NOVARTIS

אפריל 2024

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,
שלום רב,

הנדון :

<u>עדכון עלוני התכשיר</u>

<u>ZOLGENSMA, suspension for infusion, I.V</u>
<u>זולג'נסמה, תרחיף לעירוי תוך-ורידי</u>

חברת נוברטיס ישראל בע"מ מבקשת להודיע על עדכון בעלון לצרכן ועלון לרופא של התכשיר שבנדון.
העלונים לרופא ולצרכן עודכנו באפריל 2024.

בהודעה 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.

<u>התווית התכשיר:</u>

Zolgensma is indicated for the treatment of:

- **patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or**
- **patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.**

<u>חומר פעיל:</u>

Onasemnogene abeparvovec 2.0×10^{13} vg/mL

<u>עלון לרופא</u>

העדכונים המהווים עדכון במידע בטיחותי מודגשים בצהוב

4.4 Special warnings and precautions for use

…

<u>Hepatotoxicity</u>

Immune-mediated hepatotoxicity is generally manifested as elevated ALT and/or AST levels. Acute serious liver injury and acute liver failure, including fatal cases, have been reported with onasemnogene abeparvovec use, typically within 2 months after infusion and despite receiving corticosteroids before and after infusion. Immune-mediated hepatotoxicity may require adjustment of the immunomodulatory regimen including longer duration, increased dose, or prolongation of the corticosteroid taper (see section 4.8).

…

- Data from a small study in children weighing ≥8.5 kg to ≤21 kg (aged approximately 1.5 to 9 years), indicate a higher frequency of AST or ALT elevations (in 23 out of 24 patients) compared with frequencies of AST/ALT elevations observed in other studies in patients weighing <8.5 kg (in 31 out of 99 patients) (see section 4.8).

…

Novartis Israel Ltd.
P.O.Box 7126, 6 Tozeret Haaretz street, Tel Aviv
Tel: 972-3-9201111 Fax: 972-3-9229331

נוברטיס ישראל בע"מ.
תוצרת הארץ 6, ת"ד 7126, תל אביב
טלפון : 03-9201111 פקס: 03-922-9331

Thrombocytopenia

…

Post-marketing cases with platelet count <25 x 10^9/L have been reported to occur within three weeks following administration.

Platelet counts should be obtained before onasemnogene abeparvovec infusion and should be closely monitored within the first three weeks following infusion and on a regular basis afterwards, at least weekly for the first month and every other week for the second and third months until platelet counts return to baseline.

Data from a small study in children weighing ≥8.5 kg to ≤21 kg (aged approximately 1.5 to 9 years), indicate a higher frequency of thrombocytopenia (in 20 out of 24 patients) compared with frequencies of thrombocytopenia observed in other studies in patients weighing <8.5 kg (in 22 out of 99 patients) (see section 4.8).

Thrombotic microangiopathy

Several cases of thrombotic microangiopathy (TMA) have been reported with onasemnogene abeparvovec (see section 4.8). Cases generally occurred within the first two weeks after onasemnogene abeparvovec infusion. TMA is an acute and life-threatening condition, which is characterised by thrombocytopenia and microangiopathic haemolytic anaemia. Fatal outcomes have been reported. Acute kidney injury has also been observed. In some cases, concurrent immune system activation (e.g. infections, vaccinations) has been reported (see sections 4.2 and 4.5 for information on administration of vaccinations).

Thrombocytopenia is a key feature of TMA, therefore platelet counts should be closely monitored within the first three weeks following infusion and on a regular basis afterwards (see sub-section 'Thrombocytopenia'). In case of thrombocytopenia, further evaluation including diagnostic testing for haemolytic anaemia and renal dysfunction should be undertaken promptly. If patients show clinical signs, symptoms or laboratory findings consistent with TMA, a specialist should be consulted immediately to manage TMA as clinically indicated. Caregivers should be informed about signs and symptoms of TMA and should be advised to seek urgent medical care if such symptoms occur.

…

4.8 Undesirable effects

…

Table 3 Tabulated list of adverse reactions to onasemnogene abeparvovec

Adverse Reactions by MedDRA SOC/PT and Frequency	
Blood and lymphatic system disorders	
Common	Thrombocytopenia[1)]
~~Not known~~ Uncommon	Thrombotic microangiopathy[2)3)]
Gastrointestinal disorders	
Common	Vomiting

Novartis Israel Ltd.
P.O.Box 7126, 6 Tozeret Haaretz street, Tel Aviv
Tel: 972-3-9201111 Fax: 972-3-9229331

נוברטיס ישראל בע"מ.
תוצרת הארץ 6, ת"ד 7126, תל אביב
טלפון: 03-9201111 פקס: 03-922-9331

Hepatobiliary disorders	
Common	Hepatotoxicity[4)]
~~Not known~~ Uncommon	Acute liver failure[2)3)]
~~Not known~~	~~Acute liver injury~~ [2)]
General disorders and administration site conditions	
Common	Pyrexia
Investigations	
Very common	Hepatic enzyme increased[5)]
Common	Troponin increased[6)]

[1)]Thrombocytopenia includes thrombocytopenia and platelet count decreased.
[2)]Treatment-related adverse reactions reported outside of pre-marketing clinical studies, including in the post-marketing setting.
[3)]Includes fatal cases.
[4)]Hepatotoxicity includes hepatic steatosis and hypertransaminasaemia.
[5)]Hepatic enzyme increased includes: alanine aminotransferase increased, ammonia increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, hepatic enzyme increased, liver function test increased and transaminases increased.
[6)]Troponin increased includes troponin increased, troponin-T increased, and troponin-I increased (reported outside of clinical studies, including in the post-marketing setting).

…

Description of selected adverse reactions

In a study (COAV101A12306) including 24 children weighing ≥8.5 kg to ≤21 kg (aged approximately 1.5 to 9 years; 21 discontinued previous SMA treatment) increased transaminases were observed in 23 out of 24 patients. The patients were asymptomatic and there were no elevations of bilirubin. The AST and ALT elevations were managed with the use of corticosteroids, typically with prolonged duration (at Week 26, 17 patients were continuing prednisolone, at Week 52, 6 patients were still receiving prednisolone) and/or a higher dose.

Transient thrombocytopenia
In the clinical development program (see section 5.1), transient thrombocytopenia was observed at multiple time points post-dose and normally resolved within two weeks. Decreases in platelet counts were more prominent during the first week of treatment. Post-marketing cases with transient decrease in platelet count to levels <25 x 10^9/L within three weeks of administration have been reported (see section 4.4).

In a study (COAV101A12306) including 24 children weighing ≥8.5 kg to ≤21 kg (aged approximately 1.5 to 9 years), thrombocytopenia was observed in 20 out of 24 patients.

…

עלון לצרכן:

העדכונים המהווים עדכון במידע בטיחותי מודגשים בצהוב

2. לפני השימוש בתרופה

…

בדיקות ומעקב

…

זולג'נסמה עלולה להביא לירידה בספירת הטסיות בדם (תרומביציטופניה).
יש לשים לב לסימנים אפשריים של ספירת טסיות דם נמוכה לאחר מתן זולג'נסמה לילדך, כגון חבלות או דימומים

Novartis Israel Ltd.
P.O.Box 7126, 6 Tozeret Haaretz street, Tel Aviv
Tel: 972-3-9201111 Fax: 972-3-9229331

נוברטיס ישראל בע"מ.
תוצרת הארץ 6, ת"ד 7126, תל אביב
טלפון: 03-9201111 פקס: 03-922-9331

חריגים. (ראה סעיף 4 למידע נוסף). רוב המקרים המדווחים של ספירת טסיות דם נמוכה התרחשו במהלך שלושת השבועות הראשונים לאחר מתן זולג'נסמה לילד.

...

4. תופעות לוואי

...

תופעות לוואי שאינן שכיחות (uncommon) - מופיעות ב 1-10 משתמשים מתוך 1000:

~~**שכיחות אינה ידועה (לא ניתן להעריך את התדירות מהנתונים הזמינים):**~~

• הקאות, צהבת (הצהבה של העור או של לובן העיניים) או ערנות מופחתת - אלה עלולים להיות סימנים של פגיעה בכבד (כולל אי ספיקת כבד)

• הופעת חבורות בקלות, פרכוסים, ירידה במתן השתן - אלה עשויים להיות סימנים של מיקרואנגיופתיה תרומבוטית

...

בברכה,
נוברטיס ישראל בע"מ

Novartis Israel Ltd.
P.O.Box 7126, 6 Tozeret Haaretz street, Tel Aviv
Tel: 972-3-9201111 Fax: 972-3-9229331

נוברטיס ישראל בע"מ.
תוצרת הארץ 6, ת"ד 7126, תל אביב
טלפון: 03-9201111 פקס: 03-922-9331