FOR PROVIDERS

AlnylamAct®

Genetic Testing and Counseling Program*† for **Acute Hepatic Porphyria (AHP)** Offered at No Charge‡

Consider genetic testing and counseling for your patients; Alnylam Act® provides one option for eligible individuals

*While program is sponsored by Alnylam Pharmaceuticals, all services are performed by independent third parties.

†Both genetic testing and genetic counseling are available in the US and Canada

‡To patients, healthcare professionals, or payers.

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About Acute Hepatic Porphyria (AHP)

What is AHP?

AHP refers to a family of rare genetic diseases characterized by potentially life-threatening attacks and, for some patients, chronic, debilitating symptoms. AHP may inflict years of suffering and impaired quality of life. The symptoms of AHP can often resemble those of other more common conditions such as irritable bowel syndrome (IBS), fibromyalgia, and endometriosis. Consequently, patients afflicted with AHP are often misdiagnosed or remain undiagnosed for up to 15 years after symptom onset.[1-5]

How is it diagnosed?

The two most common techniques to help inform a diagnosis of AHP are a urine test and a genetic test:

- **Urine Test:** Initial testing for AHP can include a random (spot) urine tested for PBG (porphobilinogen), ALA (aminolevulinic acid), and porphyrin levels. The optimal time to test is during or shortly after an attack when ALA and PBG levels have spiked. In most cases, PBG and ALA remain elevated between attacks; however, levels may normalize in some patients with less common forms of AHP (e.g., HCP and VP). Porphyrin analyses may help identify the specific type of AHP, but should not be used alone to test for AHP as they can be elevated for several reasons. Additional tests on plasma or stool samples may also be used to aid in a diagnosis.[1,6-10]
- **Genetic Test:** Genetic testing can help confirm a diagnosis and determine the specific type of AHP. It can be performed regardless of whether a person is currently experiencing attack symptoms. Penetrance in AHP is low, so people with a genetic variant for AHP may be asymptomatic and never develop symptoms.[8,10]

Why use genetic testing for AHP?

Delays in diagnosis may lead to unnecessary surgeries and increased disease burden. Genetic testing for AHP (associated genes include *HMBS, CPOX, PPOX,* and *ALAD*) can help confirm a diagnosis which may help shorten the diagnostic journey and allow timely management of AHP.[1,5]

Is family screening important?

AHP is generally an inherited disorder and may affect multiple individuals within a family. If you have a patient with AHP, consider genetic testing in blood relatives as part of at-risk family member screening. Consultation with a genetic counselor is recommended to help understand the risk of inheriting this disease.[7]

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Getting Started

Once the decision to undergo genetic testing and counseling has been made:

Step 1 Determine eligibility for genetic testing*

To be eligible for genetic testing through Alnylam Act®, patients must be pubescent or older in the U.S. and Canada and meet the requirements below:

- Family history of AHP, **or**
- Elevated (>ULN) urinary porphobilinogen (PBG) or aminolevulinic acid (ALA) levels, **or**
- Combination of AHP symptoms

Step 2 Order a genetic test

Start your order

- Request Invitae® specimen collection kits to get started at **invitae.com/request-a-kit**
- Complete the Invitae requisition form for Alnylam Act® (AHP), and fax it to **415-276-4164**, or insert the form in the Invitae specimen collection kit before shipment
- Note: You can also place an order for a genetic test through the online ordering portal at: **invitae.com/alnylam-act-ahp**

Submit patient sample

- Collect a sample using Invitae's specimen collection kit
- Follow the collection and shipping instructions inside the Invitae collection kit
- Note: Invitae offers the ability to send specimen collection kits directly to patients

Receive results

- Receive results in 10-21 calendar days, on average
- Receive a notification email once the test results are ready. If you created an online account, you can view the status of your order by logging into your account

Questions about variant of uncertain significance (VUS) results? Invitae's Clinical Support Services are available to help aid in interpretation and resolution of VUS results. To discuss, please email **clinconsult@invitae.com** or call **1-800-436-3037**.

*Refer to the Alnylam Act® AHP requisition form for full details about eligibility criteria.

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Getting Started *(continued)*

Step 3 Genetic Counseling (optional)

Refer patient for genetic counseling at any time*

- Instruct your patient to call Invitae at **800-436-3037** if they have questions for a genetic counselor
- Patient may ask questions throughout the process, and an appointment may be scheduled through the patient portal once testing is completed

Prepare patient for the appointment

We recommend the patient sets aside thirty minutes free from interruptions or distractions. The patient may consider asking family members about their family medical history ahead of the appointment. It is helpful for the genetic counselor to understand if any family members have been diagnosed with medical conditions and at what age they were diagnosed

Receive results

Invitae will provide you with a detailed summary report through the online portal

*Both genetic testing and genetic counseling are available in the U.S. and Canada.

FOR QUESTIONS ABOUT GENETIC TESTING AND COUNSELING

Contact Invitae at **invitae.com/contact** or **1.800.436.3037**

Alnylam Act®

About Alnylam Act®

What is Alnylam Act®?

Alnylam Act® is a sponsored, no-charge, third-party genetic testing and counseling program for patients with a family history or suspected diagnosis of AHP. The Alnylam Act® program was developed to reduce barriers to genetic testing and counseling to help people make more informed decisions about their health.

What genes are tested through Alnylam Act®?

Genetic testing for AHP is provided through the Invitae® Comprehensive Porphyrias Panel, which contains a total of 10 genes. This panel includes the four genes associated with AHP and six genes associated with other non-AHP forms of porphyria such as cutaneous porphyria.

How much does genetic testing and counseling cost through Alnylam Act®?

Through the Alnylam Act® program, the genetic testing and counseling services are provided at no charge to patients, healthcare professionals, or payers, including government payers.

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam may use healthcare professional contact information for research purposes.
- Both genetic testing and genetic counseling are available in the U.S. and Canada
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No patients, healthcare professionals, or payers, including government payers, are billed for this program

References: 1. Anderson KE, Bloomer JR, Bonkovsky HL, et al. *Ann Intern Med.* 2005;142(6):439-450. **2.** Gouya L, Bloomer JR, Balwani M, et al. Presented at: 2018 International Congress on Porphyrins and Porphyrias; June 26, 2017; Bordeaux, France. **3.** Simon A, Pompilus F, Querbes W, et al. *Patient.* 2018;11(5):527-537. **4.** Ko JJ, Murray S, Merkel M, et al. Poster presented at: American College of Gastroenterology Annual Meeting; October 5-10, 2018; Philadelphia, PA. **5.** Bonkovsky HL, Maddukuri VC, Yazici C, et al. *Am J Med.* 2014;127(12):1233-1241. **6.** Bissell DM, Anderson KE, Bonkovsky HL. *N Engl J Med.* 2017;377(9):862-872. **7.** Balwani M, Wang B, Anderson KE, et al; for the Porphyrias Consortium of Rare Diseases Clinical Research Network. *Hepatology.* 2017;66(4):1314-1322. **8.** Ventura P, Cappellini MD, Biolcati G, Guida CC, Rocchi E; Gruppo Italiano Porfiria (GrIP). *Eur J Intern Med.* 25(6):497-505. **9.** Pischik E, Kauppinen R. *Appl Clin Genet.* 2015;8:201-214. **10.** Ramanujam VM, Anderson KE. *Curr Protoc Hum Genet.* 2016;86:17.20.1-17.20.26.

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MED-US-AS1-1900144 03.2023