

OXLUMO® (lumasiran)

Product Fact Sheet

- OXLUMO® (lumasiran) subcutaneous injection is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients.¹
 - » OXLUMO is the first approved PH1 treatment for patients of all ages and stages of kidney function.
 - » OXLUMO is Alnylam's first RNA interference (RNAi) therapeutic FDA-approved for use in children, including infants.
- PH1 is an ultra-rare, inherited disease in which overproduction of oxalate – an unneeded end-product of metabolism – in the liver results in the deposition of calcium oxalate crystals in the kidneys and urinary tract and can lead to the formation of painful and recurrent kidney stones and nephrocalcinosis, which can progress to kidney failure. PH1 can also lead to oxalate deposition in multiple organs beyond the kidney, a condition known as systemic oxalosis.^{2,3}
- OXLUMO targets the messenger RNA, or mRNA, of the hydroxyacid oxidase 1 (*HAO1*) gene. *HAO1* encodes glycolate oxidase (GO) – the liver enzyme involved in the overproduction of oxalate and upstream of the enzyme deficient in patients with PH1. By degrading the *HAO1* mRNA and reducing the synthesis of GO, OXLUMO inhibits production of oxalate – the metabolite that directly contributes to the pathophysiology of PH1.¹
- The efficacy and safety of OXLUMO were evaluated in three pivotal clinical trials as part of the ILLUMINATE clinical program.
- Injection site reactions (ISRs) were the most common drug-related adverse reaction.⁴
- OXLUMO is a subcutaneous injection administered by a healthcare professional. The dose of OXLUMO is determined based on a patient's actual body weight; three starting doses are administered monthly followed by ongoing quarterly or monthly doses (depending on the weight of the patient).¹
- For more information about OXLUMO, please visit [OXLUMO.com](https://oxlumo.com).

OXLUMO Research at a Glance

- The FDA approval of OXLUMO in November 2020 was based on the positive results from the ILLUMINATE-A and ILLUMINATE-B studies. In October 2022, the FDA approved a supplemental New Drug Application (sNDA) for OXLUMO, and the indication was expanded based on ILLUMINATE-C 6-month data. The sNDA approval also included the addition of open-label extension data from ILLUMINATE-A and ILLUMINATE-B.¹
- ILLUMINATE-A is a randomized, double-blind, placebo-controlled multinational Phase 3 study (N=39) to evaluate the safety and efficacy of OXLUMO with a 6-month primary analysis period and an extended 54-month dosing period.⁴
 - » The study enrolled 39 patients with PH1, ages six and above, with relatively preserved kidney function (an estimated glomerular filtration rate [eGFR] ≥ 30 mL/min/1.73m²), at 16 study sites, in eight countries around the world.⁴
 - » OXLUMO achieved the ILLUMINATE-A primary endpoint of percent reduction from baseline, relative to placebo, in 24-hour urinary oxalate excretion averaged across months 3 to 6 and corrected for body surface area.
 - » Specifically, treatment with OXLUMO resulted in a 65% least-squares (LS) mean reduction in urinary oxalate relative to baseline versus 12% reduction reported in response to placebo, resulting in a between-group LS mean difference of 53% relative to placebo ($p=1.7 \times 10^{-14}$) at 6 months.⁵ Reduced urinary oxalate levels were sustained through 54 to 60 months.¹¹
 - » At Month 6, all tested secondary endpoints were met, including the proportion of patients treated with OXLUMO achieving at or below the upper limit of normal* (13/25 patients or 52%; $p=0.001$) and at or below 1.5x upper limit of normal† (21/25 patients or 84%; $p=8.3 \times 10^{-7}$) levels of urinary oxalate, compared to none (0/13) of the patients receiving placebo.⁵

Please see [Important Safety Information](#) and full [Prescribing Information](#) on Page 3.

* Normalization was defined as urinary oxalate levels \leq upper limit of normal (0.514 mmol/24 hr/1.73 m²)

† Near-normalization was defined as urinary oxalate levels ≤ 1.5 x the upper limit of normal (0.771 mmol/24hr/1.73m²)

- » In the 6 month period, no serious or severe adverse events were reported. ISRs were the most common drug-related adverse reaction, reported in 10 out of 26, or 38%, of patients receiving OXLUMO® (lumasiran). No ISRs were reported in patients receiving placebo. These symptoms were generally mild and resolved within one day of the injection and did not lead to discontinuation of treatment.^{1,4}
- ILLUMINATE-B is a single arm, open-label, multinational Phase 3 study (N=18) with a 6-month primary analysis period and an extended 54-month dosing period.⁶
 - » The study enrolled 18 patients under the age of six with an eGFR \geq 45 mL/min/1.73 m² or normal serum creatinine, if less than 12 months old.¹
 - » The primary endpoint of the study was the percent change from baseline to month 6 in spot urinary oxalate:creatinine ratio (UOx:Cr) averaged across months 3 to 6.
 - » In the 6-month primary analysis, patients treated with OXLUMO achieved a 72% mean reduction in spot UOx:Cr from baseline. Sustained reductions in UOx excretion were observed with continued OXLUMO treatment through month 30.¹
- ILLUMINATE-C is a single arm, open-label, multinational Phase 3 study with a 6-month primary analysis period and an extended 54-month dosing period.⁷
 - » The approval of the sNDA was based on positive 6-month primary analysis results.¹
 - » The study enrolled 21 patients of all ages with severe kidney impairment (eGFR \leq 45 mL/min/1.73m² or elevated serum creatinine for patients <12 months of age), including six patients with advanced PH1 who do not yet require dialysis (Cohort A) and 15 patients who are hemodialysis-dependent (Cohort B).
 - » The primary endpoint of the study for Cohort A was the percent change in plasma oxalate (POx) from baseline to month 6, and for Cohort B, the percent change in pre-dialysis plasma oxalate from baseline to month 6.
 - » At 6 months, treatment with OXLUMO led to a 33% (95% CI: - 81.8, 15.2) LS mean reduction in POx from baseline in Cohort A, and a 42% (95% CI: - 50.7, -34.1) LS mean reduction in POx from baseline in Cohort B. Sustained reductions in plasma oxalate levels were observed through 24 months of treatment.¹¹
- In the two single-arm studies in patients with PH1, ILLUMINATE-B and ILLUMINATE-C, the OXLUMO safety profile was similar to that seen in ILLUMINATE-A.¹

RNAi as a Class of Medicines

- Historically, RNA was only thought to be involved in protein synthesis. However, in recent years, RNA has been identified to also play significant roles in regulatory functions within the cell.⁸
- A specific class of RNA, called small-interfering RNA (siRNA), appeared to exert cellular control resulting in gene silencing.⁹ In 2001, researchers confirmed that siRNA-mediated gene silencing did occur in human cells.¹⁰ This form of gene silencing has since become widely known as RNA interference, or RNAi for short and has been the subject of a Nobel Prize in Medicine in 2006.
- The FDA approval of OXLUMO reinforces RNAi as a key platform for the development of therapeutics for complex, serious conditions for patients with limited treatment options.

Access to OXLUMO: Alnylam Assist®

The Alnylam Assist® program offers support services to patients throughout their treatment with OXLUMO, including helping patients understand their insurance coverage and options for financial support based on eligibility. An Alnylam Case Manager will work with a patient to begin treatment with and maintain access to OXLUMO. An Alnylam Patient Education Liaison can provide education to help patients and their family members better understand the disease and answer questions about OXLUMO. Learn more about Alnylam Assist by visiting AlnylamAssist.com/OXLUMO.

Please see [Important Safety Information](#) and full [Prescribing Information](#) on Page 3.

IMPORTANT SAFETY INFORMATION

Adverse Reactions

The most common ($\geq 20\%$) adverse reaction reported in patients treated with OXLUMO was injection site reaction. Injection site reactions included erythema, swelling, pain, hematoma, pruritus, and discoloration.

Pregnancy and Lactation

No data are available on the use of OXLUMO in pregnant women. No data are available on the presence of OXLUMO in human milk or its effects on breastfed infants or milk production. Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for OXLUMO and any potential adverse effects on the breastfed child from OXLUMO or the underlying maternal condition.

INDICATION

OXLUMO® (lumasiran) is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in children and adults.

For additional information about OXLUMO, please see the full [Prescribing Information](#).

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