

**Qinlock 50 mg****קינלוק 50 מ"ג****TABLETS**

מרכיב פעיל : ripretinib

הריני להודיעכם כי העלון לרופא של התכשיר עודכן:

התוויה מאושרת :

QINLOCK is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

להלן העדכונים בעלון לרופא (הוספה בכחול ומחיקה באדום):

**5.4 Cardiac Dysfunction**

In INVICTUS, cardiac failure occurred in 1.2% of the 85 patients who received QINLOCK. In the pooled safety population, cardiac dysfunction (including cardiac failure, acute left ventricular failure, diastolic dysfunction, and ventricular hypertrophy) occurred in 1.7% of 351 patients, including Grade 3 adverse reactions in 1.1%.

In INVICTUS, Grade 3 decreased ejection fraction occurred in ~~2.6~~1.3% of the 77 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram. In the pooled safety population, Grade 3 decreased ejection fraction occurred in ~~3.4~~1.9% of the 263 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram.

**12.3 Pharmacokinetics**

[...]

**Drug Interaction Studies***Clinical Studies and Model-Informed Approaches*

[CYP Enzymes: No clinically significant differences in the pharmacokinetics of repaglinide \(a sensitive substrate for CYP2C8\) were observed when used concomitantly with QINLOCK.](#)

*Strong CYP3A Inhibitors:* Coadministration of QINLOCK with itraconazole (a strong CYP3A inhibitor and also a P-gp inhibitor) increased ripretinib  $C_{max}$  by 36% and  $AUC_{0-inf}$  by 99% and also increased DP-5439  $AUC_{0-inf}$  by 99% with no change in its  $C_{max}$ .

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**Strong CYP3A Inducers:** Coadministration of QINLOCK with rifampin (a strong CYP3A inducer) decreased ripretinib  $C_{max}$  by 18% and  $AUC_{0-inf}$  by 61% and also decreased DP-5439  $AUC_{0-inf}$  by 57% with increased  $C_{max}$  by 37%.

**Moderate CYP3A Inducers:** Coadministration of QINLOCK with efavirenz (a moderate CYP3A inducer) was predicted to decrease ripretinib  $C_{max}$  by 24% and decrease  $AUC_{0-inf}$  by 56%.

**Proton Pump Inhibitors:** No clinically significant differences in the plasma exposure to ripretinib and DP-5439 were observed when QINLOCK was coadministered with pantoprazole (a proton pump inhibitor).

#### *In Vitro Studies*

**CYP Enzymes:** Ripretinib and DP-5439 are **inhibitors of CYP2C8. Ripretinib and DP-5439 are** not inducers of CYP1A2, CYP2B6, or CYP3A4.

**Transporter Systems:** Ripretinib and DP-5439 are substrates for P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP). Ripretinib is an inhibitor of P-gp and BCRP. DP-5439 is an inhibitor of BCRP and Multidrug And Toxin Extrusion Protein 1 (MATE1).

[UGT1A Substrates: Ripretinib is an inhibitor of UGT1A1, UGT1A3, UGT1A4, UGT1A7, and UGT1A8.](#)

העלון לרופא נמצא בקישור, וכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום.

בברכה,

מדיסון פארמה בע"מ