**INDICATIONS FOR TESTING**

Suspected hemoglobinopathy

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

**ORDER**

- Ferritin

Low

- **Iron deficiency anemia (see related algorithm)**

Indeterminate

- **Microcytosis (MCV <80 fL)**

- **ORDER**
  - Hemoglobin Evaluation Reflexive Cascade
  - OR Hemoglobin Evaluation with Reflex to Electrophoresis and/or RBC solubility

**HbA₂ elevated**

- **β thalassemia likely**

  - **ORDER**
    - Beta Globin (HBB) Gene Sequencing

  Pathogenic variant detected

  - **β thalassemia confirmed**

  - **ORDER**
    - Beta Globin (HBB) Gene Sequencing

  Pathogenic variant detected

  - **β thalassemia confirmed**

Other variant hemoglobin

- **Non-HbS/C/E**

  - **ORDER**
    - alpha or β globin sequencing

  No pathogenic variant detected

  - **β thalassemia confirmed**

  - **ORDER**
    - Beta Globin (HBB) Gene Sequencing

  Pathogenic variant detected

  - **β thalassemia confirmed**

  - **ORDER**
    - Hemoglobin S, Sickle Solubility

  Positive results

- **HbS/C/E**

  - **RULE OUT**
    - Sickle cell disease likely (HbSS, HbSC, HbSE, HbS/β thalassemia, HbS/Hb Lepore)

  - **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

Patient from population with common deletion

- **No**

  - **ORDER**
    - Alpha Thalassemia (HBA1 and HBA2) Deletions
     - Deletions

  No variant detected

  - **α thalassemia**

  - **ORDER**
    - Alpha Globin (HBA1 and HBA2) Sequencing

  Pathogenic variant detected

  - **α thalassemia**

- **Yes**

  - **ORDER**
    - Alpha Thalassemia (HBA1 and HBA2) 7 Deletions

  Variant detected

  - **α thalassemia**

  - **ORDER**
    - Alpha Globin (HBA1 and HBA2) Se equencing

  Pathogenic variant detected

  - **α thalassemia**

- **Abnormal results on peripheral smear**

  - **Target cells**
    - Sickle cells
    - Heinz bodies

  - **RULE OUT**
    - Splenectomy, splenic atrophy

  - **Consider**
    - G6PD deficiency, unstable hemoglobinopathies, hemoglobin H disease

  - **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

Low

- **Indeterminate**

- **Iron deficiency anemia (see related algorithm)**

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 -α3.7, -α4.2, -α(α20.5, --SEA, --MED-I, --FLI, and --THA.I.