Givosiran: Monthly Dosing Timeframe

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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.

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SUMMARY

- As part of the ENVISION study protocol, givosiran 2.5 mg/kg was administered subcutaneously once monthly. Study drug administration was initially aligned with monthly study visits, scheduled every 28 days (±7 days). Starting in April 2020, the protocol was adjusted to account for complications posed by COVID-19, extending the scheduling interval to every 28 days (±14 days).[1,2]

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CLINICAL DATA

ENVISION Study

The phase 3 ENVISION study was a 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.[3,4]

Study drug administration was aligned with monthly study visits which were scheduled every 28 (±7) days.[1] In April 2020, changes to the protocol of the ENVISION study were made to account for complications of scheduling assessments due to COVID-19. This included expanding the study drug administration (and study visit) window from 28 (±7) days to 28 (±14) days. Study visit scheduling was acceptable in that time range as long as the study drug doses were administered at least 14 days apart.[2]

GIVLAARI PRESCRIBING INFORMATION – RELEVANT CONTENT

The DOSAGE AND ADMINISTRATION section provides the following information[5]:

The recommended dose of GIVLAARI is 2.5 mg/kg administered via subcutaneous injection once monthly. Dosing is based on actual body weight.

Missed Dose

Administer GIVLAARI as soon as possible after a missed dose. Resume dosing at monthly intervals following administration of the missed dose.

Dose Modification for Adverse Reactions

In patients with severe or clinically significant transaminase elevations, who have dose interruption and subsequent improvement, reduce the dose to 1.25 mg/kg once monthly [see Warnings and Precautions (5.2)]. In patients who resume dosing at 1.25 mg/kg once monthly without recurrence of severe or clinically significant transaminase elevations, the dose may be increased to the recommended dose of 2.5 mg/kg once monthly.

ABBREVIATIONS

AHP = acute hepatic porphyria; AIP = acute intermittent porphyria; OLE = open-label extension.

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REFERENCES

1. 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.
2. Alnylam Pharmaceuticals. Data on file. MED-ALL-AS1-2100016.
3. 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
4. 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
5. GIVLAARI (givosiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.