MAYO CLINIC LABORATORIES

Test Definition: MPS2R

Endogenous Mucopolysaccharidosis Type II (I2S [Iduronate-2-Sulfatase]) Biomarker Reflex, Blood Spot

Overview

Useful For

Second-tier testing of newborns with an abnormal primary screening result for mucopolysaccharidosis type II (MPS II, decreased iduronate-2-sulfatase) where quantitation of the glycosaminoglycans dermatan and heparan sulfate is desired in the presence of elevated endogenous MPS II biomarkers

Follow-up testing for evaluation of an abnormal newborn screening result for MPS II.

This test is **not useful** a monitoring test for individuals with MPS II.

This test is **not appropriate** for carrier detection.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MPSBS	Mucopolysaccharidosis, BS	Yes	No

Genetics Test Information

This test is a second-tier assay for newborns and infants who have abnormal newborn screening results for mucopolysaccharidosis type II (MPS II) with reduced iduronate-2-sulfatase activity.

Testing Algorithm

Testing begins with analysis of the mucopolysaccharidosis type II (MPS II) specific endogenous biomarker. If it is within the normal range, testing is complete. If the MPS II specific endogenous biomarker is elevated, quantification of heparan sulfate, dermatan sulfate, and keratan sulfate will be performed at an additional charge.

If the patient has abnormal newborn screening results for MPS II, timely action should be taken. Refer to the appropriate American College of Medical Genetics and Genomics Newborn Screening ACT Sheet.(1)

For more information see Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans.

Special Instructions

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions
- Newborn Screening Follow up for Mucopolysaccharidosis Type II: Decreased Iduronate 2-Sulfatase Activity and Elevated Blood Glycosaminoglycans

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Highlights

This assay provides an analysis of a glycosaminoglycan (GAG) fragment that is specific to mucopolysaccharidosis type II (MPS II) with reflex to quantitative values of heparan sulfate, dermatan sulfate, and keratan sulfate when elevated.

Elevations of the MPS II specific endogenous biomarker and the GAGs heparan and dermatan sulfate are suggestive of a diagnosis of MPS II.

This assay can help differentiate true cases of MPS II from false-positive cases (such as carriers and pseudodeficiency of the iduronate-2-sulfatase enzyme).

Additional biochemical or molecular testing is required to confirm a diagnosis of MPS II.

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This test is recommended for assessment of newborns and infants with a positive newborn screen for mucopolysaccharidosis type II (MPS II). This test is **not intended** to be used as a monitoring test for individuals with confirmed MPS II.

Shipping Instructions

Specimens stored at ambient temperatures for more than 13 days after collection may result in false-positive results in carrier and other unaffected individuals.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood Spot Collection Card
Acceptable: Whatman Protein Saver 903 paper, PerkinElmer 226 filter paper, Munktell filter paper, local newborn screening card, or postmortem screening card.
Specimen Volume: 2 Blood spots
Collection Instructions
1. An alternative blood collection option for patient older than 1 year is a fingerstick. For detailed instructions, see How

to Collect Dried Blood Spot Samples.

2. Completely fill at least 2 circles on filter paper card (approximately 100 microliters blood per circle).
3. Let blood dry on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.

Additional Information:

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

Forms

1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

1 Blood spot

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers/applications	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated (preferred)	30 days	FILTER PAPER
	Ambient	13 days	FILTER PAPER
	Frozen	90 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Mucopolysaccharidosis II (MPS II; Hunter syndrome) is an X-linked lysosomal disorder caused by the deficiency of iduronate-2-sulfatase enzyme due to variants in the *IDS* gene. Clinical features and severity of symptoms are widely variable ranging from severe infantile onset disease to an attenuated form, which generally has a later onset with a

milder clinical presentation. Symptoms may include coarse facies, short stature, enlarged liver and spleen, hoarse voice, stiff joints, cardiac disease, and profound neurologic involvement leading to developmental delays and regression. As an X-linked disorder, MPS II occurs primarily in male patients with an estimated incidence of 1 in 120,000 male births, although symptomatic carrier females have been reported. Treatment availability, including hematopoietic stem cell transplantation and enzyme replacement therapy, makes early diagnosis desirable, as early initiation of treatment has been shown to improve clinical outcomes. Newborn screening for MPS II has been implemented in some states.

Individuals with MPS II typically demonstrate elevated levels of the glycosaminoglycans (GAGs) dermatan sulfate and heparan sulfate (see MPSQU / Mucopolysaccharides Quantitative, Random, Urine; or MPSBS / Mucopolysaccharides, Blood Spot), as well as elevated levels of GAG fragments known as endogenous disaccharide biomarkers that are specific to the deficiency of iduronate-2-sulfatase. Reduced or absent activity of iduronate-2-sulfatase (see I2SWB / Iduronate-2-Sulfatase, Leukocytes) can confirm a diagnosis of MPS II but may also be deficient in unaffected individuals with pseudodeficiency as well as in individuals with multiple sulfatase deficiency. Enzymatic testing is not reliable to detect carriers. Molecular genetic testing of the *IDS* gene allows for detection of the disease-causing variant in affected patients and subsequent carrier detection in female relatives (see MPS2Z / Hunter Syndrome, Full Gene Analysis, Varies).

Reference Values

An interpretive report will be provided.

Interpretation

The qualitative measurement of mucopolysaccharidosis type II (MPS II) specific endogenous biomarker is compared to the reference value. This report is in text form only, indicating if the MPS II specific endogenous biomarker value is or is not suggestive of a biochemical diagnosis of MPS II. In any specimen where the MPS II specific endogenous biomarker value is elevated, quantitative analysis of heparan, dermatan, and keratan sulfate will be performed.

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. To verify a preliminary diagnosis, independent biochemical (ie, in vitro enzyme assay or quantitative glycosaminoglycan measurement) or molecular genetic analyses are required, many of which are offered within Mayo Clinic Laboratories. Recommendations for additional biochemical testing and confirmatory studies (biomarker, enzyme assay, molecular analysis) are provided in the interpretative report.

Cautions

Individuals with multiple sulfatase deficiency may also have abnormal levels of mucopolysaccharidosis type II specific biomarker and heparan and dermatan sulfate.

Clinical Reference

1. ACMG Newborn Screening ACT Sheets. Newborn Screening ACT Sheet [Iduronate 2-Sulfatase Deficiency] Mucopolysaccharidosis Type II. American College of Medical Genetics and Genomics; 2022 .Accessed October 23, 2024. Available at www.acmg.net/PDFLibrary/MPS-II.pdf

2. Saville JT, Herbst ZM, Gelb MH, Fuller M. Endogenous, non-reducing end glycosaminoglycan biomarkers for the mucopolysaccharidoses: Accurate diagnosis and elimination of false positive newborn screening results. Mol Gen Metab. 2023;140(3):107685

3. Herbst ZM, Hong X, Urdaneta L, et al. Endogenous, non-reducing end glycosaminoglycan biomarkers are superior to

internal disaccharide glycosaminoglycan biomarkers for newborn screening of mucopolysaccharidoses and GM1 gangliosidosis. Mol Genet Metab. 2023;140(1-2):107632
4. Peck DS, Lacey JM, White AL, et al. Incorporation of second-tier biomarker testing improves the specificity of newborn screening for mucopolysaccharidosis type I. Int J Neonatal Screen. 2020;6(1):10. doi:10.3390/ijns6010010

Performance

Method Description
Sample preparation consists of extraction from dried blood spots using aqueous buffer and the addition of reagents to aid in removing the analytes from the filter paper. The resulting extracted analytes are chemically derived to aid in chromatographic separation and to increase signal intensity. A liquid/liquid extraction is preformed to remove the derived analytes from bulk matrix. The sample is then analyzed via liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Mondays, Thursdays

Report Available
3 to 6 days

Specimen Retention Time
6 months

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.

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CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPS2R	MPS II Biomarker Reflex, BS	In Process

Result ID	Test Result Name	Result LOINC® Value
622364	Interpretation	59462-2
622365	Reviewed by	18771-6