MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: September 25, 2023
Effective Date: October 26, 2023

Glucose-6-Phosphate Dehydrogenase (*G6PD*) Full Gene Sequencing, Varies

Test ID: G6PDZ

Useful for:

- Genetic test for individuals at high risk for glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Aiding in the diagnosis of G6PD deficiency
- Determining G6PD deficiency status in individuals with inconclusive or unexpected phenotyping results
- Differentiation of heterozygotes with skewed X-inactivation from homozygotes and compound heterozygotes
- Definitive diagnosis of carrier status
- Evaluation of neonates with unexplained jaundice
- Identifying individuals at risk of drug-induced acute hemolytic anemia related to G6PD deficiency

Genetics Information:

- **This test is for molecular sequencing of the *G6PD* gene and does not assess glucose-6-phosphate dehydrogenase (G6PD) enzyme activity**. Enzymatic testing may be suggested as follow-up to this assay. For G6PD enzyme testing order G6PD1 / Glucose 6-Phosphate Dehydrogenase Enzyme Activity, Blood.
- G6PD deficiency is a common X-linked condition, estimated to affect up to 500 million people worldwide. Both male and female patients may be impacted due to how common G6PD deficiency is in the population.
- Acute hemolytic anemia (AHA) can be triggered in individuals with G6PD deficiency by fava beans, several types of medications (including rasburicase, dapsone-containing combinations of antimalarial drugs, and methylene blue), and infection. Less commonly, chronic congenital nonspherocytic hemolytic anemia (CNSHA) may occur in severe forms of G6PD deficiency.
- US Food and Drug Administration labeling and Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines recommend that G6PD testing be undertaken in high-risk populations before prescribing drugs known to cause AHA. Knowing a patient's genotype is generally sufficient to avoid contraindicated drugs, but follow-up with the phenotyping (enzyme) assay may be necessary to clarify results in some cases.
- This test involves full gene sequencing of all exons and exon/intron boundaries of the *G6PD* gene. A comprehensive interpretation will be provided including congenital and pharmacogenomic implications of results. Testing should be considered before prescribing medication associated with hemolysis in individuals with G6PD deficiency.

Methods:

Polymerase Chain Reaction (PCR) followed by DNA Sequence Analysis

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Submit only 1 of the following specimens:

Specimen Type:	**Whole blood**
Preferred:	Lavender top (EDTA)
Specimen Volume:	3 mL
Collection Instructions:	1. Invert several times to mix blood 2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information:	Ambient (preferred) 9 days/Refrigerated 30 days
Minimum Volume:	0.45 mL

Specimen Type:	**Saliva**
Patient Preparation:	Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies:	Saliva Swab Collection Kit (T786)
Specimen Volume:	1 Swab
Collection Instructions:	Collect and send specimen per kit instructions.
Specimen Stability Information:	Ambient 30 days

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Ordering Guidance:

For initial or time-sensitive screening for glucose-6-phosphate dehydrogenase deficiency, order G6PD1 / Glucose 6-Phosphate Dehydrogenase Enzyme Activity, Blood.

Necessary Information:

Include physician name and phone number with specimen.

Interpretation:

All detected alterations will be evaluated according to the latest American College of Medical Genetics and Genomics recommendations and the most recent World Health Organization system for classifying genetic variants of *G6PD*.(1-2) Variants will be classified based on known, predicted, or possible effect on gene pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions:

- Patients who have received a non-leukocyte reduced blood transfusion within the preceding 6 weeks, or who have received an allogeneic hematopoietic stem cell transplant, can have inaccurate genetic test results due to the presence of both donor and recipient DNA.
- For patients who have been transfused within the preceding 6 weeks, the glucose-6-phosphate dehydrogenase (G6PD) enzyme assay will also be affected, so it is **not** an appropriate alternative test.
- Patients who have received an allogeneic hematopoietic stem cell transplant would be expected to convert G6PD status to that of donor. However, if the patient's transplant was partially successful or if there is a relapse of an underlying hematologic malignancy, a mixture of donor and recipient genotype may be seen on genetic analysis. The enzyme assay can be run after transplantation; order G6PD1 / Glucose 6-Phosphate Dehydrogenase Enzyme Activity, Blood.
- Rare variants exist that could lead to false-negative or false-positive results. Other variants in the primer binding regions can affect the testing, and ultimately, the genotype assessment made.
- Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Large deletions or rearrangements are not detected by this assay.
- Sometimes a genetic alteration of unknown significance may be identified. In this case, testing of appropriate family members may be useful to determine pathogenicity of the alteration.
- This test is not designed to provide specific dosing or drug selection recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.
- Skewed X-inactivation in heterozygous female patients has been reported to result in G6PD deficiency. In these cases, the phenotyping (enzyme) assay is necessary to determine G6PD activity level and assign G6PD deficiency status.
- Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

CPT Code:

81249

Day(s) Performed: Monday, Wednesday **Report Available:** 3 to 7 days

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.