09/2023

Ultomiris 100 mg/ml

אולטומיריס 100 מ"ג למ"ל

RAVULIZUMAB 100 MG/ML

CONCENTRATE FOR SOLUTION FOR INFUSION

Ultomiris 10 mg/ml

אולטומיריס 10 מ"ג למ"ל

RAVULIZUMAB 10 MG/ML

CONCENTRATE FOR SOLUTION FOR INFUSION

רופא /ה, רוקח/ת נכבד

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

העלון עודכן בתאריך 09/2023.

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.

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

4.4 Special warnings and precautions for use

(…)

Infusion-related reactions

Administration of ravulizumab may result in systemic infusion-related reactions and allergic or hypersensitivity reactions, including anaphylaxis (see section 4.8).

~~In clinical trials, infusion reactions were common (1%). These events, which were mild to moderate in severity and transient, included lower back pain, drop in blood pressure, elevation in blood pressure, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste) and drowsiness.~~

In case of systemic infusion-related reaction, if signs of cardiovascular instability or respiratory compromise occur, administration ~~infusion~~ of ravulizumab should be interrupted and appropriate supportive measures should be instituted ~~if signs of cardiovascular instability or respiratory compromise occur~~.

(…)

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.

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

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4.8 Undesirable effects

The most common adverse ~~drug~~ reactions with ravulizumab ~~(very common frequency)~~ are headache (26.6%), nasopharyngitis (17.5%), upper respiratory tract infection (16.8%), diarrhoea (14.2%), pyrexia (12.2%), nausea (12.2%), arthralgia (11.3%), fatigue (11.2%), back pain (10.4%), and abdominal pain (10.1%) ~~upper respiratory tract infection, nasopharyngitis and headache~~. The most serious adverse reactions ~~in patients in clinical trials~~ are meningococcal infection (0.6%) ~~and~~ including meningococcal sepsis and encephalitis meningococcal (see section 4.4).

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], Gonococcal infection [b]
Immune system disorders		Hypersensitivity [d]	~~Hypersensitivity,~~ Anaphylactic reaction [c]
Nervous system disorders	Headache	Dizziness	
Gastrointestinal disorders	Diarrhoea, Nausea, Abdominal pain	Vomiting, ~~Abdominal pain~~ Dyspepsia	
Skin and subcutaneous tissue disorders		Urticaria, Rash, Pruritus	
Musculoskeletal and connective tissue disorders	Arthralgia, Back pain	~~Arthralgia, Back pain,~~ Myalgia, Muscle spasms	
General disorders and administration site conditions	Pyrexia, Fatigue	~~Pyrexia,~~ Influenza like illness, Chills, Asthenia	~~Chills~~
Injury, poisoning and procedural complications		Infusion-related reaction	

[a] Meningococcal infection includes preferred terms of meningococcal infection, ~~and~~ meningococcal sepsis, and encephalitis meningococcal ~~Estimated from post-marketing experianse~~

[b] Gonococcal infection includes disseminated gonococcal infection ~~Meningococcal infection includes preferred terms of meningococcal infection and meningococcal sepsis~~

[c] Estimated from post-marketing experience ~~Gonococcal infection includes disseminated gonococcal infection~~

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

(…)

Description of selected adverse reactions

Meningococcal infection/sepsis/encephalitis

Vaccination reduces, but does not eliminate, the risk of meningococcal infections. In clinical trials, ~~3 out of 261~~ < 1% of ~~adult PNH~~ patients developed serious meningococcal infections~~/sepsis~~ while receiving treatment with ravulizumab; all ~~3~~ were adult patients who had been vaccinated. ~~All 3 recovered while continuing treatment with ravulizumab. In the study in paediatric patients with PNH, no meningococcal infections occurred among 13 patients receiving treatment with ravulizumab. In aHUS studies, no meningococcal infections occurred among 89 patients receiving treatment with ravulizumab. In the gMG study, no meningococcal infections occurred among 86 patients receiving treatment with ravulizumab during the Randomized Controlled Period.~~ Please refer to section 4.4 for information on prevention and treatment of suspected meningococcal infection. In patients treated with ravulizumab, meningococcal infections have presented as meningococcal sepsis and encephalitis meningococcal. Patients should be informed of the signs and symptoms of meningococcal infection ~~septicaemia~~ and advised to seek medical care immediately.

Infusion-related reactions
In clinical trials, infusion-related reactions were common (≥1%). These events, which were mild to moderate in severity and transient, included back pain, abdominal pain, muscle spasms, drop in blood pressure, elevation in blood pressure, rigors, limb discomfort, drug hypersensitivity (allergic reaction), dysgeusia (bad taste), and drowsiness. These reactions did not require discontinuation of ravulizumab.

Immunogenicity
~~Treatment with any therapeutic protein may induce an immune response.~~
(…)

4.9 Overdose
~~No case of overdose has been reported to date~~.
Patients who experience overdose should have immediate interruption of their infusion and be closely monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted**.**

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