04.2025

SOLIRIS
סוליריס

ECULIZUMAB
Concentrate for solution for infusion IV

רופא/ה ,רוקח/ת נכבד/ה,

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

ההתוויה הרשומה לתכשיר בישראל:

Soliris is indicated for the treatment of patients with:
-Paroxysmal nocturnal haemoglobinuria (PNH). Evidence of clinical benefit is demonstrated in patients with haemolysis with clinical symptom(s) indicative of high disease activity, regardless of transfusion history. Eculizumab has not been studied in clinical trials in patients with PNH below 11 years of age.
-Atypical haemolytic uremic syndrome (aHUS).
- Refractory generalized myasthenia gravis (gMG) in patients aged 6 years and above who are antiacetylcholine receptor (AChR) antibody-positive

Soliris is indicated in adults for the treatment of:
-Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibodypositive with a relapsing course of the disease who have received prior therapy

בהודעה זו מצוינים העדכונים המהותיים בעלון לרופא
מידע שהוסר – מסומן ב~~קו אדום חוצה~~
תוספת – כתב כחול
עדכון בטיחות – מסומן ברקע צהוב

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

(…)
Excipients with known effect: Sodium (5 mmol per vial), **polysorbate 80 (6.6 mg per vial).**

4.4 Special warnings and precautions for use

(…)
Excipients with known effect

Sodium ~~**content**~~:
Once diluted with sodium chloride 9 mg/mL (0.9%) solution for injection, this medicinal product contains 0.88 g sodium per 240 mL at the maximal dose, equivalent to 44.0% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Once diluted with sodium chloride 4.5 mg/mL (0.45%) solution for injection, this medicinal product contains 0.67 g sodium per 240 mL at the maximal dose, equivalent to 33.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Polysorbate 80
This medicinal product contains 6.6 mg of polysorbate 80 in each vial (30mL vial) which is equivalent to 0.66 mg/kg or less at the maximum dose for adult patients and paediatric patients with body weight more than 10 kg and is equivalent to 1.32 mg/kg or less at the maximum dose for paediatric patients with body weight 5 to <10 kg. Polysorbates may cause allergic reactions.

4.8 Undesirable effects

(…)

MedDRA System Organ Class	Very Common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)
(…)				
Endocrine disorders				~~Basedow's~~ Grave's disease

(…)

[b] Meningococcal infection includes the following group of PTs: Meningococcal infection, Meningococcal sepsis, Meningitis meningococcal~~, Neisseria infection~~.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Complement Inhibitors ~~Selective immunosuppressants~~, ATC code: L04AJ01 ~~L04AA25~~

(…)

An event of clinical deterioration (MG crisis) was observed in 1 patient (9.1%) during the Primary Evaluation Treatment Period requiring rescue therapy (PE) which was administered between the Week 22 and Week 24 study visits. As a result and due to physician decision, this patient did not have QMG, MG-ADL or other efficacy assessments after Week 20 and did not enter the extension period. **Another 2 patients experienced clinical deteriorations (MG crisis) during the Extension Period requiring rescue therapy (PE and IVIg for clinical deterioration in one case and IVIg and 2 supplemental treatments of eculizumab in the second case)**.

During the **entire study period** ~~Primary Evaluation Treatment Period~~ in paediatric patients with refractory gMG (study ECU-MG-303), ~~1~~ **4** out of 11 patients (~~9~~**36**.~~1~~**4**%) decreased **their** daily dose of anticholinesterase **IST or anticholinesterase therapy due to improved MG symptoms. An additional patient (9.1%) decreased and subsequently increased their daily dose during the Extension Period due to improved and worsened MG symptoms respectively and 1 patient started a new corticosteroid treatment due to worsened MG symptoms** ~~and 3 out of 11 patients (27.3%) decreased their daily dose of corticosteroid, due to improved MG symptoms~~.

Long-term efficacy

All patients who completed the Primary Treatment Period (N=10) entered the Extension Period of up to 208 weeks of treatment. Only two patients completed the Extension Period. Eight participants discontinued the study during the Extension Period including 4 participants transitioned to either commercially available Soliris or Ultomiris or transferred to another ongoing Ultomiris paediatric study.

Patients consistently maintained the response through the study, which was of similar magnitude to that reported to during the initial treatment period.

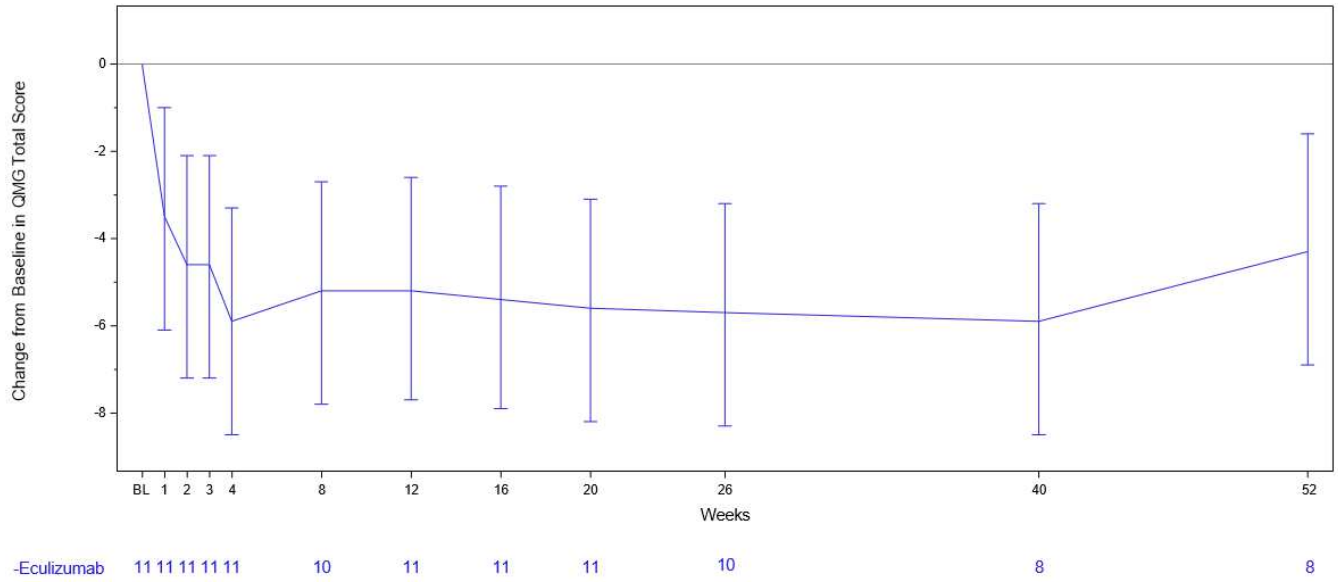

Figure 3: Change from Baseline in QMG Total Score (LS Mean and 95% CI) regardless of Rescue Therapy) during Week 1 to Week 52 Using a Repeated Measures Model

Abbreviations:; LS=Least square; CI=Confidence Interval.

Note: Baseline is defined as the last available assessment value prior to first study drug infusion.

Note: Estimates are based on MMRM that included terms of visit and baseline value.

Mean equal to 0. A compound symmetry covariance structure was used.

(…)

Special Populations

Dedicated studies have not been conducted to evaluate the pharmacokinetics of Soliris in special patient populations identified by gender, race, age (geriatric), or the presence of renal or hepatic impairment. Population PK **(PopPK)** analysis on data collected across studies in PNH, aHUS, gMG and NMOSD patients showed that gender, race, age (geriatric), or the presence of renal or hepatic impairment function do not influence the PK of eculizumab. ~~**Body weight was a significant covariate resulting in a lower eculizumab clearance in pediatric patients, requiring body weight based dosing in pediatric patients**~~.

Paediatric population

The pharmacokinetics of eculizumab was evaluated in Study M07-005 in PNH paediatric patients (aged from 11 to less than 18 years) and in Studies C08-002, C08-003, C09-001r and C10-003 in aHUS pediatric patients (aged 2 months to less than 18 years) and in Study ECU-MG-303 paediatric patients with refractory gMG (aged from 12 years to less than 18 years) **PopPK analysis showed that for PNH, aHUS, refractory gMG, and NMOSD, body weight was a significant covariate requiring body weight-based dosing for pediatric patients** ~~**with body-weight based dose regimen.**~~

~~**Weight was a significant covariate resulting in a lower eculizumab clearance 0.0105 L/h in the adolescent PNH patients.**~~

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

העלון נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום

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בברכה,

עוז וולך הרוקח הממונה של בעל הרישום