INDICATIONS FOR TESTING
Suspected hemoglobinopathy

ORDER
CBC with Platelet Count and Automated Differential
Blood Smear with Interpretation

Abnormal results on peripheral smear

RULE OUT
Splenectomy, splenic atrophy

Consider HbE or HbC disease, thalassemia

CONSIDER
• Hemoglobin evaluation
• Hemoglobin S, Sickle Solubility
• Beta Globin (HBB) Gene Sequencing

CONSIDER
• Genetic testing
• Isopropanol heat stability testing
• G6PD enzyme testing
• Evaluation for α thalassemia

ORDER
Hemoglobin Evaluation with Reflex to Electrophoresis and/or RBC solubility

Other variant hemoglobin

HbA2 elevated

β thalassemia likely

ORDER
Beta Globin (HBB) Gene Sequencing

Pathogenic variant detected

β thalassemia confirmed

No pathogenic variant detected

α or β globin sequencing

HbS/C/E

ORDER
Beta Globin (HBB) Gene Sequencing

Pathogenic variant detected

β thalassemia confirmed

Non-HbS/C/E

ORDER
Beta Globin (HBB) Gene Sequencing

Pathogenic variant detected

β thalassemia confirmed

ORDER
Hemoglobin S, Sickle Solubility

Pathogenic variant detected

Sickle cell disease

ORDER
Alpha Globin (HBA1 and HBA2) Deletion/Duplication

Variant detected

α thalassemia

No variant detected

No variant detected, but suspicion persists

ORDER
Alpha Globin (HBA1 and HBA2) Sequencing

Pathogenic variant detected

α thalassemia

ORDER
Alpha Thalassemia (HBA1 and HBA2) 7 Deletions

Variant detected

α thalassemia

Normal or HbH

Patient from population with common deletion

Low

Iron deficiency anemia (see related algorithm)

Indeterminate

HbA2 elevated

Other variant hemoglobin

Non-HbS/C/E

HbS/C/E

ORDER
Beta Globin (HBB) Deletion/Duplication

Pathogenic variant detected

β thalassemia confirmed

Pathogenic variant detected

α thalassemia

Key
G6PD Glucose-6-phosphate dehydrogenase
Hb Hemoglobin
MCV Mean corpuscular volume

*See the Hemolytic Anemias Testing Algorithm for additional possible abnormal findings.
*Test reflex pattern follows algorithm until a diagnosis is reached.
*Common deletions are α-3.7, α-4.2, -α(20.5), --SEA, --MED-I, --FIL, and --THAI.