Lumasiran: Injection Site Reactions

The following information is provided in response to your unsolicited inquiry. It is intended to provide you with a review of the available scientific literature and to assist you in forming your own conclusions in order to make healthcare decisions. This document is not for further dissemination or publication without authorization.

The full Prescribing Information for OXLUMO® (lumasiran) is provided here. Alnylam Pharmaceuticals does not recommend the use of its products in any manner that is inconsistent with the approved Prescribing Information. This resource may contain information that is not in the approved Prescribing Information.

If you are seeking additional scientific information related to Alnylam medicines, you may visit the Alnylam US Medical Affairs website at RNAiScience.com.

SUMMARY

- In placebo-controlled and open-label clinical studies the most common adverse reaction reported was injection site reaction. Injection site reactions included erythema, swelling, pain, hematoma, pruritus, and discoloration. These symptoms were generally mild and resolved within one day of the injection and did not lead to discontinuation of treatment.[1]
- There were no protocols for the management of ISRs in patients receiving lumasiran injection in the lumasiran clinical studies. Healthcare professionals should exercise their clinical judgement for the management of ISRs.

INDEX

OXLUMO PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following section(s) of the OXLUMO Prescribing Information[1]:

- DOSAGE AND ADMINISTRATION Section 2.2 Administration Instructions
- ADVERSE REACTIONS Section 6.1 Clinical Trials Experience

CLINICAL DATA

Phase 1 Study and Phase 1/2 OLE Study

The Phase 1/2 study was a single-blind, placebo-controlled, single and multiple ascending dose study to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamics of subcutaneously administered lumasiran in healthy adult subjects and patients with PH1.[2]

- In Part A of the study, 32 healthy volunteers were randomized to receive a single SC dose of lumasiran 0.3 mg/kg (n=6), 1.0 mg/kg (n=6), 3.0 mg/kg (n=6), 6.0 mg/kg (n=6), or placebo (n=8).[2,3]

- In Part B of the study, 20 patients with PH1 were randomized (3:1) to receive multiple doses of either placebo (n=3), 1.0 mg/kg of lumasiran every 28 days for 3 doses (n=3), 3.0 mg/kg every 28 days for 3 doses (n=3), or 3.0 mg/kg every 84 days for 2 doses (n=3).[2]
- The OLE cohorts received doses of lumasiran at a dosage of either 1.0 mg/kg every 28 days for 3 doses (n=4) or 3.0 mg/kg every 28 days for 3 doses (n=4).[2]

In Part A of the study, self-limiting ISRs were reported in 4 (17%) patients who received lumasiran. In Part B of the study, self-limiting ISRs were reported in 3 (15%) patients who received lumasiran. These ISRs were mild or moderate in severity and did not lead to treatment interruption or discontinuation.[2,3]

Phase 2 OLE Study

The Phase 2 OLE study of lumasiran was a multicenter, open-label, extension study to evaluate the long-term safety and tolerability of lumasiran in patients with PH1 (N=20) who were previously dosed in the lumasiran Phase 1/2 study.[4]

Through 54 months of the Phase 2 OLE study, ISRs were reported in 8 (40%) patients who received lumasiran. These ISRs were mild and resolved, generally within 3 days. ISR's were the most frequently reported TEAEs. Of 427 total doses of lumasiran, 13 (3%) were associated with ISRs, all of which occurred in the first 18 months of the study.[4]

ILLUMINATE-A Study

ILLUMINATE-A was a phase 3, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of lumasiran in adults and children ≥6 years old with PH1 and an eGFR ≥30 mL/min/1.73m^2. Patients were randomized (2:1) to receive subcutaneous injections of lumasiran 3 mg/kg (N=26) or placebo (N=13) once monthly for 3 loading doses, followed by maintenance doses once every 3 months beginning 1 month after the last loading dose. The primary endpoint was the percent change from baseline in 24-hour UOx excretion corrected for BSA at 6 months (average of visits from month 3 through 6). After the 6-month double-blind treatment period, all patients received lumasiran in an optional 54-month OLE.[5] Of the 39 patients enrolled, 13 of the 13 in the placebo crossover arm and 24 of the 26 in the continuous lumasiran group completed treatment in the 54-month OLE.[6]

<u>Double-Blind Phase</u>

During the six-month double-blind period, ISRs were reported in 10 (38%) patients (N=26) who received lumasiran compared with 0 in patients on placebo (N=13). Symptoms included pain, pruritus, and discomfort, which were mild in severity, transient, and did not lead to discontinuation of treatment.[5]

<u>Open-Label Extension Phase</u>

At 54 months, ISRs were reported in 14 (36%) patients (N=39) who received lumasiran. These ISRs were transient, mild in severity, and resolved without sequelae.[6]

ILLUMINATE-B Study

ILLUMINATE-B (N=18) was a phase 3, open-label, single-arm study with a 6-month primary analysis period followed by an ongoing 54-month extension period to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in infants and young children <6 years old with PH1 and an eGFR >45 mL/min/1.73m^2 (or normal serum creatinine for infants <12 months old). Patients

received subcutaneous injections of lumasiran as determined by a body weight-based dosing regimen. The primary endpoint was the percent change from baseline in spot UOx:Cr at 6 months.[7]

At 30 months, ISRs were reported in 3 (17%) patients who received lumasiran. Symptoms included erythema, discoloration, and pain at the injection site, which were transient, mild in severity, and did not result in treatment interruptions or discontinuation.[7]

ILLUMINATE-C Study

The ILLUMINATE-C study was a phase 3, open-label, single-arm study with a 6-month primary analysis period followed by an ongoing 54-month extension period to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in full term infants to adult patients with advanced PH1 with an eGFR ≤45 mL/min/1.73m^2 (or elevated serum creatinine if <12 months old) and POx ≥20 µmol/L. Patients enrolled in the study included those not receiving hemodialysis in Cohort A (N=6) and those receiving hemodialysis in Cohort B (N=15). Patients received subcutaneous injections of lumasiran as determined by a body weight-based dosing regimen. The primary endpoints were the percent change from baseline in POx at 6 months (Cohort A) and percent change from baseline in predialysis POx at 6 months (Cohort B).[8]

At 24 months, ISRs were reported in 5 (24%) patients who received lumasiran. ISRs were mild in severity.[9]

ABBREVIATIONS

BSA = body surface area; Cr = creatinine; eGFR = estimated glomerular filtration rate; ISR = injection site reaction; OLE = open-label extension; PH1 = primary hyperoxaluria type 1; POx = plasma oxalate; TEAE = treatment-emergent adverse event; UOx = urinary oxalate.

Updated 21 January 2026

REFERENCES

1. OXLUMO (lumasiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals.
2. Frishberg Y, Deschênes G, Groothoff JW, et al. Phase 1/2 study of lumasiran for treatment of primary hyperoxaluria type 1: A placebo-controlled randomized clinical trial. *Clin J Am Soc Nephrol*. 2021;16(7):1025-1036. doi:10.2215/CJN.14730920
3. Supplement to: Frishberg Y, Deschênes G, Groothoff JW, et al. Phase 1/2 study of lumasiran for treatment of primary hyperoxaluria type 1: A placebo-controlled randomized clinical trial. *Clin J Am Soc Nephrol*. 2021;16(7):1025-1036. doi:10.2215/CJN.14730920
4. Frishberg Y, Groothoff JW, Hulton S-A, et al. Long-term lumasiran therapy final results from a phase 2 open-label extension study in primary hyperoxaluria. *Nephrol Dial Transplant*. September 2025. doi:10.1093/ndt/gfaf188
5. Garrelfs SF, Frishberg Y, Hulton SA, et al. Lumasiran, an RNAi therapeutic for primary hyperoxaluria type 1. *N Engl J Med*. 2021;384(13):1216-1226. doi:10.1056/NEJMoa2021712
6. Frishberg Y, Saland JM, Lieske JC, et al. Final results of the ILLUMINATE-A phase 3 clinical trial of lumasiran for primary hyperoxaluria 1. *Clin J Am Soc Nephrol*. December 2025. doi:10.2215/CJN.0000000916
7. Frishberg Y, Hayes W, Shasha-Lavsky H, et al. Efficacy and safety of lumasiran for infants and young children with primary hyperoxaluria type 1: 30-month analysis of the phase 3 ILLUMINATE-B trial. *Front Pediatr*. 2024;12. doi:10.3389/fped.2024.1392644
8. Michael M, Groothoff JW, Shasha-Lavsky H, et al. Lumasiran for advanced primary hyperoxaluria type 1: Phase 3 ILLUMINATE-C trial. *Am J Kidney Dis*. 2023;81(2):145-155. doi:10.1053/j.ajkd.2022.05.012
9. Sellier-Leclerc A-L, Magen D, Shasha-Lavsky H, et al. Efficacy and safety of lumasiran for advanced primary hyperoxaluria type 1: 24-month follow-up of the phase 3 ILLUMINATE-C trial. *Am J Kidney Dis*. 2025;86(2):285-288. doi:10.1053/j.ajkd.2025.01.016