

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

הריני להודיעכם כי העלונים לרופא ולצרכן של התכשיר עודכנו:

Braftovi 75 mg**ברפטובי 75 מ"ג****HARD GELATIN CAPSULES**

מרכיב פעיל : encorafenib

התוויה מאושרת :

BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma

Encorafenib is a kinase inhibitor indicated, in combination with binimetinib, for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation.

BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)

Encorafenib is indicated in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an approved test after prior therapy.

להלן העדכונים בעלון לרופא (מסומנים בצהוב):

7.1 Effect of Other Drugs on BRAFTOVI

[...]

Strong ~~or Moderate~~ CYP3A4 Inducers

Coadministration of BRAFTOVI with a strong ~~or moderate~~ CYP3A4 inducer may decrease encorafenib plasma concentrations [see *Clinical Pharmacology (11.3)*] and may decrease encorafenib efficacy. Avoid coadministration of BRAFTOVI with strong ~~or moderate~~ CYP3A4 inducers.

7.2 Effect of BRAFTOVI on Other Drugs**Sensitive CYP3A4 Substrates**

BRAFTOVI is a strong CYP3A4 inducer at steady-state. Concomitant use Coadministration of BRAFTOVI with sensitive CYP3A4 substrates may increase adverse reactions or decrease efficacy of these agents.

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~~Coadministration of BRAFTOVI with the plasma concentrations of CYP3A4 substrates (including hormonal contraceptives (CYP3A4), [see Clinical Pharmacology (12.1.3)], which may reduce the efficacy of these substrates) can result in decreased concentrations and loss of hormonal contraceptive efficacy.~~ Avoid ~~the~~ coadministration of BRAFTOVI with ~~hormonal contraceptives [see Use in Specific Populations (8.3)].~~ CYP3A4 substrates for which a decrease in plasma concentration may lead to reduced efficacy of the substrate. If the coadministration cannot be avoided, see the CYP3A4 substrate product labeling for recommendations.

8.1 Pregnancy

[...]

~~In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.~~

11.3 Pharmacokinetics

[...]

Strong CYP3A4 Inducers: The effect of a **strong** CYP3A4 inducer on encorafenib exposure has not been studied. ~~However, [see Drug Interactions (7.1)].~~

Moderate CYP3A4 Inducers: Repeat dose administration of BRAFTOVI 450 mg once daily and binimetinib 45 mg twice daily with modafinil, a moderate CYP3A4 inducer, decreased encorafenib ~~(CYP3A4 inducer in vitro) exposures were lower at~~ steady-state **AUC by 24% and C_{max} by 20%**, compared to **BRAFTOVI alone.**

Effect of encorafenib on CYP3A4 Substrates: Repeat dose administration of BRAFTOVI 450 mg once daily and binimetinib 45 mg twice daily with a single dose of midazolam 2 mg, a sensitive CYP3A4 substrate, decreased midazolam AUC by 82% and C_{max} by 74% relative to midazolam 2 mg alone.

Effect of encorafenib on Other CYP Substrates: There was no clinically significant effect of repeat dose administration of BRAFTOVI 450 mg once daily and binimetinib 45 mg twice daily ~~on the first dose in clinical studies, suggesting CYP3A4 auto-induction induction~~ exposure of substrates of CYP1A2, CYP2B6, CYP2C9, CYP2C19, and CYP2D6.

[...]

In Vitro Studies

CYP/UGT Enzymes: Encorafenib is a reversible inhibitor of UGT1A1, **CYP1A2, CYP2B6, CYP2C8/9, CYP2D6, and CYP3A,** and a time-dependent inhibitor of CYP3A4 at clinically relevant plasma concentrations. Encorafenib is an inducer of **CYP2B6, CYP2C9, and CYP3A4** at clinically relevant plasma concentrations.

להלן העדכונים בעלון לצרכן המהווים החמרות (מסומנים בצהוב):

4. תופעות לוואי

[...]

תופעות לוואי שכיחות מאוד (תופעות שמופיעות ביותר ממשתמש אחד מעשרה) **המופיעות בעת נטילת ברפטובי וסיטוקסימאב יחד:**

[...]

- הקאות

העלון לרופא והעלון לצרכן נמצאים בקישור, וכן מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בברכה,

מדיסון פארמה בע"מ