FDA approves givosiran for acute hepatic porphyria

On November 20, 2019, the Food and Drug Administration approved givosiran (GIVLAARI, Alnylam Pharmaceuticals, Inc.) for adults with acute hepatic porphyria (AHP).

Efficacy was evaluated in ENVISION (NCT03338816), a randomized, double–blind, placebo–controlled, multinational trial enrolling 94 patients with AHP. Patients were randomized (1:1) to receive once monthly subcutaneous injections of givosiran 2.5 mg/kg or placebo during a 6–month double–blind period.

The primary efficacy outcome measure was the rate of porphyria attacks requiring hospitalizations, urgent healthcare visit, or intravenous hemin administration at home. The mean rates of attacks over a 6-month time period were 1.9 (95% CI:1.3,2.8) for patients receiving givosiran and 6.5 (95% CI:4.5, 9.3) for those on placebo. On average, patients with AHP on givosiran experienced 70% (95% CI: 60%, 80%) fewer porphyria attacks compared to placebo.

The most common adverse reactions (>20% of patients) included nausea and injection site reactions. The label contains warnings for anaphylactic reactions, hepatic and renal toxicities, and injection site reactions. Hepatic toxicity was mostly transaminase elevation. Renal toxicity was mostly serum creatinine elevation and decreases in estimated glomerular filtration rate.

The recommended givosiran dose is 2.5 mg/kg once monthly by subcutaneous injection.

View full prescribing information for GIVLAARI (https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/0212194s000lbl.pdf).

FDA granted this application priority review and orphan product and breakthrough therapy designations. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics).

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm) or by calling 1-800-FDA-1088.

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate (https://www.fda.gov/about-fda/oncology-center-excellence/project-facilitate) at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov (mailto:OncProjectFacilitate@fda.hhs.gov).

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