Introducing GIVLAARI™ (givosiran)

NOW APPROVED

to treat **acute hepatic porphyria (AHP) in adults**

What is GIVLAARI?

GIVLAARI is a prescription medicine used to treat acute hepatic porphyria (AHP) in adults.

Important Safety Information

Do not use GIVLAARI if you have ever had a severe allergic reaction to GIVLAARI.

Please see Important Safety Information throughout this brochure and full Prescribing Information.

About GIVLAARI™ (givosiran)

What is GIVLAARI?

GIVLAARI is the first and only FDA-approved medicine for the treatment of adults with acute hepatic porphyria (AHP). There are 4 types of AHP:

- Acute intermittent porphyria (AIP)
- Variegate porphyria (VP)
- Hereditary coproporphyria (HCP)
- ALAD-deficiency porphyria (ADP)

What is AHP?

Acute hepatic porphyria, or AHP, is a family of rare, genetic diseases that can cause severe and potentially life-threatening attacks. Some people with AHP also have chronic, debilitating symptoms when they are not having an attack.

In people with AHP, the heme production process in the liver does not work properly because of a genetic mutation. In the liver, this process is controlled by an enzyme called delta-aminolevulinate synthase 1 (ALAS1).

When ALAS1 is activated, the heme production process is unable to keep up. This causes neurotoxic substances called aminolevulinic acid (ALA) and porphobilinogen (PBG) to build up. ALA and PBG are associated with attacks and other AHP symptoms.

GIVLAARI reduces the amount of ALAS1 in the liver, which leads to a reduction in levels of the neurotoxins ALA and PBG.

Important Safety Information

GIVLAARI can cause a severe allergic reaction:

Tell your doctor or nurse right away if you experience any of the following signs or symptoms of a severe allergic reaction during treatment:

- Swelling – mainly of the lips, tongue or throat which makes it difficult to swallow or breathe
- Breathing problems or wheezing
- Feeling dizzy or fainting
- Rash or hives
- Itching

If you have a severe allergic reaction, your doctor or nurse will stop GIVLAARI treatment right away and you may need to take other medicines to control the symptoms.

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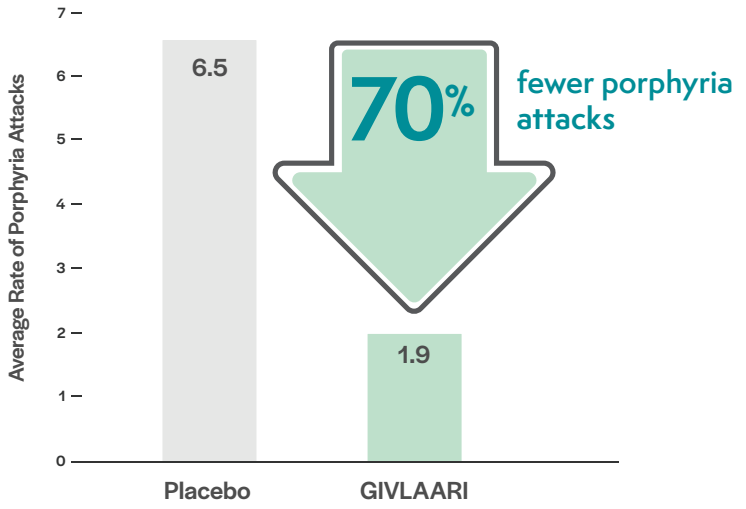
GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL

In a 6-month study:

GIVLAARI™ (givosiran) reduced AHP attacks compared to placebo

GIVLAARI was tested against a placebo in a clinical study of 94 adults with AHP who had ≥2 attacks* in the past 6 months. In the study, patients received either GIVLAARI or a placebo (an injection that did not contain any medication) once monthly over a 6-month period.

Patients with AHP taking GIVLAARI experienced 70% fewer porphyria attacks* on average compared to those on placebo



*Attacks were defined as those that required hospitalization, urgent healthcare visit, or intravenous (IV) hemin at home.

GIVLAARI is given as an injection under the skin once a month by a healthcare professional.

Important Safety Information

GIVLAARI can cause injection site reactions:

GIVLAARI is given as an injection under the skin (called a "subcutaneous injection"). Reactions to this injection may happen during treatment with GIVLAARI.

Tell your doctor or nurse right away if you experience any of the following symptoms of an injection site reaction during treatment: redness, pain, itchiness, rash, discoloration, or swelling around the injection site.

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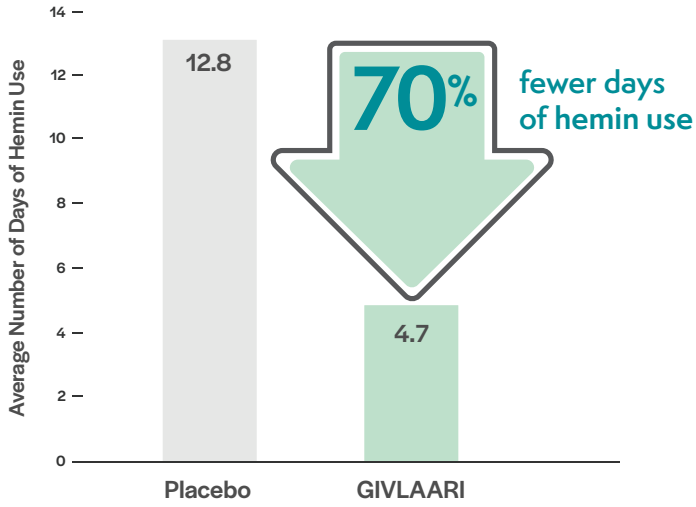
GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL

In a 6-month study:

GIVLAARI™ (givosiran) also reduced days of hemin use compared to placebo

Patients with AHP taking GIVLAARI had 70% fewer days of hemin use on average compared to those on placebo



Important Safety Information

GIVLAARI can cause liver problems:
Your doctor will check your liver function by doing blood tests:

- Before you start using GIVLAARI
- Once a month for the first 6 months of treatment
- And when they think it is needed

If these tests show abnormal results, your doctor or nurse will decide whether to temporarily interrupt or stop treatment with GIVLAARI.

GIVLAARI can cause kidney problems:
Your doctor will check how your kidneys are working while you are using GIVLAARI.

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GIVLAARI™ (givosiran) safety information

The most common side effects in patients treated with GIVLAARI in the 6-month study are in the table below.

	GIVLAARI (N=48)	PLACEBO (N=46)
Nausea	13 (27%)	5 (11%)
Injection site reactions	12 (25%)	0
Rash	8 (17%)	2 (4%)
Changes in kidney function	7 (15%)	2 (4%)
Changes in liver function	6 (13%)	1 (2%)
Fatigue	5 (10%)	2 (4%)

Important Safety Information

What are the common side effects of GIVLAARI?

The most common side effects of GIVLAARI are nausea and injection site reactions. These are not all the possible side effects of GIVLAARI. Talk to your doctor about side effects that you experience. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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Getting started on GIVLAARI™ (givosiran)

Alnylam Assist® is here to help

As you begin your treatment with GIVLAARI, Alnylam Assist® will provide you with a dedicated Alnylam Case Manager and Patient Education Liaison for ongoing support throughout treatment.

What is Alnylam Assist®?

Alnylam Assist® is a personalized support program for patients receiving GIVLAARI. Our services include:

Navigating your insurance benefits

We will review your insurance coverage and answer questions about your insurance benefits for GIVLAARI.

Financial assistance

Alnylam is committed to making GIVLAARI available to those who need it. When you and your doctor decide to start treatment, your Case Manager will work with you to determine eligibility for one of Alnylam's financial assistance programs.*

- If you have commercial insurance, our Copay Program offers assistance with drug-related out-of-pocket expenses—including copays and co-insurance—regardless of your financial status
- If you do not have insurance, or are unable to pay for treatment, our Patient Assistance Program may be able to provide you with GIVLAARI at no cost
- Talk to your Case Manager to learn more about Alnylam financial assistance program eligibility

A dedicated support team

Whether you have questions about navigating insurance, getting started on treatment, or locating additional resources for people with AHP, there is a dedicated team ready to help. Call Alnylam Assist® to speak to your Case Manager or Patient Education Liaison to learn more.

*Individuals must meet specified eligibility criteria to qualify for assistance. Alnylam reserves the right to make eligibility determinations and to modify or discontinue the program at any time.

GIVLAARI™ (givosiran) injection for subcutaneous use 189 mg/mL

Partner with your dedicated support team

A dedicated Case Manager

When you and your healthcare professional choose to begin treatment with GIVLAARI™ (givosiran), you will be partnered with a dedicated Alnylam Case Manager. Case Managers are experienced in helping individuals get started on treatment and providing ongoing support. They will tailor their level of contact based on your personal needs.

A dedicated Patient Education Liaison

Our Patient Education Liaisons have backgrounds in nursing and genetic counseling, and are experienced in educating people and their families about matters related to AHP. Your Patient Education Liaison can help you in a variety of ways, such as:

- Supporting you with disease education
- Providing you with product information
- Connecting you to additional resources
- Answering questions about treatment

For more information about Alnylam Assist® or to access downloadable materials, visit www.AlnylamAssist.com.

Alnylam ASSIST®

Monday-Friday, 8 AM-6 PM ET
CALL: 1-833-256-2748

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GIVLAARI™ (givosiran) at a glance

GIVLAARI is the first and only FDA-approved medicine for the treatment of adults with acute hepatic porphyria (AHP).

- **GIVLAARI reduces levels of aminolevulinic acid (ALA) and porphobilinogen (PBG)**
  ALA and PBG are neurotoxins and are associated with attacks and other AHP symptoms
- **Once-monthly dosing**
  GIVLAARI is given as an injection under the skin by a healthcare professional

GIVLAARI was studied in a 6-month trial of patients with AHP who received either GIVLAARI or placebo once a month. Patients in the trial treated with GIVLAARI had:

- **70% fewer porphyria attacks that required hospitalization, urgent healthcare visit, or intravenous (IV) hemin at home**
  Patients on GIVLAARI had an average of 1.9 porphyria attacks compared to 6.5 in patients on placebo
- **70% fewer days of hemin use**
  Patients on GIVLAARI had an average of 4.7 days of hemin use compared to 12.8 in patients on placebo
- **The most common side effects were nausea and injection site reactions**
  27% of patients on GIVLAARI experienced nausea and 25% had injection site reactions

Important Safety Information

Do not use GIVLAARI if you have ever had a severe allergic reaction to GIVLAARI.

GIVLAARI can cause:

- Severe allergic reaction
- Liver problems
- Kidney problems
- Injection site reactions

Please see more details on Important Safety Information throughout this brochure, and full Prescribing Information.

Talk to your doctor about GIVLAARI.

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