Prescribing Information: Cerdelga ▼ 84 mg (eliglustat) hard capsules

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each hard capsule contains 84.4 mg of eliglustat (as tartrate).

Indication: The long-term treatment of adult patients with Gaucher disease type 1 (GD1), who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs). Additionally, for the long-term treatment of paediatric patients with GD1 ≥6 years with a minimum body weight of 25 kg, who are stable on enzyme replacement therapy (ERT), and who are CYP2D6 PMs, IMs or EMs.

Dosage and administration: Therapy with Cerdelga should be initiated and supervised by a physician knowledgeable in the management of Gaucher disease. Before initiation of treatment, patients must be genotyped for CYP2D6 to determine the CYP2D6 metaboliser status. Cerdelga should not be used in ultra-rapid metabolisers (URMs) and indeterminate metabolisers. The recommended dose in adults is 84 mg eliglustat twice daily in CYP2D6 IMs and EMs and 84 mg once daily in CYP2D6 PMs. If a dose is missed, the prescribed dose should be taken at the next scheduled time; the next dose should not be doubled. Cerdelga is to be taken orally and swallowed whole, preferably with water, and must not be crushed or dissolved. The capsules may be taken with or without food.

Special populations: Paediatric population: Cerdelga is to be taken orally in children who can swallow the intact capsule. In children ≥6 years of age and weighing ≥50 kg, the recommended dose is 84 mg eliglustat twice daily in CYP2D6 IMs and EMs and 84 mg once daily in CYP2D6 PMs. In children ≥6 years of age and weighing 25 kg to <50 kg, 84 mg eliglustat should be given twice daily in CYP2D6 IMs and EMs, the appropriate dose is not available for CYP2D6 PMs. Safety and efficacy data of Cerdelga eliglustat are limited in paediatric patients below the age of 6 years. Elderly: Data available (from limited treatment experience) indicates no dose adjustment is required. Hepatic impairment: No dose adjustment is required in CYP2D6 EMs with mild hepatic impairment (Child-Pugh class A). Cerdelga is not recommended in CYP2D6 EMs with moderate hepatic impairment (Child-Pugh class B) or in CYP2D6 EMs with mild or moderate hepatic impairment taking a strong CYP2D6 inhibitor. In CYP2D6 EMs with mild hepatic impairment taking a weak CYP2D6 inhibitor or a strong, moderate or weak CYP3A inhibitor, a once daily dose should be considered. Use of Cerdelga in CYP2D6 IMs or PMs with any degree of hepatic impairment is not recommended. Renal impairment: No dose adjustment is required in CYP2D6 EMs with mild, moderate or severe renal impairment. Cerdelga is not recommended in CYP2D6 EMs with end stage renal disease (ESRD) or in CYP2D6 IMs or PMs with mild, moderate or severe renal impairment, or ESRD.

Contraindications: Hypersensitivity to the active substance or to any of the excipients. Cerdelga is also contraindicated in: CYP2D6 EMs with severe hepatic impairment (Child-Pugh Class C), including in those who are also taking any other CYP inhibitors; CYP2D6 EMs also taking a strong or moderate CYP2D6 inhibitor; CYP2D6 EMs or IMs taking a strong or moderate CYP2D6 inhibitor with a strong or moderate CYP3A inhibitor; CYP2D6 PMs who are taking a strong CYP3A inhibitor.

Warnings and Precautions: Patients with pre-existing cardiac conditions: use of Cerdelga should be avoided in patients with cardiac disease (congestive heart failure, recent acute myocardial infarction, bradycardia, heart block, ventricular arrhythmia), long QT syndrome, and in combination with Class IA (e.g. quinidine) and Class III (e.g. amiodarone, sotalol) antiarrhythmic medicinal products. Patients with hepatic impairment and concomitant use with other medicinal products: Concomitant use of eliglustat with CYP2D6 or CYP3A4 inhibitors in CYP2D6 EMs with mild hepatic impairment can elevate eliglustat plasma concentrations (depending on enzyme inhibited and inhibitor potency); once daily dose is recommended. Monitoring of clinical response: Some treatment-naïve patients showed less than 20% spleen volume reduction (sub-optimal results) after 9 months of treatment. For these patients, monitoring for further improvement or an alternative treatment modality should be considered. For patients with stable disease who switch from ERT to eliglustat, monitoring for disease progression (e.g. after 6 months with regular monitoring thereafter) should be performed for all disease domains to evaluate disease stability. Reinstitution of ERT or an alternative treatment modality should be considered in individual patients who have a sub-optimal response. Excipients of known effect: This product contains lactose. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interactions: Agents that may increase eliglustat exposure: *CYP2D6 inhibitors (in IMs and EMs):* Once a day dosing of eliglustat is recommended when a strong CYP2D6 inhibitor (e.g. paroxetine, fluoxetine, quinidine, bupropion) is used concomitantly. Caution should be used with moderate CYP2D6 inhibitors (e.g. duloxetine, terbinafine, moclobemide, mirabegron, cinacalcet, dronedarone). *CYP3A inhibitors (in IMs and EMs):* Caution should be used with strong CYP3A inhibitors (e.g. clarithromycin, ketoconazole, itraconazole, cobicistat, indinavir, lopinavir, ritonavir, saquinavir, telaprevir, tipranavir, posaconazole, voriconazole, telithromycin, conivaptan, boceprevir) and moderate CYP3A inhibitors (erythromycin, ciprofloxacin, fluconazole, diltiazem, verapamil, aprepitant, atazanavir, darunavir, fosamprenavir, imatinib, cimetidine). *CYP3A inhibitors (in PMs):* Strong CYP3A inhibitors are contraindicated, and moderate CYP3A inhibitors are not recommended. Caution should be used with weak CYP3A inhibitors (e.g. amlodipine, cilostazol, fluvoxamine, goldenseal, isoniazid, ranitidine, ranolazine). *CYP2D6 inhibitors used simultaneously with CYP3A inhibitors (in IMs and EMs):* Consumption of grapefruit or its juice should be avoided. Agents that may decrease eliglustat exposure: *Strong CYP3A inducers (in IMs, EMs and PMs):* Use of a strong CYP3A inducer (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin, rifabutin and St. John's wort) with eliglustat is not recommended. Agents whose exposure may be increased by eliglustat: *P-gp substrates:* Lower doses of P-gp substrates (e.g. digoxin, colchicine, dabigatran, phenytoin, pravastatin) may be required. *CYP2D6 substrates:* Lower doses of CYP2D6 substrates (e.g. metoprolol, (tricyclic antidepressants, e.g. nortriptyline, amitriptyline, imipramine, and desipramine), phenothiazines, dextromethorphan and atomoxetine) may be required. The list of substances mentioned here is not exhaustive, prescribers should consult SmPCs of other prescribed medicines for potential drug-drug interactions with eliglustat.

Fertility, pregnancy and lactation: There are limited data from the use of eliglustat in pregnant women. As a precautionary measure, it is recommended to avoid the use

of Cerdelga during pregnancy. It is unknown whether Cerdelga or its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. When deciding whether to discontinue breast-feeding or to discontinue from Cerdelga therapy, the benefit of the breast-feeding child and the benefit of therapy for the woman must be taken into account.

Adverse Reactions: Common: headache, dizziness, dysgeusia, palpitations, throat irritation, cough, dyspepsia, abdominal pain upper, diarrhoea, nausea, constipation, abdominal pain, gastroesophageal reflux disease, abdominal distension, gastritis, dysphagia, vomiting, dry mouth, flatulence, dry skin, urticaria, arthralgia, pain in extremity, back pain and fatigue. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal Category: POM.

List Price: £19,165 (56 capsules).

Marketing Authorisation Number: PLGB 04425/0763

Marketing Authorisation Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

Further information is available from: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com