Elbasvir/Grazoprevir (Zepatier)

Manufacturer: Merck and Co., Inc., Kenilworth, New Jersey

Date of Approval: January 28, 2016

Indication: The fixed-dose combination of elbasvir and grazoprevir is indicated for the treatment of chronic hepatitis C virus (HCV) genotypes 1 or 4 infection in adults.

Drug Class: Elbasvir is an HCV NS5A inhibitor, and grazoprevir is an HCV NS3/4A protease inhibitor. Both are direct-acting antiviral agents against HCV.

Uniqueness of Drug: The approval of Zepatier provides another oral treatment option for patients with genotypes 1 and 4 HCV infections without requiring the use of interferon.

Warnings and Precautions:
- Alanine aminotransferase (ALT) elevations. Clinicians should perform hepatic laboratory testing before the initiation of therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, clinicians should perform additional hepatic laboratory testing at treatment week 12.
- Risk associated with ribavirin combination treatment. If elbasvir/grazoprevir is administered with ribavirin, the warnings and precautions for ribavirin also apply.

Dosage and Administration: Zepatier is a two-drug, fixed-dose combination product containing 50 mg of elbasvir and 100 mg of grazoprevir in a single tablet. The recommended dosage of Zepatier is one tablet taken orally once daily with or without food. Zepatier is used in combination with ribavirin in certain patient populations.

Commentary: The safety and efficacy of elbasvir/grazoprevir were evaluated in clinical trials involving a total of 1,373 participants with chronic HCV genotype 1 or 4 infections with and without cirrhosis. The subjects received elbasvir/grazoprevir with or without ribavirin once daily for 12 or 16 weeks. The overall sustained virologic response rates ranged from 94% to 97% in genotype-1-infected subjects and from 97% to 100% in genotype-4-infected subjects across the studies. The most common adverse effects of elbasvir/grazoprevir without ribavirin were fatigue, headache, and nausea. The most common adverse effects of elbasvir/grazoprevir with ribavirin were anemia and headache.

Sources: Merck, Zepatier prescribing information

Sumatriptan Nasal Powder (Onzetra Xsail)

Manufacturer: Avanir Pharmaceuticals, Aliso Viejo, California

Date of Approval: January 28, 2016

Indication: Sumatriptan nasal powder is indicated for the acute treatment of migraine with or without aura in adults.

Drug Class: Sumatriptan is a selective 5-hydroxy-tryptamine receptor subtype 1 (5-HT1) agonist (triptan).

Uniqueness of Drug: Onzetra Xsail is the first breath-powered intranasal medication delivery system for the acute treatment of migraine.

Warnings and Precautions:
- Myocardial ischemia/infarction and Prinzmetal’s angina. Clinicians should perform a cardiac evaluation in patients with multiple cardiovascular risk factors.
- Arrhythmias. Onzeta Xsail should be discontinued if arrhythmias occur.
- Chest, throat, neck, or jaw pain, tightness, pressure, or heaviness. These events generally are not myocardial ischemia; clinicians should evaluate high-risk patients for coronary artery disease.
- Cerebral hemorrhage, subarachnoid hemorrhage, and stroke. Onzeta Xsail should be discontinued if these events occur.
- Gastrointestinal ischemia and infarction events, peripheral vasospastic reactions. Onzeta Xsail should be discontinued if these events occur.
- Medication overuse headache. Detoxification may be necessary.
- Serotonin syndrome. Onzeta Xsail should be discontinued if serotonin syndrome occurs.
- Seizures. Onzeta Xsail should be used with caution in patients with epilepsy or a lowered seizure threshold.

Dosage and Administration: The recommended dosage of Onzeta is 22 mg of sumatriptan nasal powder (two nosepieces), administered using the Xsail breath-powered delivery device. If the migraine has not resolved within two hours after taking Onzeta Xsail, or returns after a transient improvement, a second dose of 22 mg may be administered at least two hours after the first dose. The maximum recommended dose that may be given in 24 hours is two doses of Onzeta Xsail (44 mg/four nosepieces) or one dose of Onzeta Xsail and one dose of another sumatriptan product, separated by at least two hours.

Commentary: Onzeta Xsail is an intranasal medication delivery system consisting of low-dose (22 mg) sumatriptan powder, the most commonly prescribed migraine medication. The powder is delivered intranasally using the Xsail breath-powered delivery device, which is activated by the user’s breath to propel the medication deep into the nasal cavity. The user exhales into the device, automatically closing the soft palate and sealing off the nasal cavity. Through a sealing nosepiece placed into the nostril, the exhaled breath carries medication from the device directly into one side of the nose. Narrow nasal passages are expanded, and the medication is dispersed deep into the nasal cavity, reaching areas where it can be rapidly absorbed. As the medication is delivered, the air flows around to the opposite side of the nasal cavity and exits through the other nostril. Closure of the soft palate helps prevent swallowing and reduce gastrointestinal absorption.

Sources: Avanir Pharmaceuticals, Onzeta Xsail prescribing information

Eribulin Mesylate (Halaven)

Manufacturer: Eisai Inc., Woodcliff Lake, New Jersey

Date of Approval: January 28, 2016

Indication: Eribulin mesylate was approved for the treatment of patients with metastatic breast cancer in 2010. The...
new approval expands the product’s label to include the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

**Drug Class:** Eribulin mesylate is a non-taxane microtubule dynamics inhibitor. It is a synthetic analogue of halichondrin B, a product isolated from the marine sponge *Halichondria okadai*.

**Uniqueness of Drug:** Eribulin mesylate is the first drug approved for patients with advanced liposarcoma that has demonstrated an improvement in survival time.

**Warnings and Precautions:**

Neutropenia. Clinicians should monitor peripheral blood cell counts and adjust the dose as appropriate.

Peripheral neuropathy. Clinicians should monitor for signs of neuropathy. If neuropathy is present, it should be managed with dose delay and adjustment.

**Use in pregnancy.** Fetal harm can occur when eribulin mesylate is administered to a pregnant woman.

**QT prolongation.** Clinicians should monitor for prolonged QT intervals in patients with congestive heart failure, bradyarrhythmias, drugs known to prolong the QT interval, and electrolyte abnormalities. Clinicians should avoid the use of eribulin mesylate in patients with congenital long QT syndrome.

**Dosage and Administration:** The recommended dosage of eribulin mesylate is 1.4 mg/m² administered intravenously over two to five minutes on days 1 and 8 of a 21-day cycle.

**Commentary:** Eribulin mesylate was evaluated in 143 clinical trial participants with advanced liposarcoma that was unresectable or had spread to nearby lymph nodes (locally advanced) or other parts of the body (metastatic), and who had been treated with chemotherapy. Participants were treated with eribulin mesylate or another chemotherapy drug, dacarbazine, until their disease spread or until they were no longer able to tolerate the adverse effects of treatment. The study was designed to measure overall survival (OS). The median OS for patients with liposarcoma receiving eribulin mesylate was 15.6 months compared with 8.4 months for those who received dacarbazine.

**Sources:** Eisai, Inc., Halaven prescribing information

---

**Pharmaceutical Approval Update**

Extended-Release Amphetamine (Adzenys XR-ODT)

**Manufacturer:** Neos Therapeutics, Grand Prairie, Texas

**Date of Approval:** January 27, 2016

**Indication:** Adzenys XR-ODT is indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) in patients 6 years of age and older.

**Drug Class:** Amphetamine is a central nervous system (CNS) stimulant.

**Uniqueness of Drug:** Adzenys XR-ODT is the first and only extended-release orally disintegrating tablet (ODT) for the treatment of ADHD.

**Warnings and Precautions:**

**Boxed warning.** CNS stimulants, including Adzenys XR-ODT, other amphetamine-containing products, and methylphenidate, have a high potential for abuse and dependence.

**Serious cardiovascular reactions.** Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Treatment with Adzenys XR-ODT should be avoided in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, or coronary artery disease.

**Blood pressure and heart rate increases.** Clinicians should monitor the patient’s blood pressure and pulse. Benefits and risks should be considered before using Adzenys XR-ODT in patients for whom blood pressure increases may be problematic.

**Psychiatric adverse reactions.** Adzenys XR-ODT may cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Clinicians should evaluate patients for bipolar disorder before using a stimulant.

**Long-term suppression of growth.** Clinicians should monitor height and weight in pediatric patients during treatment.

**Peripheral vasculopathy, including Raynaud’s phenomenon.** Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud’s phenomenon. Careful observation for digital changes is necessary during treatment with ADHD stimulants.

**Dosage and Administration:** In pediatric patients (6 to 17 years of age), the starting dosage is 6.3 mg once daily in the morning. The maximum dosage is 18.8 mg once daily for patients 6 to 12 years of age, and 12.5 mg once daily for patients 13 to 17 years of age. In adults, the recommended dosage is 12.5 mg once daily in the morning. Adzenys XR-ODT may be taken with or without food.

**Commentary:** Adzenys XR-ODT contains amphetamine loaded onto a mixture of immediate-release and polymer-coated, delayed-release resin particles. It is not a generic version of amphetamine mixed salts extended-release capsules.

**Sources:** Neos Therapeutics, Adzenys XR-ODT prescribing information