New drugs 2014 PART 2

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THIS ARTICLE FEATURES seven recently approved drugs, including

> an important advance for treatment of hepatitis C infection.

> the first drug specifically approved to treat Cushing disease.

> a monoclonal antibody for treatment and prevention of inhalational anthrax, a potential biological terrorism threat.

Unless otherwise specified, the information in the following summaries applies to adults, not children. Consult a pharmacist or the package insert for information on drug safety during pregnancy and breastfeeding. Consult a pharmacist, the package insert, or a comprehensive and current 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.; 2014.

Nursing 2014 Drug Handbook. Ambler, PA: Lippincott Williams & Wilkins; 2014.

Physicians' Desk Reference. 68th ed. Montvale, NJ: Medical Economics; 2014.

*Common adverse reactions are italicized throughout this article.

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Simeprevir
Sofosbuvir

Hepatitis C virus (HCV) infection is characterized by inflammation of the liver, which can lead to hepatic dysfunction and failure. Following initial infection with HCV, most people develop chronic HCV infection. Many patients with the infection don't experience signs or symptoms until liver damage occurs, which may take several years. Some develop cirrhosis leading to liver damage with complications such as bleeding, jaundice, ascites, infections, and/or liver cancer. An estimated 3.2 million Americans are infected with HCV.[1]

For many years, the standard of treatment for chronic HCV infection was a combination regimen of peginterferon alfa, which is administered parenterally, plus ribavirin for 48 weeks. This treatment failed to attain sustained virologic response (SVR) in 50% of patients and was associated with adverse reactions such as flulike symptoms, fatigue, and depression. Additionally, ribavirin is contraindicated during pregnancy.

In 2011, the approval and marketing of boceprevir and telaprevir, classified as HCV protease inhibitors, marked an important advance in the treatment of chronic HCV infection. Administered orally, each of these agents is used in combination with peginterferon alfa and ribavirin. Three-drug regimens that include an HCV protease inhibitor are more effective and permit a shorter course of treatment in many patients. However, both boceprevir and telaprevir may cause some serious adverse events, interact with numerous medications, and have a short duration of action that requires patients to take boceprevir three times a day and telaprevir twice a day.

Late last year, the FDA approved two new drugs, simeprevir and sofosbuvir. Both are administered orally just once a day as part of a combination regimen. Sofosbuvir is the first agent that permits the use of combination regimens that for some patients doesn't include interferon. This represents an important advance in the development of combination regimens for chronic HCV infection that don't include either interferon or, in the not-too-distant future, ribavirin. Combination regimens that include one of these new drugs offer the hope for treatments that are more effective, better tolerated, and shorter in duration.

REFERENCE

1. FDA. FDA approves new treatment for hepatitis C virus. News release. November 22, 2013.

Simeprevir

New player in a 3-drug regimen

Like boceprevir and telaprevir, simeprevir (*Olysio*, Janssen) is a direct-acting antiviral agent against HCV that inhibits the HCV NS3/4A protease needed for viral replication. It's indicated to treat chronic HCV infection as a component of a combination antiviral treatment regimen.[1] Its efficacy has been established in combination with peginterferon alfa and ribavirin in HCV genotype 1 infected patients with compensated liver disease (including cirrhosis). It must not be used as monotherapy.[1]

Simeprevir was evaluated in studies designed to measure whether a patient's HCV was no longer detected in the blood at least 12 weeks after finishing treatment, indicating SVR. Of treatment-naive patients treated with simeprevir, peginterferon alfa, and ribavirin, 80% achieved a SVR, compared with 50% of those treated with peginterferon alfa and ribavirin. In a study in prior relapse patients, 79% of those treated with the 3-drug regimen achieved SVR, compared with 37% of those treated with peginterferon alfa and ribavirin. In another study, the regimen with simeprevir improved response rates in partial responders and those who hadn't responded to prior therapy (null responders). However, the new drug hasn't been evaluated in patients who'd previously failed therapy with a treatment regimen that included an HCV protease inhibitor.

The effectiveness of simeprevir is substantially reduced in patients infected with HCV genotype 1a with an NS3 Q80K polymorphism at baseline. Screening of patients with HCV genotype 1a infection for the presence of virus with this polymorphism at baseline is strongly recommended and, if it's identified, alternative therapy should be considered.

The product labeling should be consulted for recommendations for discontinuation of treatment for patients who experience an inadequate virologic response to therapy as indicated by HCV RNA determinations during treatment with simeprevir.

Precautions: (1) The combination regimen that includes ribavirin, simeprevir, and peginterferon alfa is classified in Pregnancy Category X because ribavirin can cause fetal injury and death. This regimen is contraindicated in pregnant women and in men whose female partners are pregnant. (2) Simeprevir is associated with an increased frequency of adverse reactions in patients of East Asian ancestry. Anticipated benefits and risks should be carefully evaluated before therapy is initiated in these patients. (3) Simeprevir may cause severe photosensitivity, especially during the first 4 weeks of treatment. Patients should limit sun exposure during treatment and protect themselves from sun when outdoors. (4) The concurrent use of moderate or strong inhibitors of CYP3A may significantly increase the concentration of simeprevir, raising the risk of adverse reactions; the use of moderate or strong inducers of CYP3A may significantly reduce its

concentration and efficacy. Simeprevir isn't recommended for use with a moderate or strong CYP3A inhibitor (such as clarithromycin, itraconazole, certain HIV protease inhibitors, and milk thistle), or moderate or strong CYP3A inducers (such as rifampin, carbamazepine, phenobarbital, phenytoin, systemic dexamethasone, efavirenz, and St. John's wort). (5) When simeprevir is used concurrently with atorvastatin or rosuvastatin, the daily dose of the latter two drugs shouldn't exceed 40 mg and 10 mg, respectively.

Adverse reactions: *rash, photosensitivity, pruritus, nausea*, myalgia, dyspnea

Supplied as: 150 mg oral capsules

Dosage: 150 mg once a day with food in a combination regimen with peginterferon alfa and ribavirin. The recommended duration of this 3-drug regimen is 12 weeks. Consult the product insert for therapy adjustments recommended for treatment-naive patients, prior-relapse patients, and prior nonresponder patients.

Nursing considerations: (1) For women of childbearing potential, obtain a negative pregnancy test immediately before treatment starts. Tell both male and female patients to use two effective contraceptive methods during treatment and for 6 months after ending treatment. (2) Warn patients about the risk of photosensitivity and advise them to avoid sun exposure and tanning devices, and to take sun-protective measures when outdoors. (3) Teach patients to take the drug with food.

REFERENCE

1. Prescribing information. Olysio (simeprevir) capsules, for oral use. http://www.olysio.com.

Sofosbuvir

Hailed as a "breakthrough therapy" for HCV infection

Another direct-acting antiviral agent, sofosbuvir (*Sovaldi*, Gilead) inhibits the HCV NS5B RNA-dependent RNA polymerase that's essential for viral replication. It has a unique mechanism of action against HCV and has been active against all HCV genotypes in *in vitro* studies, including strains that are resistant to protease inhibitors.[1,2]

Although sofosbuvir must also be used in a combination regimen, it's the first drug for which effectiveness has been demonstrated when used in regimens that don't include interferon. Its unique mechanism of action and demonstrated effectiveness offer the potential to construct combination regimens that will be more effective, safer, and shorter in duration than previous regimens. It represents such an important advance in the treatment of HCV infection that the FDA designated it as a "breakthrough therapy" and expedited approval in its priority-review program.[3]

Sofosbuvir is specifically indicated for the treatment of chronic HCV infection as a component of a combination antiviral treatment regimen. Its efficacy has been established in patients with HCV genotype 1, 2, 3, and 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 coinfection.

In patients with HCV infection or HCV/HIV-1 coinfection, a regimen of sofosbuvir and ribavirin has been effective in the treatment of HCV genotype 2 or 3 infections. Although a 3-drug regimen that also includes peginterferon alfa is recommended for patients with genotype 1 or 4 infections, some patients are ineligible to receive an interferon-based regimen; in such cases, a sofosbuvir/ribavirin regimen can be considered as an option. This 2-drug regimen can also be used in patients with hepatocellular carcinoma awaiting liver transplantation to prevent posttransplant HCV reinfection.

The approval of the HCV protease inhibitor simeprevir just before the approval of sofosbuvir provides the opportunity to use these two drugs in combination in regimens that avoid the need to use interferon or ribavirin. Other antiviral drugs are also being evaluated for use in combination regimens that will be more effective, better tolerated, and more convenient to use than previous regimens.

Precautions: (1) Not for concurrent use with potent P-glycoprotein (P-gp) inducers in the intestine (such as rifampin and St. John's wort), which may decrease the concentration and pharmacologic action of sofosbuvir, a substrate of P-gp. Other medications known to induce metabolic pathways (such as carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, and tipranavir/ritonavir) may also reduce the concentration and action of sofosbuvir and concurrent use isn't recommended. (2) A combination regimen that includes ribavirin is contraindicated in pregnant women and in men whose female partners are pregnant.

Adverse reactions: With a sofosbuvir/ribavirin regimen, *fatigue, headache*. With a 3-drug regimen containing peginterferon alfa and ribavirin, *fatigue, headache, nausea, insomnia, anemia*.

Supplied as: 400 mg oral tablets

Dosage: 400 mg once a day. See the product insert for recommended combination treatment regimens and adjustments to therapy based on HCV genotype and specific medical conditions, such as HCV/HIV coinfection and hepatocellular carcinoma.

Nursing considerations: (1) Tell patients they can take sofosbuvir without regard to food. (2) For women of childbearing potential, obtain a negative pregnancy test immediately before treatment starts. Tell both male and female

patients to use two effective contraceptive methods during treatment and for 6 months after ending treatment.

REFERENCES

1. Prescribing information. Sovaldi (sofosbuvir) tablets, for oral use. http://www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf.

2. FDA. Approval of Sovaldi (sofosbuvir) tablets for the treatment of chronic hepatitis C. http://www.fda.gov/forconsumers/byaudience/forpatientadvocates/ucm377920.htm.

3. FDA. FDA approves Sovaldi for chronic hepatitis C. News release. December 6, 2013.

DRUG FOR HIV INFECTION

Dolutegravir sodium

Blocking HIV replication

Like HIV reverse transcriptase and HIV protease, HIV integrase is an enzyme that has an important role in the replication of HIV. Inhibiting this enzyme helps manage HIV infection. Dolutegravir sodium (*Tivicay*, GlaxoSmithKline; ViiV) is the third HIV-1 integrase strand transfer inhibitor (INSTI) to be approved, joining raltegravir and elvitegravir, which is included with cobicistat, emtricitabine, and tenofovir in the combination product Stribild.

Dolutegravir is indicated for use in combination with other antiretroviral agents to treat HIV-1 infection in adults and in children age 12 and older and weighing at least 88 lb (40 kg).[1] It can be used to treat patients with HIV infection who are treatment-naive or treatment-experienced, including adults who've been treated with other INSTIs.

In clinical trials, dolutegravir was effective in reducing viral loads in treatment-naive patients and in treatment-experienced, INSTI-naive patients. It's also been evaluated in treatment-experienced, INSTI-experienced patients and may be effective in some patients who've developed resistance to other INSTIs.

The effectiveness and safety of dolutegravir haven't been established in pediatric patients who are INSTI-experienced with documented or suspected resistance to other INSTIs. Research involving pediatric patients under age 12 or weighing less than 40 kg is very limited; dolutegravir use isn't recommended in these patients.

As with most other HIV antiretroviral regimens, immune reconstitution syndrome and fat redistribution/accumulation have been reported with the use of combination regimens that include dolutegravir.

Precautions: (1) Although rare, hypersensitivity reactions characterized by rash, systemic reactions, and possible liver injury have been reported. Treatment should be immediately discontinued if signs and symptoms of hypersensitivity develop. The drug shouldn't be used again in patients who've experienced a hypersensitivity reaction to it. (2) Not recommended for use in patients with severe hepatic impairment. (3) Patients with underlying hepatitis B or C virus infection may be at increased risk for development of or worsening transaminase elevations during treatment with dolutegravir. Patients with underlying hepatic disease should undergo appropriate lab testing prior to initiating treatment with a regimen that includes dolutegravir and monitored for hepatotoxicity during therapy. (4) Concurrent use with dofetilide is contraindicated because of the increased risk of dofetilide toxicity. (5) Concurrent use with metformin should be closely monitored; the dosage of metformin may need adjusting. (6) Avoid concurrent use of certain metabolic inducers such as carbamazepine, oxcarbazepine, phenobarbital, phenytoin, and St. John's wort because data are insufficient for dosage recommendations. Consult the product insert for more details on potential drug interactions and recommended dosage adjustments.

Adverse reactions: *insomnia, headache*

Supplied as: 50 mg film coated tablets

Dosage: In treatment-naive or treatment-experienced INSTI-naive patients, 50 mg once a day. 50 mg twice a day is recommended for adult patients also taking a potent UGT1A/CYP3A inducer such as efavirenz, fosamprenavir/ritonavir, tipranavir/ritonavir, or rifampin, and for adults who are INSTI-experienced and have certain INSTI-associated resistance substitutions or suspected INSTI resistance.

Nursing considerations: (1) Dolutegravir may be taken without regard to food. (2) Certain antacids and laxatives, oral calcium supplements, oral iron supplements, and buffered medications may reduce the activity of dolutegravir. Tell patients to take the new drug either 2 hours before or 6 hours after taking one of these medications. (3) If appropriate, warn female patients not to breast-feed during treatment because of the risk of HIV transmission through breast milk.

REFERENCE

1. Prescribing information. Tivicay (dolutegravir) tablets for oral use. http://www.viivhealthcare.com/media/58599/us_tivicay.pdf.

DRUG FOR INHALATIONAL ANTHRAX

Raxibacumab

I.V. treatment and prophylaxis for adults and children

Anthrax is a potential biological terrorism threat because the spores of the bacterium *Bacillus anthracis* resist destruction and can be easily spread through the air. The toxins released by the bacterium can cause irreversible tissue damage and death. The management of inhalational anthrax has included use of anthrax vaccine adsorbed and a 60-day course of treatment with an appropriate antibiotic, usually

ciprofloxacin or doxycycline. Raxibacumab (GlaxoSmithKline) is a monoclonal antibody that neutralizes toxins produced by *B. anthracis*. It doesn't have direct antibacterial activity but binds to the bacterium's protective antigen (PA). By inhibiting the binding of PA to its cellular receptors, raxibacumab prevents lethal toxins from entering cells.

Administered I.V., raxibacumab is indicated to treat adult and pediatric patients with inhalational anthrax due to *B. anthracis* in combination with appropriate antibacterial drugs. It's also indicated for prophylaxis of inhalational anthrax when alternative therapies aren't available or appropriate.[1]

Raxibacumab was approved using the FDA's Animal Efficacy Rule, which permits efficacy findings from adequate and well-controlled animal studies to support FDA approval when conducting trials in humans isn't ethical or feasible. The safety and pharmacokinetic characteristics of raxibacumab have been evaluated in healthy human volunteers. Infusion-related reactions such as rash, urticaria, and pruritus have been reported.

Raxibacumab hasn't been studied in pediatric patients; dosage recommendations for children were derived using a population pharmacokinetic approach. Raxibacumab doesn't cross the blood-brain barrier and doesn't prevent or treat anthrax meningitis.

Precaution: Premedicate patients with diphenhydramine as prescribed to mitigate any infusion reactions.

Adverse reactions experienced by healthy volunteers: *rash, pain in extremity, pruritus*, somnolence

Supplied as: single-use vials containing 1,700 mg of the drug in 34 mL (50 mg/mL)

Dosage: For adults, a single dose of 40 mg/kg administered I.V. over 2 hours and 15 minutes after dilution in 0.9% sodium chloride injection to a final volume of 250 mL. Consult the product insert for dosage recommendations for pediatric patients and for information about the preparation and administration of infusion solutions.

Nursing considerations: (1) To reduce the risk of infusion reactions, administer a dose of diphenhydramine (25-50 mg) within 1 hour before initiating the raxibacumab infusion, as prescribed. Diphenhydramine may be administered orally or I.V. based on proximity to the start of the raxibacumab infusion. (2) Store vials in the refrigerator.

REFERENCE

1. Prescribing information. Raxibacumab injection for intravenous use. http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/125349s000lbl.pdf.

DRUG FOR SHORT BOWEL SYNDROME

Teduglutide

Indicated to reduce the volume of parenteral nutrition needed

Short bowel syndrome (SBS) is characterized by a significant reduction in length of functioning intestine (for example, to less than 200 cm [78.7 in] of small intestine).[1] Although it may occur in children as a congenital defect, it most often results from the partial or complete surgical removal of the small and/or large intestine in patients with disorders such as Crohn disease.[2] An estimated 10,000 to 15,000 American adults have SBS.[3] Many of them experience poor absorption of fluids and nutrients from food, resulting in malnutrition, dehydration, diarrhea, and weight loss. Besides dietary adjustments, treatment for SBS often includes parenteral nutrition, I.V. fluids, antimotility drugs such as loperamide, and drugs to reduce gastric acid secretion such as omeprazole and ranitidine.

Administered via subcutaneous injection, teduglutide (*Gattex*, NPS) is the third drug approved to treat adults with SBS who require parenteral support, joining somatropin and glutamine.[4] Produced using recombinant DNA technology, it binds to and activates glucagon-like peptide-2 (GLP-2) receptors in several types of intestinal cells, resulting in the local release of multiple mediators, including insulin-like growth factor (IGF)-1, nitric oxide, and keratinocyte growth factor. The effect is to increase intestinal absorption of fluids and nutrients, which has been shown to help reduce the volume of parenteral nutrition patients need. In two placebo-controlled studies, 46% and 63% of patients treated with teduglutide achieved the clinical response of at least a 20% reduction in the volume of weekly parenteral nutrition after 20 and 24 weeks of treatment, compared with 6% and 30%, respectively, of those receiving placebo. A few patients in the studies were weaned off parenteral nutrition.

Several risks associated with teduglutide are the basis for development of a Risk Evaluation and Mitigation Strategy (REMS) consisting of a communication plan and training for prescribers.[5]

- Because the drug has the potential to accelerate neoplastic growth, it shouldn't be prescribed for patients with active gastrointestinal (GI) malignancy. Colonoscopy of the entire colon with removal of polyps should be done within 6 months before initiation of treatment with teduglutide. A follow-up colonoscopy (or alternate imaging) is recommended at the first year of treatment, and subsequent colonoscopies should be done every 5 years or more often as needed. Patients should also be monitored clinically for small bowel neoplasia.

• Some patients in clinical trials experienced intestinal obstruction and biliary and pancreatic disease. In patients who develop intestinal or stomal obstruction, treatment should be temporarily suspended until the obstruction is resolved. To monitor for the potential for biliary disease and pancreatic disease, patients should undergo lab assessment within 6 months before starting teduglutide for bilirubin and alkaline phosphatase, and lipase/amylase, respectively. Repeat assessments should be performed at least every 6 months during treatment, or more frequently if needed.
• Some patients have experienced fluid overload and congestive heart failure, presumably as a result of increased fluid absorption associated with teduglutide treatment. Parenteral support should be adjusted as needed. If this or other cardiovascular manifestations can't be readily resolved, teduglutide may need to be discontinued.
• Some patients who were being treated concurrently with a benzodiazepine experienced altered mental status that may have been associated with increased absorption of the benzodiazepine. Patients taking concomitant oral drugs that require titration and/or have a narrow therapeutic index, such as benzodiazepines and phenothiazines, may require dosage adjustments.

Precautions: (1) Contraindicated in patients with active GI malignancy. In patients with active non-GI malignancy and in those who are considered to be at increased risk for malignancy, teduglutide should be used only if the anticipated benefit outweighs the risk. (2) Assess and monitor patients for biliary and pancreatic disorders as recommended. (3) Monitor patients for fluid overload and adjust parenteral nutrition volume as needed. (4) Use caution with concomitant use of oral drugs that require titration and/or have a narrow therapeutic range.

Adverse reactions: *abdominal pain, injection site reactions, nausea, headache*, abdominal distension, upper respiratory tract infection, vomiting, fluid overload

Supplied as: a lyophilized powder in single-use vials containing 5 mg of the drug

Dosage: 0.05 mg/kg once a day via subcutaneous injection. The dosage should be reduced by 50% in patients with moderate or severe renal impairment (creatinine clearance less than 50 mL/minute) and end-stage renal disease.

Nursing considerations: (1) Don't administer teduglutide I.M. or I.V. (2) Reconstitute vial contents by slowly injecting 0.5 mL of preservative-free sterile water for injection provided in a prefilled syringe. Upon reconstitution, the vial provides a maximum of 0.38 mL of the sterile solution, which contains 3.8 mg of teduglutide. Administer the medication within 3 hours after reconstitution. Consult the product labeling for details about dispensing the medication and preparing doses. (3) Teach patients to prepare and self-administer the drug, if indicated, and to alternate injection sites, which may include the thighs, arms, and abdominal quadrants. (4) If patients miss a dose, they should take the next dose as soon as possible on that day, but warn them not to administer two doses on the same day. (5) If treatment is discontinued, closely monitor patients for fluid and electrolyte imbalances. (6) Teach patients to store vials in a refrigerator.

REFERENCES

1. Teduglutide injection (Gattex) for short bowel syndrome. *Med Lett Drugs Ther.* 2013;55(1414):29-30.
2. National Digestive Diseases Information Clearinghouse. Short bowel syndrome. http://digestive.niddk.nih.gov/ddiseases/pubs/shortbowel/index.aspx?control=Pubs.
3. Crane M. FDA approves teduglutide to treat short bowel syndrome. Medscape news release. December 21, 2012. http:www.medscape.com.
4. FDA. FDA approves Gattex to treat short bowel syndrome. News release. December 21, 2013.
5. Prescribing information. http://www.gattex.com.

DRUG FOR CUSHING DISEASE

Pasireotide diaspartate

First drug specifically approved for Cushing disease

Resulting from excessive cortisol production by the adrenal glands, Cushing disease is caused by a tumor in the pituitary gland that increases secretion of adrenocorticotrophic hormone (ACTH), which overstimulates the adrenal glands. It's associated with the overexpression of human somatostatin receptor subtypes (hsst), particularly hsst5.

Cushing disease is often characterized by increased weight, glucose intolerance or diabetes, high BP, easy bruising, and increased risk for infections. The first-line treatment is surgical removal of the pituitary tumor.

Pasireotide diaspartate (*Signifor*, Novartis) is a cyclohexapeptide somatostatin analogue that has a high affinity for hsst5. By binding and activating hsst receptors, it inhibits ACTH secretion, which reduces cortisol secretion. Administered subcutaneously, it's indicated for adults with Cushing disease for whom pituitary surgery isn't an option or hasn't been curative. It's the first drug to be specifically approved for treatment of Cushing disease, although other drugs such as ketoconazole, octreotide, and lanreotide are often prescribed off-label.

The effectiveness of pasireotide was demonstrated in two studies in patients with Cushing disease, in which urine cortisol concentrations were reduced to the normal range in approximately 20% of patients. The reduction in cortisol concentrations was observed as early as 1 month after starting treatment.[1]

Precautions: (1) Anticipate elevations of blood glucose concentrations. Assess fasting plasma glucose (FPG) or A1C before initiating treatment. (2) Due to the risk of cholelithiasis, gallbladder ultrasonography before treatment and at 6- to 12-month intervals during treatment is recommended. (3) Because pasireotide suppresses ACTH secretion, monitor patients for hypocortisolism. As prescribed, temporarily reduce the dosage or interrupt treatment and initiate short-term, low-dose glucocorticoid replacement therapy if indicated. (4) Pasireotide has been associated with bradycardia and prolongation of the QT interval. A baseline ECG is recommended, as is monitoring the drug's effect on the QT interval. Hypokalemia and hypomagnesemia should be corrected before treatment starts. Use pasireotide with caution in patients with other risk factors for QT prolongation (for example, patients with congenital long QT prolongation or clinically significant bradycardia), and in those being treated concurrently with other drugs that are known to cause QT prolongation such as antiarrhythmic drugs or moxifloxacin. (5) Pasireotide shouldn't be used in patients with severe hepatic impairment. A dosage reduction is recommended for patients with moderate hepatic impairment. (6) Monitor liver function tests after 1 to 2 weeks of treatment, then monthly for 3 months and every 6 months thereafter. Some patients have experienced alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) elevations greater than three times the upper limit of normal. (7) Pasireotide may inhibit pituitary hormones other than ACTH. Monitor pituitary function before starting therapy and periodically during treatment. (8) Concurrent use of pasireotide with cyclosporine may reduce the availability of the latter, requiring a dosage adjustment of cyclosporine. (9) Pasireotide may increase the concentration and action of bromocriptine; reduce the dosage of bromocriptine as prescribed if the two drugs are used concurrently.

Adverse reactions: *diarrhea, nausea, hyperglycemia, cholelithiasis, headache*, abdominal pain, diabetes mellitus, fatigue, injection site reactions

Supplied as: single-use ampules in quantities that provide pasireotide base in concentrations of 0.3 mg/mL, 0.6 mg/mL, and 0.9 mg/mL

Dosage: initially, 0.6 mg or 0.9 mg twice a day by subcutaneous injection. For patients in whom treatment was initiated with a dosage of 0.6 mg twice a day, the dosage may be increased to 0.9 mg twice a day based on response to treatment. In patients with moderate hepatic impairment, the recommended initial dosage is 0.3 mg twice a day and the maximum recommended dosage is 0.6 mg twice a day.

Nursing considerations: (1) Inform patients that they must perform self-monitoring of blood glucose and/or FPG assessments every week for the first 2 to 3 months and periodically thereafter. (2) Teach patients to administer subcutaneous injections in the abdomen or upper thigh and to rotate sites. (3) Patients should be evaluated for a treatment response based on a clinically meaningful reduction in 24-hour urinary free cortisol levels and/or improvement in signs and symptoms of the disease. Maximum urinary free cortisol reduction is usually seen by 2 months of treatment, and treatment may be continued for as long as patients continue to benefit.

REFERENCE

1. Prescribing information. Signifor (pasireotide) injection, for subcutaneous use. http://www.pharma.us.novartis.com/product/pi/pdf/signifor.pdf.

DRUG FOR VITREOMACULAR ADHESION

Ocriplasmin

Sight-saving therapy combats macular damage

During the normal aging process, the eye's gel-like vitreous may begin to separate from the retina. However, some vitreous may remain attached at a site of the retina that includes the macula. The resulting vitreomacular adhesion (VMA) is associated with traction on the macula that can lead to macular damage, including macular hole formation, macular edema, and vision loss. Signs and symptoms include photopsia (flashes of light) and reduced, distorted, and/or impaired vision. The standard treatment for worsening disease is surgical vitrectomy.

Ocriplasmin (*Jetrea*, ThromboGenics), the first drug to be approved for symptomatic VMA, represents an alternative to surgery. Produced by recombinant DNA technology, the new drug is a truncated form of human plasmin. It exhibits proteolytic activity against protein components of the vitreous body and the vitreoretinal interface, and dissolves the protein matrix responsible for VMA.[1]

Administered by intravitreal injection, ocriplasmin is approved for the treatment of symptomatic VMA. In two studies, 26% of the patients treated with the drug experienced resolution of the VMA, compared with 10% of those in the placebo group.[2]

Although ocriplasmin provides an important alternative to surgery for some patients with VMA, most patients didn't experience the intended benefit and approximately 20% of those in whom treatment with the drug was considered successful subsequently required surgical vitrectomy.[3]

In clinical trials, a few patients experienced decreased vision that was considered to be due to VMA progression in most cases and usually required surgical intervention. The potential also exists for lens subluxation, retinal detachment, and dyschromatopsia (yellowish vision). The intravitreal injection procedure is associated with certain adverse reactions, including intraocular inflammation/infection, intraocular hemorrhage, and increased intraocular pressure.

Precautions: (1) Repeated administration into the same eye isn't recommended. (2) If the drug is to be used to treat VMA in both eyes, the second treatment shouldn't be administered within 7 days of the initial treatment in order to permit adequate monitoring of the postinjection course, including the potential for decreased vision in the treated eye.

Adverse reactions: *vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision*, macular hole, reduced visual acuity, visual impairment, retinal edema

Supplied as: single-use vials containing 0.5 mg of the drug in 0.2 mL of solution.

Dosage: 0.125 mg (0.1 mL of the diluted solution) by intravitreal injection to the affected eye once as a single dose

Nursing considerations: (1) Store the vials frozen and protect them from light by keeping them in the original package until the time of use. (2) When the drug is to be administered, remove the vial from the freezer and allow it to thaw at room temperature (within a few minutes). (3) The solution in the vial must be diluted before use by adding 0.2 mL of 0.9% sodium chloride injection and gently swirling the vial until the solutions are mixed. (4) Adequate anesthesia and a broad-spectrum microbiocide should be administered. Consult the product labeling for detailed recommendations for administration and monitoring. ■

REFERENCES

1. Prescribing information. Jetrea (ocriplasmin) Intravitreal Injection, 2.5 mg/mL. http://jetrea.com/JETREAPrescribingInformation.pdf.

2. FDA. FDA approves Jetrea for symptomatic vitreomacular adhesion in the eyes. News release. October 18, 2012.

3. Ocriplasmin (Jetrea) for vitromacular adhesion. *Med Lett Drugs Ther.* 2013;55(1422):63-64.

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