MAYO CLINIC LABORATORIES

Test Definition: OROT

Orotic Acid, Random, Urine

Overview

Useful For

Evaluation of the differential diagnosis of hyperammonemia and hereditary orotic aciduria

Sensitive indicator of ornithine transcarbamylase (OTC) activity after administration of allopurinol or a protein load to identify OTC carriers

Special Instructions

- Biochemical Genetics Patient Information

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Urine

Necessary Information

Patient's age is required.

Specimen Required

Supplies: Urine Tubes, 10 mL (T068)
Container/Tube: Plastic, 10-mL urine tube
Specimen Volume: 3 mL
Collection Instructions:
1. Collect a random urine specimen.
2. No preservative needed.

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

2 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Urine	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Urinary excretion of orotic acid, an intermediate in pyrimidine biosynthesis, is increased in many urea cycle disorders and in a number of other disorders involving the metabolism of arginine. The determination of orotic acid can be useful to distinguish between various causes of elevated ammonia (hyperammonemia). Hyperammonemia is characteristic of all urea cycle disorders, but orotic acid is only elevated in some, including ornithine transcarbamylase (OTC) deficiency, citrullinemia, and argininosuccinic aciduria. Orotic acid is also elevated in the transport defects of dibasic amino acids (lysinuric protein intolerance and hyperornithinemia, hyperammonemia, and homocitrullinuria [HHH] syndrome) and is greatly elevated in patients with hereditary orotic aciduria (uridine monophosphate synthase [UMPS] deficiency).

Ornithine transcarbamylase deficiency is an X-linked urea cycle disorder that affects patients to varying degrees based on their sex and severity of molecular *OTC* variant. It is thought to be the most common urea cycle disorder, with an estimated incidence of 1:56,000. In OTC deficiency, carbamoyl phosphate accumulates and is alternatively metabolized into orotic acid. Allopurinol inhibits orotidine monophosphate decarboxylase and, when given to OTC carriers (who may have normal orotic acid excretion), can cause increased excretion of orotic acid. When orotic acid is measured after a protein load or administration of allopurinol, its excretion is a very sensitive indicator of OTC activity. A carefully monitored allopurinol challenge followed by several determinations of a patient's orotic acid excretion can be useful to identify OTC carriers, as approximately 5% to 10% of *OTC* variants are not detectable by current molecular genetic testing methods.

Reference Values

< or =6 years: < or =4 mmol/mol creatinine
7-18 years: < or =3 mmol/mol creatinine
> or =19 years: < or =5 mmol/mol creatinine

Interpretation

The value for orotic acid concentration is reported. The interpretation of the result must be correlated with clinical and other laboratory findings.

Cautions

Pregnant individuals will normally excrete up to twice the upper limit of the adult reference range.

Clinical Reference

1. Singh RH, Rhead WJ, Smith W, et al. Nutritional management of urea cycle disorders. Crit Care Clin. 2005;21(4 Suppl):S27-35

2. Lee B, Singh RH, Rhead WJ, et al. Considerations in the difficult-to-manage urea cycle disorder patient. Crit Care Clin. 2005;21(4 Suppl):S19-25
3. Brusilow SW, Horwich AL. Urea cycle enzymes. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed February 12, 2026. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225084071
4. Webster DR, Becroft DO, van Gennip AH, Van Kuilenburg AP. Hereditary orotic aciduria and other disorders of pyrimidine metabolism. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease., McGraw-Hill; 2019. Accessed February 12, 2026. Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225090376
5. Simpson KL, MacLeod EL, Kakajiwala A, Gropman AL, Ah Mew N. Urea cycle disorders overview. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2003. Updated July 3, 2025. Accessed February 12, 2026. Available at www.ncbi.nlm.nih.gov/books/NBK1217

Performance

Method Description
Diluted, filtered urine is mixed with an internal standard mixture and analyzed for orotic acid by liquid chromatography-tandem mass spectrometry. The ratio of the extracted peak area of orotic acid to the added internal standard is used to calculate the concentration present in the sample.(la Marca G, Casetta B, Malvagia S, et al. Implementing tandem mass spectrometry as a routine tool for characterizing the complete purine and pyrimidine metabolic profile in urine samples. J Mass Spectrom. 2006;41[11]:1442-1452; Monostori P, Klinke G, Hauke J, et al. Extended diagnosis of purine and pyrimidine disorders from urine: LC MS/MS assay development and clinical validation. PLoS One. 2019;14[2]:e0212458. doi:10.1371/journal.pone.0212458)

PDF Report
No

Day(s) Performed
Tuesday, Thursday

Report Available
3 to 7 days

Specimen Retention Time
1 month

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.

CPT Code Information

83921

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
OROT	Orotic Acid, U	17869-9

Result ID	Test Result Name	Result LOINC® Value
8905	Orotic Acid, U	17869-9