

NewDrugs

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PART 1

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THIS ARTICLE REVIEWS six drugs recently approved by the FDA, including:

- the first drug approved to treat hyperkalemia in 50 years.
- a breakthrough drug for treating Parkinson disease psychosis.
- an I.V. antiasthmatic medication indicated for add-on maintenance treatment in patients with severe asthma and an eosinophilic phenotype.

Unless otherwise specified, the information in the following summaries applies to adults, not children. Consult a pharmacist or the package insert for information on drug safety during pregnancy and breastfeeding. Consult a pharmacist, the package insert, or a current and comprehensive drug reference for more details on precautions, drug interactions, and adverse reactions for all these drugs.

SELECTED REFERENCES

Drug Facts and Comparisons. St. Louis, MO: Facts and Comparisons, Inc.; 2017.
Nursing2017 Drug Handbook. Philadelphia, PA: Lippincott Williams & Wilkins; 2017.
Physician's Desk Reference. 70th ed. Montvale, NJ: Medical Economics; 2017.

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DRUG FOR HYPERKALEMIA

Patiromer sorbitex calcium

First new drug for hyperkalemia in 50 years

Hyperkalemia is characterized by a serum potassium concentration greater than 5.0 mEq/L and may be associated with complications such as cardiac dysrhythmias. It's most often experienced by patients with kidney disease or heart failure, particularly those taking medications that inhibit the renin-angiotensin-aldosterone system (RAAS). Examples include angiotensin-converting enzyme inhibitors such as lisinopril, angiotensin receptor blockers such as valsartan, the direct renin inhibitor aliskiren, and aldosterone antagonists such as spironolactone and eplerenone.

Management of chronic mild or moderate hyperkalemia may involve reduction in dosage or use of therapeutic alternatives to medications that increase serum potassium concentrations, restriction of foods and beverages with a high potassium content, and use of diuretics that promote the excretion of potassium as well as sodium.

Indicated to treat hyperkalemia, patiromer sorbitex calcium (*Veltassa*, Relypsa) is the first drug to be approved for this disorder in more than 50 years. It consists of patiromer, a nonabsorbed potassium-binding polymer, and calcium-sorbitol counterion (an ion that is to be exchanged for another ion). When administered orally, the calcium-sorbitol counterion is exchanged for potassium that binds with patiromer in the lumen of the gastrointestinal (GI) tract. This exchange reduces potassium absorption and increases fecal potassium

excretion, thereby reducing serum potassium concentrations.

The new drug may reduce the risk of hyperkalemia for patients with chronic diseases such as chronic kidney disease (CKD), heart failure, and diabetes for whom the continued use of RAAS inhibitors is beneficial despite their tendency to increase serum potassium concentrations. Its effectiveness was evaluated in hyperkalemic patients with CKD who were on stable doses of at least one RAAS inhibitor. Following 4 weeks of treatment, 76% of patients experienced a reduction in serum potassium concentrations to the target range (3.8 mEq/L–5.1 mEq/L).

In a study of hyperkalemic patients with CKD and type 2 diabetes on RAAS inhibitor therapy, the effectiveness of patiromer in reducing serum potassium concentrations was maintained during continued therapy for up to 52 weeks.

Precautions: (1) Because patiromer has a delayed onset of action, it shouldn't be used as an emergency treatment for life-threatening hyperkalemia. (2) Patiromer should be avoided in patients with severe constipation or bowel obstruction or impaction, including abnormal postoperative bowel motility disorders, because the drug may be ineffective and worsen GI disorders. (3) Monitor lab values and assess for signs and symptoms of hypokalemia (serum potassium less than 3.5 mEq/L), which was reported in 5% of patients in clinical trials. (4) Because patiromer binds to magnesium in the colon, approximately 9% of patients in the clinical trials developed hypomagnesemia (serum magnesium less than 1.4 mg/dL). Monitor serum magnesium concentrations and administer a magnesium supplement if pre-

scribed. (5) Administer other oral medications at least 3 hours before or 3 hours after patiromer. Patiromer binds to many oral drugs, which may reduce their absorption and effectiveness. If separating the administration of medications by at least 3 hours isn't possible, a decision should be made to administer either patiromer or the other oral medication.

Adverse reactions: constipation, diarrhea, nausea, abdominal discomfort, flatulence, hypomagnesemia

Supplied as: single-use packets containing 8.4 g, 16.8 g, and 25.2 g of patiromer powder for oral suspension. Each dose should be prepared immediately before administration.

Dosage: The recommended starting dosage is 8.4 g once a day. Adjust the dosage as prescribed based on the potassium concentration and the desired target range. The dosage may be increased at 1-week or longer intervals, in increments of 8.4 g, up to the maximum dosage of 25.2 g once a day.

Nursing considerations: (1) Teach patients how to prepare a dose of patiromer: Empty the contents of a packet into a glass or cup containing about 1 oz of water, stir the mixture thoroughly, add an additional 2 oz of water, and mix thoroughly. Inform patients that the powder won't dissolve and the mixture will look cloudy. Instruct them to drink the mixture immediately after preparation. (2) If some powder remains in the glass after drinking, patients should add more water, stir, and drink the mixture. They should repeat this process as needed until the entire dose is administered. (3) Tell patients to take

each dose with food but not to add it to heated foods or liquids. (4) Tell patients to take other oral medications either 3 hours before or 3 hours after a dose of patiromer, as directed by the healthcare provider. (5) Instruct patients to store the drug packets in a refrigerator and to avoid heating the drug when preparing it for administration. (6) If stored at room temperature, packets must be used within 3 months of being taken out of the refrigerator.

REFERENCE

Veltassa (patiromer) for oral suspension. Prescribing information. <https://www.veltassa.com/pi.pdf>.

ANTIDIABETIC DRUG

Insulin degludec

The third long-acting human insulin analog on the market

Joining insulin glargine and insulin detemir, insulin degludec (*Tresiba*, Novo Nordisk) is the third long-acting human insulin analog. It's prepared using recombinant DNA technology. Following subcutaneous administration, it forms multihexamers that result in a depot of the drug and delayed absorption from subcutaneous tissues. It's administered once a day and has a duration of action of approximately 42 hours. In contrast, insulin glargine (Lantus) is administered once a day but its duration of action is approximately 24 hours. A new formulation of insulin glargine (Toujeo) has a duration of action that's slightly longer than 24 hours. Insulin detemir's duration of action is somewhat less than 24 hours and it's administered once or twice a day. Insulin glargine (both Lantus and Toujeo) and insulin detemir should be administered at the same time each day, but insulin degludec may be administered at any time of the day.

Insulin degludec is indicated to improve glycemic control in adults

with type 1 and type 2 diabetes mellitus. Its effectiveness was evaluated in multiple clinical studies in which it was demonstrated to be noninferior to insulin glargine and insulin detemir in lowering A1C concentrations.

All insulins may cause hypoglycemia and this is the most important concern with their use. In some studies, the frequency of nocturnal hypoglycemia with insulin degludec was lower than with the other insulin analogs. In another study, insulin degludec was determined to be more effective than sitagliptin in lowering A1C concentrations, but it was also more likely to cause hypoglycemia. Patients with type 2 diabetes treated with insulin degludec for 1 year experienced an average weight gain of 3 kg.

Precautions: (1) Insulin degludec, like other long-acting insulins, isn't indicated to treat patients with diabetic ketoacidosis for whom I.V. administration of a rapid-acting or short-acting insulin is usually indicated. (2) Insulin degludec is contraindicated during episodes of hypoglycemia. Closely monitor patients for this risk when changes are made in insulin dosage, other glucose-lowering medications are used concurrently, and during changes in meal patterns and/or physical activity. (3) The risk of hypoglycemia may also be increased by angiotensin-converting enzyme inhibitors such as lisinopril and angiotensin II receptor blockers such as valsartan. (4) Use insulin degludec with caution in patients with hepatic or renal impairment. (5) The concurrent use of medications such as a thiazide diuretic or corticosteroid may reduce insulin degludec's blood glucose-lowering effect. The activity of insulin degludec may also be altered by the consumption of alcoholic beverages or the concurrent use of a beta-blocker. (6) Concurrent use of beta-blockers and other antiadrenergic drugs such as clonidine may mask

signs and symptoms of hypoglycemia. (7) Monitor serum potassium concentrations in patients at risk for hypokalemia. Thiazolidinedione antidiabetic drugs such as pioglitazone may also cause edema and, when used concurrently with insulin degludec or other insulins, may cause fluid retention and heart failure. If heart failure occurs, reduce the dosage or discontinue treatment as prescribed.

Adverse reactions: hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, rash, edema, weight gain

Supplied as: prefilled pens (Flex-Touch) containing 100 units/mL (U-100; 3 mL) and 200 units/mL (U-200; 3 mL). The pens enable, respectively, maximum doses of 80 units and 160 units per single injection. The dose window for both pens shows the number of insulin units to be delivered; dose conversion is *not* needed.

Dosage: individualized based on the patient's metabolic needs, blood glucose results, and glycemic control goal. In *insulin-naïve patients with type 1 diabetes*, the recommended starting dose is approximately one-third to one-half of the total daily insulin dose. For *insulin-naïve patients with type 2 diabetes*, the recommended starting dose is 10 units once a day. The recommended interval between dosage increases is 3 to 4 days. Consult the prescribing information for detailed recommendations for patients with type 1 or type 2 diabetes, including guidelines for patients already on insulin therapy.

Nursing considerations: (1) Teach patients to use the pens correctly. Detailed instructions are provided in the labeling. (2) Insulin degludec should be clear and colorless. Tell patients not to use medication that looks cloudy or discolored. (3) Teach patients to administer

insulin degludec subcutaneously into the thigh, upper arm, or abdomen once a day. (4) Although the drug can be given at any time of the day, advise patients to administer it at approximately the same time each day to help them adhere to the medication regimen. (5) Stress the importance of rotating injection sites to reduce the risk of lipodystrophy. (6) If a dose is missed, patients should inject the daily dose during waking hours when they realize a dose has been missed. At least 8 hours should separate the administration of consecutive doses. (7) Before use, insulin degludec pens should be stored in a refrigerator. Once in use, the pens may be refrigerated or kept at room temperature for 56 days. (8) Warn patients not to store pens with the needle attached. Storing without the needle helps prevent leaking or air entering the pen. (9) If not refrigerated, pens in use should be disposed of after 56 days, even if they still contain insulin. Refrigerated pens may be used until their expiration date. (10) Tell patients to protect pens from heat and light. (11) Make sure all patients with diabetes can recognize signs and symptoms of hypo- and hyperglycemia and know how to respond appropriately.

REFERENCE

Tresiba, insulin degludec injection 100 U/mL, 200 U/mL. Prescribing information. www.novo-pi.com/tresiba.pdf.

ANTIPSYCHOTIC DRUGS

Cariprazine hydrochloride

Indicated for schizophrenia and bipolar mania

Cariprazine hydrochloride (*Vraylar*, Allergan) is an atypical antipsychotic drug that acts at certain dopamine and serotonin receptors and at histamine H₁ receptors. It's indi-

cated to treat schizophrenia and for the acute treatment of manic or mixed episodes associated with bipolar I disorder. Although the specific mechanism of action of cariprazine is unknown, its actions may be mediated through a combination of partial agonist activity at central dopamine D₂ and serotonin 5-HT_{1A} receptors and antagonist activity at serotonin 5-HT_{2A} receptors.

The effectiveness of cariprazine for treating patients with schizophrenia was demonstrated in three 6-week, placebo-controlled studies; the new drug was superior to placebo in all three studies. For the acute treatment of patients with bipolar mania, cariprazine was evaluated in three 3-week, placebo-controlled trials, and the new drug was superior to placebo in all of these studies as well.

As with other antipsychotic drugs, the labeling for cariprazine includes a boxed warning that older adults with dementia-related psychosis are at increased risk for death if treated with an antipsychotic drug, none of which has been approved for treating patients with dementia-related psychosis. The use of antipsychotic drugs in these patients has been reported to increase the risk of cerebrovascular adverse events such as stroke and transient ischemic attack.

Numerous other risks associated with the use of the atypical antipsychotic drugs also apply to cariprazine. These include neuroleptic malignant syndrome, tardive dyskinesia, seizures, orthostatic hypotension and syncope, body temperature dysregulation, dysphagia, metabolic changes (such as hyperglycemia/diabetes, dyslipidemia, weight gain), leukopenia, neutropenia, agranulocytosis, and the potential for cognitive and motor impairment. Patients who are at greater risk or who've experienced signs and symptoms that are characteristic of these events

should be closely monitored. In some patients, the type and/or extent of the adverse reaction will warrant discontinuation of treatment—for example, neuroleptic malignant syndrome and severe neutropenia (absolute neutrophil count less than 1,000/mm³).

Plasma concentrations of cariprazine and its active metabolites accumulate over time and adverse reactions may not be evident until several weeks after treatment starts. Patient response and adverse reactions should be monitored for several weeks after starting treatment and with each dosage change.

Taken during pregnancy, cariprazine may harm the unborn child. In addition, neonates whose mothers have been exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. A pregnancy exposure registry (1-866-961-2388) monitors pregnancy outcomes in women who've been exposed to atypical antipsychotic drugs during pregnancy.

Precautions: (1) Not recommended for patients with severe renal impairment or severe hepatic impairment. (Dosage adjustment isn't necessary in patients with mild-to-moderate renal impairment or mild-to-moderate hepatic impairment.) (2) Because the concurrent use of a strong CYP3A4 inhibitor such as clarithromycin or itraconazole increases the exposure of cariprazine and its active metabolites, reduce the dosage of the new drug in patients taking a strong CYP3A4 inhibitor. (3) The concurrent use of cariprazine and a CYP3A4 inducer such as carbamazepine or rifampin hasn't been evaluated and isn't recommended.

Adverse reactions: *In patients with schizophrenia:* extrapyramidal symptoms (such as bradycardia, cogwheel rigidity, drooling, dyskinesia,

hypokinesia, tremor, musculoskeletal stiffness), akathisia. *In patients with bipolar mania:* extrapyramidal symptoms, akathisia, nausea, vomiting, dyspepsia, somnolence, restlessness.

Supplied as: 1.5 mg, 3 mg, 4.5 mg, and 6 mg oral capsules

Dosage: Initially 1.5 mg once a day. *In patients with schizophrenia*, the recommended dosage range is 1.5 mg to 6 mg once daily, and the dosage can be increased to 3 mg on Day 2. *In patients with bipolar mania*, the recommended dosage is 3 mg to 6 mg once a day, and the dosage should be increased to 3 mg on Day 2. Depending on clinical response and tolerability, further dosage adjustments can be made in 1.5 mg or 3 mg increments. Consult the prescribing information for specific dosage recommendations for patients taking a strong CYP3A4 inhibitor concurrently.

Nursing considerations: (1) Cariprazine can be taken without regard to food. (2) Because atypical antipsychotic medications have the potential to impair judgment, thinking, or motor skills, caution patients to avoid operating hazardous machinery, including motor vehicles, until they know how cariprazine affects them. (3) Warn patients about the risk of orthostatic hypotension and syncope, especially early in treatment. (4) Educate patients about signs and symptoms of tardive dyskinesia, a syndrome consisting of potentially irreversible repetitive involuntary movements, and tell them to contact the healthcare provider immediately if they experience these abnormal movements.

REFERENCE

Vraylar (cariprazine) capsules, for oral use. Prescribing information. www.allergan.com/assets/pdf/vraylar_pi.

Pimavanserin tartrate

Breakthrough therapy for Parkinson disease psychosis

Approximately one million Americans have Parkinson disease, and an estimated 50,000 individuals are diagnosed with the disease each year. Most patients experience tremors as an early manifestation of the disease and, as the disease worsens, the increasing severity of the tremors may interfere with daily activities, including eating. As many as 50% of patients with Parkinson disease experience symptoms of psychosis such as hallucinations and delusions and this is a major reason for long-term-care admissions of patients with Parkinson disease.¹

Because Parkinson disease is characterized by a reduction in dopamine activity, a goal of treatment with medications such as levodopa is to increase dopamine concentrations and activity. The occurrence of psychosis in a patient with Parkinson disease presents a formidable treatment challenge because most antipsychotic drugs exhibit a dopamine antagonist action and may cause extrapyramidal (Parkinson-like) effects that compromise the benefits of dopaminergic medications prescribed for Parkinson disease.

Serotonin 5-HT_{2A} receptors are thought to play an important role in Parkinson disease psychosis. Pimavanserin tartrate (*Nuplazid*, *Acadia*) is an atypical antipsychotic drug that has a unique mechanism of action: It preferentially targets 5-HT_{2A} receptors and its action is mediated through a combination of inverse agonist and antagonist activity at these receptors. Unlike other antipsychotic drugs, it doesn't act at dopamine receptors, so it doesn't interfere with patients' dopaminergic therapy or impair motor function. In addition, its unique mechanism of action may

reduce the risk of certain serious adverse reactions infrequently associated with other antipsychotic drugs, such as tardive dyskinesia and neuroleptic malignant syndrome.²

Pimavanserin is the first drug to be approved for treatment of hallucinations and delusions associated with Parkinson disease psychosis. The FDA granted pimavanserin a breakthrough therapy designation, an initiative established to expedite the development and review of drugs that are intended to treat a serious disorder and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy.

Pimavanserin is metabolized to a major active metabolite. Its effectiveness was evaluated in a 6-week placebo-controlled study that included 199 patients. The new drug was demonstrated to be superior to placebo in decreasing the frequency and/or severity of both hallucinations and delusions without worsening the primary motor symptoms of Parkinson disease.

As with cariprazine and other atypical antipsychotics, the labeling for pimavanserin includes a boxed warning regarding an increased risk of death in older adults with dementia-related psychosis. The new drug isn't approved to treat dementia-related psychosis that's unrelated to the hallucinations and delusions associated with Parkinson disease psychosis.

Precautions: (1) Pimavanserin prolongs the QT interval and may increase the risk of cardiac dysrhythmias. Avoid using it in patients with known QT prolongation and/or a history of cardiac dysrhythmias or other disorders that may increase the risk of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia, or hypomagnesemia. (2) Pimavanserin shouldn't be used

concurrently with other medications known to prolong the QT interval, including Class 1A antiarrhythmics (such as quinidine, procainamide, and disopyramide), Class 3 antiarrhythmics (such as amiodarone and sotalol), certain antipsychotic medications (such as ziprasidone, chlorpromazine, and thioridazine), and certain antibacterial agents (such as moxifloxacin). (3) The concurrent use of a strong CYP3A4 inhibitor such as clarithromycin, itraconazole, or ketoconazole may increase the exposure and activity of pimavanserin, and the dosage of the new drug should be reduced. (4) The concurrent use of a strong CYP3A4 inducer such as carbamazepine, phenytoin, rifampin, or St. John's wort may reduce the exposure and effectiveness of pimavanserin, and an increase in dosage may be necessary.

Adverse reactions: nausea, peripheral edema, confusion

Supplied as: 17 mg film-coated oral tablets

Dosage: 34 mg once a day. For patients being treated concurrently with a strong CYP3A4 inhibitor, the recommended dosage is 17 mg/day.

Nursing considerations: (1) Pimavanserin may be administered without regard to food. (2) Tell patients to inform the healthcare provider of any changes in their use of medications, including dietary supplements and over-the-counter drugs, because of the potential for adverse medication interactions. (3) Monitor QT intervals as indicated in patients at risk for QT interval prolongation.

REFERENCES

1. Food and Drug Administration. FDA approves first drug to treat hallucinations and delusions associated with Parkinson's disease. News release. April 29, 2016.
2. Nuplazid (pimavanserin) tablets, for oral use. Prescribing information. https://www.nuplazidhcp.com/pdf/NUPLAZID_Prescribing_Information.pdf.

ANTIASTHMATIC DRUG

Reslizumab

I.V. medication for certain patients with severe asthma

Many patients with asthma effectively manage symptoms with a beta₂-adrenergic agonist, muscarinic antagonist, and/or a corticosteroid administered by oral inhalation. Corticosteroids such as prednisone are sometimes taken orally by patients with more severe symptoms. Even though these regimens are effective for most of the more than 20 million Americans with asthma, many patients don't experience adequate reduction of symptoms and have associated complications with conventional therapy, and more than 400,000 asthma-related hospitalizations occur each year.¹

Multiple cell types, including eosinophils, and mediators such as cytokines are involved in the inflammatory process that occurs in the airways. Interleukin-5 (IL-5) is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. In 2015, mepolizumab was approved as the first IL-5 antagonist for add-on maintenance treatment for patients with severe asthma and with an eosinophilic phenotype. It's administered subcutaneously and acts by reducing the production and survival of eosinophils.

Reslizumab (*Cinqair*, Teva) is the second IL-5 antagonist to be approved. Like mepolizumab, it's a monoclonal antibody indicated for add-on maintenance treatment in patients with severe asthma and with an eosinophilic phenotype. However, unlike mepolizumab, reslizumab is administered once a month by I.V. infusion and isn't indicated in patients under age 18.² (The labeled indications for mepolizumab include patients as young as age 12.) Neither reslizumab nor mepolizumab is indicated to treat other eosinophilic disorders, acute bronchospasm, or status asthmaticus.

The effectiveness of reslizumab was demonstrated in four placebo-controlled studies in patients with severe asthma who were being treated with other antiasthmatic medications. Two of the studies continued for 52 weeks. Reslizumab provided a significant reduction in the rate of asthma exacerbations, including those that required the use of a systemic corticosteroid as well as those that required hospitalization or an ED visit. Reslizumab also significantly improved lung function as reflected by increases in forced expiratory volume in 1 second (FEV₁) determinations.

The most important risk associated with reslizumab is anaphylaxis, which was reported in 0.3% of patients in the clinical studies. This is the subject of a boxed warning in the new drug's labeling. However, the drug was generally well tolerated in the clinical studies.

Malignant neoplasms occurred in a small number of patients (0.6% compared with 0.3% of those in the placebo group). These responses were diverse and not associated with any particular tissue type, but the risk is identified in the warnings in reslizumab's labeling.

Precautions: (1) Contraindicated in patients with known hypersensitivity to the drug or any excipients in the formulation. (2) Reslizumab should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis, and patients should be observed for an appropriate period afterward. If severe systemic reactions occur, drug administration should be stopped immediately and appropriate medical treatment provided. (3) Because eosinophils may be involved in the immunologic response to some helminth infections, patients with known parasitic infections were excluded from participation in the clinical studies of reslizumab. Although whether reslizumab would influence a patient's response against

a parasitic infection is unknown, preexisting helminth infections should be treated before initiating therapy. If a helminth infection occurs during treatment with reslizumab and doesn't respond to antihelminth treatment, reslizumab therapy should be discontinued until the infection resolves. (4) Reslizumab must be given via I.V. infusion, not I.V. bolus. (5) Reslizumab isn't indicated for patients under age 18. Among 39 patients in the 12-to-17 age range participating in clinical studies, the asthma exacerbation rate was higher for patients taking reslizumab than for those receiving placebo. (6) If use of reslizumab permits a reduction in the dosage of corticosteroids that have been part of a patient's maintenance treatment, the dosage should be reduced gradually. Abrupt discontinuation of a corticosteroid may be associated with systemic withdrawal symptoms and/or unmask disorders previously suppressed by systemic corticosteroid therapy.

Adverse reactions: oropharyngeal pain, myalgia

Supplied as: single-use vials containing the drug in a concentration of 100 mg/10 mL

Dosage: 3 mg/kg once every 4 weeks, infused over 20 to 50 minutes

Nursing considerations: (1) Store vials in a refrigerator. (2) Withdraw the volume of solution needed to provide the dose of reslizumab from the vial and slowly add it to an infusion bag containing 50 mL of 0.9% Sodium Chloride Injection. (3) To minimize foaming, avoid shaking the vial or the infusion bag.

REFERENCES

1. Food and Drug Administration. FDA approves Cinquair to treat severe asthma. News release. March 23, 2016.

2. Cinquair (reslizumab) injection, for intravenous use. Prescribing information. <http://cinquair.com/pdf/PrescribingInformation.pdf>.

ANTIEPILEPTIC DRUG

Brivaracetam

Adjunctive therapy in the treatment of partial-onset seizures

Over 5 million people in the United States have a history of epilepsy, and almost 3 million have active epilepsy.¹ Partial-onset seizures, the most common type of epilepsy, affect a limited or localized area of the brain but can spread to other parts of the brain.

Brivaracetam (*Briviact*, UCB) is an analog of the antiepileptic drug (AED) levetiracetam. The effectiveness of these drugs in the treatment of seizure disorders is thought to be due to their affinity for synaptic vesicle protein 2A in the brain. Both drugs may be administered orally or I.V.

Brivaracetam is indicated as adjunctive therapy in the treatment of partial-onset seizures in patients age 16 and older with epilepsy.² Its effectiveness in reducing the frequency of seizures was demonstrated in three placebo-controlled trials involving 1,550 patients who were also taking other AEDs concomitantly. Levetiracetam was a concomitant AED in approximately 20% of the patients in two of the studies, and brivaracetam provided no added benefit for these patients. Brivaracetam and levetiracetam haven't been directly compared in clinical studies.

Brivaracetam is included in Schedule V under the provisions of the Controlled Substances Act. Levetiracetam isn't a controlled substance.

The effectiveness and safety of brivaracetam in patients younger than age 16 haven't been established. For patients with partial-onset seizures, levetiracetam is indicated for patients as young as 1 month.

Precautions: (1) Sedation and other neurologic adverse reactions are more likely early in treatment but

can occur at any time. The concurrent use of other central nervous system depressants including alcoholic beverages may increase the likelihood of neurologic adverse reactions. (2) Contraindicated in patients known to be hypersensitive to the drug or any of the inactive ingredients in the formulation. Hypersensitivity reactions such as bronchospasm and angioedema have been reported infrequently. Discontinue brivaracetam if such events occur. (3) Like other AEDs, brivaracetam increases the risk of suicidal thoughts or behavior. Monitor patients for emerging or worsening depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Other psychiatric adverse reactions, including psychotic symptoms such as hallucinations and paranoia and nonpsychotic symptoms such as anxiety, irritability, and mood swings have been experienced by some patients. (4) Patients who are CYP2C19 poor metabolizers or who are taking a CYP2C19 inhibitor concurrently may require a reduction in dosage of brivaracetam. (5) The exposure of brivaracetam is increased in patients with hepatic impairment. A reduction in dosage is recommended for patients with all stages of hepatic impairment. (6) Closely monitor patients taking phenytoin concurrently. Brivaracetam has also been reported to increase plasma concentrations of phenytoin. Consult the prescribing information for details about other possible drug interactions. (7) Like most AEDs, brivaracetam should be withdrawn gradually when treatment is to be discontinued because of the risk of increased seizure frequency and status epilepticus. However, rapid discontinuation can be considered if withdrawal is needed because of a serious adverse reaction.

Adverse reactions: somnolence/sedation, dizziness, fatigue, nausea/vomiting

Supplied as:

- oral tablets (provided as 10 mg, 25 mg, 50 mg, 75 mg, and 100 mg tablets)
- oral solution (provided in a 300 mL glass bottle containing 10 mg/mL)
- I.V. injection (provided in single-dose vials containing 50 mg/5 mL)

Dosage: *Oral administration:* Initially, 50 mg twice a day. Based on individual patient tolerability and therapeutic response, the dosage may be reduced to 25 mg twice a day or increased to 100 mg twice a day. Consult the prescribing information for recommended dosage adjustments for patients with hepatic impairment and certain other patient populations. *I.V. injection:* When oral administration isn't fea-

sible, brivaracetam may be administered I.V. over 2 to 15 minutes at the same dosage and same frequency as with oral administration.

Nursing considerations: (1) Tell patients to swallow tablets whole with liquid and not to chew or crush them. Doses can be taken without regard to food. (2) Teach patients using the oral solution to measure doses with a calibrated measuring device, not a household utensil. The oral solution doesn't require dilution and may also be administered via nasogastric or gastrostomy tube. (3) Tell patients to discard any remaining oral solution after 5 months of first opening the bottle. (4) Brivaracetam injection may be administered I.V. without further dilution or may be mixed with 0.9% Sodium

Chloride Injection, 5% Dextrose Injection, or Lactated Ringer's Injection. The diluted solution shouldn't be stored for more than 4 hours at room temperature. (5) Warn patients about the risk of sedation and caution them not to drive or operate machinery until they determine how the medication affects them. (6) Warn patients that discontinuing brivaracetam abruptly increases the risk of seizures. ■

REFERENCES

1. Food and Drug Administration. FDA approves Briviact to treat partial onset seizures. News release. February 19, 2016.
2. Briviact (brivaracetam) tablets for oral use; oral solution; and injection for intravenous use. Prescribing information. <https://www.briviact.com/briviact-PI.pdf?v=1479316368>.

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