

Givosiran: Use in Patients with Pre-Existing Renal Impairment

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 GIVLAARI® (givosiran) 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

- The ENVISION study a phase 3, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of givosiran in patients with a documented diagnosis of AHP.¹
 - Patients with an eGFR of less than 30 mL/min/1.73m² were excluded from the study.²
 - At baseline, 25% of patients had a medical history of renal impairment, and 34% of patients had an eGFR of less than 60 mL/min/1.73m².³
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns regarding the use of givosiran in patients with ESRD or on dialysis.⁴
- No clinically meaningful differences in givosiran pharmacokinetics or pharmacodynamics (percent reduction in urinary ALA and PBG) were observed based on age (19 to 65 years), sex, race/ethnicity, mild, moderate or severe renal impairment (eGFR \geq 15 to <89 mL/min/1.73m² estimated by the Modification of Diet in Renal Disease [MDRD] formula).⁵

INDEX

[Clinical Data](#) – [Global Safety Database](#) – [Label Information](#) – [Abbreviations](#) – [References](#)

CLINICAL DATA

ENVISION Study

The ENVISION study was a phase 3, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of givosiran in patients with a documented diagnosis of AHP. Enrolled patients were randomized on a 1:1 basis to receive subcutaneous injections of givosiran 2.5 mg/kg or placebo once a month for 6 months, followed by an optional 30-month OLE.¹

Patients with an eGFR of less than 30 mL/min/1.73m² were excluded from the study.² At baseline, 25% of patients had a medical history of renal impairment, and 34% of patients had an eGFR of less than 60 mL/min/1.73m².³ Subgroup analyses regarding the use of givosiran in patients with renal impairment have not been conducted.

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any new safety concerns regarding the use of givosiran in patients with ESRD or on dialysis. An analysis of the available data did not change the benefit-risk balance of givosiran. The use of givosiran in patients with ESRD or on dialysis is closely monitored through routine pharmacovigilance activities.⁴

GIVLAARI PRESCRIBING INFORMATION – RELEVANT CONTENT

The **CLINICAL PHARMACOLOGY** section provides the following information⁵:

Pharmacokinetics

Specific Populations

No clinically meaningful differences in givosiran pharmacokinetics or pharmacodynamics (percent reduction in urinary ALA and PBG) were observed based on age (19 to 65 years), sex, race/ethnicity, mild, moderate or severe renal impairment (eGFR ≥ 15 to < 89 mL/min/1.73m² estimated by the Modification of Diet in Renal Disease [MDRD] formula), and mild hepatic impairment (bilirubin $\leq 1 \times$ ULN and AST $> 1 \times$ ULN, or bilirubin $> 1 \times$ ULN to $1.5 \times$ ULN). The effect of end-stage renal disease (eGFR < 15 mL/min/1.73m²), and moderate to severe hepatic impairment on givosiran pharmacokinetics is unknown.

ABBREVIATIONS

AHP = acute hepatic porphyria; ALA = aminolevulinic acid; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; OLE = open-label extension; PBG = porphobilinogen; ULN = upper limit of normal.

Updated 1 May 2025

REFERENCES

1. Kuter DJ, Bonkovsky HL, Monroy S, et al. Efficacy and safety of givosiran for acute hepatic porphyria: Final results of the randomized phase III ENVISION trial. *J Hepatol.* 2023;79(5):1150-1158. doi:10.1016/j.jhep.2023.06.013
2. Protocol for: Balwani M, Sardh E, Ventura P, et al. Phase 3 trial of RNAi therapeutic givosiran for acute intermittent porphyria. *N Engl J Med.* 2020;382(24):2289-2301. doi:10.1056/NEJMoa1913147
3. Balwani M, Sardh E, Ventura P, et al. Phase 3 trial of RNAi therapeutic givosiran for acute intermittent porphyria. *N Engl J Med.* 2020;382(24):2289-2301. doi:10.1056/NEJMoa1913147
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-GIVO-2500004.
5. GIVLAARI (givosiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.