PrCerdelga™
(eliglustat) capsules

GUIDE FOR PRESCRIBER

This guide contains the checklist of actions to be completed before and after treatment initiation. This checklist is part of the CERDELGA Risk Management Plan and is to be used in conjunction with the CERDELGA Product Monograph.

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Guide for Prescriber

CERDELGA (eliglustat) is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 poor metabolizers (PMs), intermediate metabolizers (IMs) or extensive metabolizers (EMs), as determined by CYP2D6 genotype testing.

This guide has been developed as part of the CERDELGA Risk Management Plan (RMP) and is intended for physicians who initiate and supervise CERDELGA treatment. Please refer to the approved Product Monograph for full prescribing information.

It contains:

1. Checklist of actions to be completed before and after treatment initiation
2. Information on CYP2D6 genotyping assessment
3. Information on reporting suspected adverse reactions

In addition, a *Patient Alert Card* has been developed as part of the RMP for patients initiated on CERDELGA treatment. If needed, cards are available upon request from Medical Information (1-800-589-6215 or medicalinfolaval@sanofi.com). This card is a liaison tool to inform any healthcare professionals who are treating patients receiving CERDELGA about drug-drug interactions that should be considered before prescription or delivery of any additional medicinal products, including herbal products. The patient (or caregivers when appropriate) should be told to carry and show this card at all times to any healthcare professional who may be prescribing or delivering additional medicinal products.

Moreover, it contains information to remind the patient about the risk of self-medication and consumption of grapefruit products. An example of this card is attached in **Appendix 1**.

For more information on CERDELGA, please refer to the full Product Monograph or contact Sanofi Genzyme: Medical Information (1-800-589-6215 or medicalinfolaval@sanofi.com).

1. Prescriber Checklist

Before treatment initiation, it should be verified if the patient is appropriate for CERDELGA treatment:

Three steps must be achieved to confirm patient's eligibility for CERDELGA treatment initiation:

STEP 1:
Patient must be an adult with Gaucher disease type 1

STEP 2:
Patient must be a CYP2D6 poor (PM), intermediate (IM) or extensive metaboliser (EM)

STEP 3:
Depending on the patient's CYP2D6 phenotype defined at step 2, the following situations are to be taken into account, based on concomitant medication use, as well as hepatic and renal status. For additional information, please refer to the full Product Monograph.

<table>
<tr><th colspan="4">DOSING RECOMMENDATIONS</th></tr>
<tr><th>CYP2D6 Phenotype</th><th>Extensive Metabolizers (EMs)</th><th>Intermediate Metabolizers (IMs)</th><th>Poor Metabolizers (PMs)</th></tr>
<tr><td>Standard dosing</td><td>84 mg twice daily (BID)</td><td>84 mg BID</td><td>84 mg once daily (OD)</td></tr>
<tr><td colspan="4">Concomitant use of CYP2D6 and/or CYP3A inhibitors increase plasma concentration of eliglustat.</td></tr>
<tr><td>Strong CYP3A Inhibitors used concomitantly with Strong/ Moderate CYP2D6 Inhibitors</td><td rowspan="2">Contraindicated</td><td rowspan="2">Contraindicated</td><td>Contraindicated</td></tr>
<tr><td>Moderate CYP3A Inhibitors used concomitantly with Strong/ Moderate CYP2D6 Inhibitors</td><td>Not recommended</td></tr>
</table>

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DOSING RECOMMENDATIONS (CONT'D)			
CYP2D6 Phenotype	**Extensive Metabolizers (EMs)**	**Intermediate Metabolizers (IMs)**	**Poor Metabolizers (PMs)**
Strong CYP2D6 Inhibitors	Not recommended	Not recommended	84 mg OD
Moderate CYP2D6 Inhibitors	84 mg OD	84 mg OD	84 mg OD
Weak CYP2D6 Inhibitors	84 mg BID	No data available[a]	84 mg OD
Strong CYP3A Inhibitors	84 mg OD	Contraindicated	Contraindicated
Moderate CYP3A Inhibitors	84 mg OD	84 mg OD	Not recommended
Weak CYP3A Inhibitors	84 mg BID	No data available[a]	Not recommended
Grapefruit products fall under the category of strong CYP3A inhibitors and can increase plasma concentration of eliglustat. Consumption of grapefruit or its juice should be avoided.			
Concomitant use of strong CYP3A inducers decrease plasma concentration of eliglustat.			
Strong CYP3A Inducers	Not recommended	Not recommended	Not recommended
Concomitant use of agents whose exposure may be increased by eliglustat.			
P-gp Substrates	Lower doses of other substrates which are P-gp substrates may be required.		
CYP2D6 Substrates	Lower doses of medicinal products that are CYP2D6 substrates may be required and titrate to clinical effect.		

[a] No clinical data provided to make a dosing recommendation

DOSING RECOMMENDATIONS (CONT'D)			
Patients with hepatic impairment	[EMs]	[IMs]	[PMs]
Mild Hepatic Impairment (Child-Pugh Class A)	84 mg OD	Contraindicated	Contraindicated
Mild Hepatic Impairment + Strong CYP2D6 Inhibitors	Contraindicated		
Mild Hepatic Impairment + Moderate CYP2D6 Inhibitors			
Mild hepatic impairment + Weak CYP2D6 Inhibitors	84 mg OD		
Mild Hepatic Impairment + Strong CYP3A Inhibitors	Contraindicated		
Mild Hepatic Impairment + Moderate CYP3A Inhibitors	84 mg OD		
Mild Hepatic Impairment + Weak CYP3A Inhibitors			
Moderate or Severe Hepatic Impairment (Child-Pugh Class B or C)	Contraindicated	Contraindicated	Contraindicated
Patients with renal impairment	[EM]	[IM]	[PM]
Mild, Moderate or Severe Renal Impairment (eCrCl: ≥15-≤80 ml/min)	84 mg BID	Not recommended	Not recommended
End Stage Renal Disease (ESRD) (eCrCl: <15 ml/min)	Not recommended	Not recommended	Not recommended

Patient education

- ☑ You have informed the patient about the drug-drug interactions that could occur with CERDELGA and the importance of informing all healthcare professionals about the patient's current medications and treatment
- ☑ You have instructed the patient about the risk of self-medication and consumption of grapefruit products
- ☑ You have provided the *Patient Alert Card* to the patient and instructed him/her about its use (i.e., you have discussed with them the importance of showing the card to all their healthcare professionals)

AT PATIENT FOLLOW-UP, CHECK THE FOLLOWING:

Medical conditions

- ☑ Inquire about any changes in medical history or new medications since last visit (including over the counter medication or herbal products) and use of grapefruit products
- ☑ Check for suspected adverse reactions

Patient education

- ☑ Check for appropriate use of the *Patient Alert Card*
- ☑ Remind patient about the risk of self-medication and consumption of grapefruit products

2. Predicted Cytochrome P450 2D6 Metabolic Activity

CERDELGA is to be used only in patients who have a predicted CYP2D6 poor, intermediate or extensive metabolizer phenotype based on genotyping. Determination of the patient's CYP2D6 phenotype prior to starting CERDELGA is required.

Genotyping to determine the patient's CYP2D6 phenotype is to be performed using an established genetic laboratory test that is able to detect a specific set of CYP2D6 alleles[#] with adequate accuracy, sensitivity and specificity in order to ensure consistent identification of CYP2D6 metabolizer status. DNA for genotyping can be collected using a blood sample.

For patients who meet eligibility criteria defined in the full Product Monograph, Sanofi Genzyme can provide laboratory services for CYP2D6 metabolizer genotyping. For more information about this service contact Medical information (1-800-589-6215).

3. Reporting of Suspected Adverse Reactions

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (www.healthcanada.gc.ca/medeffect) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: You can also report any adverse events to Sanofi Genzyme at 1-800-589-6215.

[#] At least the following alleles: *2, *3, *4, *5, *7, *8, *9, *14A, *14B, *17, *41, *1XN, *2N, *4XN, *10XN, *17N, *41N, *39.

4. If you want more information about CERDELGA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals by visiting the Health Canada website; the manufacturer's website www.sanofigenzyme.ca, or by calling 1-800-589-6215.

5. APPENDIX 1: Patient Alert Card

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Patient's name:

Date CERDELGA first prescribed:

Treating doctor's name:

Treating doctor's phone number:

Metabolizer Status:

☐ Poor Metabolizer ☐ Intermediate Metabolizer ☐ Extensive Metabolizer

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PATIENT ALERT CARD

Information for the patient[1]

Please carry this card with you at all times and show it to any healthcare professional in order to inform them about your current treatment with CERDELGA

- Do not start any new prescription medication, over-the-counter medication, or herbal products without telling your doctor or pharmacist
- Do not consume grapefruit products

REFERENCE: 1. CERDELGA™ Product Monograph, December 6, 2018.

CERDELGA is a registered trademark of Sanofi Genzyme.

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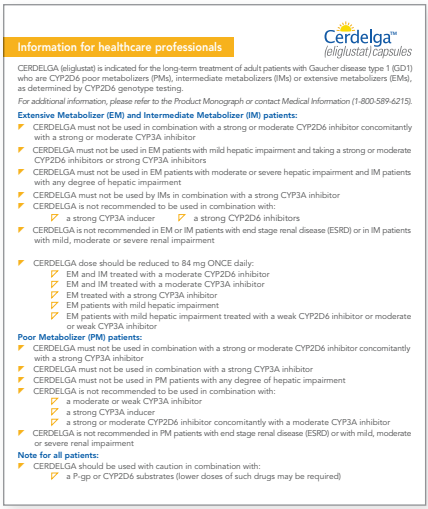

Information for healthcare professionals

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CERDELGA (eliglustat) is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 poor metabolizers (PMs), intermediate metabolizers (IMs) or extensive metabolizers (EMs), as determined by CYP2D6 genotype testing.

For additional information, please refer to the Product Monograph or contact Medical Information (1-800-589-6215).

Extensive Metabolizer (EM) and Intermediate Metabolizer (IM) patients:

- CERDELGA must not be used in combination with a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor
- CERDELGA must not be used in EM patients with mild hepatic impairment and taking a strong or moderate CYP2D6 inhibitors or strong CYP3A inhibitors
- CERDELGA must not be used in EM patients with moderate or severe hepatic impairment and IM patients with any degree of hepatic impairment
- CERDELGA must not be used by IMs in combination with a strong CYP3A inhibitor
- CERDELGA is not recommended to be used in combination with:
  - a strong CYP3A inducer
  - a strong CYP2D6 inhibitors
- CERDELGA is not recommended in EM or IM patients with end stage renal disease (ESRD) or in IM patients with mild, moderate or severe renal impairment

- CERDELGA dose should be reduced to 84 mg ONCE daily:
  - EM and IM treated with a moderate CYP2D6 inhibitor
  - EM and IM treated with a moderate CYP3A inhibitor
  - EM treated with a strong CYP3A inhibitor
  - EM patients with mild hepatic impairment
  - EM patients with mild hepatic impairment treated with a weak CYP2D6 inhibitor or moderate or weak CYP3A inhibitor

Poor Metabolizer (PM) patients:

- CERDELGA must not be used in combination with a strong or moderate CYP2D6 inhibitor concomitantly with a strong CYP3A inhibitor
- CERDELGA must not be used in combination with a strong CYP3A inhibitor
- CERDELGA must not be used in PM patients with any degree of hepatic impairment
- CERDELGA is not recommended to be used in combination with:
  - a moderate or weak CYP3A inhibitor
  - a strong CYP3A inducer
  - a strong or moderate CYP2D6 inhibitor concomitantly with a moderate CYP3A inhibitor
- CERDELGA is not recommended in PM patients with end stage renal disease (ESRD) or with mild, moderate or severe renal impairment

Note for all patients:

- CERDELGA should be used with caution in combination with:
  - a P-gp or CYP2D6 substrates (lower doses of such drugs may be required)

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