Product Focus

HEALTHDIRECT PHARMACY SERVICES

Aspruzyo Sprinkle® [Ranolazine]

December 2022

Description:

ASPRUZYO Sprinkle contains ranolazine, an antianginal available as white to off-white coated extended-release granules filled in unit-dose sachets containing 500 mg or 1000 mg.

Indications & Dosage:

ASPRUZYO Sprinkle is indicated for the treatment of chronic angina.

ASPRUZYO Sprinkle may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers.

Oral Dosage, Adults:

- 500 mg orally twice daily; may increase to 1000 mg orally twice daily if needed, based on clinical symptoms

Maximum Daily Dose: 1000 mg PO twice daily (2000 mg/ day).

If a dose of ASPRUZYO Sprinkle is missed, take the prescribed dose at the next scheduled time; do not double the next dose.

Dose adjustments may be needed when ASPRUZYO Sprinkle is taken in combination with other drugs- see drug interactions for more details.

Administration:

Avoid concurrent use with alcohol. Alcohol causes a rapid release of ranolazine from the extended-release granules and may increase the risk of adverse events.

Administration with soft foods (e.g., applesauce and yogurt):

- Sprinkle granules on 1 tablespoonful (15 mL) of soft food and have the patient swallow immediately. Do not prepare dose in advance.
- Do not crush or chew the granules.

Administration via nasogastric or gastric tube:

- *Nasogastric (NG) tube*: Open the sachet and empty intact granules into a catheter tip syringe. Add 50 mL of water to the syringe. Gently shake the syringe for approximately 15 seconds. Promptly administer through a 12-French or larger NG-tube. Ensure no granules are left in the syringe. If needed, rinse with approximately 15 mL of additional water.
- *Gastronomy/Gastric (G) tube*: Open the sachet and empty intact granules into a catheter tip syringe. Add 30 mL of water to the syringe. Gently shake the syringe for approximately 15 seconds. Promptly administer through a 12-French or larger G-tube. Rinse with 20 mL of water in the syringe. Ensure no granules are left in the syringe. If needed, rinse with approximately 15 mL of additional water.

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Warnings and Precautions:

QT Prolongation: Ranolazine blocks I_{Kr} and prolongs the QT_c interval in a dose-related manner. Clinical experience in an acute coronary syndrome population did not show an increased risk of proarrhythmia or sudden death. However, there is little experience with high doses (> 1000 mg twice daily) or exposure, other QT-prolonging drugs, potassium channel variants resulting in a long QT interval, in patients with a family history of (or congenital) long QT syndrome, or in patients with known acquired QT interval prolongation.

Renal Failure: Acute renal failure has been observed in patients with severe renal impairment (creatinine clearance [CrCL] < 30 mL/min) while taking ranolazine. If acute renal failure develops (e.g., marked increase in serum creatinine associated with an increase in blood urea nitrogen [BUN]), discontinue ASPRUZYO Sprinkle and treat appropriately. Monitor renal function after initiation and periodically in patients with moderate to severe renal impairment (CrCL < 60 mL/min).

Adverse Reactions:

In controlled clinical trials of angina patients, the most frequently reported treatment-emergent adverse reactions (> 4% and more common on ranolazine than on placebo) were dizziness (6.2%), headache (5.5%), constipation (4.5%), and nausea (4.4%). Dizziness may be dose-related.

Contraindications:

Aspruzyo Sprinkle is contraindicated in patients:

- Taking strong inhibitors of CYP3A4 (e.g. ketoconazole, nefazodone, ritonavir, clarithromycin)
- Taking inducers of CYP3A (e.g. rifampin, phenobarbital, phenytoin, carbamazepine)
- With liver cirrhosis (regardless of Child-Pugh classification)

Drug Interaction Management:

AVOID USE: In patients receiving strong inhibitors of CYP3A4 or inducers of CYP3A isoenzymes.

Moderate CYP3A inhibitors: Limit dose of ASPRUZYO Sprinkle to 500 mg twice daily.

- (e.g., diltiazem, verapamil, erythromycin):

P-gp inhibitors: Increased exposure of ranolazine, titrate ASPRUZYO Sprinkle slowly based on clinical response. (e.g. cyclosporine)

CYP3A substrates: Limit simvastatin to 20 mg when used with ASPRUZYO Sprinkle. Doses of other sensitive CYP3A substrates (e.g., lovastatin) and CYP3A substrates with narrow therapeutic range (e.g., cyclosporine, tacrolimus, sirolimus) may need to be reduced with ASPRUZYO Sprinkle.

OCT2 substrates: Limit the dose of metformin to 1700 mg daily when used with ASPRUZYO Sprinkle 1000 mg twice daily. Doses of other OCT2 substrates may require adjusted doses.

Drugs transported by P-gp (e.g., digoxin), or drugs metabolized by CYP2D6 (e.g., tricyclic antidepressants) may need reduced doses when used with ASPRUZYO Sprinkle.

Alcohol: An in-vitro dissolution study was conducted to evaluate the impact of alcohol on extended-release characteristics of ASPRUZYO Sprinkle. The in-vitro study showed that alcohol causes a rapid release of ranolazine from ASPRUZYO Sprinkle that may increase the risk of adverse events associated with ASPRUZYO Sprinkle. Patients should not consume alcohol when taking ASPRUZYO Sprinkle.

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Special Populations:

Geriatric Use: There were no differences in safety for patients ≥ 65 years compared to younger patients, but patients ≥ 75 years of age on ranolazine, compared to placebo, had a higher incidence of adverse events, serious adverse events, and drug discontinuations due to adverse events. In general, dose selection for an elderly patient should usually start at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease, or other drug therapy.

Hepatic Impairment: ASPRUZYO Sprinkle is contraindicated in patients with liver cirrhosis, due to an increased risk of QT prolongation.

Renal Impairment: Monitor renal function after initiation and periodically in patients with moderate to severe renal impairment (CrCL < 60 mL/min). Discontinue ASPRUZYO Sprinkle if acute renal failure develops.

Hemodialysis: Use in this population has not been studied. Since ranolazine is about 62% bound to plasma proteins, hemodialysis is unlikely to be effective in clearing ranolazine.

Pregnancy: There are no data on the use of ranolazine during pregnancy to inform any drug-associated risks.

Lactation: There are no data on the presence of ranolazine in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ranolazine and any potential adverse effects on the breastfed infant from ranolazine or from the underlying maternal condition.

Storage and Handling:

Store ASPRUZYO Sprinkle at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature].

References:

1. Aspruzyo Sprinkle (ranolazine) extended-release granules. Cranbury, NJ; Sun Pharmaceuticals, Inc.: 2022 Feb.

Sun Pharma is committed to providing a portfolio of alternative-formulation products designed to address the unmet needs of LTC residents who cannot or will not swallow solid medication dosage forms. Visit http://www.sunltc.com/ for more information.