RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Gaucher disease is an inherited lysosomal storage disorder in humans that results in the inability to produce glucocerebroside, 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 (1,2).

Zavesca is an oral administration 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 glucocerebroside the body produces (2).

Regulatory Status
FDA-approved indication: Zavesca is a glucosylceramide synthase inhibitor 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 (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) (2).

Clinically significant adverse reactions may occur with Zavesca therapy including peripheral neuropathy, tremor, reduction in platelet count, diarrhea and weight loss. Based on the severity of the adverse reaction, Zavesca therapy should have a dose reduction or discontinued. Patients with mild to moderate renal insufficiency should have a dose reduction. Use of Zavesca in patients with severe renal impairment (creatinine clearance < 30mL/min/1.73 m²) is not recommended. Therapy should be directed by physicians knowledgeable in the management of patients with Gaucher disease (3).

Safety and effectiveness of Zavesca in pediatric patients have not been established (3).

Summary
Zavesca is an oral administration 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. Clinically
significant adverse reactions may occur with Zavesca therapy including peripheral neuropathy, tremor, reduction in platelet count, diarrhea and weight loss. Based on the severity of the adverse reaction, Zavesca therapy should have a dose reduction or discontinued. Patients with mild to moderate renal insufficiency should have a dose reduction and not recommended in patients with severe renal impairment. Therapy should be directed by physicians knowledgeable in the management of patients with Gaucher disease. Safety and effectiveness of Zavesca in pediatric patients have not been established (3).

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

References
2. Understanding your Zavesca therapy, how it works. Zavesca website.