

## Overview

### Useful For

Preferred first test for screening for catecholamine-secreting tumors in a random urine specimen when requesting both homovanillic acid and vanillylmandelic acid

Supporting a diagnosis of neuroblastoma

Monitoring patients with a treated neuroblastoma

### Highlights

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

HVA measurement is also useful for diagnosing children with disorders of catecholamine metabolism, such as monoamine oxidase-A deficiency and dopamine beta-hydroxylase deficiency, which result in decreased or elevated urinary HVA values, respectively.

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

### 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

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**Necessary Information****1. Patient's age is required.**

- All patients receiving L-dopa should be identified to the laboratory when this test is ordered.
- 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 homovanillic acid and 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:**

- Collect a random urine specimen.
- Adjust the urine pH to a level between 1 and 5 by adding 50% acetic acid or hydrochloric acid dropwise and checking the pH.

**Forms**

If not ordering electronically, complete, print, and send an [Oncology Test Request](#) (T729) 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	Refrigerated (preferred)	28 days	
	Frozen	180 days	

**Clinical & Interpretive****Clinical Information**

Elevated values of homovanillic acid (HVA), vanillylmandelic acid (VMA), and other catecholamine metabolites (eg, dopamine) may be suggestive of the presence of a catecholamine-secreting tumor (eg, neuroblastoma, pheochromocytoma, or other neural crest tumors). HVA and VMA levels may also be useful in monitoring patients who have been treated as a result of the above-mentioned tumors. HVA levels may also be altered in disorders of catecholamine metabolism: monamine oxidase-A deficiency can cause decreased urinary HVA values, while a deficiency of dopamine beta-hydroxylase (the enzyme that converts dopamine to norepinephrine) can cause elevated urinary HVA values.

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**Reference Values**

Vanillylmandelic acid

&lt;1 year: &lt;25.0 mg/g creatinine

1 year: &lt;22.5 mg/g creatinine

2-4 years: &lt;16.0 mg/g creatinine

5-9 years: &lt;12.0 mg/g creatinine

10-14 years: &lt;8.0 mg/g creatinine

&gt; or =15 years: &lt;7.0 mg/g creatinine

Homovanillic acid

&lt;1 year: &lt;35.0 mg/g creatinine

1 year: &lt;30.0 mg/g creatinine

2-4 years: &lt;25.0 mg/g creatinine

5-9 years: &lt;15.0 mg/g creatinine

10-14 years: &lt;9.0 mg/g creatinine

&gt; or =15 years: &lt;8.0 mg/g creatinine

**Interpretation**

Homovanillic acid (HVA) and vanillylmandelic acid (VMA) concentrations are elevated in more than 90% of patients 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 HVA and VMA values are suggestive of a pheochromocytoma, but they are not diagnostic.

**Cautions**

Administration of L-dopa may falsely increase homovanillic acid (HVA) and vanillylmandelic acid (VMA) results. Patients receiving L-dopa should stop taking it for 24 hours before the collection.

All patients receiving L-dopa should be identified to the laboratory when HVA or VMA tests are ordered.

All patients taking Bactrim should be identified to the laboratory when HVA or VMA 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
2. 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
3. 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
4. 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  
5. 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

#### Homovanillic Acid:

Homovanillic acid (HVA) is measured by solid-phase extraction (SPE) of a 1-mL aliquot of urine. A known amount of stable isotope-labeled HVA internal standard (IS) is added to each urine specimen prior to SPE. HVA and IS are eluted from the SPE column with methanol. The methanol is evaporated and the HVA and IS are redissolved in liquid chromatography tandem-mass spectrometry (LC-MS/MS) mobile phase. A portion of this prepared extract is injected onto a LC column that separates HVA and IS from the bulk of any remaining specimen matrix. The HVA and IS are measured by mass spectrometry/tandem-mass spectrometry using the selected reaction monitoring mode. HVA is quantified using the ratio to IS versus urine calibrators. (Magera MJ, Stoor A, Helgeson JK, Matern D, Rinaldo P. Determination of homovanillic acid in urine by stable isotope dilution and electrospray tandem mass spectrometry. *Clin Chim Acta.* 2001;306[1-2]:35-41; 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)

#### Vanillylmandelic Acid:

Vanillylmandelic acid (VMA) is measured by SPE of a 1-mL aliquot of urine. A known amount of stable isotope-labeled VMA 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 LC-MS/MS 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 MS/MS 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

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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

83150-HVA

84585-VMA

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VH	VMA and HVA, Random, U	90250-2

Result ID	Test Result Name	Result LOINC® Value
2143	Vanillylmandelic Acid, VH	3124-5
2144	Homovanillic Acid, VH	11146-8