Overview

Useful For
Second-tier newborn screen for tyrosinemia type 1 (HT-1) when primary screen showed nonspecific elevations of tyrosine

Diagnosis of HT-1 when used in conjunction with testing for urine organic acids (OAU), liver function tests, alpha-fetoprotein, and molecular genetic analysis of FAH

Genetics Test Information
This test is a second-tier newborn screen for tyrosinemia type 1 (HT-1).

Special Instructions
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions

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

NY State Available
Yes

Specimen

Specimen Type
Whole blood

Necessary Information
Patient’s age is required.

Specimen Required
Submit only 1 of the following specimen types:

Preferred:
Specimen Type: Blood Spot

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

Container/Tube:
Preferred: Blood Spot Collection Card

Acceptable: Whatman Protein Saver 903 Paper, Ahlstrom 226 filter paper, Munktell filter paper, or blood collected in tube containing heparin, ACD or EDTA and dried on filter paper.

Specimen Volume: 2 blood spots

Collection Instructions:
1. At least 1 spot should be complete, i.e., unpunched.

2. Do not expose specimen to heat or direct sunlight.

3. Do not stack wet specimens.

4. Keep specimen dry.

5. If collection of a new specimen is necessary, let blood dry on the Blood Spot Collection Card (T493) at ambient temperature in a horizontal position for 3 hours.

**Specimen Stability Information:** Ambient (preferred) 90 days/Refrigerated 90 days/Frozen 90 days

**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.

**Acceptable**

**Specimen Type:** Whole Blood

**Container/Tube:**

**Preferred:** Lavender top (EDTA)

**Acceptable:** Green top (sodium or lithium heparin) and yellow top (ACD)

**Specimen Volume:** 2 mL

**Collection Instructions:** Send specimen in original tube.

**Specimen Stability Information:** Refrigerate (preferred) 4 days/Ambient 4 days

**Forms**

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

**Specimen Minimum Volume**

Blood Spot: 1
Whole Blood: 0.5 mL

**Reject Due To**

<table>
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<tr>
<th>Other</th>
<th>Blood spot specimen that shows serum rings or has multiple layers. Insufficient specimen Unapproved filter papers</th>
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Specimen Stability Information

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

Clinical Information
Tyrosinemia type 1 (hepatorenal tyrosinemia, HT-1) is an autosomal recessive condition caused by a deficiency of the enzyme fumarylacetoacetate hydrolase (FAH). HT-1 primarily affects the liver, kidneys, and peripheral nerves causing severe liver disease, renal tubular dysfunction, and neurologic crises. If left untreated, most patients die of liver failure in the first years of life, and all are at risk of developing hepatocellular carcinoma. Treatment with 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC) is available and is particularly effective when initiated in newborns. The incidence of HT-1 is approximately 1 in 100,000 live births.

While tyrosine can be determined by routine newborn screening, it is not a specific marker for tyrosinemia type I and often may be associated with common and benign transient tyrosinemia of the newborn. Succinylacetone (SUAC) is a specific marker for HT-1, but not consistently measured by newborn screening programs. This assay determines succinylacetone and tyrosine in newborn blood spots by tandem mass spectrometry. Additional follow-up testing may include confirmatory molecular analysis of the FAH gene.

Reference Values

SUC NyLACETONE

<1.00 nmol/mL

TYROSINE

<4 weeks: 40.0-280.0 nmol/mL

> or =4 weeks: 25.0-150.0 nmol/mL

Interpretation
Elevations of succinylacetone (SUAC) above the reference range with or without elevations of tyrosine (TYR) are indicative of tyrosinemia type 1.

Elevations of TYR above the reference range without elevations of SUAC may be suggestive of tyrosinemia type II, type III, transient hypertyrosinemia of the neonate, or nonspecific liver disease.

Cautions
Normal levels may be seen in affected individuals undergoing treatment.

In rare cases of tyrosinemia type I, tyrosine and/or succinylacetone may not be elevated.

Clinical Reference


**Performance**

**Method Description**

A 3-mm disk is punched out of the blood spot onto a 96-well plate. Then, tyrosine is extracted by the addition of methanol and a known concentration of isotopically labeled tyrosine as internal standards. The extract is moved to another 96-well plate and dried under a stream of nitrogen. In a parallel process, succinylacetone is extracted from the residual blood spot by the addition of a methanol solution containing isotopically labeled succinylacetone as internal standard, derivatized with an acidic hydrazine solution, evaporated and combined with the tyrosine extract. Analytes are measured by liquid chromatography tandem mass spectrometry (LC-MS/MS). The concentrations of the analytes are established by computerized comparison of ion intensities of these analytes to that of the respective internal standards.(Unpublished Mayo method)

**PDF Report**

No

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

Monday through Friday; 9 a.m.

**Analytic Time**

3 days

**Maximum Laboratory Time**

7 days

**Specimen Retention Time**

1 year

**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

84510
82542

LOINC® Information

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