Pharmaceutical Approval Update

Michele B. Kaufman, PharmD, BCGP, RPh

Secnidazole Oral Granules (Solosec)

Manufacturer: Lupin Pharmaceuticals, Baltimore, Maryland

Date of Approval: September 15, 2017

Indication: Secnidazole is indicated to treat adult women with bacterial vaginosis (BV).

Drug Class: Nitroimidazole antimicrobial

Michele B. Kaufman, PharmD, BCGP, RPh

Uniqueness of Drug: BV, the most prevalent gynecological infection in the United States, affects approximately 21 million women 14–49 years of age each year. If BV is not treated, it can increase the risk of contracting sexually transmitted diseases and can increase the risk of preterm birth and low birth weight. The most commonly prescribed oral BV treatment regimen requires twice-a-day dosing for seven days. Patient adherence to the current leading treatment has been shown to be only about 50%. Secnidazole requires just one oral dose. The product is the first new oral antibiotic to treat BV in more than a decade. The Food and Drug Administration granted secnidazole qualified infectious disease product and fast-track designations. Secnidazole will be available by mid-2018.

Warnings and Precautions:

Vulvovaginal candidiasis. Vulvovaginal candidiasis may develop with secnidazole use and require treatment with an antifungal agent.

Potential risk for carcinogenicity. Carcinogenicity has been observed in mice and rats treated chronically with nitroimidazole derivatives, which are structurally related to secnidazole. It is unclear if the positive tumor findings in lifetime rodent studies indicate a risk to patients taking a single dose of secnidazole to treat BV. Chronic use should be avoided.

Drug interactions. There were no clinically significant drug interactions between secnidazole and the combination oral contraceptive ethinyl estradiol plus norethindrone, which indicated that secnidazole can be coadministered with combination oral contraceptives.

Pregnancy. There are no available human data on effects in pregnant patients.

Lactation. Breastfeeding is not recommended. Discontinue breastfeeding for 96 hours after administration of secnidazole.

Adverse events. The most common adverse events in clinical trials were vulvovaginal candidiasis, nausea, vomiting, and dysgeusia.

Dosage and Administration: Secnidazole will be available in unit-of-use packages containing one packet of granules in an individual carton. Each packet contains 4.8 g of granules containing 2 g secnidazole (one dose). A single packet of granules should be administered once orally, without regard to meals. The entire packet should be sprinkled onto applesauce, yogurt, or pudding and consumed within 30 minutes. It should not be chewed or crunched. A glass of water may be taken after secnidazole administration to aid in swallowing. Secnidazole is not intended to be dissolved in any liquid.

Commentary: Two randomized, placebo-controlled clinical trials with similar designs were conducted to evaluate the efficacy and safety of secnidazole for treating BV (N = 333). The percentage of patients demonstrating a clinical response was consistently higher in both secnidazole-treated arms compared with placebo-treated patients. All treatment-emergent adverse events were mild or moderate in intensity; no serious adverse events were reported, and no patients discontinued treatment due to adverse events.

Sources: Lupin Pharmaceuticals, Solosec prescribing information

Triamcinolone Acetonide Extended-Release Injection (Zilretta)

Manufacturer: Flexion Therapeutics, Inc., Burlington, Massachusetts

Date of Approval: October 6, 2017

Indication: Zilretta (triamcinolone acetonide extended-release injectable suspension) is a synthetic corticosteroid indicated as an intra-articular injection for the management of osteoarthritis (OA) pain of the knee. It is not interchangeable with other formulations of injectable triamcinolone acetonide.

Drug Class: Injectable corticosteroid

Uniqueness of Drug: This is the first and only extended-release, intra-articular injection for OA pain of the knee. It is a nonopioid pain medication that uses a proprietary microsphere technology that provides more than 12 weeks of pain relief following one injection.

Warnings and Precautions:

Hypersensitivity reactions. Zilretta should not be used in patients with hypersensitivity to triamcinolone acetonide or any component of the product. Serious reactions have been reported with triamcinolone acetonide injection. Appropriate care should be utilized if an anaphylactic reaction occurs.

For intra-articular use only. Zilretta should not be administered by epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal, or subcutaneous routes.

Serious neurological adverse reactions with epidural or intrathecal administration. Serious neurological events have been reported following epidural or intrathecal corticosteroid administration. Corticosteroids, including this agent, are not approved for these routes of administration.

Joint infection and damage. This agent may cause joint pain accompanied by joint swelling. If this occurs, an appropriate evaluation should be conducted to exclude septic arthritis. Appropriate antimicrobial therapy should be started if septic arthritis is confirmed. Injecting corticosteroids into an infected site should be avoided, and local injection of a corticosteroid into a previously infected joint is not usually recommended. Examine any joint fluid present to exclude a septic process. Corticosteroid injection into unstable joints is generally not

Dr. Kaufman is a freelance medical writer living in New York City and a Pharmacist in the NewYork–Presbyterian Lower Manhattan Hospital Pharmacy Department.

recommended, and intra-articular injection may result in joint tissue damage.

Endocrine function changes. Corticosteroids can cause reversible hypothalamic–pituitary–adrenal axis suppression, with the potential for adrenal insufficiency after withdrawal of treatment, which may persist for months. In situations of stress during that period (i.e., trauma, surgery, illness), institute corticosteroid replacement therapy. Metabolic clearance of corticosteroids is decreased in patients with hypothyroidism and increased in those with hyperthyroidism.

Cardiovascular effects. Corticosteroids can cause elevated blood pressure, sodium and water retention, and increased potassium excretion. These effects are less likely to occur with synthetic derivatives. Monitor patients with congestive heart failure or hypertension for signs of edema, weight gain, and imbalance in serum electrolytes. Dietary salt restriction and potassium supplementation may be necessary.

Renal effects. Corticosteroids can cause sodium and water retention and increased excretion of potassium, which are less likely to occur with synthetic derivatives. All corticosteroids increase calcium excretion. Monitor patients with renal insufficiency for signs of edema, weight gain, and imbalance in serum electrolytes. Dietary salt restriction and potassium supplementation may be necessary.

Other adverse effects. Increased intraocular pressure, gastrointestinal perforation, alterations in bone density, and behavioral and mood disturbances have been observed with corticosteroid administration.

Drug interactions. No drug–drug interaction studies have been completed with Zilretta; however, drug interactions associated with any systemic corticosteroid apply to this product (see full prescribing information).

Dosage and Administration: Zilretta is administered as a single intra-articular injection that delivers 32 mg triamcinolone acetonide in 5 mL of diluent. It is supplied as a single-dose kit containing a vial of triamcinolone acetonide extended-release microsphere powder, a vial of sterile diluent, and a sterile vial adapter. Proper aseptic technique should be used throughout the dose preparation and administration procedure. Prior to use, the drug should be stored in a refrigerator and not frozen. Because the product is a suspension, some residue may be left on the vial walls after the dose is withdrawn. The drug should be injected promptly following dose preparation. The reconstituted suspension can be stored in the vial for up to four hours at ambient conditions. The vial should be gently swirled to resuspend the drug prior to preparing the syringe for injection.

Commentary: The efficacy of Zilretta was shown in a phase 3, multicenter, randomized, double-blind, parallel-arm, placebo- and active-controlled study at 37 centers worldwide. The included patients (N = 484) had OA knee pain and were treated and followed for 24 weeks. Patients were assigned to one of three treatment arms: Zilretta 32 mg (n = 161), saline placebo (n = 162), or active control (a crystalline suspension of immediate-release triamcinolone acetonide 40 mg; n = 161). The mean patient age was 62 years (range, 40–85 years). The baseline demographics and disease characteristics were balanced across treatment arms. Twenty-five percent of patients had previously received at least one intra-articular corticosteroid injection more than three months prior to study participation. The primary efficacy endpoint was the change from baseline at week 12 in the weekly mean of the average daily pain intensity scores as assessed by a 0–10 numeric rating scale for Zilretta-treated patients compared with placebo-treated patients.

Zilretta-treated patients showed a statistically significant pain intensity reduction at the primary endpoint compared with placebo-treated patients. Zilretta also showed a reduction in pain intensity scores weekly from weeks 1 through 12. At week 12, the time point for primary efficacy determination, 470 patients (97%) completed follow-up, and 443 patients (92%) completed to week 24. The most common adverse reactions reported were joint swelling (3%), contusions (2%), cough (2%), and sinusitis (2%).

Sources: Flexion Therapeutics, Zilretta prescribing information

Insulin Aspart Injection (Fiasp)

Manufacturer: Novo Nordisk, Inc., Plainsboro, New Jersey

Date of Approval: September 29, 2017

Indication: Fiasp is a rapid-acting human insulin analogue indicated to improve glycemic control in adults with diabetes mellitus.

Drug Class: Insulin (metabolic hormone)

Uniqueness of Drug: Fiasp (100 units/mL [U-100]) is a fast-acting mealtime insulin indicated to improve glycemic control in adults with type-1 and type-2 diabetes. It can be dosed at the beginning of a meal or within 20 minutes after starting a meal. This new product differs from the prior insulin aspart injection (NovoLog, Novo Nordisk); niacinamide (vitamin B_3) has been added to Fiasp to aid and increase the speed of initial insulin absorption, resulting in an onset of appearance in the blood in approximately 2.5 minutes.

Warnings and Precautions:

Do not share insulin pens. Insulin pens should never be shared, even if the needle has been changed.

Hyperglycemia or hypoglycemia with changes in insulin regimen. Any insulin changes (e.g., strength, manufacturer, type, or administration method) can affect glycemic control and predispose a patient to hypoglycemia or hyperglycemia. These changes should be done cautiously and under close medical supervision. The frequency of blood glucose monitoring should be increased. For patients with type-2 diabetes, dose adjustments to concomitant oral antidiabetic medications may be needed.

Hypoglycemia. Hypoglycemia may be life threatening. The frequency of blood glucose monitoring should be increased with changes to insulin dosage, coadministered glucose-lowering medications, meal pattern, or physical activity; and in patients with renal or hepatic impairment, or hypoglycemia unawareness. Fiasp should not be used during hypoglycemic episodes.

Hypoglycemia due to medication errors. Accidental mix-ups between insulin products can occur. Instruct patients to always check insulin labels before injection.

Hypokalemia. Hypokalemia may be life threatening. Potassium levels should be monitored in patients at risk for hypokalemia.

Hypersensitivity reactions. Fiasp should not be used by patients with hypersensitivity to insulin aspart or to one of the

continued on page 755

continued from page 734

excipients in the product. Severe life-threatening, generalized allergic reactions, including anaphylaxis, can occur. Fiasp should be discontinued if a hypersensitivity reaction occurs, and the patient should be monitored and treated, if indicated.

Fluid retention and heart failure with concomitant use of thiazolidinediones (TZDs). Observe patients who also take TZDs for signs and symptoms of heart failure; consider dosage reduction or discontinuation of the TZD if heart failure occurs.

Dosage and Administration: Fiasp is available in 10-mL multidose vials and in 3-mL single-patient-use FlexTouch pens. It can be administered subcutaneously (SC) or intravenously (IV).

For SC injection, Fiasp should be injected into the abdomen, upper arm, or thigh, at the start of a meal or within 20 minutes after starting a meal. Injection sites should be rotated within the same region from one injection to the next to reduce the risk of lipodystrophy. Instruct patients on basal-bolus treatment who forget a mealtime dose to monitor their blood glucose level to decide if an insulin dose is needed and to resume their usual dosing schedule at the next meal.

IV Fiasp should be administered only under medical supervision with close monitoring of blood glucose and serum potassium levels to avoid hypoglycemia and hypokalemia. Fiasp should be diluted to concentrations from 0.5 units/mL to 1.0 units/mL insulin aspart in infusion systems using polypropylene infusion bags. After dilution, the product is stable at room temperature for 24 hours in 0.9% sodium chloride or 5% dextrose infusion fluids.

Commentary: The efficacy and safety of Fiasp were demonstrated in the onset phase 3a clinical development program. The clinical trials enrolled more than 2,000 adults with type-1 and type-2 diabetes who were administered Fiasp both at mealtime and after starting a meal. Data from the trials showed that Fiasp reduced glycosylated hemoglobin levels in both type-1 and type-2 adult diabetics. Common adverse reactions (excluding hypoglycemia) that occurred in 5% or greater of Fiasp-treated patients included back pain, diarrhea, nasopharyngitis, nausea, and upper respiratory tract infection.

According to Novo Nordisk, Fiasp will launch at the same list price as NovoLog and will be offered with a savings card program for eligible patients with commercial insurance to reduce copayments.

Sources: Novo Nordisk, Fiasp prescribing information ■