What Are the Acute Hepatic Porphyrias (Also Known as Acute Porphyrias)?[1-4]

There are four types of acute hepatic porphyria: acute intermittent porphyria (AIP), variegate porphyria (VP), hereditary coproporphyria (HCP), and ALAD-deficient porphyria (ADP). The acute hepatic porphyrias (AHPs) are characterized by acute, potentially life-threatening attacks and chronic debilitating symptoms that negatively impact patients' quality of life. Attacks are commonly characterized by severe abdominal pain, vomiting, nausea, rapid heart rate (tachycardia), and constipation. During an attack, a person may also experience muscle weakness or paralysis, seizures, low sodium levels (hyponatremia), and mental changes such as anxiety, confusion, or hallucinations in severe cases. HCP and VP are classified as acute but can also have symptoms that affect the skin—specifically blistering skin lesions on sun-exposed areas. Skin symptoms can be present with or without attacks.

For more information about the acute hepatic porphyrias, visit the American Porphyria Foundation at **www.porphyriafoundation.org**

WHAT DOES A NEGATIVE GENETIC TEST MEAN FOR YOU[3,5,6]

To date, there are four genes associated with the acute hepatic porphyrias. This test uses gene sequencing with deletion/duplication testing to look for gene changes (mutations) in these four genes. Gene sequencing detects changes in the DNA sequence of a gene while deletion/duplication testing looks for deletions or duplications of DNA within a gene.

Gene mutation testing can give several possible results: a positive result, a negative result, or an ambiguous (or uncertain) result called a variant of unknown significance. A negative genetic test result indicates that a disease-associated mutation was not found, thereby making it unlikely that a person with a negative result has an acute hepatic porphyria. This is because gene sequencing when combined with deletion/duplication testing detects approximately 99% of mutations in the four genes associated with the acute hepatic porphyrias.

Although it is unlikely that a person with negative genetic testing has an acute hepatic porphyria, if suspicion continues, biochemical testing may also be considered by your doctor. Specifically, testing a person's urine for elevated levels of porphobilinogens (PBG) or aminolevulinic acid (ALA) may be used to diagnose AIP, HCP, and VP.* These tests can be performed in a random urine sample and are more accurate when normalized per gram of urine creatine – a 24-hour collection is not required. Biochemical testing is typically performed when a person is experiencing a suspected attack, since PBG and/or ALA are most elevated at this time.

Biochemical testing is not available through the Alnylam Act™ program.

Genetic and biochemical testing results should always be interpreted in the context of a person's symptoms, medical history, and family history. If genetic testing is negative, you are encouraged to follow up with your health care provider to interpret the result as well as to determine whether other tests may be indicated.

Genetic Counseling

In addition to genetic testing, Alnylam is sponsoring no-charge, third-party genetic counseling in the U.S. for the AHPs.

Genetic counseling is a service that provides information and support to people and families who have, or may be at risk for, genetic diseases. Genetic counselors are trained health care professionals who can explain genetic diseases, genes and inheritance, and genetic test results.

To schedule telephone-based genetic counseling, call **1.888.475.3128** and reference the Alnylam Act™ program.

*Urinary aminolevulinic acid (ALA) is the first-line test for ADP.

AlnylamAct™ The Alnylam Act™ program was developed to reduce barriers to genetic testing and counseling in order to help people make more informed decisions about their health. While Alnylam provides financial support for this program, all tests and services are performed by independent third parties. At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for health care providers who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S.

References: 1. Bissell DM, et al. *J Clin Transl Hepatol*. 2015;3(1):17-26. **2.** Bonkovsky, HL et al. *Am J Med*. 2014;127:1233-1241. **3.** Anderson KE, et al. *Ann Intern Med.* 2005;142(6):439-50. **4.** Anderson, et al. In: Proceedings from AASLD 2016;64(1):285A. **5.** Whatley, et al. *Clin Chem.* 2009;55:1406–14. **6.** Bissell, et al. *N Engl J Med*. 2017;377:862-872.