Lumasiran: Pregnancy and Lactation

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

- No data on the safety of lumasiran are available in pregnant or lactating women.
- In lumasiran preclinical studies, there was no impact on fertility endpoints observed in male or female rats.[1]
- In the Phase 2 OLE study and ILLUMINATE-A, ILLUMINATE-B, and ILLUMINATE-C studies, which evaluated the safety and efficacy of lumasiran in full term infants to adult patients with PH1[2–9]:
  - Pregnant or breastfeeding women were excluded from participation, and females of childbearing potential were required to initiate an effective birth control method.
  - The need for contraception and compliance with contraception requirements was assessed at every visit for adolescent patients.
  - Pregnancy testing was performed before every dose for women of childbearing potential throughout the study. For any women with a positive pregnancy test during the study, the study drug was discontinued but the patient was followed for safety outcomes.
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns associated with exposure to lumasiran in pregnant or lactating women. The use of lumasiran in pregnant or lactating women and effects on pregnancy outcomes remains missing information and continues to be closely monitored through pharmacovigilance activities.[10]

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PRECLINICAL DATA

Placental Transfer

Placental, fetal liver, and fetal tissue concentrations of lumasiran were measured concomitantly with studies on embryo-fetal development in rats and rabbits. Lumasiran was not detected in fetal tissue and liver samples. No lumasiran was detected in the placenta of the low dose group (3 mg/kg) and only in low concentrations in the higher dose groups (10 mg/kg and 30 mg/kg) of both species.[11]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns associated with exposure to lumasiran in pregnant or lactating women. The use of lumasiran in pregnant or lactating women and effects on pregnancy outcomes remains missing information and continues to be closely monitored through pharmacovigilance activities.[10]

OXLUMO PRESCRIBING INFORMATION – RELEVANT CONTENT

The **USE IN SPECIFIC POPULATIONS** section provides the following information[1]:

Pregnancy

Risk Summary

There are no available data with the use of OXLUMO in pregnant women to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

No adverse effects on pregnancy or embryo-fetal development related to OXLUMO were observed in rats at 45 times and in rabbits at 90 times the maximum recommended human dose in women (see Data).

The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an embryo-fetal development study in pregnant rats, lumasiran was administered subcutaneously at doses of 3, 10, and 30 mg/kg/day during organogenesis (gestational days 6-17). Administration of lumasiran resulted in no effects on embryo-fetal survival or fetal body weights and no lumasiran-related fetal malformations were observed. The 30-mg/kg/day dose in rats is 45 times the maximum recommended human dose (MRHD) for women of 3 mg/kg/month normalized to 0.1 mg/kg/day, based on body surface area. In an embryo-fetal development study in female rabbits, lumasiran was administered subcutaneously at doses of 3, 10, and 30 mg/kg/day during organogenesis (gestational days 7-19). There were decreases in maternal food consumption and decreases in maternal body weight gains at doses ≥3 mg/kg/day. There were no lumasiran-related fetal findings identified at doses up to 30 mg/kg/day (90 times the normalized MRHD based on body surface area).

In a postnatal development study, lumasiran administered subcutaneously to pregnant female rats on gestational days 7, 13, 19 and on lactation days 6, 12, and 18 through weaning at doses up to 50 mg/kg did not produce maternal toxicity or developmental effects in the offspring.

Lactation

Risk Summary

There are no data on the presence of OXLUMO in human milk, the effects on the breastfed child, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OXLUMO and any potential adverse effects on the breastfed child from OXLUMO or from the underlying maternal condition.

ABBREVIATIONS

BSA = body surface area; MRHD = maximum recommended human dose; PH1 = primary hyperoxaluria type 1; OLE = open-label extension.

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