פברואר 2020

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

שלום רב,

הנדון : **<u>עדכוני בטיחות בעלוני התכשיר</u>**
Jakavi 5/10/15/20 mg, tablets
ג'קאבי 5/10/15/20 מ"ג, טבליות

חברת נוברטיס ישראל בע"מ מבקשת להודיע על עדכון בעלון לרופא של התכשירים **Jakavi 5/10/15/20 mg**.

התוויות התכשיר:

<u>Myelofibrosis (MF)</u>

Jakavi is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

<u>Polycythaemia vera (PV)</u>

Jakavi is indicated for the treatment of adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.

חומר פעיל:

Ruxolitinib (as phosphate) 5/10/15/20 mg

בהודעה זו מפורטים העדכונים המהווים עדכון במידע בטיחותי בלבד .למידע מלא יש לעיין בעלוני התכשיר.
העלונים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות ,וניתן לקבלם מודפסים על-ידי פניה לבעל הרישום:
נוברטיס ישראל בע"מ.
תוצרת הארץ 6, ת.ד. 7126, תל אביב

העלון לרופא עודכן בנובמבר 2020, להלן העדכונים המהווים עדכון במידע בטיחותי (החמרה במידע בטיחותי מודגשת בצהוב):

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4.4 Special warnings and precautions for use

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<u>Infections</u>

Serious bacterial, mycobacterial, fungal, viral and other opportunistic infections have occurred in patients treated with Jakavi. Patients should be assessed for the risk of developing serious infections. Physicians should carefully observe patients receiving Jakavi for signs and symptoms of infections and initiate appropriate treatment promptly. Treatment with Jakavi should not be started until active serious infections have resolved.

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Tuberculosis has been reported in patients receiving Jakavi. Before starting treatment, patients should be evaluated for active and inactive ("latent") tuberculosis, as per local recommendations. This can include medical history, possible previous contact with tuberculosis, and/or appropriate screening such as lung x-ray, tuberculin test and/or interferon-gamma release assay, as applicable. Prescribers are reminded of the risk of false negative tuberculin skin test results, especially in patients who are severely ill or immunocompromised.
Hepatitis B viral load (HBV-DNA titre) increases, with and without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking Jakavi. It is recommended to screen for HBV prior to commencing treatment with Jakavi. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines.

4.8 Undesirable effects

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Tabulated list of adverse drug reactions from clinical studies

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Table 1 Frequency category of adverse drug reactions reported in the phase 3 studies (COMFORT-I, COMFORT-II, RESPONSE, RESPONSE 2)

Adverse drug reaction	Frequency category for MF patients	Frequency category for PV patients
Infections and infestations		
Urinary tract infections[a,e]	Very common	Very common
Herpes zoster[a,e]	Very common	Very common
Pneumonia	Very common	Common
Sepsis	Common	Uncommon
Tuberculosis[f]	Uncommon	Not known[g]
HBV reactivation	Not known[g]	Uncommon
Blood and lymphatic system disorders[b,e]		
Anaemia[b]		
CTCAE[d] grade 4 (<6.5g/dl)	Very common	Uncommon
CTCAE[d] grade 3 (<8.0 – 6.5g/dl)	Very common	Common
Any CTCAE[d] grade	Very common	Very common
Thrombocytopenia[b]		
CTCAE[d] grade 4 (<25,000/mm^3)	Common	Uncommon
CTCAE[d] grade 3 (50,000 – 25,000/mm^3)	Very common	Common

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Any CTCAE[d] grade	Very common	Very common
Neutropenia[b]		
CTCAE[d] grade 4 (<500/mm^3)	Common	Uncommon
CTCAE[d] grade 3 (<1,000 – 500/mm^3)	Common	Uncommon
Any CTCAE[d] grade	Very common	Common
Pancytopenia[b, c]	Common	Common
Bleeding (any bleeding including intracranial, and gastrointestinal bleeding, bruising and other bleeding)	Very common	Very common
Bruising	Very common	Very common
Gastrointestinal bleeding	Very common	Common
Intracranial bleeding	Common	Uncommon
Other bleeding (including epistaxis, post-procedural haemorrhage and haematuria)	Very common	Very common
Metabolism and nutrition disorders		
Hypercholesterolaemia[b] any CTCAE[d] grade	Very common	Very common
Hypertriglyceridaemia[b] any CTCAE[d] grade	Very common	Very common
Weight gain[a]	Very common	Very common
Nervous system disorders		
Dizziness[a]	Very common	Very common
Headache[a]	Very common	Very common
Gastrointestinal disorders		
Elevated lipase, any CTCAE[d] grade	Very common	Very common
Constipation[a]	Very common	Very common
Flatulence[a]	Common	Common
Hepatobiliary disorders		
Raised alanine aminotransferase[b]		
CTCAE[d] grade 3 (> 5x – 20 x ULN)	Common	Common
Any CTCAE[d] grade	Very common	Very common
Raised aspartate aminotransferase[b]		
Any CTCAE[d] grade	Very common	Very common

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Vascular disorders		
Hypertension[a]	Very common	Very common

[a] Frequency is based on adverse event data.
- A subject with multiple occurrence of an adverse drug reaction (ADR) is counted only once in that ADR category.
- ADRs reported are on treatment or up to 28 days post treatment end date.

[b] Frequency is based on laboratory values.
- A subject with multiple occurrences of an ADR is counted only once in that ADR category.
- ADRs reported are on treatment or up to 28 days post treatment end date.

[c] Pancytopenia is defined as haemoglobin level <100 g/l, platelet count <100x10^9/l, and neutrophil count <1.5x10^9/l (or low white blood cell count of grade 2 if neutrophil count is missing), simultaneously in the same lab assessment

[d] Common Terminology Criteria for Adverse Events (CTCAE) version 3.0; grade 1 = mild, grade 2 = moderate, grade 3 = severe, grade 4 = life-threatening

[e] These ADRs are discussed in the text.

[f] Frequency is based on all patients exposed to ruxolitinib in clinical studies (N=4755)

[g] ADR derived from post-marketing experience

העלון לצרכן עודכן בנובמבר 2020, להלן העדכונים המהווים עדכון במידע בטיחותי (החמרה במידע בטיחותי מודגשת בצהוב):

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4. תופעות לוואי

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תופעות לוואי נוספות:

תופעות לוואי שכיחות (common) - תופעות העלולות להופיע בעד 1 מתוך 10 מטופלים:

- ירידה במספר כל שלושת הסוגים של תאי דם – תאי דם אדומים, לבנים וטסיות (pancytopenia)
- כמות עודפת של גזים במערכת העיכול (נפיחות)

תופעות לוואי שאינן שכיחות (uncommon) - תופעות העלולות להופיע בעד 1 מתוך 100 מטופלים:

- שחפת
- חזרה של זיהום הפטיטיס B (שיכול לגרום להצהבה של העור והעיניים, שתן כהה בצבע חום, כאב בטן בצד ימין, חום, בחילה והקאה)

בברכה,

לריסה חייקין
רוקחת ממונה

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