08/2024

# Ultomiris 100 mg/ml

# אולטומיריס 100 מ"ג למ"ל

RAVULIZUMAB 100 MG/ML

CONCENTRATE FOR SOLUTION FOR INFUSION

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**רופא /ה, רוקח/ת נכבד**

חברת אלקסיון פארמה ישראל בע"מ מבקשת להודיע על עדכון העלון לרופא של התכשיר שבנידון.

העלון עודכן בתאריך 08/2024.

ההתוויה הרשומה לתכשיר בישראל:

• Ultomiris is indicated in the treatment of adult and paediatric patients with a body weight of 10 kg or above with paroxysmal nocturnal haemoglobinuria (PNH):

* In patients with haemolysis with clinical symptom(s) indicative of high disease activity.
* In patients who are clinically stable after having been treated with eculizumab for at least the past 6 months.

• Ultomiris is indicated in the treatment of patients with a body weight of 10 kg or above with atypical haemolytic uremic syndrome aHUS who are complement inhibitor treatment naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab.

• Ultomiris is indicated in the treatment of adult patients with generalized myasthenia gravis (gMG) who are antiacetylcholine receptor (AChR) antibody-positive.

• Ultomiris is indicated in the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive.

## בהודעה זו מצוינים העדכונים המהותיים בלבד בעלון לרופא:

מידע שהוסר -מסומן בקו אדום חוצה ~~XXX~~

תוספת -כתב **כחול**

תוספת חמרה - כתב **כחול** -מסומן בצהוב מרקר

מידע שעבר מקום - כתב ירוק

**4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed. Based on the potential inhibitory effect of ravulizumab on complement-dependent cytotoxicity of rituximab, ravulizumab may reduce the expected pharmacodynamic effects of rituximab.

Chronic intravenous human immunoglobulin (IVIg) treatment may interfere with the endosomal neonatal Fc receptor (FcRn) recycling mechanism of monoclonal antibodies such as ravulizumab and thereby decrease serum ravulizumab concentrations.

See Section 4.2 for guidance in case of concomitant PE, PP, or IVIg treatment.

**4.8 Undesirable effects**

The most common adverse reactions with ravulizumab are headache (~~26.6~~ 28.2%), ~~nasopharyngitis (19.5%),~~ upper respiratory tract infection (~~16.8~~ 19.9%), nasopharyngitis (~~17.5~~ 19.5%), diarrhoea (~~14.2~~ 16.9%), pyrexia (~~12.2~~ 16.4%), nausea (~~12.2~~ 13.7%), arthralgia (~~11.3~~ 13.2%), fatigue (~~11.2~~ 13.1%), back pain (~~10.4~~ 12.6%), abdominal pain (~~10.1~~ 11.8%) and dizziness (10.1%). The most serious adverse reactions are meningococcal infection (~~0.6~~ 0.7%) including meningococcal sepsis, encephalitis meningococcal, meningococcal infection (see section 4.4) and disseminated gonococcal infection (0.1%).

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Tabulated list of adverse reactions

(…)

**Table 8: Adverse reactions from clinical trials and postmarketing experience**

| MedDRA System Organ Class | Very common (≥ 1/10) | Common (≥ 1/100 to < 1/10) | Uncommon (≥ 1/1,000 to < 1/100) |
|---|---|---|---|
| **Infections and infestations** | Upper respiratory tract infection, Nasopharyngitis | Urinary tract infection | Meningococcal infection [a], Disseminated Gonococcal infection [b] |
| **Immune system disorders** | | Hypersensitivity [d] | Anaphylactic reaction [c] |
| **Nervous system disorders** | Headache Dizziness | ~~Dizziness~~ | |
| **Gastrointestinal disorders** | Diarrhoea, Nausea, Abdominal pain | Vomiting, Dyspepsia | |
| **Skin and subcutaneous tissue disorders** | | Urticaria, Pruritus, Rash | |
| **Musculoskeletal and connective tissue disorders** | Arthralgia, Back pain | Myalgia, Muscle spasms | |
| **General disorders and administration site conditions** | Pyrexia, Fatigue | Influenza like illness, Chills, Asthenia | |
| **Injury, poisoning and procedural complications** | | Infusion-related reaction | |

[a] Meningococcal infection includes preferred terms of meningococcal infection, meningococcal sepsis, and encephalitis meningococcal

[b] Disseminated gonococcal infection includes preferred terms of disseminated gonococcal infection and gonococcal infection

[c] Estimated from post-marketing experience

[d] Hypersensitivity is a group term for Preferred Term drug hypersensitivity with related causality and Preferred Term hypersensitivity

(…)

Description of selected adverse reactions

(…)

*Paediatric population*

*Paroxysmal nocturnal haemoglobinuria (PNH)*

In paediatric PNH patients (N=13, aged 9 to 17 years old) enrolled in the paediatric PNH Study (ALXN1210-PNH-304), the safety profile appeared similar to that observed in adult PNH patients. The most common adverse reactions reported in paediatric PNH patients were abdominal pain, nausea, ~~and~~ nasopharyngitis and headache, which occurred in ~~2~~ 3 patients (~~15.4~~ 23.1%).

(…)

## 5.1 Pharmacodynamic properties

**(…)**

*Study in complement-inhibitor naïve adult patients with PNH (ALXN1210-PNH-301)*

The complement-inhibitor naïve study was a 26-week, multicentre, open-label, randomised, active-controlled, Phase 3 study conducted in 246 patients who were naïve to complement inhibitor treatment prior to study entry and was followed by a long-term extension period where all patients received ravulizumab. Eligible patients to enter this trial had to demonstrate high disease activity, defined as LDH level ≥ 1.5 × upper limit of normal (ULN) at screening along with the presence of 1 or more of the following PNH-related signs or symptoms within 3 months of screening: fatigue, haemoglobinuria, abdominal pain, shortness of breath (dyspnoea), anaemia (haemoglobin < 10 g/dL), history of a major adverse vascular event (including thrombosis), dysphagia, or erectile dysfunction; or history of packed red blood cell (pRBC) transfusion due to PNH.

(…)

The final efficacy analysis for the study included all patients ever treated with ravulizumab (n=244) and had a median treatment duration of 1423 days. The final analysis confirmed that ravulizumab treatment responses observed during the Primary Evaluation Period were maintained throughout the duration of the study.

*Study in adult PNH patients previously treated with eculizumab (ALXN1210-PNH-302)*

The eculizumab-experienced study was a 26-week, multicentre, open-label, randomised, active-controlled Phase 3 study conducted in 195 patients with PNH who were clinically stable (LDH ≤ 1.5 x ULN) after having been treated with eculizumab for at least the past 6 months and was followed by a long-term extension period where all patients received ravulizumab.
(…)

*Study in paediatric patients with PNH (ALXN1210-PNH-304)*
(…)
Long term efficacy results through end of study over a median treatment duration of 915 days resulted in a sustained treatment response in paediatric patients with PNH.
(…)

**קיימים בעלון עדכונים נוספים**, למידע נוסף יש לעיין בעלון לרופא המעודכן.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום (אלקסיון פארמה ישראל בע"מ, ת.ד. 7063, פתח תקווה 4917001; טלפון: 03-9373753 ; פקס: 03-9373774)

בברכה,
עוז וולך הרוקח הממונה של בעל הרישום