

## Liquid Chromatography-Tandem Mass Spectrometry for Measurement of Urine Metanephrines

### Background Information

Pheochromocytomas are neuroendocrine tumors that may produce excess catecholamines (epinephrine, norepinephrine and dopamine) and metanephrines (metanephrine and normetanephrine) and can present as unexplained hypertension.<sup>1</sup> Urinary fractionated metanephrines assay has been recommended as one of the first-line tests for diagnosis of pheochromocytoma.<sup>1,2</sup>

Metanephrine and normetanephrine are derived from epinephrine and norepinephrine, respectively. Metanephrines are primarily produced in the adrenal chromaffin cells, with some production occurring in the extraneuronal tissues.<sup>1</sup>

Although liquid chromatography with electrochemical detection (LC-ECD) represents one of the most commonly used techniques for measuring urinary metanephrines, it suffers from analytical interference, tedious sample preparation and relatively high imprecision.<sup>2</sup> New methods have recently been reported using LC with tandem mass spectrometric detection (LC-MS/MS), which offers better specificity, less manual sample preparation and shorter chromatographic time.<sup>3,4</sup>

### Clinical Indications

Elevated levels of metanephrines in urine may assist the diagnosis of pheochromocytoma.

### Interpretation

- Metanephrine reference range: 52 - 341  $\mu\text{g}/24\text{hr}$
- Normetanephrine reference range: 88 - 444  $\mu\text{g}/24\text{hr}$

### Limitations of the Assay

1. The method is linear from 42 - 5406 ng/mL and 61 - 2666 ng/mL for metanephrine and normetanephrine, respectively.
2. Minimum sample size of 1.5 mL is required.
3. This is a laboratory-validated assay that uses analyte specific reagents (ASR), which will be indicated.

### Methodology<sup>5</sup>

This assay measures total metanephrines after hydrolysis.

1. Urine metanephrines are extracted by solid phase extraction and analyzed by liquid chromatography-tandem mass spectrometry.
2. Specimen pH should be adjusted to < 3 immediately upon arrival in the laboratory.
3. Specimen should be kept at 4°C until assayed.

### References

1. Eisenhofer G, Siegert G, Kotzerke J, Bornstein SR, Pacak K. Current progress and future challenges in the biochemical diagnosis and treatment of pheochromocytomas and paragangliomas. *Horm Metab Res*. 2008;40:329-37.
2. Barron J. Pheochromocytoma: diagnostic challenges for biochemical screening and diagnosis. *J Clin Pathol*. 63:669-74.
3. Whiting MJ. Simultaneous measurement of urinary metanephrines and catecholamines by liquid chromatography with tandem mass spectrometric detection. *Ann Clin Biochem*. 2009;46:129-36.
4. Taylor RL, Singh RJ. Validation of liquid chromatography-tandem mass spectrometry method for analysis of urinary conjugated metanephrine and normetanephrine for screening of pheochromocytoma. *Clin Chem*. 2002;48:533-9.
5. Gabler J, Miller A, Wang S. A simple liquid chromatography-tandem mass spectrometry method for measuring metanephrine and normetanephrine in urine. *Clinical Chemistry and Laboratory Medicine*. 2011;49(7):1213-1216.

### Related tests

- Plasma metanephrines
- Plasma catecholamines
- Urine catecholamines

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**Test Overview**

<b>Test Name</b>	Metanephrines, urine 24hr; Metanephrines, urine random
<b>Metanephrine Reference Range</b>	52 – 341 $\mu\text{g}/24\text{hr}$
<b>Normetanephrine Reference Range</b>	88 – 444 $\mu\text{g}/24\text{hr}$
<b>Patient Preparation</b>	N/A
<b>Specimen Requirements</b>	2.5 mL urine
<b>Disclaimers or Notations</b>	Not FDA-approved
<b>Test Ordering Information</b>	UMETRA; UMETAN
<b>Billing Code</b>	83835
<b>CPT Code</b>	83835

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