Overview

Useful For
Identifying mutations within the *IDUA* gene

Confirmation of a diagnosis of mucopolysaccharidosis type I (MPS-I)

Carrier testing when there is a family history of MPS-I, but disease-causing mutations have not been previously identified

Genetics Test Information
Testing includes full gene sequencing of the *IDUA* gene.

Reflex Tests

<table>
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<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>CULFB</td>
<td>Fibroblast Culture for Genetic Test</td>
<td>Yes</td>
<td>No</td>
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</table>

Testing Algorithm
If skin biopsy is received, fibroblast culture for genetic test will be added and charged separately.

The following algorithms are available in Special Instructions:

- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I

For more information, see Newborn Screening Act Sheet Mucopolysaccharidosis Type I: Decreased Alpha-L-Iduronidase in Special Instructions.

Special Instructions
- Molecular Genetics: Biochemical Disorders Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Mucopolysaccharidoses Type I: Decreased Alpha-L-Iduronidase
- Newborn Screen Follow-up for Mucopolysaccharidosis Type I
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1

Method Name
Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis

NY State Available
Yes
**Specimen**

**Specimen Type**  
Varies

**Shipping Instructions**  
Specimen preferred to arrive within 96 hours of draw.

**Specimen Required**  

**Patient Preparation:** A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

**Preferred:**

**Specimen Type:** Whole blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA) or yellow top (ACD)

**Acceptable:** Any anticoagulant

**Specimen Volume:** 3 mL

**Collection Instructions:**

1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred)/Refrigerated

**Specimen Type:** Cultured fibroblasts

**Container/Tube:** T-75 or T-25 flask

**Specimen Volume:** 1 Full T-75 flask or 2 full T-25 flasks

**Specimen Stability Information:** Ambient (preferred)/Refrigerated <24 hours

**Specimen Type:** Skin biopsy

**Container/Tube:** Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin. Tubes can be supplied upon request (Eagle's minimum essential medium with 1% penicillin and streptomycin [T115]).

**Specimen Volume:** 4-mm punch
Specimen Stability Information: Refrigerated (preferred)/ Ambient

Acceptable:

Specimen Type: Blood spot

Supplies: Card - Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper or Blood Spot Collection Card (T493)

Specimen Volume: 2 to 5 Blood spots

Collection Instructions:

1. An alternative blood collection option for a patient >1 year of age is finger stick.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Additional Information:

1. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.
2. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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 in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. Molecular Genetics: Biochemical Disorders Patient Information (T527) in Special Instructions

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
Test Definition: MPS1Z
Hurler Syndrome, Full Gene Analysis

Blood: 1 mL
Blood Spots: 5, 3-mm diameter

Reject Due To
All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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Clinical and Interpretive

Clinical Information

Mucopolysaccharidosis type I (MPS-I) can be categorized into 3 syndromes, Hurler syndrome, Scheie syndrome, and Hurler-Scheie syndrome. MPS-I, inherited in an autosomal recessive manner, is caused by mutations in the IDUA gene. Furthermore, MPS-I is characterized by reduced or absent activity of the alpha-L-iduronidase enzyme.

Hurler syndrome (severe MPS-I) has early onset and consists of skeletal deformities, coarse facial features, corneal clouding, hepatosplenomegaly, cardiac involvement, hearing loss, and respiratory tract infections. Developmental delay is noticed as early as 12 months with death occurring usually before 10 years of age.

Hurler-Scheie syndrome and Scheie syndrome (attenuated MPS-I) have onset between 3 to 10 years of age and consist of corneal clouding, cardiac involvement, moderate-to-severe hearing loss, and progressive pulmonary disease. Typically skeletal and joint involvement is the most significant source of discomfort for attenuated MPS-I. Intellect with attenuated MPS-I is typically normal or nearly normal.

The IDUA gene is located on chromosome 4 and has 14 exons. IDUA is the only known gene to be associated with MPS-I, and the 3 syndromes appear to be caused by different combinations of mutations.

The recommended first-tier test for MPS-I is biochemical testing that measures alpha-L-iduronidase enzyme activity in blood or fibroblasts: IDSWB / Alpha-L-Iduronidase, Blood or IDST / Alpha-L-Iduronidase, Fibroblasts. Individuals with decreased or absent enzyme activity are more likely to have 2 identifiable mutations in the IDUA gene by molecular genetic testing. However, enzymatic testing is not reliable to detect carriers.

Reference Values
An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of mucopolysaccharidosis type I (MPS-I) may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of MPS-I. The preferred approach to carrier testing is to first document the presence of an IDUA gene mutation in an affected family member.
In some cases, DNA alterations of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

**Clinical Reference**


5. Vijay S, Wraith JE: Clinical presentation and follow-up of patients with the attenuated phenotype of mucopolysaccharidosis type I. Acta Paediatr 2005;94(7):872-877

**Performance**

**Method Description**

Bi-directional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the *IDUA* gene. (Unpublished Mayo method)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Performed weekly; Varies

**Analytic Time**

14 days

**Maximum Laboratory Time**

20 days

**Specimen Retention Time**

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

**Performing Laboratory Location**

Rochester
Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81406 IDUA (iduronidase, alpha-L-) (eg, mucopolysaccharidosis type I), full gene sequence
Fibroblast Culture for Genetic Test
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

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