BlueCross BlueShield Federal Employee Program

ZAVESCA/ YARGESA (miglustat)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Gaucher disease is an inherited lysosomal storage disorder in humans that results in the inability to produce glucocerebrosidase, an enzyme necessary for fat metabolism. The enzyme deficiency causes fat materials (lipids) to collect and build up over time, causing problems in the spleen, liver, and bone marrow. Accumulation of lipids in these areas results in the enlargement of the liver and spleen, anemia, thrombocytopenia, lung disease and bone abnormalities (1).

Zavesca and Yargesa are oral medications for the long-term treatment of adult patients with the type 1 form of Gaucher disease. The drug reduces the harmful buildup of the fatty materials by reducing the amount of glucosylceramide- based glycosphingolipids the body produces (1-2).

Regulatory Status

FDA-approved indication: Zavesca and Yargesa are glucosylceramide synthase inhibitors indicated as monotherapy for treatment of adult patients with mild/moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (1-2).

Zavesca and Yargesa are also used in combination with Miplyffa (arimoclomol) for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older (3).

People with type 1 Gaucher disease also may have lowered levels of hemoglobin (a substance in red blood cells) and platelets (blood-clotting cells) that may cause anemia (low red blood cell count) (1).

Clinically significant adverse reactions may occur with Zavesca and Yargesa therapy including peripheral neuropathy, tremor, reduction in platelet count, diarrhea, and weight loss. Based on the severity of the adverse reaction, Zavesca and Yargesa therapy should have a dose reduction or discontinued. Patients with mild to moderate renal insufficiency should have a dose reduction. Use of Zavesca and Yargesa in patients with severe renal impairment (creatinine clearance < 30mL/min/1.73 m^2) is not recommended. Therapy should be directed by physicians knowledgeable in the management of patients with Gaucher disease (1-2).

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Safety and effectiveness of Zavesca and Yargesa in pediatric patients with Gaucher disease have not been established. Safety and effectiveness of Zavesca and Yargesa in pediatric patients less than 2 years of age with NPC have not been established (1-3).

Summary

Zavesca and Yargesa are oral medications for the long-term monotherapy treatment of adult patients with mild/moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option due to constraints such as allergy, hypersensitivity, or poor venous access. Zavesca and Yargesa are also used for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC). Safety and effectiveness of Zavesca and Yargesa in pediatric patients with Gaucher disease have not been established. Safety and effectiveness of Zavesca and Yargesa in pediatric patients less than 2 years of age with NPC have not been established (1-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Zavesca and Yargesa while maintaining optimal therapeutic outcomes.

References

1. Zavesca [package insert]. San Francisco, CA: Actelion Pharmaceuticals US Inc.; August 2022.
2. Yargesa [package insert]. Parsippany, NJ: Edenbridge Pharmaceuticals, LLC.; October 2023.
3. Miplyffa [package insert]. Celebration, FL: Zevra Therapeutics, Inc.; September 2024.