ינואר 2022

Cerdelga™
(eliglustat) capsules

Hard capsules
Eliglustat 84.4 mg

רופא/ה רוקח/ת נכבד/ה,
חברת סאנופי-אוונטיס ישראל בע"מ מבקשת להודיע על עדכון העלון לרופא של התכשיר **סרדלגה.**

ההתוויה המאושרת:
Cerdelga is indicated for 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).

מפורטים להלן רק תתי הסעיפים בהם נעשו העדכונים העיקריים בעלון לרופא:

4.2 Posology and method of administration

…

Patients with hepatic impairment

~~Cerdelga has not been studied in patients with hepatic impairment. Therefore, no dose recommendations can be made.~~

In CYP2D6 extensive metabolisers (EMs) with severe (Child-Pugh class C) hepatic impairment, eliglustat is contraindicated (see sections 4.3 and 5.2).

In CYP2D6 extensive metabolisers (EMs) with moderate hepatic impairment (Child-Pugh class B), eliglustat is not recommended (see sections 4.4 and 5.2).

In CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment (Child-Pugh class A), no dosage adjustment is required and the recommended dose is 84 mg eliglustat twice daily.

In CYP2D6 intermediate metabolisers (IMs) or poor metabolisers (PMs) with any degree of hepatic impairment, eliglustat is not recommended (see sections 4.4 and 5.2).

In CYP2D6 extensive metabolisers (EMs) with mild or moderate hepatic impairment taking a strong or moderate CYP2D6 inhibitor, Cerdelga is contraindicated (see sections 4.3 and 5.2).

In CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment taking a weak CYP2D6 inhibitor or a strong, moderate or weak CYP3A inhibitor, a dose of 84 mg eliglustat once daily should be considered (see sections 4.4 and 5.2).

Patients with renal impairment

~~Cerdelga has not been studied in patients with renal impairment. Therefore, no dose recommendations can be made.~~

In CYP2D6 extensive metabolisers (EMs) with mild, moderate or severe renal impairment, no dosage adjustment is required and the recommended dose is 84 mg eliglustat twice daily (see sections 4.4 and 5.2).

In CYP2D6 EMs with end stage renal disease (ESRD), eliglustat is not recommended (see sections 4.4 and 5.2).

סאנופי אוונטיס ישראל, רח' בני גאון 10, פארק פולג, ת.ד. 8090, נתניה דרום 42504
טל': 09-8633700 פקס: 09-8851444

In CYP2D6 intermediate metabolisers (IMs) or poor metabolisers (PMs) with mild, moderate or severe renal impairment or ESRD, eliglustat is not recommended (see sections 4.4 and 5.2).

4.3 Contraindications

…

Due to significantly increased eliglustat plasma concentrations, Cerdelga is contraindicated in CYP2D6 extensive metabolisers (EMs) with severe hepatic impairment and in CYP2D6 extensive metabolisers (EMs) with mild or moderate hepatic impairment taking a strong or moderate CYP2D6 inhibitor (see sections 4.2 and 5.2).

4.4 Special warnings and precautions for use

…

Patients with hepatic impairment

Limited data are available in CYP2D6 extensive metabolisers (EMs) with moderate hepatic impairment. Use of eliglustat in these patients is not recommended (see sections 4.2. and 5.2).

Limited or no data are available in CYP2D6 intermediate metabolisers (IMs) or poor metabolisers (PMs) with any degree of hepatic impairment. Use of eliglustat in these patients is not recommended (see sections 4.2 and 5.2).

Concomitant use of eliglustat with CYP2D6 or CYP3A4 inhibitors in CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment can result in further elevation of eliglustat plasma concentrations, with the magnitude of the effect depending on the enzyme inhibited and the potency of the inhibitor. In CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment taking a weak CYP2D6 inhibitor or strong, moderate or weak CYP3A inhibitor, a dose of 84 mg eliglustat mg once daily should be considered (see sections 4.2 and 5.2).

Patients with renal impairment

Limited or no data are available in CYP2D6 extensive metabolisers (EMs), intermediate metabolisers (IMs) or poor metabolisers (PMs) -with ESRD and in CYP2D6 intermediate metabolisers (IMs) or poor metabolisers (PMs) with mild, moderate, or severe renal impairment; use of eliglustat in these patients is not recommended (see sections 4.2 and 5.2).

4.5 Interaction with other medicinal products and other forms of interaction

CYP2D6 inhibitors

…*In extensive metabolisers (EMs) with mild or moderate hepatic impairment:* see sections 4.2, 4.3 and 4.4.

In extensive metabolisers (EMs) with severe hepatic impairment: see sections 4.2 and 4.3.

CYP3A inhibitors

…*In extensive metabolisers (EMs) with mild hepatic impairment:* see sections 4.2 and 4.4.

In extensive metabolisers (EMs) with moderate or severe hepatic impairment: see sections 4.2 and 4.3.

5.2 Pharmacokinetic properties

Hepatic impairment:

Effects of mild and moderate hepatic impairment were evaluated in a single dose phase 1 study. After a single 84 mg dose, eliglustat C_{max} and AUC were 1.2- and 1.2-fold higher in CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment, and 2.8- and 5.2-fold higher in

CYP2D6 extensive metabolisers (EMs) with moderate hepatic impairment compared to healthy CYP2D6 extensive metabolisers (EMs).
After repeated 84 mg twice daily doses of Cerdelga, C_{max} and AUC_{0-12} are predicted to be 2.4- and 2.9-fold higher in CYP2D6 extensive metabolisers (EMs) with mild hepatic impairment and 6.4- and 8.9-fold higher in CYP2D6 extensive metabolisers (EMs) with moderate hepatic impairment compared to healthy CYP2D6 extensive metabolisers (EMs).
After repeated 84 mg once daily doses of Cerdelga, C_{max} and AUC_{0-24} are predicted to be 3.1- and 3.2 -fold higher in CYP2D6 extensive metabolisers (EMs) with moderate hepatic impairment compared to healthy CYP2D6 extensive metabolisers (EMs) receiving Cerdelga 84 mg twice daily (see sections 4.2 and 4.4).
Steady state PK exposure could not be predicted in CYP2D6 intermediate metabolisers (IMs) and poor metabolisers (PMs) with mild and moderate hepatic impairment due to limited or no single-dose data. The effect of severe hepatic impairment was not studied in subjects with any CYP2D6 phenotype (see sections 4.2, 4.3 and 4.4).
Renal impairment:
Effect of severe renal impairment was evaluated in a single dose phase 1 study. After a single 84 mg dose, eliglustat C_{max} and AUC were similar in CYP2D6 extensive metabolisers (EMs) with severe renal impairment and healthy CYP2D6 extensive metabolisers (EMs).
Limited or no data were available in patients with ESRD and in CYP2D6 intermediate metabolisers (IMs) or poor metabolisers(PMs) with severe renal impairment (see sections 4.2 and 4.4).

מפורטים להלן רק תתי הסעיפים בהם נעשו העדכונים העיקריים בעלון לצרכן:

2. לפני השימוש בתרופה
אין להשתמש בתרופה אם:

.....
- הינך בעל מטבוליזם (פירוק) מהיר והינך סובל מפגיעה חמורה בתפקודי הכבד.
- הינך בעל מטבוליזם (פירוק) מהיר וסובל מפגיעה קלה או בינונית בתפקודי הכבד, בזמן שהינך נוטל תרופות שהינן מעכבי CYP2D6 חזקים או בינוניים.

אזהרות מיוחדות הנוגעות לשימוש בתרופה. לפני הטיפול בסרדלגה, ספר לרופא אם:

....
- הינך בעל מטבוליזם (פירוק) מהיר והינך סובל מפגיעה בינונית בתפקודי הכבד.
- הינך בעל מטבוליזם (פירוק) בינוני או איטי והינך סובל מפגיעה בחומרה כלשהי בתפקודי הכבד.
- הינך בעל מטבוליזם (פירוק) בינוני או איטי והינך סובל מפגיעה בתפקודי הכליה.
- הינך סובל ממחלת כליה סופנית (ESRD).

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום, סאנופי-אוונטיס ישראל בע"מ, רח' בני גאון 10 נתניה או בטלפון: 09-8633700.

בברכה,

חברת סאנופי אוונטיס ישראל בע"מ