מאי 2021

AUBAGIO film coated tablets

חומר פעיל: Teriflunomide 14 mg

ההתוויה המאושרת:

Aubagio is indicated for the treatment of adult patients with relapsing remitting forms of Multiple Sclerosis (MS) to reduce the frequency of clinical relapses and to delay the progression of physical disability.

חברת סאנופי אוונטיס מבקשת להודיע על עדכון העלון לרופא והעלון לצרכן באפריל 2021.

העדכונים העיקרים מופיעים בסעיפים הבאים:

בעלון לרופא:

4.4 Special warnings and precautions for use

Monitoring

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- Alanine aminotransferase / serum glutamic pyruvic transaminase (ALT/SGPT)
  - Liver enzymes should be assessed at least every ~~two~~four weeks during the first 6 months oftreatment~~,~~ and ~~every 8 weeks~~regularly thereafter.
  - Consider additional monitoring when AUBAGIO is given in patients with pre-existing liver disorders, given with other potentially hepatotoxic drugs or as indicated by clinical signs and symptoms such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. Liver enzymes should be assessed every two weeks during the first 6 months of treatment, and at least every 8 weeks thereafter for at least 2 years from initiation of treatment.

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Cases of drug-induced liver injury (DILI) have been observed during treatment with teriflunomide, sometimes life-threatening. Most cases of DILI occurred with time to onset of several weeks or several months after treatment initiation of teriflunomide, but DILI can also occur with prolonged use.

The risk for liver enzyme increases and DILI with teriflunomide might be higher in patients with pre-existing liver disorder, concomitant treatment with other hepatotoxic drugs, and/or consumption of substantial quantities of alcohol. Patients should therefore be closely monitored for signs and symptoms of liver injury.

Teriflunomide therapy should be discontinued and accelerated elimination procedure considered if liver injury is suspected~~; consider discontinuing~~. Consider to discontinue teriflunomide therapy if elevated liver enzymes (greater than3-fold ULN) are confirmed.

~~Patients with pre-existing liver disease and/or who consume substantial quantities of alcohol may be at increased risk of developing elevated liver enzymes when taking teriflunomide and should be closely monitored for signals of liver disease.~~

~~Hypoproteinaemia~~

In case of treatment discontinuation, liver tests should be pursued until normalisation of transaminase levels.

Hypoproteinaemia

Since teriflunomide is highly protein bound and as the binding is dependent upon the concentrations of albumin, unbound plasma teriflunomide concentrations are expected to be increased in patients with hypoproteinaemia, e.g. in nephrotic syndrome. Teriflunomide should not be used in patients with conditions of severe hypoproteinaemia.

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Skin reactions

Cases of ~~severe~~serious skin reactions ~~have been reported postmarketing (~~, sometimes fatal including Stevens-Johnson syndrome ~~and~~(SJS), toxic epidermalnecrolysis~~).~~

~~In patients treated~~ (TEN), and drug reaction with ~~leflunomide, the parent compound, very rare cases of Drug Reaction with Eosinophilia~~eoseinophilia and ~~Systemic Symptoms~~systemic symptoms (DRESS~~)~~), have ~~also~~ been reported~~.~~ with AUBAGIO.

~~In case of ulcerative stomatitis, teriflunomide administration should be discontinued.~~ If skin and /or mucosal reactions (ulcerative stomatitis) are observed which raise the suspicion of severe generalised major skin reactions (Stevens-Johnson syndrome, ~~or~~ toxic epidermal necrolysis-Lyell's syndrome,or drug reaction with eosinophilia and systemic symptoms), teriflunomide and any other possibly associatedtreatment must be discontinued, and an accelerated procedure initiated immediately. In such cases patients should not be re-exposed to teriflunomide (see section 4.3).

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4.8 Undesirable effects

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System organ class	Very common	Common	Uncommon	Rare	Very rare	Not known
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Hepatobiliary disorders	Alanine aminotransferase (ALT) increase[b]	Gamma-glutamyltransferase (GGT) increase[b], Aspartate aminotransferase increase[b]		Acute hepatitis		~~Acute hepatitis~~Drug- induced liver injury (DILI)
Skin and subcutaneous tissue disorders	Alopecia	Rash, Acne	Nail disorders, Severe skin reactions[a]			Psoriasis (including pustular)b

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5.1 Pharmacodynamic properties

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Mechanism of action

Teriflunomide is an immunomodulatory agent with anti-inflammatory properties that selectively and reversibly inhibits the mitochondrial enzyme dihydroorotate dehydrogenase (DHO-DH), ~~required for~~which functionally connects with the ~~de novo pyrimidine synthesis.~~respiratory chain. As a consequence of the inhibition, teriflunomide generally reduces theproliferation of rapidly dividing cells that ~~need~~depend on de novo synthesis of pyrimidine to expand. The exact mechanism by which teriflunomide exerts its therapeutic effect in MS is not fully understood, but this is mediated by a reduced number of T-lymphocytes.

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בעלון לצרכן:

2. לפני השימוש בתרופה

אין להשתמש בתרופה אם:

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- פיתחת בעבר פריחה חמורה בעור או קילוף בעור, שלפוחיות ו/או פצעים בפה לאחר נטילת טריפלונומיד או לפלונומיד.
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4. תופעות לוואי

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תופעות לוואי חמורות
פנה מיד לרופא שלך אם אתה מבחין באחת מתופעות הלוואי החמורות שלהלן:

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- תגובות חמורות בעור שיכולות לכלול תסמינים של פריחה בעור, שלפוחיות, חום, או כיבים בפה.
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תופעות לוואי שאינן שכיחות (עלולות להשפיע על עד 1 מתוך 100 אנשים):

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- בעיות בציפורניים, תופעות עוריות חמורות

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תופעות לוואי נדירות (עלולות להשפיע על עד 1 מתוך 1,000 אנשים):

- דלקת או פגיעה בכבד

תופעות לוואי ששכיחותן אינה ידועה (תופעות ששכיחותן טרם נקבעה):

- .....
- ~~תופעות עוריות חמורות~~
- .....

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום- סאנופי-אוונטיס ישראל בע"מ, רח' בני גאון 10 נתניה או בטלפון : 09-8633700 .

להלן הקישור לאתר משרד הבריאות: https://data.health.gov.il/drugs/index.html#/byDrug

בברכה,

אסנת מירון – עוזרי
רוקחת ממונה

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