MAYO CLINIC LABORATORIES

# Test Definition: AGAW

Alpha-Galactosidase, Leukocytes

## Overview

### Useful For

Diagnosis of Fabry disease in male patients

Verifying abnormal serum alpha-galactosidase results in male patients with a clinical presentation suggestive of Fabry disease

This test is **not useful for** patients undergoing a work-up for a meat or meat-derived product allergy.

### Genetics Test Information

Fabry disease is caused by deficient activity of the enzyme alpha-galactosidase A and results in damage to multiple organs including the kidney, heart, and brain.

Treatment with enzyme replacement therapy is available for individuals with Fabry disease.

### Testing Algorithm

Additional information is available:

-Fabry Disease: Newborn Screen-Positive Follow-up

-Fabry Disease Diagnostic Testing Algorithm

If the patient has abnormal newborn screening results for Fabry disease. Refer to the appropriate ACMG Newborn Screening ACT Sheet.(1)

### Special Instructions

- Informed Consent for Genetic Testing
- Fabry Disease Diagnostic Testing Algorithm
- Fabry Disease: Newborn Screen-Positive Follow-up
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

### Method Name

Flow Injection Analysis-Tandem Mass Spectrometry (FIA-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Whole Blood ACD

## Ordering Guidance

If testing is needed for assessment of meat or meat-derived product allergy, order either ALGAL / Galactose-Alpha-1,3-Galactose (Alpha-Gal), IgE, Serum or APGAL / Galactose-Alpha-1,3-Galactose (Alpha-Gal) Mammalian Meat Allergy Profile, Serum.

Carrier detection using enzyme levels is unreliable for female patients as results may be within the normal values. Order GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, Varies for testing carrier status.

## Shipping Instructions

**For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 6 days of collection to be stabilized**. Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

## Specimen Required

**Container/Tube:**
**Preferred:** Yellow top (ACD solution B)
**Acceptable:** Yellow top (ACD solution A) or lavender top (EDTA)
**Specimen Volume:** 6 mL
**Collection Instructions:** Send whole blood specimen in original tube. **Do not aliquot**.

## Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

## Specimen Minimum Volume

4 mL

## Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |

## Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole Blood ACD | Refrigerated (preferred) | 6 days | |
| | Ambient | 6 days | |

## Clinical & Interpretive

## Clinical Information

Fabry disease is an X-linked lysosomal disorder resulting from deficient activity of the enzyme alpha-galactosidase A (alpha-Gal A) and the subsequent deposition of glycosylsphingolipids in tissues throughout the body, in particular the kidney, heart, and brain. Variants within the *GLA* gene cause Fabry disease and more than 630 genetic alterations have been identified. Severity and onset of symptoms are dependent on the amount of residual enzyme activity. The classic form of Fabry disease occurs in male patients who have less than 1% alpha-Gal A activity. Symptoms usually appear in childhood or adolescence and can include acroparesthesias (burning pain in the extremities), gastrointestinal issues, multiple angiokeratomas, reduced or absent sweating, corneal opacity, and proteinuria. In addition, progressive kidney involvement leading to end-stage kidney disease (ESRD) typically occurs in adulthood, followed by cardiovascular and cerebrovascular disease. The estimated incidence varies from 1 in 3000 infants detected via newborn screening to 1 in 10,000 male patients diagnosed after onset of symptoms.

Male patients with residual alpha-Gal A activity greater than 1% may present with 1 of 3 variant forms of Fabry disease with onset of symptoms later in life: a kidney variant associated with ESRD but without the pain or skin lesions; a cardiac variant typically presenting in the 6th to 8th decade with left ventricular hypertrophy, cardiomyopathy and arrhythmia, and proteinuria, but without ESRD; and a cerebrovascular variant presenting as stroke or transient ischemic attack. The variant forms of Fabry disease may be underdiagnosed.

Female patients who are carriers of Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Measurement of alpha-Gal A activity is not generally useful for identifying carriers of Fabry disease, as many of these individuals will have normal levels. Therefore, molecular genetic analysis of the *GLA* gene (GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, Varies) is recommended to detect carriers.

Unless irreversible damage has already occurred, treatment with enzyme replacement therapy has led to significant clinical improvement in affected individuals. In addition, some adult patients may be candidates for an oral chaperone therapy. For this reason, early diagnosis and treatment are desirable and, in a few US states, early detection of Fabry disease through newborn screening has been implemented.

Absent or reduced alpha-Gal A in leukocytes (this test) or serum (AGAS / Alpha-Galactosidase, Serum) can indicate a diagnosis of classic or variant Fabry disease. The biomarkers globotriaosylsphingosine (LGBWB / Globotriaosylsphingosine, Blood) and ceramide trihexosides (CTSU / Ceramide Trihexosides and Sulfatides, Random, Urine) may be elevated in patients with Fabry disease and may aid in the diagnostic evaluation of female patients. Molecular sequence analysis of the *GLA* gene (GLA / Fabry Disease, *GLA* Gene Sequencing with Deletion/Duplication, Varies) allows for detection of the disease-causing variant in both male and female patients.

## Reference Values

> or =10.32 nmol/hour/mg protein
An interpretative report will be provided.
**Note:** Results from this assay do not reflect carrier status because of individual variation of alpha-galactosidase enzyme levels.

## Interpretation

Values below the reference range are consistent with a diagnosis of Fabry Disease.

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their

significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing and in vitro, confirmatory studies (enzyme assay, molecular analysis), name and phone number of key contacts who may provide these studies, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

### Cautions

Individuals with pseudodeficiency allelic variants can show reduced alpha-galactosidase A enzyme activity with this assay.

### Clinical Reference

1. ACMG Newborn Screening ACT Sheets. Accessed July 22, 2025. Available at www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508
2. Desnick RJ, Ioannou YA, Eng CM: Alpha-galactosidase A deficiency: Fabry disease. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed July 22, 2025. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546984
3. De Schoenmakere G, Poppe B, Wuyts B, et al. Two-tier approach for the detection of alpha-galactosidase A deficiency in kidney transplant recipients. Nephrol Dial Transplant. 2008;23(12):4044-4048. doi:10.1093/ndt/gfn370
4. Mehta A, Hughes DA: Fabry disease. In: Adam MP, Ardinger HH, Pagon RA, et al: eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated April 11, 2024. Accessed July 22, 2025. Available at www.ncbi.nlm.nih.gov/books/NBK1292/
5. Laney DA, Bennett RL, Clarke V, et al. Fabry disease practice guidelines: recommendations of the National Society of Genetic Counselors. J Genet Couns. 2013;22(5):555-564. doi:10.1007/s10897-013-9613-3
6. Laney DA, Peck DS, Atherton AM, et al. Fabry disease in infancy and early childhood: a systematic literature review. Genet Med. 2015;17(5):323-330. doi:10.1038/gim.2014.120

## Performance

### Method Description

The specimens are incubated with a mix of substrate and internal standard for acid sphingomyelinase, beta-glucocerebrosidase, acid alpha-glucosidase, alpha-galactosidase, galactocerebrosidase and alpha-L-iduronidase. The sample is then purified by liquid-liquid extraction. The extract is evaporated and reconstituted before analysis by tandem mass spectrometry.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Preanalytical processing: Monday through Friday, Sunday
Assay performed: Monday, Thursday

### Report Available

2 to 5 days

### Specimen Retention Time

White blood cell homogenate: 1 month

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

## Fees & Codes

### Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

### Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

82657

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| AGAW | Alpha-Galactosidase, Leukocytes | 24049-9 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 606261 | Alpha-Galactosidase, Leukocytes | 24049-9 |
| 606262 | Interpretation | 59462-2 |
| 606263 | Reviewed By | 18771-6 |