliptin is administered orally as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It's not indicated to treat type 1 diabetes or diabetic ketoacidosis.

When used as monotherapy, linagliptin reduced glycosylated hemoglobin (A1C) by up to 0.7% compared to placebo in clinical trials. The reduction of A1C attributed to the new drug was slightly smaller when it was used in combination with other antidiabetic drugs, such as metformin, glimepiride, or pioglitazone.

Linagliptin hasn't been directly compared to sitagliptin or saxagliptin.

Because only 5% of a linagliptin dose is eliminated via urine, a dosage reduction isn't necessary for patients with impaired renal function. This gives linagliptin an advantage over sitagliptin and saxagliptin. Dosage for both of the older drugs should be reduced in patients with moderate or severe renal impairment or end-stage renal disease.

In clinical trials, linagliptin was well tolerated by patients. Unlike sitagliptin and saxagliptin, it's not available in combination formulations with metformin.

Precautions: (1) Hypersensitivity reactions to linagliptin were infrequently reported in clinical trials, although this isn't specifically identified as a warning in its labeling. (2) Linagliptin may have the potential to cause acute pancreatitis. Although this risk isn't included in the labeling, the labeling for the similar drug sitagliptin was revised to include this risk based on postmarketing reports. (3) Use caution when giving linagliptin concurrently with an antidiabetic drug with the potential to cause hypoglycemia, such as a sulfonylurea. Monitor patient response and lower the latter drug's dosage as prescribed. (4) Drugs that are inducers of P-glycoprotein or CYP3A4, such as rifampin, may reduce exposure to linagliptin to subtherapeutic concentrations. In patients taking these drugs, an alternative to linagliptin is strongly recommended. Consult the product labeling for complete information on potential drug interactions.

Adverse reactions: *nasopharyngitis*, hypersensitivity reactions (rare)

Supplied as: 5 mg tablets

Dosage: 5 mg once a day

Nursing considerations: (1) Tell patients they can take this drug without regard to food. (2) Teach patients how to recognize and manage signs and symptoms of hypoglycemia, such as headache, drowsiness or dizziness, weakness, confusion, hunger, irritability or a jittery feeling, tachycardia, and diaphoresis. ■

REFERENCE

Tradjenta (linagliptin) tablets [package insert]. Ridgefield, CONN: Boehringer Ingelheim Pharmaceuticals, Inc; 2011. http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing+Information/PIs/Tradjenta/Tradjenta.pdf.

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