



RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Gaucher disease is lysosomal storage disorder that results in the inability to produce glucocerebrosidase, an enzyme necessary for fat metabolism. The enzyme deficiency causes the formation of cells with excess lipids/fats, called Gaucher cells, to collect in the spleen, liver, and bone marrow, and other organs. Accumulation of lipids in these areas may result in the enlargement of the liver and spleen, anemia, thrombocytopenia, lung disease and bone abnormalities (1).

Cerdelga is an orally administered drug for the long-term treatment of adult patients with the type 1 form of Gaucher disease. The drug inhibits the accumulation of lipids/fats and hence Gaucher cells (1).

Regulatory Status

FDA-approved indication: Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test (1).

Limitations of Use:

Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers) (1).

Physicians should select patients with Gaucher disease type 1 based on their CYP2D6 metabolizer status. Patient genotypes must be established using an FDA-cleared test for determining CYP2D6 genotype (1).

Cerdelga is a CYP2D6 and CYP3A substrate. Drugs that inhibit CYP2D6 and CYP3A metabolism pathways may significantly increase the exposure to Cerdelga and result in prolongation of the PR, QTc, and/or QRS cardiac intervals that could result in cardiac arrhythmias. Cerdelga is contraindicated in the those patients due to the risk of significantly increased eliglustat plasma concentrations which may result in cardiac arrhythmias. Some inhibitors of CYP2D6 and CYP3A are contraindicated with Cerdelga depending on the patient's metabolizer status. Extensive metabolizers (EMs) or intermediate metabolizers (IMs) taking a strong or moderate CYP2D6



inhibitor concomitantly with a strong or moderate CYP3A inhibitor would be at risk for cardiac arrhythmias. And intermediate metabolizers (IMs) or PM poor metabolizers (PMs) taking a strong CYP3A inhibitor are also at risk for cardiac arrhythmias. Co-administration of Cerdelga with other CYP2D6 and CYP3A inhibitors may require dosage adjustment depending on the patient's CYP2D6 metabolizer status to reduce the risk of potentially significant adverse reactions (1).

Safety and effectiveness in pediatric patients have not been established (1).

Summary

Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test. Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve adequate concentrations of Cerdelga to achieve a therapeutic effect. A specific dosage cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers). Drugs that inhibit CYP2D6 and CYP3A metabolism pathways may significantly increase the exposure to Cerdelga and result in prolongation of the PR, QTc, and/or QRS cardiac intervals that could result in cardiac arrhythmias. Safety and effectiveness in pediatric patients have not been established (1).

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

References

1. Cerdelga [package Insert]. Waterford, Ireland: Genzyme Ireland Ltd.; January 2024.