new DRUGS

PART 2 2011

CE **2.8** ANCC CONTACT HOURS

Rx **2.8** PHARMACOLOGY CREDITS

IN THIS ARTICLE, YOU'LL LEARN ABOUT SEVEN RECENTLY APPROVED DRUGS, INCLUDING:

> fingolimod hydrochloride, an oral drug indicated to treat patients with relapsing forms of multiple sclerosis.

> ulipristal acetate, an emergency contraceptive available by prescription.

> dabigatran etexilate mesylate, the first of a group of investigational oral anticoagulants to be approved in the United States.

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.; 2011.

Nursing2011 Drug Handbook. Ambler, PA: Lippincott Williams & Wilkins; 2011.

Physicians' Desk Reference. 65th ed. Montvale, NJ: Medical Economics; 2011.

*Common adverse reactions are italicized throughout this article.

The author has disclosed that he has no significant relationship with or financial interest in any commercial companies that pertain to this educational activity.

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DRUG FOR MULTIPLE SCLEROSIS

Fingolimod hydrochloride

Oral administration offers patients a convenient treatment option.

Joining dalfampridine, fingolimod hydrochloride (*Gilenya*, Novartis) was the second new drug marketed in 2010 to treat patients with multiple sclerosis (MS). Compared with dalfampridine, fingolimod has broader indications. Other drugs with indications similar to fingolimod's, such as interferon beta 1a and interferon beta 1b, are administered parenterally. Because fingolimod is administered orally, it has an important advantage over these drugs.

Fingolimod is specifically indicated to treat patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability. The most common type of MS is the relapsing/remitting form.[1] In clinical trials, fingolimod was shown to reduce the annual relapse rate.

The pathologic changes associated with MS haven't been clearly delineated, but increased lymphocytes in the central nervous system appear to be a contributing factor. When metabolized to its active metabolite (fingolimod phosphate), the new drug blocks the ability of lymphocytes to leave lymph nodes, reducing the number of lymphocytes in peripheral blood available for migration into the central nervous system.[2] This sequestration of lymphocytes in lymph tissue results in a dose-dependent decrease in serum lymphocytes, increasing the patient's risk of infection. However, in clinical trials, infection rates in patients taking fingolimod were similar to those in the placebo group.

Initiation of treatment is associated with bradycardia and transient atrioventricular conduction delays. Most patients are asymptomatic, but some experience dizziness, palpitations, or fatigue during the first 24 hours of treatment. With ongoing treatment, heart rate returns to normal within 1 month. Conduction abnormalities usually resolve within the first 24 hours of treatment, but some patients in clinical trials required treatment with atropine or isoproterenol.

Because animal studies have shown that fingolimod may cause fetal harm, it's classified in Pregnancy Category C. If a pregnant patient is taking the drug, she should be enrolled in the pregnancy registry (1-877-598-7237).

Precautions: (1) Use caution in patients at increased risk for bradycardia or heart block/conduction delays, such as those with low heart rate, history of syncope, sick sinus syndrome, 2nd degree or higher conduction block, heart failure, or those taking a beta-blocker, calcium channel blocker, or certain antiarrhythmia drugs, such as procainamide. Before initiating treatment, obtain an ECG for patients with one or more of these risk factors. (2) Before initiating treatment with fingolimod, a recent complete blood cell count (within 6 months) should be obtained. Don't initiate treatment in patients with an active acute or chronic infection until the infection is resolved. Suspending treatment should be considered in patients who develop infections while taking fingolimod. (3) Use caution in patients concurrently taking an antineoplastic, immunosuppressive, or immune-modulating drug, and in patients changing from long-acting therapies for MS that have immune effects, such as natalizumab. (4) Patients who've never had varicella (chicken pox) or been vaccinated against varicella zoster virus (VZV) should be tested for VZV antibodies. VZV vaccination should be considered before starting fingolimod therapy in patients who are antibody-negative, and therapy should be delayed for 1 month while the vaccine takes full effect. (5) Patients with a history of uveitis and those with diabetes mellitus are at increased risk for macular edema, which was reported in 0.4% of patients treated with fingolimod in clinical trials. Patients should have a baseline ophthalmologic exam before starting treatment and regular assessments throughout treatment and whenever symptoms such as blurred vision occur. (6) Closely monitor patients with compromised respiratory function during therapy. In clinical trials, some patients experienced a decrease in pulmonary function test results or unexplained dyspnea. (7) Use caution in patients with severe hepatic impairment. In clinical trials, 8% of patients experienced elevation of liver transaminases at least 3 times the upper limit of normal. Liver transaminases and bilirubin levels should be evaluated before initiating treatment, and treatment should be discontinued if significant liver injury is suspected. (8) Closely monitor patients concurrently taking ketoconazole, which may markedly increase fingolimod's effects.

Adverse reactions: *headache, influenza, back pain, diarrhea, cough, liver transaminase elevations*, hypertension

Supplied as: 0.5 mg oral capsules

Dosage: 0.5 mg once a day

Nursing considerations: (1) Fingolimod can be taken without regard to food. (2) Observe patients for 6 hours following the first dose for signs and symptoms of bradycardia. (3) Monitor patients' BP throughout treatment; 5% of patients experienced hypertension in clinical trials. (4) Tell patients to report any vision changes, which may indicate macular edema. Instruct them to have regular eye exams as directed by the healthcare provider. (5) Tell patients to report signs and symptoms of possible hepatic dysfunction, such as nausea, abdominal pain, jaundice, or dark urine. (6) Instruct patients to report any signs and symptoms of infection, including respiratory tract infections. Continue monitoring for infection after treatment is discontinued. (7) Because fingolimod's effects, including lymphocytopenia, persist in the body for up to 2 months following the last dose, tell patients not to receive live attenuated vaccines during treatment with fingolimod and for 2 months after ending treatment. (8) Warn patients not to exceed the prescribed dosage. In trials, higher dosages weren't more effective but caused more adverse reactions. (9) Advise women of childbearing potential to use effective contraception during therapy and for 2 months after discontinuing therapy.

REFERENCES

1. National Multiple Sclerosis Society. Relapsing/remitting MS (RRMS). http://www.nationalmssociety.org/about-multiple-sclerosis/relapsing-ms/index.aspx.

2. Chun J, Hartung HP. Mechanism of action of oral fingolimod (FTY7290) in multiple sclerosis. *Clin Neuropharmacol.* 2010;33(2):91-101.

CONTRACEPTIVE

Ulipristal acetate

Emergency contraceptive available by prescription

A synthetic progesterone agonist/antagonist, ulipristal acetate (*ella*, Watson) is indicated for prevention of pregnancy following unprotected intercourse or a known or suspected contraceptive failure. Its use is most similar to that of levonorgestrel, the synthetic progestogen included in other emergency contraceptives, such as Plan B One-Step. However unlike levonorgestrel, which the FDA has approved for use without a prescription for women age 17 and older, ulipristal is available by prescription only.

Ulipristal's primary mechanism of action is thought to be inhibition or delay of ovulation. Depending on the timing of administration in relation to the menstrual cycle, it may also alter the endometrium in ways that impair implantation in the uterus. In this way it's similar to the abortifacient drug mifepristone. However, ulipristal has been evaluated only for the prevention of pregnancy, not as an abortifacient. In clincial trials, ulipristal reduced the pregnancy rate when used within 120 hours (5 days) of unprotected intercourse. It may be less effective in women with a body mass index greater than 30 kg/m^2.

Precautions: (1) Ulipristal is contraindicated in pregnancy. Because of its potential harm to the fetus, it's classified in Pregnancy Category X, and pregnancy should be excluded before its use. (2) If a patient becomes pregnant or experiences lower abdominal pain following use of ulipristal, the possibility of ectopic pregnancy should be considered. (3) Drugs or herbs that induce the CYP3A4 metabolic pathway (such as St. John's wort, rifampin, and carbamazepine) may reduce the drug's action. Its action may be increased by the use of CYP3A4 inhibitors such as itraconazole.

Adverse reactions: *headache*, *abdominal pain*, *nausea*, dysmenorrhea, fatigue, dizziness

Supplied as: 30 mg oral tablets

Dosage: one tablet as soon as possible after unprotected intercourse or a known or suspected contraceptive failure. The dose may be repeated if the patient vomits within 3 hours after taking the dose.

Nursing considerations: (1) Ulipristal can be taken without regard to food. (2) Tell patients that following use of the drug, menses may occur earlier or later than expected by a few days. If menses is delayed more than 1 week beyond the suspected time, however, pregnancy should be ruled out. (3) Tell patients to resume routine contraception immediately, but warn them that ulipristal may reduce the contraceptive action of hormonal products. Advise them to use a reliable barrier method for the duration of the current menstrual period. (4) Instruct patients to consult their healthcare provider if they become pregnant despite ulipristal use, or if they experience lower abdominal pain, which may indicate an ectopic pregnancy. (5) Inform patients that this drug doesn't protect against HIV/AIDS or any other sexually transmitted infection, and educate them about safer sex practices.

ANTICOAGULANT

Dabigatran etexilate mesylate

An effective alternative to warfarin for patients with atrial fibrillation

A direct thrombin inhibitor, dabigatran etexilate mesylate (*Pradaxa*, Boehringer Ingelheim) is the first of this group of investigational oral anticoagulants to be approved in the United States. It's indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Its safety and effectiveness was established in a clinical trial of more than 18,000 patients. At a dosage of 150 mg twice a day, dabigatran reduced stroke and systemic embolism by 35% beyond the reduction attained with warfarin. The risk of major bleeding was similar for both drugs.

Unlike warfarin, dabigatran doesn't require monitoring of blood tests and resultant dosage adjustments, an important advantage. The international normalized ratio (INR) used to monitor warfarin isn't a reliable indicator of its anticoagulant activity. The ecarin clotting time (ECT) is a better indicator and may be used to determine bleeding risk before invasive procedures. (ECT measures anticoagulation during treatment with lepirudin and other direct thrombin inhibitors.[1] For details about assessing ECT values, consult the product labeling.)

Also unlike warfarin, dabigatran has no antidote. Bleeding complications are treated by discontinuing the drug and providing clinical support.

Dabigatran has been approved in some other countries to prevent venous thromboembolism following joint replacement surgery, but this isn't a labeled indication in the United States at this time.

Precautions: (1) Contraindicated in patients with active pathologic bleeding. (2) Because of bleeding risks, dabigatran should be discontinued 1 to 2 days before surgical procedures if possible. (3) Bleeding risks are increased by the concurrent use of medications such as heparin, antiplatelet drugs, and chronic use of nonsteroidal anti-inflammatory drugs. (4) Consult the product labeling for specific recommendations and precautions when patients are being converted from therapy with warfarin or a parenteral anticoagulant to therapy with dabigatran.

Adverse reactions: *Bleeding*, *gastritis-like symptoms* (gastroesophageal reflux disease, esophagitis, erosive gastritis, gastrointestinal ulcer, gastric hemorrhage), dyspepsia

Supplied as: 75 mg and 150 mg oral capsules

Dosage: 150 mg twice a day; in patients with severe renal impairment, 75 mg twice a day

Nursing considerations: (1) Dabigatran may be taken without regard to food. Unlike warfarin, its action isn't affected by dietary changes. (2) Teach patients to take doses at the same time each day. If a dose isn't taken at the scheduled time, patients should take it as soon as possible on the same day. But if the missed dose can't be taken at least 6 hours before the next scheduled dose, it should be skipped. Warn patients not to double the dose to make up for a missed dose. (3) Stress the importance of taking the drug exactly as prescribed. Missing doses or interrupting treatment increases the risk of stroke. If therapy is interrupted (before surgery, for example), it should be resumed as soon as possible. (4) Instruct patients to swallow the capsule whole. Opening, chewing, or breaking the capsule significantly increases the drug's bioavailability. (5) Educate patients about possible adverse reactions, especially bleeding. Tell them to call their healthcare provider right away or seek emergency care if they experience unexpected, severe, and/or prolonged bleeding from the gums, nose, or any other site (including unusually heavy menstrual bleeding); pink or brown urine; red or tarry black stools; large or unexplained bruises; coughing up or vomiting blood (blood may look like coffee grounds in

vomit); and unexplained joint pain or swelling. (6) Dabigatran is supplied in bottles containing 60 capsules and in a blister package containing 60 capsules. The original package should be dispensed to protect the medication from moisture. Tell patients that the bottle should be tightly closed after each use. Once opened, the product must be used within 30 days.

REFERENCE

1. Ecarin Clotting Time. Practical-Haemostasis.com. http://www.practical-haemostasis.com/Miscellaneous/Miscellaneous%20Tests/ecarin_ct.html

DRUG FOR CERVICAL DYSTONIA

IncobotulinumtoxinA

Relief for head and neck pain

The botulinum toxins are neuromuscular blocking agents that block cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve endings. Botulinum toxin A (Botox), now designated as onabotulinumtoxinA, was the first of these products to be approved for therapeutic use.

IncobotulinumtoxinA (*Xeomin*, Merz) is the fourth botulinum toxin product to be marketed. Administered I.M., it's indicated to treat adults with cervical dystonia to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients. It's also approved to treat adults with blepharospasm who were previously treated with onabotulinumtoxinA.

The most important risk for botulinum toxin products is the potential for distant spread of the toxin from the area of injection. This is the subject of a boxed warning in the product labeling. Swallowing and breathing difficulties have been reported hours to weeks after injection and can be life-threatening. Adults with underlying conditions such as myasthenia gravis or amyotrophic lateral sclerosis are predisposed to these problems.

The dose, number, and location of I.M. injection sites varies based on the patient's condition and previous treatments, if any. If proposed injection sites are marked with a pen, the drug must not be injected through the pen marks or a permanent tattooing effect may occur. Repeat injections should generally be no more frequent than every 12 weeks.

Precautions: (1) Contraindicated in patients with a known hypersensitivity to any botulinum toxin product. (2) Contraindicated in the presence of infection at proposed injection sites. (3) Closely monitor for respiratory, swallowing, or speech difficulties in patients taking an aminoglycoside, muscle relaxant, or other drug that interferes with neuromuscular transmission. These drugs may increase the response to incobotulinumtoxinA. (4) Patients treated for cervical dystonia who have smaller neck muscle mass or who require bilateral injections into the sternocleidomastoid muscles may be at greater risk for dysphagia. (5) When used to treat blepharospasm, incobotulinumtoxinA reduces blinking, which may lead to corneal exposure, persistent epithelial defect, and corneal ulceration. (6) Use caution in patients taking drugs with anticholinergic activity because of the potential for excessive systemic anticholinergic effects.

Adverse reactions: ***When used to treat cervical dystonia***—*dysphagia*, *injection site pain*, *neck pain*, *musculoskeletal pain*, *muscular weakness*. ***When used to treat blepharospasm***—*ptosis*, *dry eye*, *visual impairment*, *dry mouth*, *diarrhea, headache*, *nasopharyngitis*, *dyspnea*, *respiratory tract infection*

Supplied as: single-use vials containing 50 units and 100 units of lyophilized drug

Dosage: The recommended initial dose for the treatment of cervical dystonia is 120 units. Treatment of blepharospasm is based on treatment history and patient response, up to a maximum dose of 35 units per eye. Consult the product labeling for detailed recommendations and dosage precautions.

Nursing considerations: (1) Unlike other botulinum toxin products, vials of incobotulinumtoxinA needn't be refrigerated. (2) Reconstitute the drug with preservative-free 0.9% sodium chloride injection. (3) Teach patients being treated for blepharospasm to use protective ophthalmic drops or ointments as prescribed. (4) Instruct patients to notify the healthcare provider or seek emergency care if they experience breathing, swallowing, or speech difficulties. Inform them that these adverse reactions can be life-threatening and may occur days or weeks after injections.

ANTINEOPLASTIC DRUGS

Cabazitaxel

Potent cytotoxic agent for hormone-refractory prostate cancer

Classified as a taxane antineoplastic agent, Cabazitaxel (*Jevtana*, Sanofi-Aventis) is indicated for use with prednisone to treat hormone-refractory metastatic prostate cancer in patients previously treated with a docetaxel-containing treatment regimen. Administered I.V., it's the first drug to be approved for advanced, hormone-refractory prostate cancer that's worsened during or after treatment with docetaxel.

Two potentially fatal adverse reactions are the subject of boxed warnings in the product labeling. The first, neutropenia, is experienced by virtually all patients treated with cabazitaxel. In clinical trials, five patients died from infection, such as sepsis. Each of these patients had grade 4 (life-threatening) neutropenia.

The second, severe hypersensitivity reaction may occur within a few minutes following infusion of the drug, particularly during the first and second infusions. Patients should be premedicated as recommended in the product labeling.

The drug can also cause severe gastrointestinal (GI) adverse reactions, such as vomiting and diarrhea, and patients being treated with cabazitaxel have died from complications associated with dehydration and electrolyte imbalances. Patients should be treated with antiemetic and antidiarrheal medications to minimize this risk.

Cabazitaxel is administered as a 1-hour I.V. infusion every 3 weeks in combination with oral prednisone 10 mg once a day throughout the treatment period.

Although cabazitaxel is approved for use only in men with prostate cancer, some practitioners may prescribe it off-label to women. Warn women of childbearing potential to avoid becoming pregnant during treatment.

Precautions: (1) Contraindicated in patients with a neutrophil count of 1,500/mm^3 or lower. Monitor complete blood cell counts weekly during cycle 1 and before each treatment cycle thereafter. Consider prophylaxis with granulocyte colony-stimulating factor in patients vulnerable to neutropenia complications, such as older adults, malnourished patients, and those with a history of febrile neutropenia. (2) Contraindicated in patients with a history of severe hypersensitivity to the new drug or other drugs formulated with polysorbate 80. (3) Hepatic impairment is likely to increase serum concentrations of cabazitaxel. The drug is contraindicated in patients with a total bilirubin equal to or greater than the upper limit of normal (ULN), or an aspartate aminotransferase or alanine aminotransferase determination of 1.5 x ULN or greater. (4) At least 30 minutes before each dose, premedicate patients as prescribed with I.V.

diphenhydramine or an equivalent antihistamine, dexamethasone or an equivalent corticosteroid, and ranitidine or an equivalent histamine$_2$ antagonist. (5) Prophylaxis with an antiemetic is recommended and may be given orally or I.V. as needed. (6) Be aware that concurrent use of a strong CYP3A inhibitor such as clarithromycin will increase the concentration and action of the new drug, and concurrent use of a strong CYP3A inducer such as carbamazepine, rifampin, or St. John's wort will reduce its concentration.

Adverse reactions: *neutropenia, leukopenia, anemia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, hematuria, asthenia, abdominal pain, anorexia, back pain*

Supplied as: a kit that includes a single-use vial containing 60 mg of the drug in 1.5-mL polysorbate 80. A vial of diluent is also provided that contains approximately 5.7 mL of 13% (w/w) ethanol in water for injection.

Dosage: 25 mg/m^2 every 3 weeks. The preparation of a dose requires two dilutions prior to administration. Consult the product labeling for detailed instructions.

Nursing considerations: (1) Because cabazitaxel is cytotoxic, take appropriate precautions to protect yourself when preparing and administering the drug. (2) After the drug has been prepared according to detailed product instructions, the final solution should be used within 8 hours (including the 1-hour infusion) if at room temperature or within 24 hours if refrigerated. (3) Administer the solution using an in-line filter of 0.22 micrometer nominal pore size during administration. (4) Premedicate patients as prescribed before treatment begins. (5) Closely observe patients for signs and symptoms of hypersensitivity reactions and other adverse events during treatment. The incidence of most adverse reactions is higher in patients over age 65 than in younger patients, so be especially vigilant with older adults. (6) Educate patients about taking oral prednisone as prescribed.

Eribulin mesylate

Another weapon against metastatic breast cancer

Developed from an agent isolated from a sea sponge, eribulin mesylate (*Halaven*, Eisai) is indicated to treat patients with metastatic breast cancer who've previously received at least two chemotherapeutic regimens for treatment of metastatic disease. Prior therapy should have included an anthracycline (such as doxorubicin) and a taxane derivative. In clinical trials comparing eribulin to other single-agent therapies, patients taking eribulin experienced an improvement in overall survival (median of 13.1 months, compared with a median of 10.6 months for patients in the control group).

Severe neutropenia (absolute neutrophil count <500/mm^3) lasting more than 1 week occurred in 12% of patients in clinical trials. Patients with elevated alanine aminotransferase, aspartate aminotransferase, or bilirubin concentrations had a higher incidence of grade 4 (life-threatening) neutropenia and febrile neutropenia.

Peripheral neuropathy, experienced by 35% of patients in clinical trials, was the most common adverse reaction resulting in discontinuation of eribulin treatment. Five percent of patients experienced neuropathy lasting more than a year.

Precautions: (1) Obtain complete blood counts prior to each dose. Increase the frequency of monitoring in patients who develop grade 3 or 4 (severe or life-threatening) cytopenias. (2) Closely monitor patients for peripheral motor and sensory neuropathy. Treatment should be withheld in patients who experience grade 3 or 4 (severe or disabling) peripheral neuropathy until resolution to grade 2 or less. (3) Eribulin has been associated with prolongation of the QT interval on ECG. Avoid use in patients with congenital long QT syndrome. ECG monitoring is recommended in patients with heart failure, bradydysrhythmias, drugs known to prolong the QT interval (such as certain antiarrhythmics), and electrolyte abnormalities. (4) Hypokalemia and/or hypomagnesemia should be corrected before therapy begins, and these electrolytes should be periodically monitored during therapy. (5) The drug dosage should be reduced in patients with mild or moderate hepatic impairment or moderate renal impairment. Eribulin hasn't been studied in patients with severe hepatic or renal impairment.

Adverse reactions: *neutropenia, anemia, asthenia/fatigue, alopecia, peripheral neuropathy, nausea, constipation*

Supplied as: single-use vials containing 1 mg of the drug in 2 mL of solution (0.5 mg/mL)

Dosage: 1.4 mg/m^2 administered I.V. over 2 to 5 minutes on days 1 and 8 of a 21-day cycle. Consult the product labeling for recommended dosage adjustments for patients with hepatic or renal impairment.

Nursing considerations: (1) Before each dose, obtain a complete blood cell count and assess for signs and symptoms of peripheral neuropathy, such as numbness, tingling, or burning sensations in hands or feet. (2) Monitor for electrolyte imbalances, particularly hypokalemia and hypomagnesemia, throughout therapy. (3) Caution women of childbearing potential to avoid pregnancy during treatment. (4) The volume of solution needed to provide one dose of the drug should be withdrawn and administered undiluted or diluted in 100 mL of 0.9% sodium chloride injection. Don't dilute in or administer the drug through an I.V. line containing dextrose solutions because precipitation may result. (5) Don't administer the drug concurrently through the same I.V. line with any other drug. (6) Diluted or undiluted solutions of eribulin may be stored in the syringe for up to 4 hours at room temperature or for up to 24 hours under refrigeration.

DRUG FOR GOUT

Pegloticase

Easing joint pain for patients with persistent symptoms

An estimated 3 to 5 million Americans suffer from gout, an arthritic disorder characterized by elevated serum uric acid concentrations and associated with pain, erythema, and edema in affected joints.[1,2] For most patients with chronic gout, the xanthine oxidase inhibitor allopurinol is highly effective in preventing uric acid synthesis and reducing its serum concentration to less than the goal of 6 mg/dL. But an estimated 3% of patients with gout don't respond adequately to allopurinol and other conventional therapies and experience persistent symptoms.

Pegloticase (*Krystexxa*, Savient), a uric acid-specific enzyme, is indicated for adults with chronic gout who are refractory to conventional therapy. It's not recommended to treat patients with hyperuricemia who are asymptomatic.

The most important risk associated with pegloticase, which is administered I.V., is anaphylaxis, the subject of a boxed warning in the product labeling. It was reported with a frequency of 6.5% in patients receiving the drug every 2 weeks (compared with none with placebo), even though patients were premedicated with an antihistamine, corticosteroid,

or acetaminophen before the infusion. Anaphylaxis may develop with any infusion of the drug, including the first infusion, and is usually evident within 2 hours. Consequently, the drug should be administered by a healthcare provider in a setting equipped to manage anaphylaxis, and the patient should be observed for an appropriate period after treatment.

Infusion reactions are also the subject of a boxed warning. The risk of an infusion reaction is higher in patients who've lost therapeutic response to this drug, probably as a consequence of antibody formation.

Initiation of treatment with pegloticase is often associated with gout flares because the changing uric acid concentrations mobilize urate from tissue deposits. Unless contraindicated or not tolerated, gout flare prophylaxis with a nonsteroidal anti-inflammatory drug or colchicine is recommended, starting at least 1 week before treatment starts and continuing for at least 6 months.

Precautions: (1) Contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency because of the potential for hemolysis and methemoglobinemia. Patients of African and Mediterranean ancestry are at higher risk for G6PD deficiency and should be screened for the disorder before therapy starts. (2) To lessen the risk of anaphylaxis, patients should be premedicated with an antihistamine or corticosteroid. Treatment should be administered in a setting equipped to provide emergency care. (3) Never administer the drug via I.V. bolus. (4) Closely monitor patients with heart failure. In clinical trials, some patients with heart failure experienced exacerbations.

Adverse reactions: *nausea, contusion or ecchymosis, nasopharyngitis, constipation, vomiting, chest pain*

Supplied as: a sterile solution in single-use vials containing 8 mg/mL of the drug

Dosage: 8 mg every 2 weeks via I.V. infusion over no less than 120 minutes via gravity feed, syringe-type pump, or infusion pump

Nursing considerations: (1) Before treatment begins, the patient's serum uric acid concentration should be determined. (2) Premedicate the patient with an oral antihistamine, I.V. corticosteroid, or acetaminophen as prescribed. (3) Prepare the dose by withdrawing 1 mL of solution from the vial and injecting it into a 250 mL bag of 0.9% sodium chloride injection or 0.45% sodium chloride injection. Invert (don't shake) the infusion bag numerous times to ensure thorough mixing. Infuse the diluted solution within 4 hours. (4) Monitor the patient for serious signs and symptoms during and after the infusion, such as urticaria, dyspnea, chest discomfort, erythema, and pruritus. As prescribed, slow the infusion, or stop the infusion and restart at a slower rate. Be prepared to provide emergency care if indicated. (5) Protect drug vials from light and store vial cartons in the refrigerator. ■

REFERENCES

1. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum.* 2008;58(1):15-25.

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DOI-10.1097/01.NURSE.0000397931.58044.99