NOVARTIS

פברואר 2024

רופא/ה, רוקח/ת נכבד/ה,

שלום רב,

הנדון: עדכון עלון התכשיר:

Rydapt 25 mg, capsules soft

ריידפט 25 מ"ג, כמוסות רכות

חברת נוברטיס ישראל בע"מ מבקשת להודיע על עדכון בעלון לרופא של התכשיר שבנדון.

בהודעה זו מפורטים העדכונים המהותיים בלבד (ללא שינוי נוסח, עריכה, אדמיניסטרציה וכו'). למידע מלא על התרופה יש לעיין בעלון לרופא העדכני של התכשיר.

(טקסט שנוסף מסומן בצבע עם קו תחתי, טקסט שהוסר מסומן בצבע ובקו חצייה ,שינויים אשר מהווים מידע בטיחות חדש מסומנים ברקע צהוב)

התווית התכשיר:

Acute myeloid leukaemia (AML):
Rydapt is indicated in combination with standard induction and consolidation chemotherapy followed by single-agent maintenance therapy for adults with newly diagnosed acute myeloid leukaemia (AML) who have an FLT3 mutation.
Advanced systemic mastocytosis (advanced SM):
Rydapt is indicated for the treatment of adult patients with advanced systemic mastocytosis (advanced SM)

חומר פעיל: MIDOSTAURIN 25 mg

עדכונים בעלון לרופא

4.2 Posology and method of administration

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Special dosage instructions

Patients with hepatic impairment

No dose adjustment is required in patients with mild or moderate (Child-Pugh A or B) hepatic impairment. (see section 5.2). Exposure to midostaurin and its active metabolite CGP62221 is substantially lower in patients with severe hepatic impairment than that in patients with normal hepatic function (see section 5.2). However, there are insufficient efficacy data in patients with severe hepatic impairment to suggest a dose adjustment is required.

[…]

Novartis Israel Ltd.
6 Totzeret Ha'arets St.
P.O.B 7126, Tel Aviv, Israel
Tel: 972-3-9201123 Fax: 972-3-9229331

נוברטיס ישראל בע"מ
רח' תוצרת הארץ 6
ת.ד. 7126 תל אביב
טלפון: 03-9201123 פקס: 03-9229331

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4.4 Special warnings and precautions for use

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[…]

5.2 Pharmacokinetic properties

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Hepatic impairment

A dedicated hepatic impairment study assessed the systemic exposure of midostaurin after oral administration of 50 mg twice daily for 6 days and a single 50 mg dose on day 7 in subjects with baseline mild or moderate (Child-Pugh Class A or B, respectively) and following a single dose administration of 50 mg in subjects with severe hepatic impairment (Child-Pugh Class C) in comparison to control subjects with normal hepatic function. The maximum concentration of midostaurin was reached between 2 and 3 hours after administration after single or repeated doses for all groups. On day 1, the AUC_{0-12} and C_{max} were 8 130 ng*h/ml and 1 206 ng/ml, respectively, for healthy subjects. AUC_{0-12} was decreased by 39% and 36% in subjects with mild and moderate hepatic impairment, respectively. On day 7, $AUC_{Ctrough}$ (exposure under the curve of C_{trough} from day 1 to day 7) was 5 410 ng*h/ml in healthy subjects and was decreased by 35% and 20% in subjects with mild and moderate hepatic impairment, respectively. AUC_{tau} was decreased by 28% and 20% on day 7, respectively.

The subjects with severe hepatic impairment had a lower geometric mean Cmax and AUC_{inf} of midostaurin compared to the control group (C_{max}: 1 360 ng/ml, AUCinf: 30 100 ng.h/ml). C_{max} and AUC_{inf} of midostaurin decreased on average by 78% and 59% respectively in subjects with severe hepatic impairment.

Finally, the long-term data from patients were analysed using a population pharmacokinetic approach. No impact of hepatic impairment could be identified in patients with mild or moderate hepatic impairment in the advanced SM and AML populations.

Overall, there was no increase in exposure (AUC) to plasma midostaurin and its metabolites (CGP62221 and CGP52421) in subjects with mild,moderate or severe hepatic impairment compared to subjects with normal hepatic function. No dose adjustment is necessary for patients with baseline mild or moderate hepatic impairment. Exposure to midostaurin and its active metabolite CGP62221 is substantially lower in patients with severe hepatic impairment than that in patients with normal hepatic function (see section 4.2). However, there are insufficient efficacy data in patients with severe hepatic impairment to suggest a dose adjustment is required.[…]

העלון נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פניה לבעל הרישום:

נוברטיס ישראל בע"מ. תוצרת הארץ 6, ת.ד. 7126, תל אביב

בברכה,

ניב טובי
רוקח ממונה

Novartis Israel Ltd.
6 Totzeret Ha'arets St.
P.O.B 7126, Tel Aviv, Israel
Tel: 972-3-9201123 Fax: 972-3-9229331

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