

מרץ 2024

רופא/ה, רוקח/ת נכבד/ה,

ברצוננו להודיע על עדכון בעלונים לרופא ולצרכן של תכשירי **Lorviqua 25 mg** ו-**Lorviqua 100 mg**:

המרכיב הפעיל:

lorlatinib 25 mg, lorlatinib 100 mg

צורת מינון:

Film-coated tablet

התוויה:

LORVIQUA® is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive.

### להלן העדכונים העיקריים בעלון לרופא:

## 2 DOSAGE AND ADMINISTRATION

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### 2.4 Concomitant Use of Strong ~~or Moderate~~ CYP3A Inducers

LORVIQUA is contraindicated in patients taking strong CYP3A inducers. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating LORVIQUA. ~~Avoid concomitant use of LORVIQUA with moderate CYP3A inducers [see Contraindications (4), Warnings and Precautions (5.1), Drug Interactions (7.1), Clinical Pharmacology (12.3)].~~

### 2.5 Concomitant Use of Moderate CYP3A Inducers

Avoid concomitant use of moderate CYP3A inducers with LORVIQUA. If concomitant use with moderate CYP3A inducers is unavoidable, increase the LORVIQUA dose to 125 mg once daily [see Drug Interactions (7.1), Clinical Pharmacology (12.3)].

### 2.8 Dosage Modification for Severe Renal Impairment

Reduce the recommended dosage of LORVIQUA for patients with severe renal impairment (creatinine clearance [CL<sub>cr</sub>] 15 to < 30 mL/min, estimated by Cockcroft-Gault) from 100 mg to 75 mg orally once daily [see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)].

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Risk of Serious Hepatotoxicity with Concomitant Use of Strong CYP3A Inducers

Severe hepatotoxicity occurred in 10 of 12 healthy subjects receiving a single dose of LORVIQUA with multiple daily doses of rifampin, a strong CYP3A inducer. Grade 4 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevations occurred in 50% of subjects, Grade 3 ALT or AST elevations occurred in 33% and Grade 2 ALT or AST elevations occurred in 8%. ALT or AST elevations occurred within 3 days and returned to within normal limits after a median of 15 days (7 to 34 days); the median time to recovery was 18 days in subjects with Grade 3 or 4 ALT or AST elevations and 7 days in subjects with Grade 2 ALT or AST elevations [see Drug Interactions (7.1)].

LORVIQUA is contraindicated in patients taking strong CYP3A inducers. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating LORVIQUA [*see Contraindications (4), Drug Interactions (7.1)*].

~~Avoid concomitant use of LORVIQUA with moderate CYP3A inducers. If concomitant use of moderate CYP3A inducers cannot be avoided, monitor AST, ALT, and bilirubin 48 hours after initiating LORVIQUA and at least 3 times during the first week after initiating LORVIQUA.~~

## 7 DRUG INTERACTIONS

### 7.1 Effect of Other Drugs on LORVIQUA

#### Effect of Strong CYP3A Inducers

Concomitant use of LORVIQUA with a strong CYP3A inducer decreased lorlatinib plasma concentrations [*see Clinical Pharmacology (12.3)*], which may decrease the efficacy of LORVIQUA. ~~The effect of concomitant use of LORVIQUA with a moderate CYP3A inducer on lorlatinib plasma concentrations has not been studied.~~

Severe hepatotoxicity occurred in healthy subjects receiving LORVIQUA with rifampin, a strong CYP3A inducer. In 12 healthy subjects receiving a single 100 mg dose of LORVIQUA with multiple daily doses of rifampin, Grade 3 or 4 increases in ALT or AST occurred in 83% of subjects and Grade 2 increases in ALT or AST occurred in 8%. A possible mechanism for hepatotoxicity is through activation of the pregnane X receptor (PXR) by LORVIQUA and rifampin, which are both PXR agonists. ~~The risk of hepatotoxicity with concomitant use of LORVIQUA and moderate CYP3A inducers that are also PXR agonists is unknown.~~

LORVIQUA is contraindicated in patients taking strong CYP3A inducers [*see Contraindication (4)*]. Discontinue strong CYP3A inducers for 3 plasma half-lives of the strong CYP3A inducer prior to initiating LORVIQUA. [*see Dosage and Administration (2.3)*].

#### Moderate CYP3A Inducers

Concomitant use of LORVIQUA with a moderate CYP3A inducer decreased lorlatinib plasma concentrations, which may decrease the efficacy of LORVIQUA [*see Clinical Pharmacology (12.3)*]. ~~Avoid concomitant use of LORVIQUA with moderate CYP3A inducers. If concomitant use of moderate CYP3A inducers cannot be avoided, monitor ALT, AST, and bilirubin as recommended with LORVIQUA. If concomitant use is unavoidable, increase the LORVIQUA dose [*see Dosage and Administration (2.3), Warnings and Precautions (5.1), Clinical Pharmacology (12.3)+4*].~~

## 8 USE IN SPECIFIC POPULATIONS

### 8.7 Renal Impairment

Reduce the dose when administering LORVIQUA to patients with severe ( $CL_{cr}$  15 to <30 mL/min, estimated by Cockcroft Gault) renal impairment [*see Dosage and Administration (2.8) and Clinical Pharmacology (12.3)*].

No dose adjustment is recommended for patients with mild or moderate renal impairment (creatinine clearance [ $CL_{cr}$ ] ~~( $CL_{cr}$  30 to 89 mL/min estimated by Cockcroft-Gault).~~ The recommended dose of LORVIQUA has not been established for patients with severe renal impairment ( $CL_{cr}$  15 to 29 mL/min, estimated by Cockcroft-Gault) renal impairment [*see Clinical Pharmacology (12.3)*].

## להלן העדכונים העיקריים בעלון לצרכן:

### 2. לפני השימוש בתרופה

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אזהרות מיוחדות הנוגעות לשימוש בתרופה

לפני הטיפול בלורביקואה ספר לרופא אם:

- יש לך בעיות בכליות

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השינויים מסומנים בקו תחתון (תוספת מידע) או קו מחיקה (הסרת מידע). השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מוצגים במכתב זה.

העלון המעודכן נשלח למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:

[מאגר התרופות\(health.gov.il\)](http://health.gov.il)

לחילופין, לקבלת עלון מלא מודפס ניתן לפנות לחברת פיזור פרמצבטיקה ישראל בע"מ, שנקר 9, ת.ד. 12133, הרצליה פיתוח, 46725.

בברכה,

מרגריטה אוליבסון פולישצ'וק

רוקחת ממונה