

## Overview

### Useful For

Screening children for catecholamine-secreting tumors using a 24-hour urine collection when requesting testing for vanillylmandelic acid only

Supporting a diagnosis of neuroblastoma

Monitoring patients with a treated neuroblastoma

### Special Instructions

- [Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens](#)

### Highlights

Vanillylmandelic acid (VMA) and other catecholamine metabolite, such as homovanillic acid (HVA), measurements in urine are used for screening children for catecholamine-secreting tumors, such as neuroblastoma and other neural crest tumors, and monitoring those who have had treatment for these tumors.

More than 90% of individuals with neuroblastoma have elevated VMA and/or HVA.

VMA is not the analyte of choice for diagnosis of pheochromocytoma, which is better detected by testing for metanephrines.

Treatment with L-dopa can impact test results and should be discontinued 24 hours prior to collection. Bactrim can impact test results and should be noted at time of collection.

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Urine

### Ordering Guidance

In the past, this test has been used to screen for pheochromocytoma. However, vanillylmandelic acid (VMA) is not the analyte of choice to rule out a diagnosis of pheochromocytoma. Recommended tests for that purpose include:  
-PMET / Metanephrines, Fractionated, Free, Plasma

-METAF / Metanephrines, Fractionated, 24 Hour, Urine  
-CATU / Catecholamine Fractionation, Free, 24 Hour, Urine

Necessary Information

- 1. Patient’s age is required.
- 2. Collection duration (in hours) and urine volume (in milliliters) are required.
- 3. All patients receiving L-dopa should be identified to the laboratory when this test is ordered.
- 4. Bactrim may interfere with detection of the analyte. All patients taking Bactrim should be identified to the laboratory when this test is ordered.

Specimen Required

**Patient Preparation:** Administration of L-dopa may falsely increase vanillylmandelic acid results. For 24 hours prior to specimen collection, the patient should **not** take L-dopa.

**Supplies:** Urine Tubes, 10 mL (T068)

**Collection Container/Tube:** Clean, plastic urine collection container

**Submission Container/Tube:** Plastic, 10-mL urine tube

**Specimen Volume:** 5 mL

Collection Instructions:

- 1. Add 25 mL of 50% acetic acid as preservative at the start of collection. Use 15 mL of 50% acetic acid for children younger than 5 years. If specimen is refrigerated during collection, preservative may be added up to 12 hours after collection. This preservative is intended to achieve a pH of between approximately 1 and 5.
- 2. Collect a 24-hour urine specimen.
- 3. If necessary, adjust urine pH to a level between 1 and 5 by adding 50% acetic acid or hydrochloric acid dropwise and checking the pH.

**Additional Information:** For multiple collections see [Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens](#).

Forms

If not ordering electronically, complete, print, and send an [Oncology Test Request](#) (T729) with the specimen.

Urine Preservative Collection Options

**Note:** For addition of preservative or application of temperature information, see Specimen Required.

Ambient (no additive)	No
Refrigerate (no additive)	No
Frozen (no additive)	No
50% Acetic Acid	Preferred
Boric Acid*	OK
Diazolidinyl Urea	No
6M Hydrochloric Acid	OK
6M Nitric Acid	OK
Sodium Carbonate	No
Toluene	No
*If boric acid is used, note on specimen container. Also, verify that pH is in desired range (pH=1-5). If pH is outside of desired range, adjust pH with a stronger acid (acetic	

acid is preferred but other acids listed above could be used if available) in a dropwise fashion to bring pH into desired range.

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	Refrigerated (preferred)	28 days	
	Frozen	180 days	

Clinical & Interpretive

Clinical Information

Vanillylmandelic acid (VMA) and other catecholamine metabolites (homovanillic acid [HVA] and dopamine) are typically elevated in patients with catecholamine-secreting tumors (eg, neuroblastoma, pheochromocytoma, and other neural crest tumors). VMA and HVA levels may also be useful in monitoring patients who have been treated as a result of one of the above-mentioned tumors.

Reference Values

- <1 year: <25.0 mg/g creatinine
- 1 year: <22.5 mg/g creatinine
- 2-4 years: <16.0 mg/g creatinine
- 5-9 years: <12.0 mg/g creatinine
- 10-14 years: <8.0 mg/g creatinine
- > or =15 years (adults): <8.0 mg/24 hours

Interpretation

Vanillylmandelic acid and/or homovanillic acid concentrations are elevated in most patients (more than 90%) with neuroblastoma; both tests should be performed. A positive test could be due to a genetic or nongenetic condition. Additional confirmatory testing is required.

A normal result does not exclude the presence of a catecholamine-secreting tumor.

Elevated values are suggestive of a pheochromocytoma, but they are not diagnostic.

Cautions

Values are more commonly elevated during a hypertensive episode.

Values may be normal in some individuals with pheochromocytoma.

All patients taking Bactrim should be identified to the laboratory when vanillylmandelic acid and homovanillic acid tests are ordered due to potential interference.

**Clinical Reference**

1. Eisenhofer G. Monoamine-producing tumors. In: Rifai N, Chiu RWK, Young I, Burnham CD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023: 765-765.e54

2. Hyland K. Disorders of neurotransmitter metabolism. In: Blau N, Duran M, Blaskovics ME, Gibson KM, eds. Physician's Guide to the Laboratory Diagnosis of Metabolic Diseases. Springer; 2003:107-122

3. Ormazabal A, Molero-Luis M, Garcia-Cazorla A, Artuch R. Biomarkers for the study of catecholamine and serotonin genetic diseases. In: Garg U, Smith LD, eds. Biomarkers in Inborn Errors of Metabolism: Clinical Aspects and Laboratory Determination. Elsevier; 2017:301-329

4. Strenger V, Kerbl R, Dornbusch HJ, et al. Diagnostic and prognostic impact of urinary catecholamines in neuroblastoma patients. *Pediatr Blood Cancer*. 2007;48(5):504-509

5. Barco S, Gennai I, Reggiardo G, et al. Urinary homovanillic and vanillylmandelic acid in the diagnosis of neuroblastoma: report from the Italian Cooperative Group for Neuroblastoma. *Clin Biochem*. 2014;47(9):848-852

6. Matthay KK, Maris JM, Schleiermacher G, et al. Neuroblastoma. *Nat Rev Dis Primers*. 2016;2:16078. doi:10.1038/nrdp.2016.78

**Performance**

**Method Description**

Vanillylmandelic acid (VMA) is measured by solid-phase extraction (SPE) of a 1-mL aliquot of urine. A known amount of stable-isotope labeled VMA internal standard (IS) is added to each urine specimen prior to SPE. VMA and IS are eluted from the SPE column with methanol. The methanol is evaporated and the VMA and IS are redissolved in liquid chromatography tandem mass spectrometry mobile phase. A portion of this prepared extract is injected onto a LC column that separates VMA and IS from the bulk of any remaining specimen matrix. The VMA and IS are measured by tandem-mass spectrometry using the selected reaction monitoring mode. VMA is quantified using the ratio to IS versus urine calibrators.(Magera MJ, Thompson AL, Stoor AL, et al. Determination of vanillylmandelic acid in urine by stable isotope dilution and electrospray tandem mass spectrometry. *Clin Chem*. 2003;49:825-826; Eisenhofer G, Grebe S, Cheung NV. Monoamine-producing tumors. In Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. Elsevier; 2018:chap 63)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday

**Report Available**

2 to 4 days

**Specimen Retention Time**

7 days

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

84585

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VMA	Vanillylmandelic Acid, 24 Hr, U	43099-1

Result ID	Test Result Name	Result LOINC® Value
3580	Vanillylmandelic Acid, Adult (>14y)	3122-9
3581	Vanillylmandelic Acid, Child (<15y)	30571-4
TM41	Collection Duration	13362-9
VL39	Urine Volume	3167-4