MAYO CLINIC LABORATORIES

Test Definition: TYRSC

Tyrosinemia Follow Up Panel, SC, BS

Overview

Useful For

Monitoring of individuals with tyrosinemia type I (hepatorenal tyrosinemia)

Genetics Test Information

This test is intended for therapeutic monitoring of 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cycohexanedione (NTBC; nitisinone) and dietin patients with tyrosinemia type 1 (HT-1).

Highlights

Blood spot specimens for this test are self-collected by the patient to send directly to Mayo Clinic Laboratories via supplied collection kit. For more information, see Specimen Required.

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

1. Patient's age is required.

2. Patient’s street address, city, state, zip code, country and home phone are required.

Specimen Required

Supplies: Blood Spot Collection-Self Collect (T858)

Container/Tube: Blood Spot Self Collection Card

Specimen Volume: 2 Blood spots

Additional Information:

1. Order test each time the patient is to collect a dried blood specimen at home and mail the specimen directly to Mayo Clinic Laboratories.

2. Order should be placed a minimum of 3 days prior to desired date of collection.

3. Enter patient’s address information for each order created, including street address, city, state abbreviation, zip code, country, and home phone number.

4. For each order, the Blood Spot Collection-Self Collect kit will be mailed directly to the patient for self-collection.

5.See Dried Blood Spot Collection Tutorial for how to collect blood spots: https://vimeo.com/508490782

Forms

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

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Unapproved filter papers	Reject

Specimen Minimum Volume

1 Blood spot

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Tyrosinemia type 1 (hepatorenal tyrosinemia: HT-1) is an autosomal recessive condition caused by a deficiency of the enzyme fumarylacetoacetate hydrolase. 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 (HCC). The incidence of HT-1 is approximately 1 in 100,000 live births.

Affected individuals can show a partial response to dietary restriction of phenylalanine and tyrosine, but dietary treatment in conjunction with the administration of 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC; nitisinone), an inhibitor of the proximal tyrosinemia pathway, is very effective when initiated in newborns. Outcome data are promising and to date, newborn patients treated with NTBC have not developed acute liver disease, neurologic crises, or HCC.

According to treatment guidelines established in 2017, monitoring of blood NTBC concentration and succinylacetone (SUAC) levels along with measuring the dietary intake of amino acids, including tyrosine and phenylalanine are part of an individualized surveillance plan for patients with HT-1.(1) Monthly analysis of SUAC, NTBC concentration, and amino acids is suggested for the first year of life with the same compounds being monitored every 3 months to age 5 years and every 6 months thereafter.

The analytes encompassed in this assay satisfy the recommendations for diagnosis and monitoring of HT-1. In particular, for NTBC, the current guidelines recommend 40 nmol/mL to 60nmol/mL plasma concentration, which corresponds to a target range for NTBC in dried blood spots of 17 nmol/mL to 26nmol/mL based on a blood to plasma conversion factor of 2.34.(2)

Data from the validation of this assay suggests that NTBC dosing could be individualized while not to exceed DBS levels of 26nmol/mL.(3)

Reference Values

TYROSINE

<4 weeks: 40.0-280.0 nmol/mL

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

PHENYLALANINE:

27.0-107.0 nmol/mL
METHIONINE:
11.0-45.0 nmol/mL
SUCCINYLACETONE:
<1.00 nmol/mL
NITISINONE:
<0.7 nmol/mL

Interpretation
Quantitative results with reference values are reported without added interpretation. When applicable, reports of abnormal results may contain an interpretation based on available clinical information.

Cautions
Bornaprine (Sormodrem) may, at least in theory, interfere with accurate measurement of 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3 cyclohexanedione (NTBC).
In rare cases of tyrosinemia type I, tyrosine or succinylacetone may not be elevated.

Clinical Reference
1. Chinsky JM, Singh R, Ficiciolglu C, et. al: Diagnosis and treatment of tyrosinemia type I: a US and Canadian consensus group review and recommendations. Genet Med. 2017 Dec;19(12). doi: 10.1038/gim.2017.101
2. Laeremans H, Turner C, Andersson T, et al: Inter-laboratory analytical improvement of succinylacetone and nitisinone quantification from dried blood spot samples. JIMD Rep. 2020 May;53(1):90-102
3. Schultz MJ, Netzel BC, Singh RH, et al: Laboratory monitoring of patients with hereditary tyrosinemia type I. Mol Genet Metab. 2020 Aug;130(4):247-254
4. Mitchell GA, Grompe M, Lambert M, Tanguay RM: Hypertyrosinemia. In: Valle D, Beaudet AL, Vogelstein B, et al, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 22, 2021. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225082825&bookid=2709
5. Blackburn PR, Hickey RD, Nace RA, et al: Silent tyrosinemia type I without elevated tyrosine or succinylacetone associated with liver cirrhosis and hepatocellular carcinoma. Hum Mutat. 2016 Oct;37(10):1097-1105. doi: 10.1002/humu.23047

Performance

Method Description
A 3-mm disk is punched out of the blood spot onto a 96-well plate. The amino acids and nitisinone are extracted by the addition of methanol and known concentrations of isotopically labeled amino acids and mesotrione 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 amino acid and nitisinone 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

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

Fees & Codes

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 US Food and Drug Administration.

CPT Code Information

84510
84030
82131
82542
80299
82542 only (if appropriate for government payers)