ינואר 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 בינואר 2019.

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

למידע נוסף, יש לעיין בעלון לרופא המצורף כפי שאושר על ידי משרד הבריאות.

העלון המעודכן לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://data.health.gov.il/drugs/index.html#/byDrug

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

העדכונים העיקריים בעלון לרופא הינם (טקסט שנוסף מסומן בכחול, טקסט שהושמט מסומן כטקסט אדום עם קו חוצה)**:**

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should ~~are strongly recommended to~~ use adequate contraception to prevent pregnancy and to continue its use for at least 18 weeks after the last treatment ~~with Entyvio~~.

Pregnancy

There are limited amount of data from the use of vedolizumab in pregnant women.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).
~~Entyvio is to be used during pregnancy only if the benefits clearly outweigh any potential risk to both the mother and foetus.~~
As a precautionary measure, it is preferable to avoid the use of Entyvio during pregnancy unless the benefits clearly outweigh any potential risk to both the mother and foetus.

Breast-feeding

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, ~~it is recommended that~~ 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.

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4.7 Effects on ability to drive and use machines

Entyvio has ~~may have a~~ minor influence on the ability to drive and use ~~or operate~~ machines, as dizziness has been reported in a small number of patients.

6.3 Shelf life

~~The expiry date of the product is indicated on the packaging materials.~~
~~Chemical and physical in-use stability of the reconstituted and diluted solution has been demonstrated for 12 hours at 20°C-25°C and 24 hours at 2°C-8°C. From a microbiological point of view, the product must be used immediately. Do not freeze the reconstituted or diluted solution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and must not be longer than a total of 24 hours. This 24 hour hold may include up to 12 hours at 20°C-25°C; any additional hold time must be at 2°C-8°C.~~
In-use stability of the reconstituted solution in the vial has been demonstrated for 8 hours at 2°C-8°C.

In-use stability of the diluted solution in sodium chloride 9 mg/mL (0.9%) solution for injection in infusion bag has been demonstrated for 12 hours at 20°C-25°C or 24 hours at 2°C-8°C.

The combined in-use stability of Entyvio in the vial and infusion bag with sodium chloride 9 mg/mL (0.9%) solution for injection is a total of 12 hours at 20°C-25°C or 24 hours at 2°C-8°C. A 24 hour period may include up to 8 hours at 2°C-8°C for reconstituted solution in the vial and up to 12 hours at 20°C-25°C for diluted solution in the infusion bag but the infusion bag must be stored in the refrigerator (2°C-8°C) for the rest of the 24 hour period.

Do not freeze the reconstituted solution in the vial or the diluted solution in the infusion bag.

	Storage Condition	
	Refrigerator (2°C- 8°C)	20°C-25°C
Reconstituted solution in the vial	8 hours	Do not hold[1]
Diluted solution in sodium chloride 9 mg/mL (0.9%) solution for injection	24 hours[2,3]	12 hours[2]

[1] Up to 30 minutes are allowed for reconstitution

[2] This time assumes the reconstituted solution is immediately diluted in the sodium chloride 9 mg/mL (0.9%) solution for injection and held in the infusion bag only. Any time that the reconstituted solution was held in the vial should be subtracted from the time the solution may be held in the infusion bag.

[3] This period may include up to 12 hours at 20°C-25°C.

6.6 Special precautions for disposal and other handling

Instructions for reconstitution and infusion

~~Entyvio should be at room temperature (20°C -25°C) when reconstituted.~~

1. Use aseptic technique when preparing Entyvio solution for intravenous infusion.
~~1.~~2. Remove flip-off cap from the vial and wipe with alcohol swab. Reconstitute vedolizumab with 4.8 ~~ml~~ mL of sterile water for injections at room temperature (20°C - 25°C), using a syringe with a 21-25 gauge needle.
~~2.~~3. Insert the needle into the vial through the centre of the stopper and direct the stream of liquid to the wall of the vial to avoid excessive foaming.
~~3.~~4. Gently swirl the vial for at least 15 seconds. Do not vigorously shake or invert.
~~4.~~5. Let the vial sit for up to 20 minutes at room temperature (20°C - 25°C), to allow for reconstitution and for any foam to settle; the vial can be swirled and inspected for dissolution during this time. If not fully dissolved after 20 minutes, allow another 10 minutes for dissolution.
~~5.~~6. Inspect the reconstituted solution visually for particulate matter and discoloration prior to dilution~~administration~~. Solution should be clear or opalescent, colourless to light yellow and free of visible particulates. Reconstituted solution with uncharacteristic colour or containing particulates must not be administered.
~~6.~~7. Once dissolved~~Prior to withdrawing reconstituted solution from vial~~, gently invert vial 3 times.
~~7.~~8. Immediately ~~Withdraw~~ withdraw 5 ~~ml~~ mL (300 mg) of reconstituted Entyvio using a syringe with a 21-25 gauge needle.
~~8.~~9. Add the 5 ~~ml~~ mL (300 mg) of reconstituted Entyvio to 250 ~~ml~~ mL of sterile ~~0.9%~~ sodium chloride 9 mg/mL (0.9%) solution for injection, and gently mix the infusion bag (5 ~~ml~~ mL of ~~0.9%~~ sodium chloride 9 mg/mL (0.9%) solution for injection does not have to be withdrawn from the infusion bag prior to adding Entyvio). Do not add other medicinal products to the prepared infusion solution or intravenous infusion set. Administer the infusion solution over 30 minutes (see section 4.2).

~~Entyvio does not contain preservatives.~~ Once reconstituted, the infusion solution should be used as soon as possible. ~~However, if necessary, the infusion solution may be stored for up to 24 hours: this 24 hour hold may include up to 12 hours at 20°C-25°C; any additional hold time must be at 2°C -8°C. Do not freeze.~~
Do not store any unused portion of the reconstituted solution or infusion solution for reuse.
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