יולי 2024

<u>זפוסיה 0.23 מ"ג, זפוסיה 0.46 מ"ג, זפוסיה 0.92 מ"ג – כמוסות</u>
<u>Zeposia 0.23 mg, Zeposia 0.46 mg, Zeposia 0.92 mg - capsules</u>

רופא/ה ,רוקח/ת יקר/ה,

חברת בריסטול-מאיירס סקוויב (ישראל) מודיעה על עדכונים בעלון לרופא ובעלון לצרכן של התכשירים שבנדון.

התוויות התכשירים כפי שאושרו ע"י משרד הבריאות:

<u>Multiple sclerosis</u>

Zeposia is indicated for the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease as defined by clinical or imaging features.

<u>Ulcerative colitis</u>

Zeposia is indicated for the treatment of moderately to severely active ulcerative colitis (UC) in adults.

המרכיב הפעיל: Ozanimod 0.23 mg, Ozanimod 0.46 mg, Ozanimod 0.92 mg per capsule

להלן העדכונים בעלון לרופא ובעלון לצרכן (ללא פירוט שינויים לא מהותיים ו/או עריכתיים).

תוספת טקסט מסומנת <u>בקו תחתון אדום</u>, מחיקת טקסט ~~בקו אמצעי אדום~~, <u>החמרה מודגשת בצהוב</u>.

העלון לרופא והעלון לצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום בריסטול-מאיירס סקוויב (ישראל) בע"מ.

בברכה,
יפעת זלינגר בן דוד
רוקחת ממונה
בריסטול-מאיירס סקוויב (ישראל)

למידע מלא על התרופה יש לעיין בעלון לרופא ובעלון לצרכן כפי שנשלחו למשרד הבריאות.

4.4 Special warnings and precautions for use

[…]

Liver injury~~function~~

Elevations of aminotransferases, gamma-glutamyl transferase (GGT) and bilirubin have been reported in patients treated with ozanimod (see section 4.8).

Clinically significant liver injury has occurred in patients treated with ozanimod in the post marketing setting. Signs of liver injury, including elevated serum hepatic enzymes and elevated total bilirubin, have occurred as early as ten days after the first dose. Severe liver injury may result in the need for a liver transplant (see section 4.8).

~~Elevations of aminotransferases may occur in patients receiving ozanimod (see section 4.8).~~

Recent (i.e. within last 6 months) transaminase and bilirubin levels should be available before initiation of treatment with ozanimod. In the absence of clinical symptoms, liver transaminases and bilirubin levels should be monitored at Months 1, 3, 6, 9 and 12 on therapy and periodically thereafter. If liver transaminases rise above 5 times the ULN, more frequent monitoring including serum bilirubin and alkaline phosphatase (ALP) should be instituted. If liver transaminases above 5 times the ULN are confirmed, or at least 3 times the ULN associated with increase of serum bilirubin more than 2 times the ULN, treatment with ozanimod should be interrupted and only re-commenced once liver transaminase values have normalised (including if an alternative cause of the hepatic dysfunction is discovered).

[…]

Prior and concomitant treatment with antineoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies

[…]

Ozanimod can generally be started immediately after discontinuation of interferon (IFN) or glatiramer.

[…]

Return of MS disease activity ~~(rebound)~~ after ozanimod discontinuation

Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of another S1P receptor modulator. In the ozanimod long-term extension study, following permanent discontinuation of ozanimod, clinical relapses were reported in 3.3% of patients, none with severe exacerbation of disease or severe increase in disability. ~~The possibility of severe exacerbation of disease after stopping ozanimod treatment should be considered.~~ Patients should be observed for ~~relevant signs of possible severe exacerbation or~~ return of ~~high~~ disease activity upon ozanimod discontinuation and appropriate treatment should be instituted as required.

[…]

4.8 Undesirable effects

[…]

Tabulated list of adverse reactions

The adverse reactions observed in patients treated with ozanimod in MS and UC clinical studies and from post-marketing experience including spontaneous case reports are listed below by system organ class (SOC) and frequency for all adverse reactions.

[…]

Table 1: Summary of adverse reactions reported ~~in MS and UC clinical studies~~

Hepatobiliary disorders	Common	Alanine aminotransferase increased, gamma-glutamyl transferase increased, blood bilirubin increased
	Rare	Liver injury****
Investigations	Common	~~Alanine aminotransferase increased, gamma-glutamyl transferase increased, blood bilirubin increased,~~ ~~p~~Pulmonary function test abnormal***

[…]

**** Adverse reactions from post-marketing reports

[…]

Description of selected adverse reactions

[…]

Severe liver injury has been reported in a post-marketing setting (see section 4.4).

[…]

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, Sphingosine-1-phosphate (S1P) receptor modulators~~selective immunosuppressants~~, ATC code: L04A~~38~~E02

[…]

Clinical efficacy and safety

Multiple sclerosis

[…]

Long-term Data

Patients with RRMS who completed the ~~Phase 3~~ SUNBEAM, ~~and~~ RADIANCE, Phase 2 extension or Phase 1 PK/PD studies could enter an open-label extension ~~study~~ (Study 3 - DAYBREAK) and received ozanimod 0.92 mg once daily to assess the long-term safety and efficacy of ZEPOSIA. ~~Of the 751 patients initially randomised to ozanimod 0.92 mg and treated for up to 3 years, the (adjusted) ARR was 0.124 after the 2nd year of treatment.~~ In total, 2494 subjects were treated in DAYBREAK with ozanimod 0.92 mg once daily (736 patients switched from interferon beta-1a IM 30 mcg once weekly, 877 switched from ozanimod 0.46 mg once daily, and 881 continued with ozanimod 0.92 mg once daily) with a median duration of treatment of 68 months up to a maximum of 81 months. The adjusted annualised relapse rate (ARR) for all subjects over the treatment period was 0.098 (95% CI: 0.082, 0.117) with 69.1% of patients remaining relapse free. Subjects who continued on ozanimod 0.92 mg into DAYBREAK had an ARR of 0.090 (95% CI: 0.073, 0.111). A total of 379 (15.2%) of subjects experienced 6-month confirmed disability progression over the study.

עדכונים בעלון לצרכן

1. למה מיועדת התרופה?

[…]

קבוצה תרפויטית: מדכאי מערכת חיסון, ~~סלקטיביים~~מודולטורים של קולטני ספינגוזין-1-פוספט (S1P)

4. תופעות לוואי

[…]

תופעות לוואי רציניות

ספר לרופא או לרוקח מיד אם הבחנת באחת מתופעות הלוואי הרציניות הבאות:

- **תופעות לוואי שכיחות (common) תופעות שמופיעות ב – 1-10 משתמשים מתוך 100:**
  - קצב לב איטי
  - זיהום בדרכי השתן
  - עלייה בלחץ הדם
- **תופעות לוואי שאינן שכיחות (uncommon) תופעות שמופיעות ב – 1-10 משתמשים מתוך 1,000:**
  - תגובה אלרגית – הסימנים יכולים לכלול פריחה
- **תופעות לוואי נדירות (rare) תופעות שמופיעות ב - 1-10 משתמשים מתוך 10,000:**
  - זיהום במוח הנקרא לויקואנצפלופתיה רב-מוקדית מתקדמת (PML) (ראה פרק 2)
  - פגיעה בכבד

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