MEDISON

ינואר 2025

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

הריני להודיעכם כי העלון לרופא של התכשיר עודכן:

Oxlumo אוקסלומו

SOLUTION FOR INJECTION

הרכב:

Each mL of solution contains lumasiran sodium equivalent to 189 mg lumasiran.

התוויה:

Oxlumo is indicated for the treatment of primary hyperoxaluria type 1 (PH1) in all age groups.

להלן העדכונים בעלון לרופא:

4.8 Undesirable effects

Tabulated list of adverse reactions

Adverse reactions associated with lumasiran obtained from clinical studies and spontaneous reporting are tabulated below. The adverse reactions are coded to preferred terms (PTs) under the MedDRA system organ class (SOC) and are presented by frequency. The frequency of the adverse reactions is expressed according to the following categories: 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); very rare (<1/10,000); not known (cannot be estimated from the available data).

Table 2: Adverse reactions

System organ class	Adverse reaction	Frequency
Immune system disorders	Hypersensitivity[a]	Not known
Gastrointestinal disorders	Abdominal pain[a,b]	Very common
General disorders and administration site conditions	Injection site reaction[b,c]	Very common

[a] Adverse reaction reported during post-marketing use.
[b] Includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort, and abdominal tenderness.
[b,c] Includes injection site reaction, injection site erythema, injection site pain, injection site pruritus, injection site swelling, injection site discomfort, injection site discolouration, injection site mass,

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injection site induration, injection site rash, injection site bruising, injection site haematoma and injection site exfoliation.

[....]

Long-term safety

ILLUMINATE-A (trial description see below)

The safety profile in the open-label extension period (median treatment duration of 55.0 months) was consistent with the known safety profile of lumasiran from the placebo-controlled double-blind period of the study.

5.1 Pharmacodynamic properties

ILLUMINATE-A

A total of 39 patients with PH1 were randomised 2:1 to receive subcutaneous doses of lumasiran or placebo during the 6-month double-blind, placebo-controlled period. Patients 6 years and older with an estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m^2 were enrolled, and received 3 loading doses of 3 mg/kg lumasiran or placebo administered once monthly, followed by quarterly maintenance doses of 3 mg/kg lumasiran or placebo (see section 4.2). After the 6-month double-blind treatment period, patients, including those originally assigned to placebo, entered an extension period with administration of lumasiran for up to 54 months. The overall lumasiran exposure was 165.7 patient years.

[....]

Reduced oxalate levels observed in the double-blind period were maintained with continued lumasiran treatment ~~through~~ up to 60~~24~~ months during the extension period of the study.

eGFR, ~~and~~ renal stone events (reported by events per person-year) and medullary nephrocalcinosis were assessed through the 6-month double-blind and extension periods for a total of up to 60~~24~~ months.

eGFR remained stable in patients administered lumasiran. The mean annual rate of change from baseline during treatment with lumasiran up to 60 months was -0.63 ml/min/1.73 m^2/year.

The rate of renal stone events per person-year reported in patients ~~treated with~~ randomised to lumasiran and placebo in ILLUMINATE-A are presented in Table 4.

Table 4: Rate of renal stone events per person-year reported in the lumasiran and placebo group

Time Period	Lumasiran Rate (95% CI)	Placebo Rate (95% CI)
12 months prior to consent	3.19 (2.57, 3.96)	0.54 (0.26, 1.13)
6-month double-blind period	1.09 (0.63, 1.88)	0.66 (0.25, 1.76)

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~~**Table 4: Rate of Renal Stone Events per Person-Year Reported in the Lumasiran Group**~~

~~Treatment~~	~~Time Period~~	~~Rate (95% CI)~~
~~No treatment~~	~~12 months prior to consent~~	~~3.19 (2.57, 3.96)~~
~~Lumasiran~~	~~6-month double-blind period~~	~~1.09 (0.63, 1.88)~~
	~~Month 6 to month 12~~	~~0.87 (0.47, 1.62)~~
	~~Month 12 to month 18~~	~~0.56 (0.25, 1.24)~~
	~~Month 18 to month 24~~	~~0.63 (0.30, 1.33)~~

~~The rate of renal stone events per person-year reported in patients treated with placebo in ILLUMINATE-A are presented in Table 5. The patients in the placebo group were initially randomised to placebo for the 6-month double-blind period and subsequently treated with lumasiran in the extension periods: month 6 to month 12, month 12 to month 18, and month 18 to month 24.~~ During extended open-label treatment with lumasiran up to 60 months, the rate of renal stone events was 0.49 per person-year, and 53.8% of the patients had no renal stone events.

~~**Table 5: Rate of Renal Stone Events per Person-Year Reported in the Placebo Group**~~

~~Treatment~~	~~Time Period~~	~~Rate (95% CI)~~
~~No treatment~~	~~12 months prior to consent~~	~~0.54 (0.26, 1.13)~~
~~Placebo~~	~~6-month double-blind period~~	~~0.66 (0.25, 1.76)~~
~~Lumasiran~~	~~Month 6 to month 12~~	~~0.16 (0.02, 1.17)~~
	~~Month 12 to month 18~~	~~0.67 (0.25, 1.78)~~
	~~Month 18 to month 24~~	~~0.00 (0.00, 0.62)~~

Medullary nephrocalcinosis results, assessed by renal ultrasound, ~~at~~ from ~~month~~ month 6 ~~and month 12~~ relative to baseline are presented in Table ~~5~~ 6.

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Table ~~65~~: ILLUMINATE-A: Patients with mMedullary nNephrocalcinosis at mMonth 6 Double blind ,placebo controlled period ~~and Month 12~~ rRelative to bBaseline*

Timepoint	Treatment (n)	Improvement	No Change	Worsening
Month 6	Lumasiran (n=23)	3	20	0
	Placebo (n=12)	0	11	1
~~Month 12~~	~~Lumasiran (n=18)~~	~~11~~	4	~~3~~
	~~Placebo/Lumasiran** (n=11)~~	~~1~~	~~9~~	1

* Patients with renal ultrasounds at baseline and the relevant timepoint were assessed.
~~** Patients received placebo for 6 months followed by lumasiran treatment for 6 months.~~

The evaluation of medullary nephrocalcinosis was performed only in a part of the study population (17/26 lumasiran/lumasiran patients and 6/13 placebo/lumasiran patients were evaluated at both baseline and at the end of the 54-month extension period). In this subpopulation a general trend for improvement over time was demonstrated.

העלון לרופא נמצא בקישור וכן מפורסם במאגר התרופות באתר משרד הבריאות וניתן לקבלו מודפס על ידי פניה לבעל הרישום.

בברכה,

שרון עמיר
רוקחת ממונה
מדיסון פארמה בע"מ

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