



navigateAPDS GENETIC TESTING PROGRAM DESCRIPTION

Pharming Healthcare, Inc. offers sponsored genetic testing and post-test genetic counseling for eligible individuals who may carry a pathogenic variant in one of two genes known to be associated with Activated PI3K Delta Syndrome (APDS), an underdiagnosed, progressive primary immunodeficiency.

The navigateAPDS testing program reduces barriers to genetic testing to help inform a diagnosis for patients suspected of having APDS and their family members.

ABOUT APDS



APDS is an underdiagnosed, progressive primary immunodeficiency that affects approximately 1-2 people per million.



Signs and symptoms of APDS start in childhood, and patients are vulnerable to repeat infections and autoimmune/inflammatory signs such as lymphoproliferation, splenomegaly, and even lymphoma.



APDS occurs when there is a disease-causing variant in either one of two specific genes, the *PIK3CD* gene or the *PIK3R1* gene, in an autosomal dominant mode of inheritance. These genes are involved in making parts of a protein that help in the growth and division of white blood cells, particularly the B-cell and T-cell lymphocytes.



Patients are often misdiagnosed with other immunodeficiencies or autoimmune disorders and have a protracted course to obtain a correct diagnosis. Genetic testing can help inform an APDS diagnosis and may identify patients for participation in clinical research.

For more information about APDS visit: www.allaboutapds-hcp.com

SPONSORED PROGRAM ELIGIBILITY*

This program is available to patients in the US, Canada, and US Territories who meet a **minimum of three** of the following criteria:

Clinical Features

- Bronchiectasis
- Lymphadenopathy/lymphoproliferation
- Chronic hepatomegaly or chronic splenomegaly
- Severe, persistent, or recurrent Herpesviridae infection (e.g. EBV, CMV, VZV, HSV)
- Recurrent sinopulmonary infections
- Recurrent pneumonia
- Recurrent otitis media
- Nodular mucosal lymphoid hyperplasia
- Autoimmune or inflammatory organ involvement consistent with immune dysregulation (e.g., autoimmune forms of hepatitis, thyroiditis, nephritis, etc)
- Autoimmune cytopenia(s)
- Enteropathy (e.g. chronic/recurrent diarrhea, inflammatory bowel disease)
- Lymphoma (0-25 years) *meets 3 eligibility criteria*
- Lymphoma ≥ 26 years of age, *requires 2 additional eligibility criteria*
- Non-food related eosinophilic esophagitis
- Developmental delay
- Short stature or history of failure to thrive
- Hypogammaglobulinemia

Laboratory

- Elevated levels of Immunoglobulin M (IgM)
- Increased number of follicular helper T cells
- Reduced number of naive B cells
- Increased transitional B cells
- Inverted CD4/CD8 ratio (low CD4+ T helper cells and high senescent effector/memory CD8+ cells)
- Hyperactive PI3K activity as assessed by phosphorylated AKT and/or phosphorylated S6

History

- Clinical diagnosis of Activated PI3K-Delta Syndrome (APDS) *meets 3 eligibility criteria*
- Common Variable Immune Deficiency (CVID) phenotype
- Family history of CVID
- Family member with *PIK3CD* or *PIK3R1* pathogenic, likely pathogenic, or VUS result *meets 3 eligibility criteria*

PANEL INFORMATION

The navigateAPDS program offers testing with the choice of either the **Invitae Primary Immunodeficiency Panel (>425 genes)** or the **Invitae Inborn Errors of Immunity and Cytopenias Panel (>570 genes)** which analyze genes that are associated with inherited disorders of the immune system. Broad panel testing allows for an efficient evaluation of several potential genes based on a single clinical indication.

CLINICAL CONSULTATION SERVICES FOR HEALTHCARE PROVIDERS

As part of the navigateAPDS program, a team of board-certified and experienced genetic counselors trained in medical genetics are available to assist clinicians by phone and/or email. Genetic counselors can be reached throughout the testing process to:

- review patient cases that may benefit from the program
- aid in explaining genetic test results
- provide result-specific background regarding variants, genes, and the condition
- identify gene-specific information including relevant literature and studies, published management guidelines if available, and patient resources

For more information or to order a test, please visit
www.invitae.com/us/sponsored-testing/navigate-apds or scan the QR code.



*While third parties and commercial organizations may provide financial support for this program, all testing is performed by Invitae (a part of Labcorp). Healthcare professionals must confirm that patients meet certain criteria to use the program. Third parties and commercial organizations may receive de-identified patient data from this program, but at no time would they receive patient identifiable information. Third parties and commercial organizations may receive contact information for healthcare professionals who use this program. Genetic testing and counseling are available in the US, Canada and US Territories only. Healthcare professionals and patients who participate in this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use or support any other products or services from third parties or commercial organizations. For full terms and conditions, see www.navigateAPDS.com.