פברואר 2019

רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

הנדון: **ENTYVIO® IV 300 mg/Vial**
אנטיביו IV 300 מ"ג/בקבוקון (ויאל)

חברת טקדה ישראל בע"מ מבקשת להודיעכם כי העלון לרופא של התכשיר שבנדון, התעדכן בפברואר 2019.

העדכונים המהותיים ביותר מופיעים במכתב זה, אך קיימים עדכונים נוספים.

למידע נוסף, יש לעיין בעלון לרופא המעודכן אשר נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://www.old.health.gov.il/units/pharmacy/trufot/PerutTrufa.asp?Reg_Number=153 58 34277 00&safa=

כמו כן, ניתן לקבלו מודפס על-ידי פנייה לבעל הרישום:

טקדה ישראל בע"מ, רח' אפעל 25, פתח-תקווה, טל': 03-3733140.

ההתוויה המאושרת לתכשיר בישראל:

Ulcerative Colitis:

Entyvio is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor alpha (TNFα) antagonist.

Crohn's Disease:

Entyvio is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor alpha (TNFα) antagonist.

מרכיב פעיל: Vedolizumab 300 mg/Vial

בברכה,

חן פרידליס
רוקחת ממונה
טקדה ישראל בע"מ

IL/EYV/0219/0014

Takeda Israel Ltd.
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העדכונים העיקריים בעלון לרופא הינם (טקסט שנוסף מסומן בכחול, טקסט שהושמט מסומן כטקסט אדום עם קו חוצה):

4.2 Posology and method of administration

Posology

Ulcerative colitis

~~Continued t~~Therapy for patients with ulcerative colitis should be discontinued~~carefully reconsidered~~ if no evidence of therapeutic benefit is observed by week 10 (see section 5.1).

Crohn's disease

Therapy for patients with Crohn's disease should ~~not~~ be discontinued if no evidence of therapeutic benefit is observed by week 14 (see section 5.1).

4.4 Special warnings and precautions for use

Infections

~~No cases of PML were reported in clinical studies of vedolizumab however, h~~Healthcare professionals should monitor patients on vedolizumab for any new onset or worsening of neurological signs and symptoms as outlined in physician education materials, and consider neurological referral if they occur.

4.6 Fertility, pregnancy and lactation

Breast-feeding

Vedolizumab has been detected in human milk. The effect of vedolizumab on infants is unknown. The use of vedolizumab in lactating women should take into account the benefit of therapy to the mother and potential risks to the infant.

~~It is unknown whether vedolizumab is excreted in human milk or absorbed systemically after ingestion. Available pharmacodynamic/toxicological data in animals have shown excretion of vedolizumab in milk (see section 5.3).~~
~~A risk to the infants cannot be excluded.~~
~~Because maternal antibodies (IgG) are excreted in breast milk, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Entyvio therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.~~

4.8 Undesirable effects

Tabulated list of adverse reactions

Infections and infestations	Very common	Nasopharyngitis
	Common	Bronchitis, Gastroenteritis, Upper respiratory tract infection, Influenza, Sinusitis, Pharyngitis
	Uncommon	Respiratory tract infection, Vulvovaginal candidiasis, Oral candidiasis, Herpes zoster
	Very rare	Pneumonia

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Description of selected adverse reactions

~~*Immunogenicity*~~

~~In GEMINI I and II controlled studies, vedolizumab showed an immunogenicity rate of 4% (56 of 1,434 patients who received continuous treatment with vedolizumab were anti-vedolizumab antibody-positive at any time during treatment). Nine out of 56 patients were persistently positive (anti-vedolizumab antibody-positive at two or more study visits) and 33 patients developed neutralizing anti-vedolizumab antibodies.~~

~~The frequency of anti-vedolizumab antibody detected in patients 16 weeks after the last dose of vedolizumab (approximately five half-lives after the last dose) was approximately 10% in GEMINI I and II.~~

~~In GEMINI I and II controlled studies, 5% (3 of 61) of the patients who had an adverse reaction assessed by the investigator as an IRR were persistently anti-vedolizumab antibody-positive.~~

~~Overall, there was no apparent correlation of anti-vedolizumab antibody development to clinical response or adverse reactions. However, the number of patients that developed anti-vedolizumab antibodies was too limited to make a definitive assessment.~~

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

… Vedolizumab reduces gastrointestinal inflammation in UC and CD patients.

Immunogenicity

Antibodies to vedolizumab may develop during vedolizumab treatment most of which are neutralising. The formation of anti-vedolizumab antibodies is associated with increased clearance of vedolizumab and lower rates of clinical remission.

Infusion related reactions after vedolizumab infusion are reported in subjects with anti-vedolizumab antibodies.

Clinical efficacy

Ulcerative colitis

… In this open-label extension study, the benefits of vedolizumab treatment as assessed by partial Mayo score, clinical remission, and clinical response were shown for up to 196 ~~124~~ weeks.

Crohn's disease

… In this open-label extension study, clinical remission and clinical response were observed in patients for up to 196~~124~~ weeks.

5.2 Pharmacokinetic properties

Elimination

Population pharmacokinetic analyses suggest that while low albumin, higher body weight and~~,~~ prior treatment with anti-TNF drugs ~~and presence of anti-vedolizumab antibody~~ may increase vedolizumab clearance, the magnitude of their effects is not considered to be clinically relevant.

5.3 Preclinical safety data

…~~ It is not known whether vedolizumab is excreted in human milk.~~

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