New Drugs part 2

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THIS ARTICLE REVIEWS 16 recently approved drugs, including:

> fidaxomicin, an antibiotic indicated for *Clostridium difficile*-associated diarrhea.

> ticagrelor, first in a new class of antiplatelet medications indicated for acute coronary syndromes.

> seven new antineoplastic drugs.

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.

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*Common adverse reactions are italicized throughout this article.

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ANTIBIOTIC

Fidaxomicin

Taking aim at *Clostridium difficile* infection

Most commonly occurring in patients being treated with an antibiotic, *Clostridium difficile*-associated diarrhea (CDAD) is experienced with increasing frequency in the United States. Particularly vulnerable are older adults, hospitalized patients, and residents of long-term care facilities. The usual treatment is oral administration of vancomycin or metronidazole (off label). However, many patients experience recurrences of infection following treatment with these drugs.

Fidaxomicin (*Dificid*, Optimer) is a macrolide antibacterial drug with a narrow spectrum of action. It's primarily active against species of clostridia, including *C. difficile*. The drug acts locally in the gastrointestinal (GI) tract and very little is absorbed systemically. For this reason, it isn't indicated to treat systemic infection.

In clinical trials, the initial response rate for fidaxomicin was similar to that for vancomycin. But fidaxomicin's sustained response rate proved superior: In two studies, fidaxomicin's rate of sustained response 25 days after the end of treatment was 70% and 72%, compared to 57% and 57% for vancomycin. The type and frequency of adverse reactions were similar for both drugs.[1]

Fidaxomicin is indicated to treat CDAD in adults over age 18.

Precaution: To optimize its effectiveness and reduce the risk of resistance, fidaxomicin should be used only to treat infections proven or strongly suspected to be caused by *C. difficile*

Adverse reactions: *nausea, vomiting, abdominal pain,* GI hemorrhage, anemia, neutropenia

Supplied as: film-coated tablets containing 200 mg of the drug

Dosage: 200 mg twice a day for 10 days

Nursing considerations: (1) Tell patients they can take the drug with or without food. (2) Teach patients to take antibiotics exactly as prescribed for the full course of treatment, even if they feel better. Warn them not to skip doses and to discard any leftover medication after they finish the course of treatment. (3) Tell patients not to share their antibiotic (or any drug) with others or take drugs prescribed for someone else.

REFERENCE

1. Dificid (fidaxomicin) tablets. Highlights of prescribing information. http://www.dificid.com/sites/www.dificid.com/files/prescribing.pdf.

ANTICOAGULANT

Rivaroxaban

Oral drug to prevent DVT, stroke, and systemic embolism

Following major orthopedic surgery, patients typically receive therapy with a subcutaneous anticoagulant such as enoxaparin to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE). Last year, an oral medication, rivaroxaban (*Xarelto*, Janssen) was approved to prevent DVT, which may lead to PE, in patients undergoing knee or hip replacement surgery. Later in the year, the drug was also approved to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

Rivaroxaban exhibits its anticoagulant activity by inhibiting factor Xa. It selectively blocks the active site of factor Xa and doesn't require a cofactor (such as anti-thrombin III) for activity.

In clinical trials involving more than 6,000 patients undergoing hip or knee replacement surgery, rivaroxaban (10 mg/day) was compared with enoxaparin (40 mg/day). Of patients undergoing knee replacement surgery, about 10% experienced venous thromboembolism (VTE), compared with 19% of patients treated with enoxaparin. In two studies involving patients undergoing hip replacement therapy, rivaroxaban was also significantly more effective at preventing VTE, including nonfatal PE and VTE-related death.[1]

In other clinical trials involving over 14,000 patients, rivaroxaban was compared with warfarin for reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. It was found to be noninferior, but not superior, to warfarin for this indication.[1]

Like other anticoagulants, rivaroxaban carries a risk of bleeding complications. Patients treated with an anticoagulant who undergo spinal/epidural analgesia or spinal puncture are at increased risk for an epidural or spinal hematoma, which can result in paralysis. This is the subject of a boxed warning in rivaroxaban's labeling.

Bleeding events were experienced by about 6% of patients taking rivaroxaban in clinical trials, but major bleeding was reported in less than 0.5% of patients.[1] The frequency of all bleeding events and major bleeding events was similar in patients treated with rivaroxaban and enoxaparin. Routine monitoring of the international normalized ratio or other coagulation parameters isn't required in patients taking rivaroxaban.

Anaphylactic reactions to rivaroxaban have been reported in postmarketing reports. Patients who experience severe hypersensitivity reactions shouldn't receive rivaroxaban.

Precautions: (1) Like other anticoagulants, rivaroxaban is contraindicated in patients with active major bleeding. (2) To minimize the bleeding risk, an epidural catheter shouldn't be removed earlier than 18 hours after the last administration of rivaroxaban, and the next dose of the drug shouldn't be administered sooner than 6 hours after catheter removal. If traumatic puncture occurs, rivaroxaban administration should be delayed for 24 hours. (3) Avoid or closely monitor concurrent use of rivaroxaban and any other medication known to increase bleeding risks, such as aspirin and other nonsteroidal anti-inflammatory drugs. Rivaroxaban shouldn't be used with another anticoagulant except during a therapeutic transition period, during which the patient must be closely monitored. (4) Rivaroxaban's effects may be increased or decreased when it's given concurrently with other drugs that are combined CYP3A4 or P-gp inhibitors or inducers, respectively. Consult the product labeling for a complete listing of potential drug interactions and precautions related to use with other drugs metabolized along these pathways. (5) Avoid use of rivaroxaban in patients with severe renal impairment (creatinine clearance <30 mL/minute) and in those with moderate or severe hepatic impairment or any hepatic disease associated with coagulopathy. (6) Use with caution in patients with moderate renal impairment. In patients age 65 and older, renal function should be assessed before rivaroxaban therapy starts.

Adverse reaction: *bleeding*

Supplied as: 10, 15, and 20 mg tablets

Dosage: *For DVT prophylaxis,* 10 mg/day for 35 days in patients having hip replacement surgery, and for 12 days in patients having knee replacement surgery. *For patients with nonvalvular atrial fibrillation*, 20 mg/day with the evening meal. *For patients with creatinine clearance between 15 and 50 mL/minute,* 15 mg/day with the evening meal.

Nursing considerations: (1) Patients undergoing hip or knee replacement surgery should take the first dose of rivaroxaban 6 to 10 hours after surgery, after hemostasis is achieved. (2) Tell patients to take rivaroxaban as prescribed at the same time each day. (3) If patients miss a dose, they should take it as soon as possible on the same day and continue at the scheduled time on the following day. (4) Teach patients to recognize and immediately report any unusual, severe, or difficult-to-control bleeding, and signs and symptoms of bleeding, such as red, pink, or brown urine; red or black tarry stools; "coffee ground" vomit; headaches; and feeling dizzy or weak.

REFERENCE

1. Xarelto (rivaroxaban) tablets, for oral use. Highlights of prescribing information. http://www.xareltohcp.com/sites/default/files/pdf/xarelto_0.pdf#zoom=100.

ANTIPLATELET DRUG

Ticagrelor

A new drug class for acute coronary syndromes

Acute coronary syndromes (ACS) include conditions characterized by myocardial ischemia and coronary artery thrombosis, such as unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). Many patients with ACS are candidates for percutaneous coronary intervention (PCI), but procedure-related platelet aggregation increases the risk of dangerous thrombus formation.

Clopidogrel and prasugrel, antiplatelet drugs commonly used to prevent thrombosis in patients with ACS, are now joined by ticagrelor (*Brilinta*, AstraZeneca), which belongs to a new chemical class. The labeled indications for ticagrelor are more limited than those for clopidogrel but broader than those for prasugrel.

Ticagrelor prevents platelet activation and aggregation by reversibly interacting with platelet $P2Y_{12}$ receptors. It's indicated to reduce the rate of thrombotic cardiovascular events in patients with ACS (UA, NSTEMI, and STEMI). In patients treated with PCI, it also reduces the rate of stent thrombosis. In a large study, ticagrelor was more effective than clopidogrel in reducing the combined endpoint of cardiovascular death, myocardial infarction, and stroke.[1]

Ticagrelor is given in a regimen that includes aspirin at a maintenance dosage of 75 to 100 mg/day. Research indicates that maintenance aspirin dosages greater than 100 mg/day reduce ticagrelor's effectiveness; this is the subject of a boxed warning in the drug's labeling. The risk of bleeding, a concern with any antiplatelet drug, is also the subject of a boxed warning.

Precautions: (1) Contraindicated in patients with active pathologic bleeding or a history of intracranial hemorrhage. (2) Contraindicated in patients with severe hepatic impairment. (3) Ticagrelor therapy shouldn't be started in patients who are to undergo urgent coronary artery bypass graft surgery. (4) If possible, ticagrelor should be discontinued at least 5 days before any surgery. (5) Risk of bleeding is increased by the concurrent use of medications such as anticoagulants, fibrinolytic agents, and chronic use of nonsteroidal anti-inflammatory drugs. (6) If possible, bleeding events should be managed without discontinuing ticagrelor; stopping the drug increases the risk of cardiovascular events. (7) The action of ticagrelor may be increased by the concurrent use of a strong CYP3A4 inhibitor (such as clarithromycin or itraconazole), and decreased by the concurrent use of a strong CYP3A4 inducer (such as carbamazepine or rifampin). Avoid concomitant use of these drugs with ticagrelor. (8) Closely monitor patients taking ticagrelor and digoxin concurrently.

Adverse reactions: *bleeding, dyspnea*, headache, cough, dizziness

Supplied as: 90 mg tablets

Dosage: loading dose of 180 mg, followed by 90 mg twice a day.

Nursing considerations: (1) Teach the patient about concurrent aspirin therapy, which is initiated with a loading dose (usually 325 mg), followed by a daily maintenance dose of 75 to 100 mg. Instruct the patient not to take more or less aspirin than prescribed. (2) A patient who misses a dose of ticagrelor should take the next dose at its scheduled time. (3) Teach the patient to recognize and immediately report any unusual, severe, or difficult-to-control bleeding, and signs and symptoms of bleeding, such as red, pink, or brown urine; red or black tarry stools; "coffee ground" vomit; headaches; and feeling dizzy or weak.

REFERENCE

1. Brillinta (ticagrelor) tablets. Highlights of prescribing information. http://www1.astrazeneca-us.com/pi/brilinta.pdf.

DRUG FOR WET AMD

Aflibercept

Vision-saving therapy

Age-related macular degeneration (AMD) is a chronic, progressive disease of the macula that can result in the loss of central vision. More than 200,000 Americans are diagnosed with AMD each year.[1]

AMD is classified as neovascular (wet) and nonneovascular (dry). In neovascular AMD, abnormal blood vessels leak blood and fluid into the retina, damaging the macula and impairing central vision. Although neovascular AMD accounts for only 10% of all AMD cases, it's more severe and rapidly progressive.[2]

Aflibercept (*Eylea*, Regeneron) is the fourth drug to be approved for treatment of neovascular AMD, joining verteporfin, pegaptanib, and ranibizumab. Administered by ophthalmic intravitreal injection, aflibercept acts as a decoy receptor that binds vascular endothelial growth factor (VEGF)-A and placental growth factor (PGF), inhibiting the binding and activation of VEGF receptors. Overexpression of VEGF and PGF causes neovascularization and vascular permeability with subsequent progressive vision loss.

In two studies comparing aflibercept with ranibizumab, patients treated with aflibercept 2 mg every 4 weeks and 2 mg every 8 weeks experienced efficacy that was clinically equivalent to patients treated with ranibizumab 0.5 mg every 4 weeks. (Efficacy was defined as maintaining vision at week 52 compared to baseline.) No additional efficacy was demonstrated when aflibercept was given every 4 weeks rather than every 8 weeks.[3]

After initiation of therapy, aflibercept is administered every 8 weeks, giving it an important advantage over ranibizumab, which is typically administered every 4 weeks.

Precautions: (1) Contraindicated in patients with ocular or periocular infection or active intraocular inflammation. (2) Intravitreal injection of VEGF inhibitors carries a risk of arterial thromboembolic events (nonfatal stroke, nonfatal myocardial infarction, or vascular death). The incidence of these events in clinical studies during the first year was 1.8%. (3) Intravitreal injections have been associated with endophthalmitis and retinal detachments. (4) Acute increases in intraocular pressure (IOP) may occur within 60 minutes of intravitreal injection. Some patients experience sustained increases in IOP.

Adverse reactions: *conjunctival hemorrhage, eye pain,* cataract, vitreous detachment, vitreous floaters, increased IOP

Supplied as: single-use vials designed to deliver 0.05 mL of a solution containing the drug in a concentration of 40 mg/mL. Needles and syringes are supplied with the medication to withdraw solution from the vial and administer it via intravitreal injection.

Dosage: 2 mg (0.05 mL) by intravitreal injection every 4 weeks for the first 12 weeks, followed by 2 mg once every 8 weeks

Nursing considerations: (1) Patients should receive adequate anesthesia and a topical broad-spectrum microbicide before the injection. (2) Because patients may experience temporary visual disturbances after treatment, instruct them not to drive or operate other machinery until their vision recovers. (3) Instruct patients to immediately call the healthcare provider if the eye becomes red, sensitive to light, or painful, or if they experience any vision changes. (4) Store drug vials in the refrigerator. Each vial is used for the treatment of only a single eye.

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2. National Eye Institute/National Institutes of Health. Facts about age-related macular degeneration. http://www.nei.nih.gov/health/maculardegen/armd_facts.asp#10.

3. Eylea (aflibercept) Injection. For intravitreal injection. Highlights of prescribing information. http://www.regeneron.com/Eylea/eylea-fpi.pdf.

ANTIVIRAL DRUG

Rilpivirine hydrochloride

Another NNRTI for treating HIV-1 infection

Rilpivirine hydrochloride (*Edurant*, Tibotec) is the fifth nonnucleoside reverse transcriptase inhibitor (NNRTI) to be marketed for treatment of HIV infection in adults. It's indicated for use in combination with other antiretroviral drugs to treat HIV-1 infection in treatment-naïve adults.

The effectiveness of rilpivirine was demonstrated in two studies comparing it with efavirenz, another NNRTI on the market. Both drugs were used with two other antiretroviral drugs in various combinations. Rilpivirine and efavirenz were similarly effective in reducing viral load, but 13% of patients treated with rilpivirine experienced virologic failure during the study period, compared with 9% of patients treated with an efavirenz regimen. Patients with a higher viral load at the beginning of therapy were less likely to respond to the rilpivirine-containing regimen than those with a lower viral load. The incidence of adverse reactions was similar for both drugs, although efavirenz was associated with a higher incidence of rash (11% versus 3%). The incidence of Grade 3 and 4 depressive disorders was 1% for both drugs.[1]

Rilpivirine is also available in a combination tablet formulation (*Complera*, Gilead) containing 25 mg rilpivirine, 300 mg tenofovir disoproxil fumarate, and 200 mg emtricitabine.

Precautions: (1) Rilpivirine shouldn't be included in a regimen with another NNRTI because the plasma concentration and activity of both drugs could be altered. (2) Use caution if rilpivirine is used concurrently with medications known to carry a risk of torsades de pointes. When given in higher-than-recommended dosages, rilpivirine has been reported to prolong the QT interval. (3) An increase in gastric pH may result in a significant decrease in rilpivirine's plasma concentration and action, so concurrent use with a proton pump inhibitor such as omeprazole is contraindicated. (4) Certain macrolide antibiotics such as clarithromycin may increase rilpivirine's action; use of another antibiotic (such as azithromycin) that's not likely to interact should be considered. (5) Concurrent use of rilpivirine with a CYP3A inducer (such as carbamazepine, phenobarbital, or phenytoin) is contraindicated. Concurrent use with these drugs may result in a loss of virologic response and resistance to rilpivirine or to the class of NNRTIs. Consult the product insert for a complete listing of potential drug interactions. (6) Closely monitor patients also being treated with methadone maintenance therapy; the methadone dosage may need adjustment. (7) Use caution and closely monitor patients with severe renal impairment or end-stage renal disease.

Adverse reactions: *depressive disorders, insomnia, headache, rash*

Supplied as: tablets containing 25 mg rilpivirine base

Dosage: 25 mg once a day

Nursing considerations: (1) Tell patients to take each dose with a meal to improve absorption. (2) As the immune system responds to treatment, some patients treated with combination antiretroviral therapy experience an inflammatory response to indolent or residual opportunistic infections. Tell patients to report any new symptoms they experience after starting therapy. (3) Antiretroviral regimens have also been associated with redistribution or accumulation of body fat, including central obesity, buffalo hump, peripheral wasting, breast enlargement, and cushingoid appearance. (4) Monitor patients for depression and instruct them to report depression and other mood changes to the healthcare provider. (5) Administer histamine H_2-receptor antagonists such as famotidine at least 12 hours before or at least 4 hours after rilpivirine. (6) Administer an antacid such as aluminum hydroxide or magnesium hydroxide at least 2 hours before or at least 4 hours after rilpivirine.

REFERENCE

1. Edurant (rilpivirine) tablets. Full prescribing information. http://www.edurant-info.com/sites/default/files/EDURANT-PI.pdf.

DRUG FOR HAE

Icatibant

Unique mechanism of action allays acute symptoms

A rare genetic disorder, hereditary angioedema (HAE) is characterized by severe, often painful edema of the extremities, face, gastrointestinal tract, and/or larynx.[1] It's caused by deficiency or dysfunction of C1 esterase inhibitor, which primarily acts to inhibit plasma kallikrein. Unregulated kallikrein activity results in excessive production of bradykinin, a vasodilator thought to be responsible for many signs and symptoms of HAE.[2]

Icatibant (*Firazyr*, Shire) has been approved for treatment of acute attacks of HAE in patients age 18 and older. Administered subcutaneously, it prevents bradykinin from binding to the B2 receptor, reducing signs and symptoms of HAE.

Three other drugs, two C1 esterase inhibitors and a kallikrein inhibitor, ecallantide, have also been approved for treatment of HAE, but icatibant's mechanism of action is unique. It was the first drug approved for self-administration by patients upon recognition of symptoms of an attack after appropriate education by a healthcare professional. (Labeling

for the C1 esterase inhibitor Berinert was expanded early this year to allow I.V. self-administration by appropriately educated patients.)

In clinical trials, the median time for patients treated with icatibant to report onset of symptom relief was 2 hours, compared with almost 20 hours in patients receiving placebo. The new drug hasn't been directly compared with the C1 esterase inhibitors or ecallantide.

Precautions: (1) Because of the potential for airway obstruction during acute laryngeal HAE attacks, patients should seek medical attention immediately in addition to treatment with icatibant. (2) Because icatibant is a bradykinin receptor antagonist, it has the potential to reduce the antihypertensive effect of angiotensin-converting enzyme inhibitors, although concurrent use with these drugs hasn't been studied.

Adverse reactions: *injection site reaction,* pyrexia, increased transaminases, dizziness, rash

Supplied as: prefilled syringes delivering 30 mg of the drug

Dosage: 30 mg via subcutaneous injection in the abdominal area

Nursing considerations: (1) If patient response to the initial dose is inadequate, additional doses may be administered at intervals of at least 6 hours. Tell the patient to administer no more than 3 doses in a 24-hour period. (2) Instruct the patient to seek care for an acute HAE attack in an appropriate healthcare facility in addition to administering icatibant because of the potential for airway obstruction. (3) Educate the patient about injection technique and injection site rotation.

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1. Pepe J, Bielory L. New hope for those with hereditary angioedema. *Nursing.* 2012;42(4):43-46.

2. Firazyr (icatibant) for injection. Highlights of prescribing information. http://pi.shirecontent.com/PI/PDFs/Firazyr_USA_ENG.pdf.

IMMUNOSUPPRESSANT

Belatacept

Preventing organ rejection after kidney transplant

Produced by recombinant DNA technology, belatacept (*Nulojix,* Bristol-Myers Squibb) is indicated for prophylaxis of organ rejection in adults receiving a kidney transplant.[1] It should be used in combination with basiliximab induction, mycophenolate mofetil, and corticosteroids. The drug is labeled with several boxed warnings, including a warning about the risk of posttransplant lymphoproliferative disorder (PTLD) predominantly involving the central nervous system (CNS), and increased risk of malignancies and serious infections. A type of malignant lymphoma, PTLD is potentially life-threatening.[2]

Belatacept isn't likely to interact with other medications, and monitoring of serum concentrations is unnecessary.

Precautions: (1) Not recommended in patients receiving liver transplants because of an increased risk of graft loss and death. (2) Because the risk of PTLD is increased in patients without immunity to Epstein-Barr virus (EBV), belatacept is contraindicated in patients who are EBV seronegative or with unknown serostatus. (3) Prophylaxis against cytomegalovirus infection is recommended for at least 3 months after transplant; prophylaxis against *Pneumocystis jiroveci* is also recommended. (4) Monitor patients for new or worsening neurologic, cognitive, or behavioral signs or symptoms. Progressive multifocal leukoencephalopathy, a rapidly progressing opportunistic infection of the CNS, has been reported with the use of belatacept.

Adverse reactions: *anemia, diarrhea, urinary tract infection, peripheral edema, constipation, hypertension, pyrexia, graft dysfunction, cough, nausea, vomiting, headache, hypokalemia, hyperkalemia, leukopenia*

Supplied as: vials containing 250 mg of the drug in a lyophilized powder

Dosage: *Initially,* 10 mg/kg I.V. over 30 minutes, administered on Day 1 (day of transplant, prior to transplantation), Day 5 (approximately 96 hours after the Day 1 dose), and at the end of weeks 2, 4, 8, and 12 after transplant. *Maintenance dosage,* 5 mg/kg administered at the end of Week 16 and every 4 weeks (plus or minus 3 days) thereafter.

Nursing considerations: (1) Store drug vials in the refrigerator. (2) Reconstitute vial contents with 10.5 mL of Sterile Water for Injection, 0.9% Sodium Chloride Injection, or 5% Dextrose Injection, using the silicone-free disposable syringe provided. The reconstituted solution contains the drug in a concentration of 25 mg/mL. The volume of the reconstituted solution required to provide the dose for infusion should be determined, and this volume of reconstituted solution should be further diluted with a suitable infusion fluid. (3) The drug dosage is based on the body weight of the patient at the time of transplant and shouldn't be modified during therapy unless body weight changes by more than 10%. (4) The initial dosage is 10 mg/kg, but the prescribed dose must be evenly divisible by 12.5 mg for the dose to be prepared accurately using the reconstituted solution and the silicone-free disposable syringe provided. A silicone-free syringe is necessary to prevent development of translucent particles, which may appear with use of siliconized syringes. (5) Instruct the patient to avoid live vaccines while undergoing treatment with belatacept. (6) To reduce the risk of skin cancer, tell the patient to limit exposure to sunlight and other ultraviolet light sources by wearing protective clothing and using a sunscreen with a high sun protection factor. (7) Teach the patient to recognize and report possible signs and symptoms of infection, including neurologic, cognitive, or behavioral changes.

REFERENCES

1. Nulojix (belacept). Highlights of prescribing information. http://packageinserts.bms.com/pi/pi_nulojix.pdf.

2. Inoue T, Satoh S, Saito M, Horikawa Y, Tsuchiya W, Habuchi T. Post-transplant lymphoproliferative disorder involving the ovary as an initial manifestation: a case report. *J Med Case Reports.* 2010; 4:184.

IRON CHELATOR

Deferiprone

New treatment for infusion-related iron overload

Patients with rare chronic blood disorders, such as thalassemia and sickle cell disease, may require frequent blood transfusions. Iron overload, a potentially life-threatening complication of frequent transfusions, can damage the heart, liver, and endocrine glands. Iron chelation therapy is used to treat transfusion-related iron overload; by binding to iron, the chelating drug facilitates its excretion.

Deferiprone (*Ferriprox*, ApoPharma) is an orally administered iron chelator indicated to treat transfusional iron overload due to thalassemia syndromes when first-line chelation therapy isn't adequate.[1] Because no controlled trials

demonstrating a direct treatment benefit have been conducted, deferiprone isn't a first-line therapy.

Deferiprone may harm fetuses and is classified in Pregnancy Category D.

Precautions: (1) The risk of agranulocytosis is the subject of a boxed warning in the labeling. Neutropenia may precede agranulocytosis, so absolute neutrophil counts should be determined before the start of therapy and monitored weekly during therapy. (2) Avoid concomitant use of deferiprone with other drugs associated with neutropenia or agranulocytosis. (3) Interrupt treatment if the patient develops an infection. (4) Use caution in patients at risk of prolonged QT interval; one patient with a history of QT prolongation developed torsades de pointes during deferiprone therapy. (5) Deferiprone may increase alanine aminotransferase (ALT) levels, which should be monitored weekly during therapy.

Adverse reactions: *nausea, vomiting, abdominal discomfort, arthralgia,* increased ALT values, neutropenia

Supplied as: scored tablets in a 500 mg potency

Dosage: *Initially*, 25 mg/kg three times a day (75 mg/kg/day). Maximum dosage: 33 mg/kg three times a day (99 mg/kg/day). Dosages should be rounded to the nearest 250 mg (half a tablet).

Nursing considerations: (1) Patients may require zinc supplementation; reductions in plasma zinc levels have been reported. (2) Tell patients to take the drug with meals in the morning, at midday, and in the evening, to minimize nausea. (3) Inform patients that they may experience chromaturia, a reddish-brown discoloration of urine resulting from iron excretion. Reassure them that this isn't harmful. (4) Because deferiprone binds to polyvalent cations (such as iron, zinc, and aluminum), give the new drug 4 hours before or 4 hours after any medications (such as antacids) or supplements containing these cations. (5) Instruct patients to contact the healthcare provider immediately if they experience signs and symptoms of infection, such as fever, sore throat, or flulike symptoms. (6) Tell patients that if they miss a dose, they should take it as soon as possible, unless it's almost time for the next dose. In that case, they should skip the missed dose and take the next scheduled dose. Warn them not to "catch up" or double dose.

REFERENCE

1. Ferriprox (deferiprone) tablets, for oral use. Highlights of prescribing information. http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/021825lbl.pdf.

DRUG FOR LIPODYSTROPHY

Tesamorelin acetate

Specifically indicated for patients with HIV

Many patients being treated with antiretroviral therapy (ART) for HIV infection experience fat accumulation in the abdomen and upper back while losing

Recently approved antineoplastic drugs[1-7]

Drug (trade name, manufacturer)	Indication	Administration route
Abiraterone acetate (*Zytiga*, Centocor Ortho Biotech)	A CYP17 inhibitor for use in combination with prednisone for treatment of metastatic castration-resistant prostate cancer in patients who've received prior chemotherapy containing docetaxel	Oral
Brentuximab vedotin (*Adcetris*, Seattle Genetics)	A CD30-directed antibody-drug conjugate for treatment of Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multiagent chemotherapy regimens in patients who aren't ASCT candidates. Also indicated for treatment of systemic anaplastic large cell lymphoma after failure of at least one prior multiagent chemotherapy regimen.	I.V.
Crizotinib (*Xalkori*, Pfizer)	A kinase inhibitor for treatment of locally advanced or metastatic non–small cell lung cancer that's positive for the abnormal anaplastic lymphoma kinase gene as detected by an FDA-approved test	Oral
Ipilimumab (*Yervoy*, Bristol-Myers Squibb)	A human monoclonal antibody that binds to and inhibits the action of the cytotoxic T-lymphocyte-associated antigen 4 blocking antibody; indicated for treatment of unresectable or metastatic melanoma	I.V.
Ruxolitinib (*Jakafi*, Incyte)	A kinase inhibitor for treatment of intermediate or high-risk myelofibrosis	Oral
Vandetanib (*Caprelsa*, AstraZenica)	A kinase inhibitor for treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable, locally advanced, or metastatic disease	Oral
Vemurafenib (*Zelboraf*, Roche)	A kinase inhibitor for treatment of unresectable or metastatic melanoma in patients with BRAF V600E mutation as detected by an FDA-approved test	Oral

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2. Adcetris (brentuximab vedotin) for injection. Highlights of prescribing information. http://www.seagen.com/pdf/ADCETRIS_US_PI.pdf.
3. Xalkori (crizotinib) capsules, oral. Highlights of prescribing information. http://labeling.pfizer.com/showlabeling.aspx?id=676.
4. Yervoy (ipilimumab). Highlights of prescribing information. http://packageinserts.bms.com/pi/pi_yervoy.pdf.
5. Jakafi (ruxolitinib) tablets, for oral use. Highlights of prescribing information. http://www.incyte.com/products/uspi_jakafi.pdf.
6. Caprelsa (vandetanib) tablets. Highlights of prescribing information. http://www1.astrazeneca-us.com/pi/caprelsa.pdf.
7. Zelboraf (vemurafenib) tablet, oral. Highlights of prescribing information. http://www.gene.com/gene/products/information/zelboraf/pdf/pi.pdf.

subcutaneous fat in the face, limbs, and buttocks (lipodystrophy). Visceral abdominal fat is a risk factor for cardiovascular disease.

Tesamorelin acetate (*Egrifta*, Serono), the first drug to be approved for lipodystrophy, is specifically indicated for reduction of excess abdominal fat in patients with HIV infection.[1] Administered subcutaneously, the new drug is an analogue of human growth hormone-releasing factor. In clinical trials, patients treated with tesamorelin experienced greater reductions in abdominal fat compared with patients receiving placebo, and some patients reported improvements in self-image. Improvements were maintained among patients who continued taking the drug, but those who were switched from tesamorelin to placebo experienced a rapid return to the degree of fat accumulation at baseline.

Tesamorelin is considered to have a weight-neutral effect and isn't indicated for weight loss management. Potential long-term cardiovascular benefits and long-term cardiovascular safety haven't been studied, and data are insufficient to determine if using the drug improves patient adherence to ART.

Tesamorelin is classified in Pregnancy Category X and is contraindicated during pregnancy.

Precautions: (1) Contraindicated in patients with disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism, pituitary tumor or surgery, head irradiation, or head trauma. (2) Contraindicated in patients with any active malignancy because it induces release of endogenous growth hormone, a known growth factor. Any preexisting malignancy should be inactive and its treatment complete before treatment with tesamorelin starts. (3) Tesamorelin stimulates release of the growth factor IGF-1, which also may influence development or progression of malignancies. Serum concentrations should be closely monitored during therapy. (4) Tesamorelin is associated with glucose intolerance. Glucose status should be evaluated before therapy starts and monitored periodically throughout treatment. (5) Discontinuing tesamorelin treatment in critically ill patients should be considered because use of growth hormone is associated with complications in patients who've had major surgery or who are experiencing acute respiratory failure. (6) Because tesamorelin stimulates growth hormone production, patients receiving glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in maintenance or stress doses following initiation of the new drug.

Adverse reactions: *arthralgia,* injection site erythema and pruritus, peripheral edema, extremity pain, myalgia, paresthesia, hypersensitivity reactions

Supplied as: single-use vials in an amount equivalent to 1 mg of tesamorelin base and vials of diluent (Sterile Water for Injection)

Dosage: 2 mg once a day via subcutaneous injection

Nursing considerations: (1) Following reconstitution, the drug concentration is 2 mg/mL. It should be administered immediately after reconstitution. (2) The abdomen is the recommended injection site; teach patients to rotate abdominal sites. (3) Store vials in the refrigerator and protect them from light. Keep vials in the original box until the time of use. (4) Inform patients that arthralgia, edema, and other musculoskeletal adverse reactions are usually transient or resolve when treatment is discontinued. ■

REFERENCE

1. Egrifta. Tesamorelin for injection. Highlights of prescribing information. http://www.egrifta.com/Pdfs/Egrifta_US_PI_1210_r2a_ltr.pdf.

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