

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205494Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CERDELGA™ safely and effectively. See full prescribing information for CERDELGA.

CERDELGA™ (eliglustat) capsules, for oral use
Initial U.S. Approval: 2014

INDICATIONS AND USAGE

CERDELGA is a glucosylceramide synthase inhibitor 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. (1)

Limitations of Use:

- CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of CERDELGA to achieve a therapeutic effect (1)
- A specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers (1)

DOSAGE AND ADMINISTRATION

- Select patients using an FDA-cleared test for determining CYP2D6 genotype (2.1)
- CYP2D6 EMs or IMs: 84 mg orally twice daily (2.2)
- CYP2D6 PMs: 84 mg orally once daily (2.2)
- Swallow capsules whole, do not crush, dissolve or open capsules (2.3)
- Avoid eating grapefruit or drinking grapefruit juice (2.3)

DOSAGE FORMS AND STRENGTHS

- 84 mg capsules (3)

CONTRAINDICATIONS

- CYP2D6 EMs and IMs taking a strong or moderate CYP2D6 inhibitor with a strong or moderate CYP3A inhibitor (4, 5.1, 7.1, 12.2)
- CYP2D6 IMs and PMs taking a strong CYP3A inhibitor (4, 5.1, 7.1, 12.2)

WARNINGS AND PRECAUTIONS

- ECG Changes and Potential for Cardiac Arrhythmias: Not recommended in patients with pre-existing cardiac disease, long QT syndrome, and concomitant use of Class IA and Class III antiarrhythmics (5.2)

ADVERSE REACTIONS

The most common adverse reactions (≥10%) are: fatigue, headache, nausea, diarrhea, back pain, pain in extremities, and upper abdominal pain (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at 1-800-745-4447 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

- Eliglustat is a CYP2D6 and CYP3A substrate. Co-administration of CERDELGA with drugs that inhibit CYP2D6 and CYP3A may significantly increase the exposure to eliglustat and result in prolongation of the PR, QTc, and/or QRS cardiac interval, which could result in cardiac arrhythmias. Consider potential drug interactions prior to and during therapy (5.1, 7.1)
- CYP2D6 IMs and PMs taking moderate CYP3A inhibitors: not recommended (7.1)
- CYP2D6 PMs taking weak CYP3A inhibitors: not recommended (7.1)
- CYP2D6 EMs and IMs taking strong or moderate CYP2D6 inhibitors and CYP2D6 EMs taking strong or moderate CYP3A inhibitors: reduce the dosage to 84 mg once daily (2.2, 7.1)
- Eliglustat is an inhibitor of P-gp and CYP2D6. Co-administration with drugs that are substrates for P-gp or CYP2D6 may result in increased concentrations of the other drug (7.2)
- See Full Prescribing Information for a list of clinically significant drug interactions (7.1, 7.2)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Only administer if the potential benefit justifies the potential risk. Based on animal data, may cause fetal harm (8.1)
- Nursing mothers: Discontinue drug or nursing based on importance of drug to mother (8.3)
- Renal impairment: Not recommended in moderate to severe impairment (8.6)
- Hepatic impairment: Not recommended (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2014

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1 FULL PRESCRIBING INFORMATION

2 1 INDICATIONS AND USAGE

3 CERDELGA is indicated for the long-term treatment of adult patients with Gaucher
4 disease type 1 (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate
5 metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test [*see*
6 *Dosage and Administration (2.1)*].

7 Limitations of Use:

- 8 • Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve
9 adequate concentrations of CERDELGA to achieve a therapeutic effect [*see*
10 *Clinical Studies (14)*].
- 11 • A specific dosage cannot be recommended for those patients whose CYP2D6
12 genotype cannot be determined (indeterminate metabolizers) [*see Clinical Studies*
13 *(14)*].

14 2 DOSAGE AND ADMINISTRATION

15 2.1 Patient Selection

16 Select patients with Gaucher disease type 1 based on their CYP2D6 metabolizer status. It
17 is recommended patient genotypes be established using an FDA-cleared test for
18 determining CYP2D6 genotype [*see Indications and Usage (1)*].

19 2.2 Recommended Adult Dosage

20 The recommended dosage of CERDELGA is 84 mg twice daily in CYP2D6 EMs and
21 IMs. The recommended dosage in CYP2D6 PMs is 84 mg once daily; appropriate
22 adverse event monitoring is recommended [*see Adverse Reactions (6.1)*]. The predicted
23 exposures with 84 mg once daily in patients who are CYP2D6 PMs are expected to be
24 similar to exposures observed with 84 mg twice daily in CYP2D6 IMs [*see Clinical*
25 *Pharmacology (12.3)*].

26 Some inhibitors of CYP2D6 and CYP3A are contraindicated with CERDELGA
27 depending on the patient's metabolizer status [*see Contraindications (4)*]. Co-
28 administration of CERDELGA with other CYP2D6 and CYP3A inhibitors may require
29 dosage adjustment depending on the patient's CYP2D6 metabolizer status to reduce the
30 risk of potentially significant adverse reactions [*see Table 3 and Table 4 in Drug*
31 *Interactions (7.1)*].

32 Reduce the dosage of CERDELGA to 84 mg once daily for:

- 33 • CYP2D6 EMs and IMs taking strong or moderate CYP2D6 inhibitors
- 34 • CYP2D6 EMs taking strong or moderate CYP3A inhibitors

35 **2.3 Important Administration Instructions**

- 36 • Swallow capsules whole, preferably with water, and do not crush, dissolve, or
37 open the capsules.
- 38 • CERDELGA can be taken with or without food.
- 39 • Avoid the consumption of grapefruit or grapefruit juice with CERDELGA
40 because grapefruit is a strong CYP3A inhibitor [see *Drug Interactions (7.1)*].
- 41 • If a dose of CERDELGA is missed, take the prescribed dose at the next scheduled
42 time; do not double the next dose.
- 43 • For patients currently treated with imiglucerase, velaglucerase alfa, or
44 taliglucerase alfa, CERDELGA may be administered 24 hours after the last dose
45 of the previous enzyme replacement therapy (ERT).

46 **3 DOSAGE FORMS AND STRENGTHS**

47 CERDELGA is supplied as 84 mg hard gelatin capsules, with a pearl blue-green opaque
48 cap and pearl white opaque body imprinted with “GZ02” in black. Each capsule contains
49 100 mg eliglustat tartrate, which is equivalent to 84 mg of eliglustat.

50 **4 CONTRAINDICATIONS**

51 CERDELGA is contraindicated in the following patients due to the risk of significantly
52 increased eliglustat plasma concentrations which may result in prolongation of the PR,
53 QTc, and/or QRS cardiac intervals that could result in cardiac arrhythmias. See Table 3
54 and Table 4 for examples of drugs in each of the categories described [see *Drug*
55 *Interactions (7.1)*]:

- 56 • EMs or IMs taking a strong or moderate CYP2D6 inhibitor concomitantly with a
57 strong or moderate CYP3A inhibitor.
- 58 • IMs or PMs taking a strong CYP3A inhibitor.

59 **5 WARNINGS AND PRECAUTIONS**

60 **5.1 Drug-Drug Interactions**

61 Eliglustat is a CYP2D6 and CYP3A substrate. Drugs that inhibit CYP2D6 and CYP3A
62 metabolism pathways may significantly increase the exposure to eliglustat and result in
63 prolongation of the PR, QTc, and/or QRS cardiac intervals that could result in cardiac
64 arrhythmias [see *Clinical Pharmacology (12.2)*]. Some drugs that are inhibitors of
65 CYP2D6 and CYP3A are contraindicated with CERDELGA depending on the patient’s

66 CYP2D6 metabolizer status [see *Contraindications (4)*]. See Table 3 and Table 4 for
67 other potentially significant drug interactions [see *Drug Interactions (7.1)*].

68 5.2 ECG Changes and Potential for Cardiac Arrhythmias

69 Use of CERDELGA in patients with pre-existing cardiac conditions has not been studied
70 during clinical trials. Because CERDELGA is predicted to cause increases in ECG
71 intervals (PR, QTc, and QRS) at substantially elevated eliglustat plasma concentrations,
72 use of CERDELGA is not recommended in patients with pre-existing cardiac disease
73 (congestive heart failure, recent acute myocardial infarction, bradycardia, heart block,
74 ventricular arrhythmia), long QT syndrome, and in combination with Class IA (e.g.,
75 quinidine, procainamide) and Class III (e.g., amiodarone, sotalol) antiarrhythmic
76 medications [see *Clinical Pharmacology (12.2)*].

77 6 ADVERSE REACTIONS

78 6.1 Clinical Trials Experience

79 Because clinical trials are conducted under widely varying conditions, adverse reaction
80 rates observed in the clinical trials of a drug cannot be directly compared to rates in the
81 clinical trials of another drug and may not reflect the rates observed in practice.

82 The most common adverse reactions to CERDELGA (occurring in $\geq 10\%$ of the 126 GD1
83 patients treated with CERDELGA across Trials 1 and 2) were fatigue, headache, nausea,
84 diarrhea, back pain, pain in extremities, and upper abdominal pain.

85 The adverse reaction profile of CERDELGA is based on two controlled studies, Trials 1
86 and 2. Table 1 presents the profile from the 9-month double-blind, randomized, placebo-
87 controlled trial of 40 treatment-naïve patients (Trial 1). Patients were between the ages
88 of 16 and 63 on the date of the first dose of study drug, and included 20 males and 20
89 females.

Table 1: Adverse Reactions Occurring in $\geq 10\%$ of Treatment-Naïve GD1 Patients and More Frequently than Placebo (Trial 1)

Adverse Reaction	CERDELGA (N=20)	Placebo (N=20)
	Patients n (%)	Patients n (%)
Arthralgia	9 (45)	2 (10)
Headache	8 (40)	6 (30)
Migraine	2 (10)	0 (0)
Flatulence	2 (10)	1 (5)

Table 1: Adverse Reactions Occurring in ≥10% of Treatment-Naïve GD1 Patients and More Frequently than Placebo (Trial 1)

Adverse Reaction	CERDELGA (N=20)	Placebo (N=20)
	Patients n (%)	Patients n (%)
Nausea	2 (10)	1 (5)
Oropharyngeal pain	2 (10)	1 (5)

90

91 Table 2 presents the profile from the 12-month open-label, randomized, imiglucerase-
92 controlled trial of 159 treated patients switching from enzyme replacement therapy (ERT)
93 (Trial 2). Patients were between the ages of 18 and 69 on the date of the first dose of
94 CERDELGA, and included 87 females and 72 males.

Table 2: Adverse Reactions Occurring in ≥5% of GD1 Patients Switching from Enzyme Replacement Therapy to CERDELGA and More Frequently than Imiglucerase (Trial 2)*

Adverse Reaction	CERDELGA (N=106)	Imiglucerase (N=53)
	Patients n (%)	Patients n (%)
Fatigue	15 (14)	1 (2)
Headache	14 (13)	1 (2)
Nausea	13 (12)	0 (0)
Diarrhea	13 (12)	2 (4)
Back pain	13 (12)	3 (6)
Pain in extremity	12 (11)	1 (2)
Upper abdominal pain	11 (10)	0 (0)
Dizziness	9 (8)	0 (0)
Asthenia	9 (8)	0 (0)
Cough	7 (7)	2 (4)
Dyspepsia	7 (7)	1 (2)
Gastroesophageal reflux disease	7 (7)	0 (0)
Constipation	5 (5)	0 (0)
Palpitations	5 (5)	0 (0)
Rash	5 (5)	0 (0)

95 *Trial 2 was not designed to support comparative claims for CERDELGA for the adverse reactions
96 reported in this table.

97 In an uncontrolled study, with up to 4 years of treatment, in 26 patients, the types and
98 incidences of adverse reactions were similar to Trials 1 and 2.

99 7 **DRUG INTERACTIONS**

100 **7.1 Potential for Other Drugs to Affect CERDELGA**

101 Eliglustat is a CYP2D6 and CYP3A substrate.

102 CYP2D6 and CYP3A Inhibitors

103 Drugs that inhibit CYP2D6 and CYP3A pathways may significantly increase the
 104 exposure to eliglustat and result in prolongation of the PR, QTc, and/or QRS cardiac
 105 interval which could result in cardiac arrhythmias:

- 106 • Some inhibitors of CYP2D6 and CYP3A are contraindicated with CERDELGA
 107 depending on the patient’s CYP2D6 metabolizer status [see *Contraindications*
 108 *(4)*].
- 109 • Co-administration of CERDELGA with other CYP2D6 and CYP3A inhibitors
 110 may require dosage adjustment depending on the patient’s CYP2D6 metabolizer
 111 status to reduce the risk of potential significant adverse reactions (see Table 3 and
 112 Table 4).

114 **Table 3: Established and Other Potentially Significant Drug Interactions:**
 115 **Alteration in CERDELGA Dosage May Be Recommended Based on Drug**
 116 **Interaction Studies or on Predicted Interaction in EMs and IMs**

CYP450 Inhibitors	Recommended CERDELGA Dosage, by CYP2D6 Metabolizer Status	
	EM	IM
Strong or Moderate CYP2D6 inhibitors concomitantly with Strong or Moderate CYP3A inhibitors	Contraindicated	Contraindicated
Strong CYP2D6 inhibitors e.g., paroxetine	84 mg once daily	84 mg once daily
Moderate CYP2D6 inhibitors e.g., terbinafine	84 mg once daily	84 mg once daily
Strong CYP3A inhibitors e.g., ketoconazole	84 mg once daily	Contraindicated
Moderate CYP3A inhibitors e.g., fluconazole	84 mg once daily	Not recommended

117

118 **Table 4: Established and Other Potentially Significant Drug Interactions:**
 119 **Alteration in CERDELGA Dosage May Be Recommended Based on Predicted**
 120 **Interaction in PMs**

CYP450 Inhibitors	Recommended CERDELGA Dosage for PMs
Strong CYP3A inhibitors e.g., ketoconazole	Contraindicated
Moderate CYP3A inhibitors e.g., fluconazole	Not recommended
Weak CYP3A inhibitors e.g., ranitidine	Not recommended

121

122 CYP3A Inducers

123 Co-administration of CERDELGA with strong CYP3A inducers significantly decreases
 124 eliglustat exposure. Use of CERDELGA with strong CYP3A inducers (e.g., rifampin,
 125 carbamazepine, phenobarbital, phenytoin, and St. John’s Wort) is not recommended in
 126 EMs, IMs, and PMs.

127 **7.2 Potential for CERDELGA to Affect Other Drugs**

128 Eliglustat is an inhibitor of P-gp and CYP2D6. Co-administration of CERDELGA with
 129 drugs that are substrates for P-gp or CYP2D6 may result in increased concentrations of
 130 the concomitant drug as shown in Table 5.

131 **Table 5: Drug Interactions that Result in Increased Concentrations of the**
 132 **Concomitant Drug**

Drug Class or Drug Name	Clinical Recommendations
Digoxin (P-gp substrate)	Measure serum digoxin concentrations before initiating CERDELGA. Reduce digoxin dose by 30% and continue monitoring.
<u>Other P-gp substrates</u> (e.g., phenytoin, colchicine, dabigatran etexilate)	Monitor therapeutic drug concentrations, as indicated, or consider reducing the dosage of the concomitant drug and titrate to clinical effect.
<u>CYP2D6 substrates</u> <ul style="list-style-type: none"> • Metoprolol; • tricyclic antidepressants (e.g., nortriptyline, amitriptyline, imipramine); • phenothiazines (e.g., perphenazine, chlorpromazine). 	

133 **8 USE IN SPECIFIC POPULATIONS**

134 **8.1 Pregnancy**

135 **Pregnancy Category C**

136 Risk Summary

137 There are no adequate or well-controlled studies with CERDELGA in pregnant women.
138 However, animal reproduction studies have been conducted for eliglustat. In these
139 animal studies, a spectrum of anomalies at doses 6 times the recommended human dose
140 were observed in orally dosed rats. No fetal harm was observed with oral administration
141 of eliglustat to pregnant rabbits at dose levels 10 times the recommended human dose.
142 CERDELGA should be used during pregnancy only if the potential benefit justifies the
143 potential risk to the fetus.

144 Clinical Considerations

145 Disease-associated maternal and embryo-fetal risk

146 Women with Gaucher disease type 1 have an increased risk of spontaneous abortion,
147 especially if disease symptoms are not treated and controlled pre-conception and during a
148 pregnancy. Pregnancy may exacerbate existing Gaucher disease type 1 symptoms or
149 result in new disease manifestations. Gaucher disease type 1 manifestations may lead to
150 adverse pregnancy outcomes including, hepatosplenomegaly which can interfere with the
151 normal growth of a pregnancy and thrombocytopenia which can lead to increased
152 bleeding and possible hemorrhage.

153 Animal Data

154 Reproduction studies have been performed in pregnant rats at oral doses up to 120
155 mg/kg/day (about 6 times the recommended human dose based on body surface area) and
156 in pregnant rabbits at oral doses up to 100 mg/kg/day (about 10 times the recommended
157 human dose based on body surface area). In rats, at 120 mg/kg/day (about 6 times the
158 recommended human dose based on body surface area), eliglustat increased the number
159 of late resorptions, dead fetuses and post implantation loss, reduced fetal body weight,
160 and caused fetal cerebral variations (dilated cerebral ventricles), fetal skeletal variations
161 (poor bone ossification) and fetal skeletal malformations (abnormal number of ribs or
162 lumbar vertebra). Eliglustat did not cause fetal harm in rabbits at oral doses up to 100
163 mg/kg/day (about 10 times the recommended human dose based on body surface area).
164 In a pre and postnatal development study in rats, eliglustat did not show any significant
165 adverse effects on pre and postnatal development at doses up to 100 mg/kg/day (about 5
166 times the recommended human dose based on body surface area).

167 8.3 Nursing Mothers

168 It is not known whether CERDELGA is present in human milk. Because many drugs are
169 present in human milk, and because of the potential for serious adverse reactions in
170 nursing infants from CERDELGA, a decision should be made whether to discontinue
171 nursing or discontinue the drug, taking into account the importance of the drug to the
172 lactating woman.

173 8.4 Pediatric Use

174 Safety and effectiveness in pediatric patients have not been established.

175 8.5 Geriatric Use

176 Clinical studies of CERDELGA did not include sufficient numbers of subjects aged 65
177 and over to determine whether they respond differently from younger subjects. Clinical
178 experience has not identified differences in responses between the elderly and younger
179 patients.

180 8.6 Renal Impairment

181 There is no dosage adjustment required for patients with mild renal impairment.
182 CERDELGA has not been studied in patients with moderate to severe renal impairment
183 or end-stage renal disease (ESRD). Use of CERDELGA in these patients is not
184 recommended.

185 8.7 Hepatic Impairment

186 CERDELGA has not been studied in patients with hepatic impairment. Use of
187 CERDELGA is not recommended in all stages of hepatic impairment or cirrhosis.

188 8.8 Poor Metabolizers

189 Dosing of CERDELGA 84 mg once daily has not been studied in PMs, however the
190 predicted systemic exposures in these patients are within the range of those observed in
191 clinical studies. Appropriate adverse event monitoring is recommended [*see Adverse*
192 *Reactions (6.1) and Clinical Studies (14)*].

193 10 OVERDOSAGE

194 The highest eliglustat plasma concentration experienced to date occurred in a single-dose,
195 dose escalation study in healthy subjects, in a subject taking a dose equivalent to
196 approximately 21 times the recommended dose for GD1 patients. At the time of the
197 highest plasma concentration (59-fold higher than normal therapeutic conditions), the

198 subject experienced dizziness marked by disequilibrium, hypotension, bradycardia,
199 nausea, and vomiting.

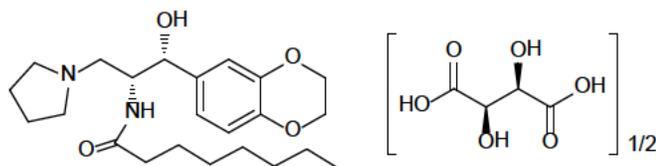
200 In the event of acute overdose, the patient should be carefully observed and given
201 symptomatic and supportive treatment.

202 Hemodialysis is unlikely to be beneficial given that eliglustat has a large volume of
203 distribution [see *Clinical Pharmacology (12.3)*].

204 11 DESCRIPTION

205 CERDELGA (eliglustat) capsules contain eliglustat tartrate, which is a small molecule
206 inhibitor of glucosylceramide synthase that resembles the ceramide substrate for the
207 enzyme, with the chemical name N-((1*R*,2*R*)-1-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-1-
208 hydroxy-3-(pyrrolidin-1-yl)propan-2-yl)octanamide (2*R*,3*R*)-2,3-dihydroxysuccinate. Its
209 molecular weight is 479.59, and the empirical formula is $C_{23}H_{36}N_2O_4 + \frac{1}{2}(C_4H_6O_6)$ with
210 the following chemical structure:

211



213

213 Each capsule of CERDELGA for oral use contains 84 mg of eliglustat, equivalent to
214 100 mg of eliglustat tartrate (hemitartrate salt). The inactive ingredients are
215 microcrystalline cellulose, lactose monohydrate, hypromellose and glyceryl behenate,
216 gelatin, candurin silver fine, yellow iron oxide, and FD&C blue 2.

217 12 CLINICAL PHARMACOLOGY

218 12.1 Mechanism of Action

219 Gaucher disease is caused by a deficiency of the lysosomal enzyme acid β -glucosidase.
220 Acid β -glucosidase catalyzes the conversion of the sphingolipid glucocerebroside into
221 glucose and ceramide. The enzymatic deficiency causes an accumulation of
222 glucosylceramide (GL-1) primarily in the lysosomal compartment of macrophages,
223 giving rise to foam cells or "Gaucher cells". CERDELGA is a specific inhibitor of
224 glucosylceramide synthase ($IC_{50} = 10$ ng/mL), and acts as a substrate reduction therapy
225 for GD1. In clinical trials CERDELGA reduced spleen and liver size, and improved
226 anemia and thrombocytopenia.

227 In this lysosomal storage disorder (LSD), clinical features are reflective of the
228 accumulation of Gaucher cells in the liver, spleen, bone marrow, and other organs. The
229 accumulation of Gaucher cells in the liver, spleen, and bone marrow leads to
230 organomegaly and skeletal disease. Presence of Gaucher cells in the bone marrow and
231 spleen lead to clinically significant anemia and thrombocytopenia.

232 **12.2 Pharmacodynamics**

233 *Electrocardiographic Evaluation*

234 QTc interval prolongation was studied in a double-blind, single dose, placebo- and
235 positive-controlled crossover study in 42 healthy subjects. Concentration-related
236 increases were observed for the placebo-corrected change from baseline in the PR, QRS,
237 and QTc intervals. Based on PK/PD modeling, eliglustat plasma concentrations of 500
238 ng/mL are predicted to cause mean (upper bound of the 95% one-sided confidence
239 interval) increases in the PR, QRS, and QTcF intervals of 22 (26), 7 (10), and 13 (19)
240 msec, respectively. At the highest geometric mean concentrations of 237 ng/mL
241 following a single supratherapeutic dose tested in the thorough QT study, CERDELGA
242 did not prolong the QT/QTc interval to any clinically relevant extent.

243 **12.3 Pharmacokinetics**

244 At a given dose, the systemic exposure (C_{max} and AUC) depends on the CYP2D6
245 phenotype. In CYP2D6 EMs and IMs, the eliglustat pharmacokinetics is time-dependent
246 and the systemic exposure increases in a more than dose proportional manner. After
247 multiple oral doses of 84 mg twice daily in EMs, eliglustat systemic exposure (AUC_{0-12})
248 increased up to about 2-fold at steady state compared to after the first dose ($AUC_{0-\infty}$). The
249 pharmacokinetics of eliglustat in CYP2D6 PMs is expected to be linear and time-
250 independent. Compared to EMs, the systemic exposure following 84 mg twice daily at
251 steady state is 7- to 9-fold higher in PMs.

252 *Absorption*

253 In CYP2D6 EMs, median time to reach maximum plasma concentrations (t_{max}) occurs at
254 1.5 to 2 hours following multiple doses of CERDELGA 84 mg twice daily. The
255 corresponding mean C_{max} values range from 12.1 to 25.0 ng/mL in EMs. The mean
256 AUC_{tau} values range from 76.3 to 143 hr*ng/mL in EMs. The C_{max} and AUC_{tau} in one
257 IM subject receiving multiple doses of CERDELGA 84 mg two time daily was 44.6
258 ng/mL and 306 hr*ng/mL, respectively. The oral bioavailability is low in EMs (<5%)
259 following single dose of CERDELGA 84 mg due to significant first-pass metabolism.

260 In PMs, median t_{\max} occurs at 3 hours following multiple doses of CERDELGA 84 mg
261 twice daily. The corresponding mean C_{\max} and AUC_{τ} values range from 113 to 137
262 ng/mL and 922 to 1057 hr*ng/mL, respectively.

263 Oral dosing of CERDELGA 84 mg once daily has not been studied in PMs. The
264 predicted C_{\max} and AUC_{0-24hr} in PMs using physiologically-based pharmacokinetic
265 (PBPK) model with 84 mg once daily are 75 ng/mL and 956 hr*ng/mL, respectively.

266 Administration of CERDELGA with a high fat meal resulted in a 15% decrease in C_{\max}
267 but no change in AUC. Food does not have a clinically relevant effect on eliglustat
268 pharmacokinetics.

269 *Distribution*

270 Eliglustat is moderately bound to human plasma proteins (76 to 83%). In the blood, it is
271 mainly distributed in plasma and not red blood cells. After intravenous (IV)
272 administration, the volume of distribution of eliglustat was 835 L in CYP2D6 EMs,
273 suggesting wide distribution to tissues (CERDELGA is only for oral use).

274 *Metabolism and Elimination*

275 CERDELGA is extensively metabolized with high clearance, mainly by CYP2D6 and to
276 a lesser extent CYP3A4. Primary metabolic pathways of eliglustat involve sequential
277 oxidation of the octanoyl moiety followed by oxidation of the 2,3-dihydro-1,4-
278 benzodioxane moiety, or a combination of the two pathways, resulting in multiple
279 oxidative metabolites. No active metabolites have been identified.

280 After oral administration of 84 mg [^{14}C]-eliglustat, the majority of the administered dose
281 is excreted in urine (41.8%) and feces (51.4%), mainly as metabolites. After 42 mg IV
282 administration in healthy volunteers, mean (CV%) of eliglustat total body clearance was
283 88 L/h (8.8%) in CYP2D6 EMs (CERDELGA is only for oral use). Following multiple
284 oral doses of CERDELGA 84 mg twice daily, eliglustat terminal elimination half-life
285 ($T_{1/2}$) was approximately 6.5 hours in EMs and 8.9 hours in PMs.

286

287 *Specific Populations*

288 Based on population PK analysis, there was no effect of mild renal impairment on
289 eliglustat PK. Furthermore, gender, body weight, age, and race had no clinically relevant
290 impact on the pharmacokinetics of eliglustat.

291 *Drug Interactions - Effect of Other Drugs on CERDELGA*

292 *In vitro*, eliglustat is metabolized primarily by CYP2D6 and to a lesser extent by
293 CYP3A4. Eliglustat is also a substrate of P-glycoprotein (P-gp).

294 *Co-administration of CERDELGA with CYP2D6 Inhibitors*

295 Systemic exposure (C_{max} and AUC_{tau}) of eliglustat increased 7.0-fold and 8.4-fold,
296 respectively, following co-administration of CERDELGA 84 mg twice daily with
297 paroxetine (a strong CYP2D6 inhibitor) 30 mg once daily in EMs (N=30), respectively.

298 Simulations using PBPK models suggested that paroxetine may increase the C_{max} and
299 AUC_{tau} of eliglustat 2.1- and 2.3-fold in IMs, respectively.

300 Compared to paroxetine, the effects of terbinafine (a moderate inhibitor of CYP2D6) on
301 the exposure of eliglustat in EMs or IMs were predicted to be smaller. Simulations using
302 PBPK models suggested that terbinafine may increase the C_{max} and AUC_{tau} of eliglustat
303 3.8- and 4.5-fold in EMs, respectively. Both C_{max} and AUC_{tau} increased 1.6-fold in IMs.

304 *Co-administration of CERDELGA with CYP3A Inhibitors*

305 CYP2D6 EMs and IMs:

306 Following co-administration of CERDELGA 84 mg twice daily with ketoconazole (a
307 strong CYP3A inhibitor) 400 mg once daily, the systemic exposure (C_{max} and AUC_{tau}) of
308 eliglustat increased 4.0-fold and 4.4-fold in EMs (N=31).

309 Simulations using PBPK models suggested that ketoconazole may increase the C_{max} and
310 AUC_{tau} of eliglustat 4.4- and 5.4-fold in IMs, respectively.

311 Compared to ketoconazole, the effects of fluconazole (a moderate inhibitor of CYP3A)
312 on the exposure of eliglustat in EMs or IMs were predicted to be smaller. Simulations
313 using PBPK models suggested that fluconazole may increase the C_{max} and AUC_{tau} of
314 eliglustat 2.8- and 3.2-fold in EMs, respectively, and 2.5- to 2.9-fold in IMs, respectively.

315 CYP2D6 PMs:

316 The effect of CYP3A inhibitors on the systemic exposure of eliglustat in PMs has not
317 been evaluated in clinical studies. Simulations using PBPK models suggest that

318 ketoconazole may increase the C_{\max} and AUC_{0-24h} of eliglustat 4.3- and 6.2-fold when co-
319 administered with CERDELGA 84 mg once daily in PMs. Simulations using PBPK
320 models suggested that fluconazole may increase the C_{\max} and AUC_{0-24h} of eliglustat 2.4-
321 and 3.0-fold, respectively, when co-administered with CERDELGA 84 mg once daily.

322 *Co-administration of CERDELGA with CYP2D6 and CYP3A inhibitors*

323 Simulations using PBPK models suggested that concomitant use of CERDELGA 84 mg
324 twice daily with paroxetine and ketoconazole may increase the C_{\max} and AUC_{τ} of
325 eliglustat 16.7- and 24.2-fold in EMs, respectively. The predicted C_{\max} and AUC_{τ} of
326 eliglustat increased 7.5- to 9.8-fold in IMs, respectively.

327 Simulations using PBPK models suggested that concomitant use of CERDELGA 84 mg
328 twice daily with terbinafine and fluconazole may increase the C_{\max} and AUC_{τ} of
329 eliglustat 10.2- and 13.6-fold in EMs. The predicted C_{\max} and AUC_{τ} of eliglustat
330 increased 4.2- to 5.0-fold in IMs, respectively.

331 *Effect of CYP3A inducers on Eliglustat PK*

332 Systemic exposures (C_{\max} and AUC_{τ}) of eliglustat decreased by approximately 90% in
333 EMs and IMs, following co-administration of CERDELGA 127 mg twice daily with
334 rifampin (a strong CYP3A inducer) 600 mg PO once daily. The only approved dose of
335 CERDELGA is 84 mg. Systemic exposures of eliglustat decreased by approximately
336 95% following co-administration of CERDELGA 84 mg twice daily with rifampin 600
337 mg PO once daily in PMs.

338 *Effect of OATP (organic anion transporting polypeptide) Inhibitors on Eliglustat PK*

339 Systemic exposures of eliglustat were similar with or without co-administration of single
340 600 mg IV dose of rifampin (a potent OATP inhibitor) regardless of subjects' CYP2D6
341 phenotypes.

342 *Effect of P-gp Inhibitors on Eliglustat PK*

343 The effect of P-gp inhibitors on the systemic exposure of eliglustat has not been studied
344 clinically.

345 *Effect of Gastric pH-Modifying Agents on Eliglustat PK*

346 Gastric pH-modifying agents (Maalox[®], Tums[®], Protonix[®]) did not have a clinically
347 relevant effect on eliglustat exposure.

348 *Drug Interactions - Effect of CERDELGA on the PK of Other Drugs*

349 Eliglustat is an inhibitor of P-gp and CYP2D6.

350 Following multiple doses of CERDELGA 127 mg twice daily, systemic exposures (C_{\max}
351 and AUC) to metoprolol (a CYP2D6 substrate) increased compared to metoprolol
352 administration alone. Mean C_{\max} and AUC increased by 1.7- and 2.3-fold, respectively,
353 in EMs and by 1.2- and 1.6-fold, respectively in IMs. The only approved dose of
354 CERDELGA is 84 mg.

355 Following multiple doses of CERDELGA 127 mg twice daily in EMs and IMs or 84 mg
356 twice daily in PMs, systemic exposures (C_{\max} and AUC) to digoxin (a P-gp substrate,
357 with narrow therapeutic index) increased compared to digoxin administration alone.
358 Mean C_{\max} and AUC increased by 1.7- and 1.5-fold, respectively. The only approved
359 dose of CERDELGA is 84 mg.

360 *In vitro*, eliglustat is a weak inhibitor of CYP3A. Repeated doses of CERDELGA 84 mg
361 twice daily did not change the exposures to norethindrone (1.0 mg) and ethinyl estradiol
362 (0.035 mg). Therefore, CERDELGA is not expected to impact the efficacy or safety of
363 oral contraceptives containing norethindrone and ethinyl estradiol.

364 **13 NONCLINICAL TOXICOLOGY**

365 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

366 *Carcinogenesis*

367 Carcinogenic potential of CERDELGA was assessed in 2-year carcinogenicity studies in
368 rats and mice. In Sprague-Dawley rats, eliglustat was administered by oral gavage at
369 doses up to 75 mg/kg/day in males (about 3.6 times the recommended human daily dose
370 of 84 mg twice daily, based on body surface area) and 50 mg/kg/day in females (about
371 2.4 times the recommended human daily dose based on body surface area). In CD-1
372 mice, eliglustat was administered to males and females at up to 75 mg/kg/day (about 1.8
373 times the recommended human daily dose based on body surface area) via dietary
374 admixture. Eliglustat did not produce any treatment-related neoplasms in rats or mice.

375 *Mutagenesis*

376 Eliglustat was negative in the Ames test, chromosome aberration test in human peripheral
377 blood lymphocytes, mouse lymphoma gene mutation assay and *in vivo* oral mouse
378 micronucleus test.

379 *Impairment of Fertility*

380 In a fertility and early embryonic development study in rats, eliglustat increased pre-
381 implantation loss at 30 (about 1.5 times the recommended human oral dose based on
382 body surface area) and 100 mg/kg/day (about 5 times the recommended human oral dose
383 based on body surface area).

384 In mature male rats, eliglustat showed reversible adverse effects on sperm morphology,
385 testes (germ cell necrosis), and sloughed cells in the epididymis at 200 mg/kg/day (about
386 10 times the recommended human oral dose based on body surface area). Similar effects
387 on sperm were not seen in mature Cynomolgus monkeys at 72 mg/kg/day (about 7 times
388 the recommended human oral dose based on body surface area).

389 **14 CLINICAL STUDIES**

390 The efficacy of CERDELGA was evaluated in three clinical trials in patients with
391 Gaucher disease type 1.

392 **14.1 CERDELGA in Treatment-Naïve GD1 Patients – Trial 1**

393 Trial 1 was a randomized, double-blind, placebo-controlled, multicenter clinical study
394 evaluating the efficacy and safety of CERDELGA in 40 treatment-naïve GD1 patients 16
395 years of age or older (median age 30.4 years) with pre-existing splenomegaly and
396 hematological abnormalities. Patients were required to have received no treatment with
397 substrate reduction therapy within 6 months or ERT within 9 months prior to
398 randomization; all but 5 patients in the study had no prior therapy. Patients were
399 stratified according to baseline spleen volume (≤ 20 or > 20 multiples of normal [MN])
400 and randomized in a 1:1 ratio to receive CERDELGA or placebo for the duration of the
401 9-month blinded primary analysis period. The CERDELGA treatment group was
402 comprised of IM (5%), EM (90%) and URM (5%) patients. Patients randomized to
403 CERDELGA treatment received a starting dose of 42 mg twice daily, with a dose
404 increase to 84 mg twice daily possible at Week 4 based on the plasma trough
405 concentration at Week 2. The majority of patients (17 [85%]) received a dose escalation
406 to 84 mg twice daily at Week 4, and 3 (15%) continued to receive 42 mg twice daily for
407 the duration of the 9-month blinded primary analysis period.

408 The primary endpoint was the percentage change in spleen volume (in MN) from
409 baseline to 9 months as compared to placebo. Secondary endpoints were absolute change
410 in hemoglobin level, percentage change in liver volume (in MN), and percentage change
411 in platelet count from baseline to 9 months compared to placebo.

412 At baseline, mean spleen volumes were 12.5 and 13.9 MN in the placebo and
 413 CERDELGA groups, respectively, and mean liver volumes were 1.4 MN for both groups.
 414 Mean hemoglobin levels were 12.8 and 12.1 g/dL, and platelet counts were 78.5 and 75.1
 415 $\times 10^9/L$, respectively.

416 During the 9-month primary analysis period, CERDELGA demonstrated statistically
 417 significant improvements in all primary and secondary endpoints compared to placebo, as
 418 shown in Table 6.

Table 6: Change from Baseline to Month 9 in Treatment-Naïve Patients with GD1 Receiving Treatment with CERDELGA in Trial 1

	Placebo (n=20)	CERDELGA (n=20)	Difference (CERDELGA – Placebo) [95% CI]	p value*
Percentage Change in Spleen Volume MN (%)	2.3	-27.8	-30.0 [-36.8, -23.2]	<0.0001
Absolute Change in Spleen Volume (MN)	0.3	-3.7	-4.1 [-5.3, -2.9]	NA
Absolute Change in Hemoglobin Level (g/dL)	-0.5	0.7	1.2 [0.6, 1.9]	0.0006
Percentage Change in Liver Volume MN (%)	1.4	-5.2	-6.6 [-11.4, -1.9]	0.0072
Absolute Change in Liver Volume (MN)	0.0	-0.1	-0.1 [-0.2, 0.0]	NA
Percentage Change in Platelet Count (%)	-9.1	32.0	41.1 [24.0, 58.2]	<0.0001
Absolute Change in Platelet Count ($\times 10^9/L$)	-7.2	24.1	31.3 [18.8, 43.8]	NA

419 MN = Multiples of Normal, CI = confidence interval, NA = Not applicable

420 *Estimates and p-value are based on ANCOVA model that includes treatment group, baseline spleen
 421 severity group ($\leq 20MN$, $>20MN$) and baseline parameter value.

422 In an uncontrolled study of treatment naïve GD1 patients, improvements in spleen and
 423 liver volume, hemoglobin level, and platelet count continued through the 4 year treatment
 424 period.

425

426 **14.2 Patients Switching from Enzyme Replacement Therapy to CERDELGA –**
427 **Trial 2**

428 Trial 2 was a randomized, open-label, active-controlled, non-inferiority, multicenter
429 clinical study evaluating the efficacy and safety of CERDELGA compared with
430 imiglucerase in 159 treated GD1 patients (median age 37.4 years) previously treated with
431 enzyme replacement therapy (≥ 3 years of enzyme replacement therapy, dosed at 30-130
432 U/kg/month in at least 6 of the prior 9 months) who met pre-specified therapeutic goals at
433 baseline. Pre-specified baseline therapeutic goals included: no bone crisis and free of
434 symptomatic bone disease within the last year; mean hemoglobin level of ≥ 11 g/dL in
435 females and ≥ 12 g/dL in males; mean platelet count $\geq 100,000/\text{mm}^3$; spleen volume < 10
436 times normal and liver volume < 1.5 times normal.

437 Patients were randomized 2:1 to receive CERDELGA or imiglucerase for the duration of
438 the 12-month primary analysis period. Seventy-five percent of patients randomized to
439 CERDELGA were previously treated with imiglucerase; 21% with velaglucerase alfa and
440 4% were unreported. Patients randomized to CERDELGA treatment received a starting
441 dose of 42 mg twice daily, with dose increases to 84 mg twice daily and 127 mg twice
442 daily possible at Weeks 4 and 8 based on plasma trough concentrations of CERDELGA
443 at Weeks 2 and 6, respectively. The percentage of patients receiving the 3 possible
444 CERDELGA doses was: 42 mg twice daily (20%), 84 mg twice daily (32%) and 127 mg
445 twice daily (48%). The CERDELGA treatment group was comprised of PM (4%), IM
446 (10%), EM (80%) and URM (4%) patients.

447 At baseline, mean spleen volumes were 2.6 and 3.2 MN in the imiglucerase and
448 CERDELGA groups, respectively, and liver volumes were 0.9 MN in both groups. Mean
449 hemoglobin levels were 13.8 and 13.6 g/dL, and platelet counts were 192 and 207 x
450 $10^9/\text{L}$, respectively.

451 The primary composite endpoint required stability in all four component domains
452 (hemoglobin level, platelet count, liver volume, and spleen volume) based on changes
453 between baseline and 12 months. Stability was defined by the following pre-specified
454 thresholds of change: hemoglobin level < 1.5 g/dL decrease, platelet count $< 25\%$
455 decrease, liver volume $< 20\%$ increase and spleen volume $< 25\%$ increase. The
456 percentages of patients meeting the criteria for stability in the individual components of
457 the composite endpoint were assessed as secondary efficacy endpoints.

458 CERDELGA met the criteria to be declared non-inferior to imiglucerase in maintaining
 459 patient stability. After 12 months of treatment, the percentage of patients meeting the
 460 primary composite endpoint was 84.8% for the CERDELGA group compared to 93.6%
 461 for the imiglucerase group. The lower bound of the 95% CI of the 8.8% difference,
 462 -17.6%, was within the pre-specified non-inferiority margin of -25%. At Month 12, the
 463 percentages of CERDELGA and imiglucerase patients respectively, who met stability
 464 criteria for the individual components of the composite endpoint were: hemoglobin level,
 465 94.9% and 100%; platelet count, 92.9% and 100%; spleen volume, 95.8% and 100%; and
 466 liver volume, 96.0% and 93.6%. Of the patients who did not meet stability criteria for the
 467 individual components, 12 of 15 CERDELGA patients and 3 of 3 imiglucerase patients
 468 remained within therapeutic goals for GD1.

469 Mean changes from baseline in the hematological and visceral parameters through 12
 470 months of treatment are shown in Table 7. There were no clinically meaningful
 471 differences between groups for any of the four parameters.

Table 7: Mean Changes from Baseline to Month 12 in Patients with GD1 Switching to CERDELGA in Trial 2

	Imiglucerase (N=47) Mean [95% CI]	CERDELGA (N=99) Mean [95% CI]
Percentage Change in Spleen Volume MN (%)*	-3.0 [-6.4, 0.4]	-6.2 [-9.5, -2.8]
Absolute Change in Spleen Volume (MN)*	-0.1 [-0.2, 0.0]	-0.2 [-0.3, -0.1]
Absolute Change in Hemoglobin Level (g/dL)	0.0 [-0.2, 0.2]	-0.2 [-0.4, -0.1]
Percentage Change in Liver Volume MN (%)	3.6 [0.6, 6.6]	1.8 [-0.2, 3.7]
Absolute Change in Liver Volume (MN)	0.0 [0.0, 0.1]	0.0 [0.0, 0.0]
Percentage Change in Platelet Count (%)	2.9 [-0.6, 6.4]	3.8 [0.0, 7.6]
Absolute Change in Platelet Count (x 10 ⁹ /L)	6.0 [-0.9, 13.0]	9.5 [1.4, 17.6]
Patients Stable for 52 Weeks, n (%) (Composite Primary Endpoint)	44 (93.6)	84 (84.8)

472 MN = Multiples of Normal, CI = confidence interval

473 * Excludes patients with a total splenectomy.

474

475 16 HOW SUPPLIED/STORAGE AND HANDLING

476 CERDELGA is supplied as 84 mg hard gelatin capsules, with a pearl blue-green opaque
477 cap and pearl white opaque body imprinted with “GZ02” in black.

478

479 CERDELGA 84 mg capsules are supplied as:

480

481 NDC-58468-0220-1 – Carton containing 4 packs of capsules (56 capsules total). Each
482 pack is composed of 1 blister card of 14 capsules and a cardboard wallet.

483

484 NDC-58468-0220-2 – Carton containing 1 pack of capsules (14 capsules total). Each
485 pack is comprised of 1 blister card of 14 capsules and a cardboard wallet.

486

487 Store at 68 °F - 77 °F (20 °C - 25 °C) with excursions permitted between 59 °F and 86 °F
488 (15 °C to 30 °C) [see USP Controlled Room Temperature].

489 17 PATIENT COUNSELING INFORMATION

490 Advise the patient to read the FDA-approved patient labeling (Medication Guide).

491 Drug Interactions

492 Advise patients to discuss all the medications they are taking, including any herbal
493 supplements or vitamins with their healthcare provider [see *Contraindications (4) and*
494 *Drug Interactions (7)*].

495 ECG Changes and Potential for Cardiac Arrhythmias

496 Advise patients to inform their healthcare provider of the following: history of
497 congestive heart failure; recent acute myocardial infarction; bradycardia; heart block;
498 ventricular arrhythmia; and long QT syndrome [see *Warnings and Precautions (5.2)*].

499 Advise patients to inform their healthcare provider if they develop new symptoms such as
500 palpitations, fainting, and dizziness.

501 Administration Instructions

502 Advise patients:

- 503 • Swallow capsules whole, preferably with water, and do not crush, dissolve, or
504 open the capsules.
- 505 • CERDELGA can be taken with or without food.
- 506 • If a dose of CERDELGA is missed, take the prescribed dose at the next scheduled
507 time; do not double the next dose.
- 508 • Avoid consumption of grapefruit or its juice.

- 509 • For patients currently treated with imiglucerase, velaglucerase alfa, or
510 taliglucerase alfa, CERDELGA may be administered 24 hours after the last dose
511 of the previous enzyme replacement therapy (ERT).

512

513 Manufactured by:
514 Genzyme Ireland, Ltd.,
515 IDA Industrial Park,
516 Old Kilmeaden Road,
517 Waterford, Ireland.

MEDICATION GUIDE
CERDELGA™ (sir-DEL-guh)
(eliglustat) capsules

What is the most important information I should know about CERDELGA?

CERDELGA can affect the way other medicines work and other medicines can affect how CERDELGA works. Using CERDELGA with other medicines or herbal supplements may cause an increased risk of side effects.

Especially tell your doctor if you take:

- St. John's Wort (Hypericum perforatum)
- Medicine for:
 - Fungal infections
 - Tuberculosis
 - Seizures
 - Heart conditions or high blood pressure
 - Depression or other mental health problems

If you take any medicines for the conditions listed above, your doctor may need to prescribe a different medicine, change your dose of other medicines, or change your dose of CERDELGA. Tell your doctor about any new medicines before you start taking them.

What is CERDELGA?

CERDELGA is a prescription medicine used for the long-term treatment of Gaucher disease type 1 (GD1) in adults.

CERDELGA is not used in certain people with Gaucher disease type 1. Your doctor will perform a test to make sure that CERDELGA is right for you.

It is not known if CERDELGA is safe and effective in children.

What should I tell my doctor before taking CERDELGA?

Before taking CERDELGA, tell your doctor about all of your medical conditions, including if you:

- have heart problems, including a condition called long QT syndrome
- have a history of a heart attack
- have kidney or liver problems
- are pregnant or planning to become pregnant. It is not known if CERDELGA will harm your unborn baby.
- are breastfeeding or planning to breastfeed. It is not known if CERDELGA passes into your breast milk. You and your doctor will decide if you should take CERDELGA or breastfeed. You should not do both.

Tell your doctor about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. See **"What is the most important information I should know about CERDELGA?"**

How should I take CERDELGA?

- Take CERDELGA exactly as your doctor tells you to take it.
- Your doctor may change your dose if needed.
- Take CERDELGA capsules whole, preferably with water. Do not open, crush, or dissolve capsules before swallowing.
- CERDELGA can be taken with or without food.
- If you miss a dose of CERDELGA, take the next dose at the usual time. Do not take two doses of CERDELGA at the same time.
- If you take too much CERDELGA, call your doctor or go to the nearest hospital emergency room right away.

What should I avoid while taking CERDELGA?

Avoid eating or drinking grapefruit products while taking CERDELGA. Grapefruit products can increase the amount of CERDELGA in your body.

What are the possible side effects of CERDELGA?

See "**What is the most important information I should know about CERDELGA?**"

- **CERDELGA, used with certain other medicines, may cause changes in the electrical activity of your heart (ECG changes) and irregular heart beat (arrhythmias).** Tell your doctor if you have new symptoms such as palpitations, fainting, or dizziness.

The most common side effects of CERDELGA include: tiredness, headache, nausea, diarrhea, and pain in the arms, legs, back, or stomach (abdomen).

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of CERDELGA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CERDELGA?

- Store CERDELGA at room temperature between 68°F to 77 °F (20°C to 25 °C).
- Keep CERDELGA and all medicines out of reach of children.

General information about the safe and effective use of CERDELGA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use CERDELGA for a condition for which it was not prescribed. Do not give CERDELGA to other people, even if they have the same symptoms you have. It may harm them.

If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about CERDELGA that is written for health professionals.

For more information, go to www.cerdelga.com or call 1-800-745-4447.

What are the ingredients in CERDELGA?

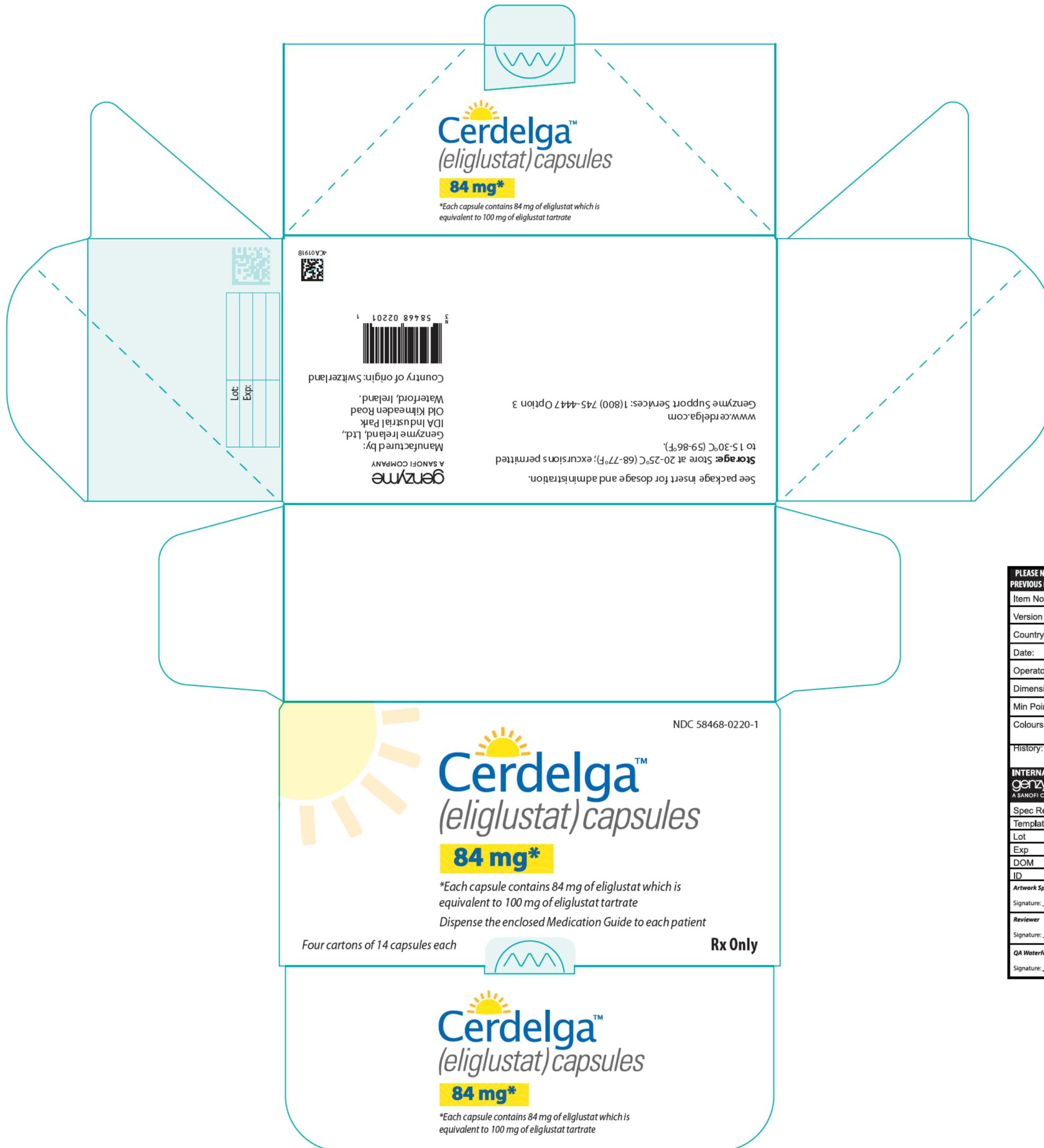
Active ingredient: eliglustat

Inactive ingredients: microcrystalline cellulose, lactose monohydrate, hypromellose, glyceryl behenate, gelatin, candurin silver fine, yellow iron oxide, and FD&C blue 2

Manufactured by: Genzyme Ireland, Ltd., IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland
CERDELGA is a trademark of Genzyme Corporation. ©2013 Genzyme Corporation. All rights reserved.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

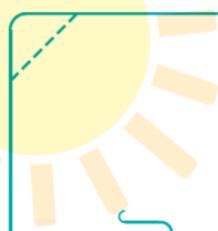
Issued: August 2014



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Min Point Size:	10pt
Colours Used:	(b) (4)
History:	(b) (4)
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genzyme	
A SANOFI COMPANY IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland.	
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Template Ref:	TBC
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Exp:	Exp
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ID:	N/A
Artwork Specialist	
Signature: _____	Date: _____
Reviewer	
Signature: _____	Date: _____
QA Waterford	
Signature: _____	Date: _____

PLEASE NOTE THIS REVISION SUPERSEDES THE PREVIOUS REVISION WHICH MUST BE DESTROYED		PREVIOUS REVISION: 4IC0004A
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genzyme		
A SANOFI COMPANY IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland.		
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Exp	Exp	
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ID	N/A	
Artwork Specialist		
Signature: _____ Date: _____		
Reviewer		
Signature: _____ Date: _____		
QA Waterford		
Signature: _____ Date: _____		

NDC 58468-0220-1



Cerdelga™

(eliglustat) capsules

84 mg*

*Each capsule contains 84 mg of eliglustat which is equivalent to 100 mg of eliglustat tartrate

14 capsules
Rx Only



Lot: _____
Exp: _____

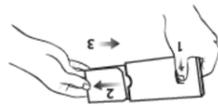


4IC0004B

Genzyme Support Services: 1(800) 745-4447 Option 3
www.cerdelga.com

Storage: Store at 20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F).

OPENING INSTRUCTIONS



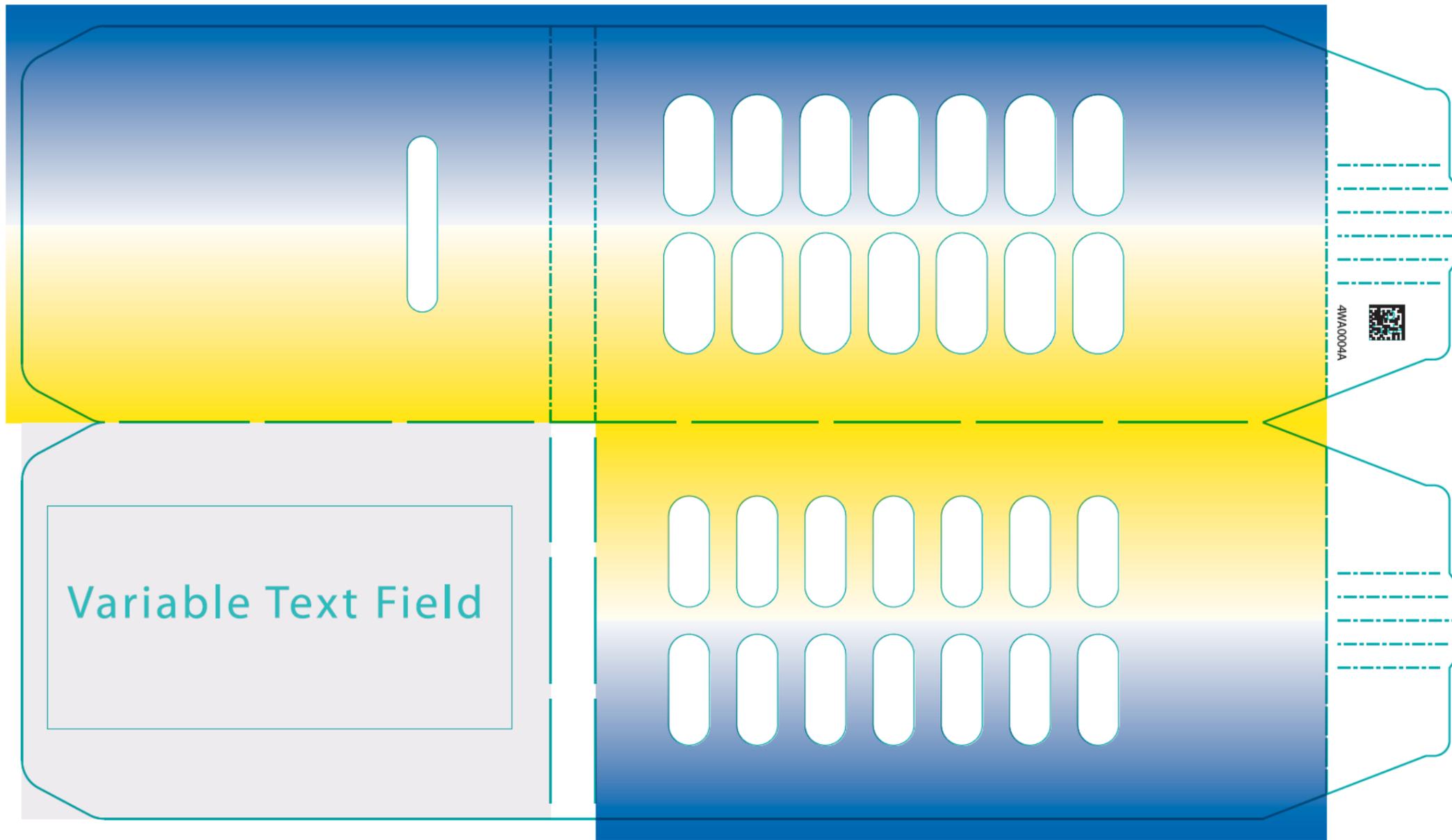
1. Push and Hold: Use thumb to push the button gently.
2. Pull: While holding the button down, pull out the wallet pack.
3. Close: Once the capsule is removed, refold the card and slide back into wallet.

See package insert for dosage and administration.



58468 02201

Manufactured by:
Genzyme Ireland, Ltd.,
IDA Industrial Park,
Old Kilmeaden Road,
Waterford, Ireland.



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ID:	N/A
History:	Cerdelga US Launch

Cerdelga
 (eliglustat) capsules
 84mg
 Rx only
 Lot:
 Exp:
 Manufactured by: Genzyme Ireland LTD.,
 IDA Industrial Park,
 Old Kilmeaden Road,
 Waterford, Ireland.

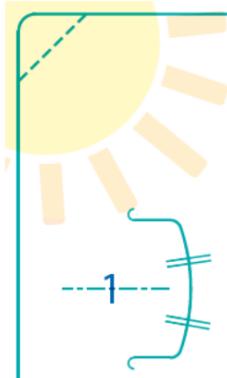


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Artwork Specialist		
Signature: _____ Date: _____		
Reviewer		
Signature: _____ Date: _____		
QA Waterford		
Signature: _____ Date: _____		

NDC 58468-0220-2



Cerdelga™ (eliglustat) capsules

84 mg*

*Each capsule contains 84 mg of eliglustat which is equivalent to 100 mg of eliglustat tartrate

14 capsules

Rx Only

2

PLEASE NOTE THIS REVISION SUPERSEDES THE PREVIOUS REVISION WHICH MUST BE DESTROYED	PREVIOUS REVISION:
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Version No:	2
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Min Point Size:	10PT
Colours Used:	(b) (4)
History:	
INTERNAL USE	
genzyme	
A SANOFI COMPANY IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland.	
Spec Ref:	PS-336
Template Ref:	TBC
Lot	Lot
Exp	Exp
DOM	N/A
ID	N/A
Artwork Specialist	
Signature: _____	Date: _____
Reviewer	
Signature: _____	Date: _____
QA Waterford	
Signature: _____	Date: _____



	Exp:
	Lot:



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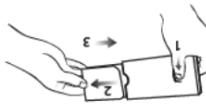


4IC0001B

Genzyme Support Services: 1(800) 745-4447 Option 3
www.cerdelga.com

Storage: Store at 20-25°C (68-77°F); excursions permitted to 15-30°C (59-86°F).

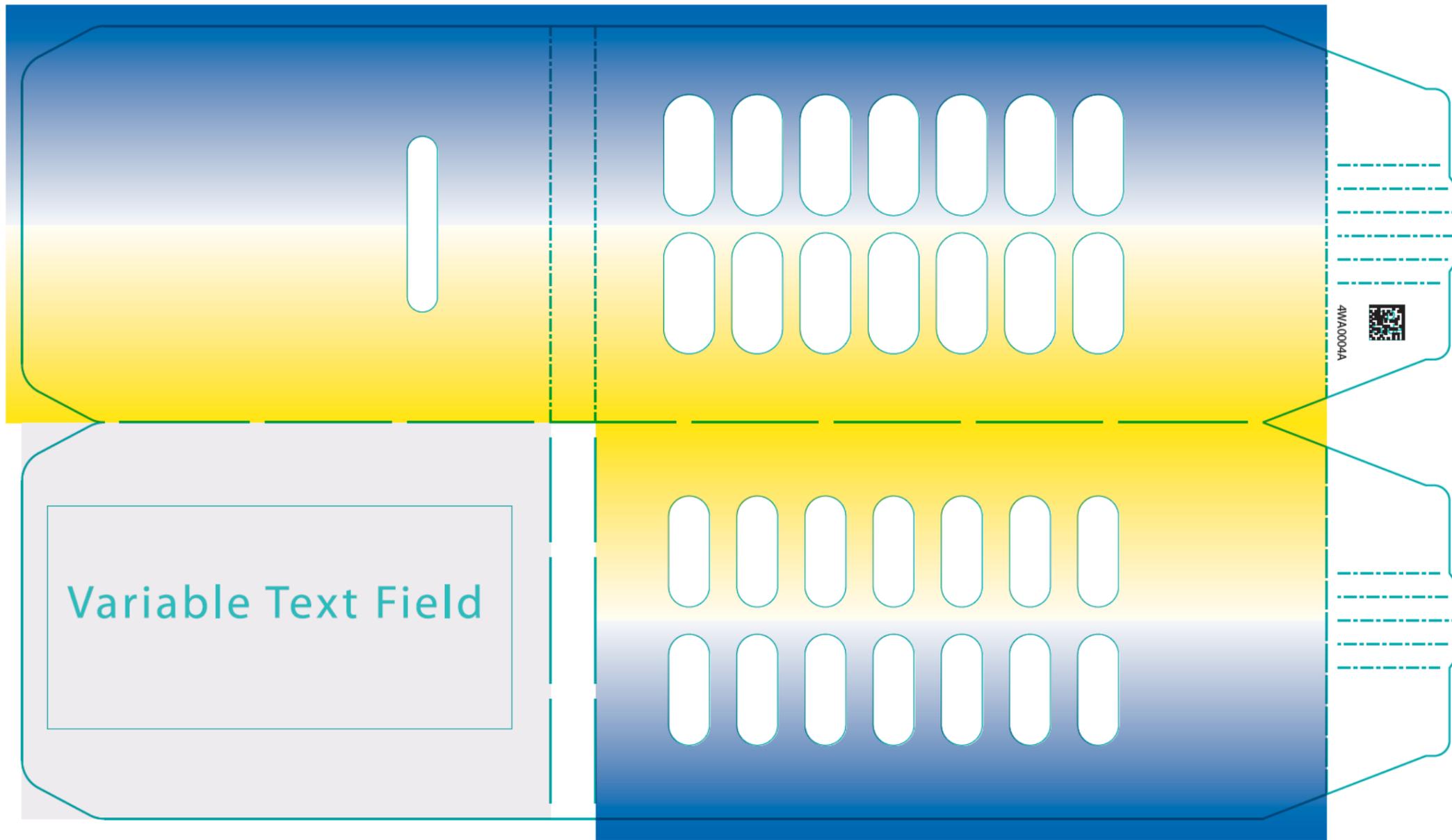
OPENING INSTRUCTIONS



1. Push and Hold: Use thumb to push the button gently.
2. Pull: While holding the button down, pull the card and slide back into wallet.
3. Close: Once the capsule is removed, refold the card and slide back into wallet.

See package insert for dosage and administration.

Manufactured by:
Genzyme Ireland, Ltd.,
IDA Industrial Park,
Old Kilmeaden Road,
Waterford, Ireland.



Variable Print Format To be printed on the line in variable text field shown in (b) (4) 4WA0004A	
Format Name:	1 us_1pack
Version No:	2
Market:	US 7 Day Pack
Date:	11 Jul 14
Operator:	(b) (4)
Colour:	Black
Lot:	Lot:
Exp:	Exp:
DOM:	N/A
ID:	N/A
History:	Cerdelga US Launch

Cerdelga
 (eliglustat) capsules
 84mg
 Rx only
 Lot:
 Exp:
 Manufactured by: Genzyme Ireland LTD.,
 IDA Industrial Park,
 Old Kilmeaden Road,
 Waterford, Ireland.



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 NDC 58468-0220-2

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/s/

AMY G EGAN
08/19/2014