Givosiran: Use in Pediatric Patients

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.

INDEX

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 (N=48) or placebo (N=46) once a month for 6 months, followed by an optional 30-month OLE. The primary endpoint was the annualized rate of composite porphyria attacks among patients with AIP at 6 months.[1]

Per the ENVISION study protocol, patients ≥12 years of age were eligible to be included in the study.[2] The youngest patient enrolled in the study was 19 years of age, as shown in **Table 1**.[1]

Table 1. Age of Enrolled Patients at Baseline in ENVISION.[1]

	Placebo crossover (N=46)	Continuous givosiran (N=48)	All givosiran (N=94)
Age at screening, years, median (range)	36.0 (20-60)	42.0 (19-65)	37.5 (19-65)

ELEVATE Registry

The ELEVATE registry (NCT04883905) is a global, prospective, observational study designed to characterize the real-world long-term safety and efficacy of givosiran and to describe the natural history and management of patients with AHP. Patient characteristics at enrollment are available for 93 patients who have received givosiran. The youngest patient enrolled in the study was 14 years of age, as shown in **Table 2**.[3]

Table 2. Age of Enrolled Patients at Baseline in ELEVATE.[3]

	Patients[a] Ever Treated with Givosiran			
	AIP (N=84, 90.3%)	VP (N=7, 7.5%)	HCP (N=2, 2.2%)	Total (N=93)
Age at entry, years, median (range)	41.5 (14-71)	43 (34-62)	54.5 (43-66)	42 (14-71)

[a]None of the enrolled patients had ADP.
Abbreviations: ADP = ALAD deficient porphyria; AIP = acute intermittent porphyria; HCP = hereditary coproporphyria; VP = variegate porphyria.

Prospective data collection is ongoing.[3] No additional data from clinical studies are available regarding the use of givosiran in pediatric patients.

CASE REPORTS

The following information provides an overview of a published case report regarding a pediatric patient who received givosiran. It is not intended to be an all-inclusive list or summary of relevant publications, abstracts, and manuscripts.

Mazzoli M, et al. Recovery of chronic motor neuropathy due to acute intermittent porphyria after givosiran treatment in a young boy: a case report. *Eur Rev Med Pharmacol Sci*. 2024;28(8):3268-3274. doi:10.26355/eurrev_202404_36055[4]

- A case report detailed the treatment outcome of a 12-year-old patient with AIP and severe chronic porphyric neuropathy. The patient was diagnosed at 5 years of age after an acute porphyric attack, and genetic analysis confirmed a pathogenic mutation in the HMBS gene.
- The patient was initially treated with routine heme arginate infusions and continued to experience frequent porphyric attacks. The patient's neuropathy progressively worsened over time, necessitating the use of a wheelchair due to severe walking impairment. Givosiran treatment was initiated at 2.5 mg/kg monthly. Clinical assessments were performed at baseline and at 3, 6, 9, and 12 months after treatment initiation with givosiran. Neurophysiologic evaluations were performed at baseline and at 6 and 12 months after treatment initiation.
- During the 12 months of givosiran treatment, there were no acute porphyric attacks, and urinary ALA and PBG levels decreased. No SAEs were reported, and heme arginate infusions were discontinued at the beginning of treatment. Neurological scales demonstrated improvement in distal limb muscle strength, pain, disability, and QOL.

GIVLAARI PRESCRIBING INFORMATION – RELEVANT CONTENT

The INDICATIONS AND USAGE section provides the following information[5]:

GIVLAARI is indicated for the treatment of adults with acute hepatic porphyria (AHP).

The USE IN SPECIFIC POPULATIONS section provides the following information[5]:

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ABBREVIATIONS

ADP = ALAD deficient porphyria; AHP = acute hepatic porphyria; AIP = acute intermittent porphyria; ALA = aminolevulinic acid; HCP = hereditary coproporphyria; HMBS = hydroxymethylbilane synthase; OLE = open-label extension; PBG = porphobilinogen; QOL = quality of life; SAE = serious adverse event; VP = variegate porphyria.

Updated 21 May 2024

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. Wang B, Cassiman D, Gouya L, et al. Characteristics of patients treated with givosiran in ELEVATE, a global observational longitudinal registry of patients with acute hepatic porphyria. Presented at: American Association for the Study of Liver Diseases (AASLD) The Liver Meeting; November 10-14, 2023; Boston, MA, USA.
4. Mazzoli M, Ricci A, Vaudano AE, et al. Recovery of chronic motor neuropathy due to acute intermittent porphyria

after givosiran treatment in a young boy: a case report. *Eur Rev Med Pharmacol Sci*. 2024;28(8):3268-3274. doi:10.26355/eurrev_202404_36055
5. GIVLAARI (givosiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.