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

REDISCOVER YOUR EVERYDAY

With the possibility of fewer attacks

"My life today with fewer attacks is very different from a few years ago."

Lina, on her experience during treatment

What is GIVLAARI® (givosiran)?

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 on page 13 and full Prescribing Information.

YOU DON'T HAVE TO WAIT FOR YOUR NEXT ATTACK:

Ask your doctor about GIVLAARI® (givosiran), a monthly treatment for AHP.

Acute hepatic porphyria (AHP) attacks may show up differently from one person to another, but any one of them can be devastating.

While attacks may come and go, it's important to remember that AHP is an ongoing condition that can be treated, and fewer attacks may be possible.

See inside how monthly treatment with GIVLAARI may help reduce the frequency of attacks.

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Important Safety Information

GIVLAARI® (givosiran) can cause 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.

Please see Important Safety Information on page 13 and full Prescribing Information.

WHAT IS AHP?

Acute hepatic porphyria (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.

WHAT ARE THE SYMPTOMS OF AN AHP ATTACK?

While most people with AHP experience severe abdominal pain during attacks, symptoms vary from person to person and change over time. Not every person with AHP will experience all the symptoms listed here, and some will experience symptoms more frequently or more severely than others.

- Limb, back, or chest pain
- Nausea
- Vomiting
- Confusion
- Anxiety
- Insomnia
- Seizures
- Weak limbs
- Dark or reddish urine
- Constipation
- Diarrhea
- Hallucinations

IN THE US, ABOUT
1 PERSON IN 100,000
IS DIAGNOSED WITH AHP
AND HAS SYMPTOMS.

THERE ARE 4 TYPES OF AHP:

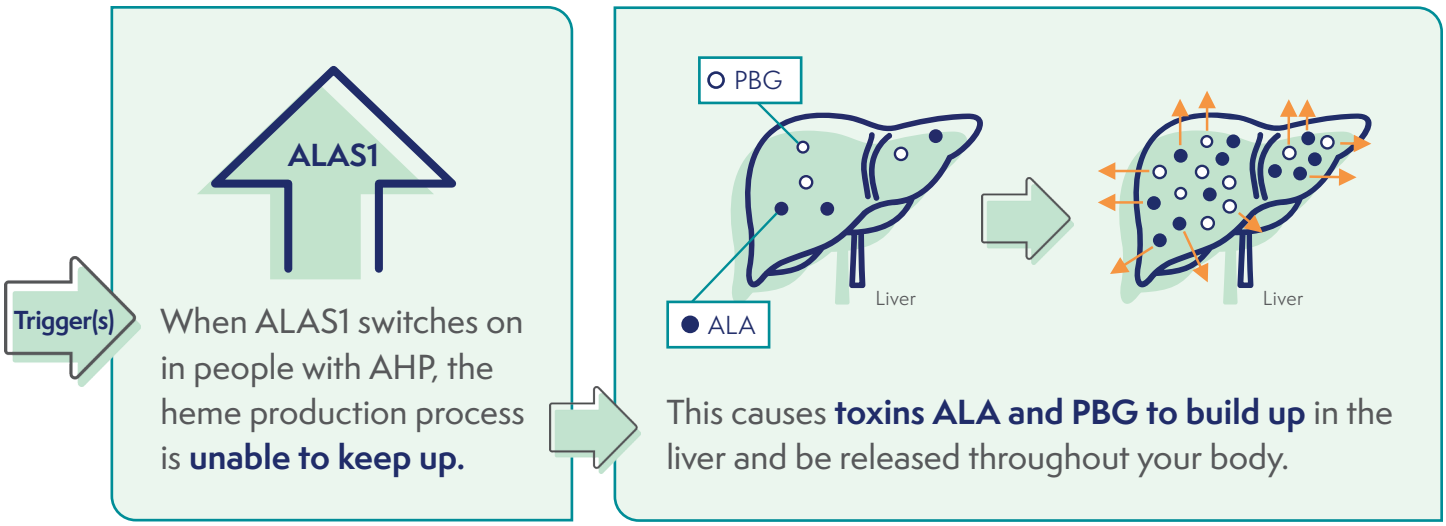
Acute intermittent porphyria (AIP)	Variegate porphyria (VP)	Hereditary coproporphyria (HCP)	ALAD-deficiency porphyria (ADP)

Most common — **Extremely rare**

ALAD=aminolevulinic acid dehydratase.

HOW AHP AFFECTS YOUR BODY

Heme is an important molecule that is made in the liver. An enzyme called ALAS1 is the "start switch" that controls the process of making heme. When ALAS1 switches on in people with acute hepatic porphyria (AHP), the heme production process is unable to keep up. This causes **toxins ALA and PBG** to build up in the liver and be released throughout your body.



ALA and PBG are associated with attacks and other AHP symptoms. Be sure to tell your healthcare providers about all the symptoms you're experiencing

DID YOU KNOW SOME FACTORS CAN WORSEN YOUR AHP?

SOME POTENTIAL ATTACK TRIGGERS INCLUDE:

- ✔ Hormonal fluctuations
- ✔ Infection
- ✔ Stress
- ✔ Use of certain medications
- ✔ Alcohol consumption
- ✔ Fasting/extreme dieting

ALAS1=aminolevulinic acid synthase 1; ALA=aminolevulinic acid; PBG=porphobilinogen.

"Now that I'm experiencing fewer attacks, I can finally focus on other things in my life."

Mike, on his experience during treatment

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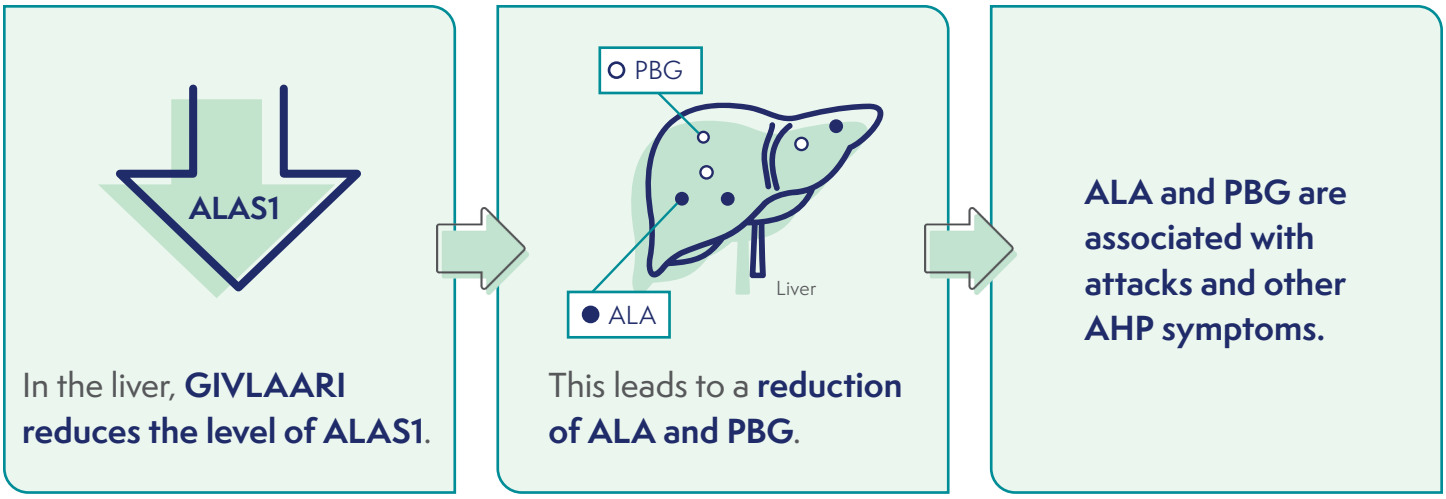
HOW GIVLAARI® (givosiran) WORKS

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



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

GIVLAARI is given as an injection under the skin (subcutaneous) by a healthcare professional. Depending on your doctor's recommendations and your insurance plan, home administration by a nurse or other healthcare professional may be an option.

GIVLAARI IS GIVEN ONCE A MONTH BY A HEALTHCARE PROFESSIONAL.

ALAS1=aminolevulinic acid synthase 1; AHP=acute hepatic porphyria; ALA=aminolevulinic acid; PBG=porphobilinogen.

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.

Please see Important Safety Information on page 13 and full Prescribing Information.

HOW GIVLAARI® (givosiran) WAS STUDIED

GIVLAARI was tested against a placebo (an injection that did not contain any medication) in a clinical study of 94 adults with acute hepatic porphyria (AHP) who had recurrent attacks (2 or more attacks in the 6 months prior to starting the study).

- During the study, 48 patients received GIVLAARI and 46 patients received a placebo once monthly for 6 months. Thereafter, all patients who remained in the study (93 patients) received GIVLAARI once a month
- Attacks measured in the study were defined as those that required hospitalization, urgent healthcare visit, or intravenous (IV) hemin at home

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.

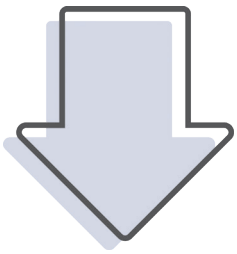
Please see Important Safety Information on page 13 and full Prescribing Information.

In a 6-month study,

PATIENTS TAKING GIVLAARI® (givosiran) EXPERIENCED

70%

fewer attacks
on average, compared to those who received placebo



70%

fewer days of hemin use
to treat AHP attacks, on average, compared to those on placebo

- GIVLAARI was studied in adults with AHP who were experiencing recurrent AHP attacks
- After the first 6 months of treatment, patients on GIVLAARI had an average of 1.9 AHP attacks compared to 6.5 for those on placebo

- In the study, patients who experienced an attack were treated according to local standards of care, which could include hemin
- Using hemin to prevent an attack was not allowed during the study
- After the first 6 months of treatment, patients on GIVLAARI had an average of 4.7 days of hemin use compared to 12.8 days for patients on placebo

Important Safety Information

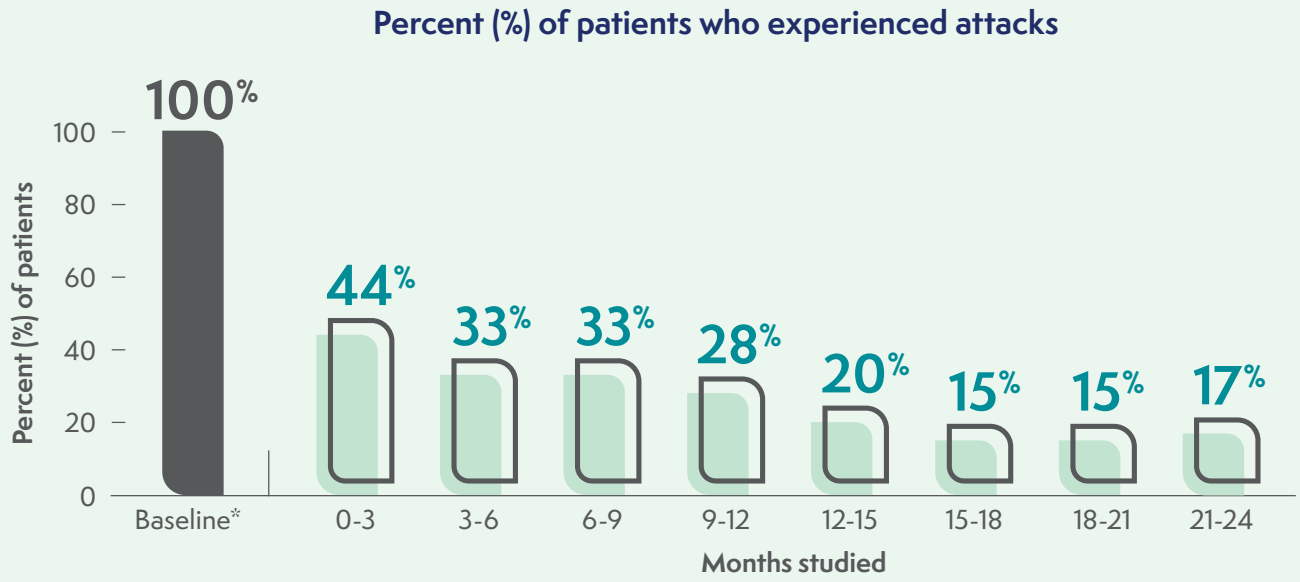
GIVLAARI can cause kidney problems:

Your doctor will check how your kidneys are working while you are using GIVLAARI.

Please see Important Safety Information on page 13 and full Prescribing Information.

FEWER PATIENTS EXPERIENCED AHP ATTACKS OVER 24 MONTHS

After the 6-month study, all eligible patients who remained in the study received GIVLAARI® (givosiran) once a month. The graph below shows the percent of patients who started on and continued taking GIVLAARI who experienced acute hepatic porphyria (AHP) attacks throughout the study.



*All patients experienced at least 2 attacks in the 6 months prior to starting in the study.

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

These results were observed in the clinical trial. Keep in mind that everyone responds to GIVLAARI differently.

Important Safety Information

Increased blood homocysteine levels

GIVLAARI may cause increased levels of homocysteine (a type of amino acid) in your blood. Your doctor will check your homocysteine levels before and during treatment by doing blood tests. If your levels are increased, your doctor may check your folate, vitamins B12 and B6, and tell you to take a vitamin B6 supplement.

Please see Important Safety Information on page 13 and full Prescribing Information.

GIVLAARI® (givosiran) SAFETY PROFILE

Safety during the first 6 months of the study

- In the first 6 months of the study, 1 patient taking GIVLAARI stopped treatment due to changes in liver function. No patients taking placebo stopped treatment

The most common side effects in patients treated with GIVLAARI compared to those taking placebo in the first 6 months of the study were:

	GIVLAARI (48 patients)	Placebo (46 patients)
Nausea	27%	11%
Injection site reactions	25%	0%
Rash	17%	4%
Changes in kidney function	15%	4%
Changes in liver function	13%	2%
Fatigue	10%	4%

Safety after the first 6 months

- The most common side effects in patients treated with GIVLAARI were injection site reactions (37%), nausea (34%), fatigue (23%), nasopharyngitis (23%), and headache (20%)
- After the initial 6-month study, 3 patients stopped treatment due to a side effect. One stopped because of a severe allergic reaction, and the other 2 stopped due to increased blood homocysteine levels
- Serious side effects were reported in 28 (30%) of patients during the study. Serious side effects that were reported in more than 1 patient included blood homocysteine increased, chronic kidney disease, device breakage, fever, and urinary tract infections (all reported in 2 patients).
- During this period, increased blood homocysteine levels were found in 15 of 93 patients (16%)

Please see Important Safety Information on page 13 and full Prescribing Information.

"Your pain is real; it is valid, and you don't have to go through it alone."

Amalia, patient with AIP

Please see Important Safety Information on page 13 and full Prescribing Information.

IMPORTANT SAFETY INFORMATION

Do not use GIVLAARI® (givosiran) if you have ever had a severe allergic reaction to GIVLAARI.

GIVLAARI can cause:

• 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.

• 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.

• Kidney problems

Your doctor will check how your kidneys are working while you are using GIVLAARI.

• 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.

• Increased blood homocysteine levels

GIVLAARI may cause increased levels of homocysteine (a type of amino acid) in your blood. Your doctor will check your homocysteine levels before and during treatment by doing blood tests. If your levels are increased, your doctor may check your folate, vitamins B12 and B6, and tell you to take a vitamin B6 supplement.

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.

For additional information about GIVLAARI, please see full Prescribing Information.

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WITH ALNYLAM ASSIST®, YOU ARE NOT ALONE

Alnylam ASSIST®

Once you and your doctor decide GIVLAARI® (givosiran) is right for you, Alnylam Assist® offers support specialists to help you every step of the way.

LEARN FROM AN ALNYLAM PEL

Our dedicated Alnylam Patient Education Liaisons (PELs) have a background in nursing and are experienced in educating people and their families about matters related to acute hepatic porphyria (AHP).

The purpose of the Alnylam Patient Education Liaisons (PELs) is to provide education to patients, their families, and caregivers. PELs are employees of Alnylam Pharmaceuticals. They are not acting as healthcare providers and are not part of your healthcare team. PELs do not provide medical care or advice. All diagnosis and treatment decisions should be made by you and your doctor.

Your Alnylam PEL will:

- Support you with disease education
- Connect you to additional resources
- Answer questions about GIVLAARI treatment

Connect with an Alnylam PEL today.
Visit www.GIVLAARIpel.com to learn how.

Please see Important Safety Information on page 13 and full Prescribing Information.

"Alnylam Assist®, and our Case Manager, really helped us navigate the approval process."

Amalia, on her experience getting started with GIVLAARI® (givosiran)

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SUPPORT IS AVAILABLE TO YOU

We are committed to making GIVLAARI® (givosiran) available to those who need it. When you and your healthcare provider decide to start treatment, Alnylam Assist® will provide you with a dedicated **Alnylam Case Manager** who can provide personalized support throughout the GIVLAARI treatment process.

SPEAK TO A DEDICATED ALNYLAM CASE MANAGER

Alnylam 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.

Your Alnylam Case Manager can:

Help you understand your insurance benefits

Determine your eligibility for Alnylam Assist's financial assistance programs*

Provide you with personalized support to get started on treatment

Please see Important Safety Information on page 13 and full Prescribing Information.

Alnylam ASSIST®

Most commercial insurance companies **offer coverage for GIVLAARI® (givosiran)**; however, if you have concerns about the cost or if you don't have coverage for GIVLAARI, Alnylam may be able to help if you're eligible.

ASK ABOUT ALNYLAM'S FINANCIAL ASSISTANCE PROGRAMS*†

- **If you have commercial insurance**, our **Alnylam Assist Commercial Copay Program** enables you to pay $0 out of pocket for medication and administration costs
  - Patients with Medicare, Medicaid, or other government-sponsored insurance are not eligible for Alnylam's Commercial Copay Program
- If you do not have insurance, or do not have coverage for GIVLAARI, our **Patient Assistance Program** may be able to provide you with GIVLAARI at no cost
- **Talk to your Alnylam Case Manager** to learn more about **Alnylam Assist financial assistance program** eligibility

*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.

†Some state laws may impact or restrict some aspects of these programs.

For more information about Alnylam Assist® or to access downloadable materials:

Visit: AlnylamAssist.com
Call: **1-833-256-2748**
Monday-Friday, 8 AM-6 PM ET

Please see Important Safety Information on page 13 and full Prescribing Information.

FREQUENTLY ASKED QUESTIONS

Can GIVLAARI® (givosiran) be used for any type of AHP?

GIVLAARI is a prescription medicine used to treat AHP in adults. There are 4 types of AHP:

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

Most patients in the 6-month study had AIP, the most common type of AHP.

How is GIVLAARI given?

GIVLAARI is given once a month as a subcutaneous injection (under the skin) by a healthcare professional.

Will I need any tests while taking GIVLAARI?

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 healthcare provider 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.

GIVLAARI may cause increased levels of homocysteine (a type of amino acid) in your blood. Your doctor will check your homocysteine levels before and during treatment by doing blood tests.

Can I use hemin while using GIVLAARI?

In clinical studies of GIVLAARI, some people on GIVLAARI used hemin to treat AHP attacks. Use of GIVLAARI with regularly scheduled (prophylactic) hemin was not studied in clinical trials of GIVLAARI. Talk to your doctor if you have questions about your treatment plan.

Is GIVLAARI safe to use during pregnancy?

GIVLAARI has not been studied in women who are pregnant. If you are pregnant or plan to become pregnant, it is important to discuss your treatment plan with your doctor.

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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Talk to your doctor about GIVLAARI® (givosiran).

Please scan the QR code to visit **www.GIVLAARI.com** for more information.

Please see Important Safety Information on page 13 and full Prescribing Information.

Alnylam® PHARMACEUTICALS