Overview

Useful For
Evaluating patients suspected of having systemic mastocytosis
Identification of aspirin sensitivity in patient respiratory diagnoses

Highlights
Systemic mastocytosis (SM) is a heterogeneous disorder; including N-methylhistamine (NMH), and 11 beta-prostaglandin F2 alpha (23BPG) provides a clinical sensitivity above 90% and specificity above 60%.

Testing Algorithm
When leukotriene E4 testing is performed, urine creatinine will always be performed at no additional charge.

Special Instructions

- Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens

Method Name
LTE4: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)
AACT: Enzymatic Colorimetric Assay

NY State Available
Yes

Specimen

Specimen Type
Urine

Specimen Required
Submit only 1 of the following specimens:

Patient Preparation: Patients taking 5-lipoxygenase inhibitor Zileuton/Zyflo may have decreased concentrations of leukotriene E4 (LTE4) if dosage has not been discontinued for 48 hours. If possible, discontinue for 48 hours before testing.

Preferred: 24-hour urine collection

Container/Tube: Plastic, 5-mL tube (T465)

Specimen Volume: 4mL

Collection Instructions:
1. Collect urine for 24 hours.
2. Refrigerate specimen during collection, aliquot 4 mL of urine into plastic tube, and send specimen refrigerated.
Additional Information: See Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens in Special Instructions for multiple collections.

Acceptable: Random collection

Container/Tube: Plastic, 5-mL tube (T465)

Specimen Volume: 4mL

Collection Instructions:

1. Collect a random urine specimen.

2. Refrigerate specimen after collection and send specimen refrigerated or frozen; do not add any preservative.

Urine Preservative Collection Options

Note: The addition of preservative or application of temperature controls must occur within 4 hours of completion of the collection.

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Ambient</td>
<td>OK</td>
</tr>
<tr>
<td>Refrigerate</td>
<td>Preferred</td>
</tr>
<tr>
<td>Frozen</td>
<td>OK</td>
</tr>
<tr>
<td>50% Acetic Acid</td>
<td>OK</td>
</tr>
<tr>
<td>Boric Acid</td>
<td>OK</td>
</tr>
<tr>
<td>Diazolidinyl Urea</td>
<td>No</td>
</tr>
<tr>
<td>6M Hydrochloric Acid</td>
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</tr>
<tr>
<td>6M Nitric Acid</td>
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<tr>
<td>Sodium Carbonate</td>
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<tr>
<td>Thymol</td>
<td>No</td>
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<tr>
<td>Toluene</td>
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</table>

Specimen Minimum Volume

1 mL

Reject Due To

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

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Urine</td>
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<tr>
<td></td>
<td>Frozen</td>
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<tr>
<td></td>
<td>Ambient</td>
<td>24 hours</td>
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Test Definition: LTE4  
Leukotriene E4, U

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<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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Clinical and Interpretive

Clinical Information

Leukotrienes (LT) are eicosanoids generated from arachidonic acid via the 5-lipoxygenase pathway. Leukotriene E4 (LTE4) is the stable end product of this pathway and, therefore, regarded as a biomarker of total cysteinyl leukotriene (cys-LT) production. Assessment of LTE4 in urine allows for noninvasive specimen collection and avoids artifactual formation of LT during phlebotomy. Generation of LTE4 occurs nonspecifically from active mast cells, basophils, eosinophils, and macrophages, and modulated through a variety of mechanisms. Elevated concentrations of LTE4 are associated with inflammatory and accelerated mast cell activation conditions, specifically in patients with systemic mast cell disease.\(^{(1)}\)

Systemic mastocytosis (SM), or systemic mast cell disease, is a myeloproliferative neoplasm that has infiltrated extracutaneous organs. Release of mast cell inflammatory mediators leads to disease symptoms including those associated with allergic and anaphylactic reactions, while increased mast cell number leads to organ dysfunction. Consensus diagnostic criteria for SM include 1 major criterion: imaging of the multifocal infiltrates; and 4 minor criteria: 1) identifying morphological features of greater than 25% of mast cells from bone marrow biopsy, 2) detection of the point mutation at codon 816 in the \textit{KIT} gene, 3) CD2 and/or CD25 expression in mast cells, and 4) persistently elevated serum tryptase. Diagnosis requires either 1 major plus 1 minor criterion or 3 minor criteria.\(^{(2)}\)

Measurement of urinary mast cell activation biomarkers can aid in the initial evaluation of suspected cases of systemic mast cell disease, potentially avoiding the need for imaging and bone marrow examination. Patients with SM frequently have elevated urine concentrations of LTE4,\(^{(1)}\) N-methylhistamine,\(^{(3,4)}\) and 2,3-dinor 11 beta-prostaglandin F2 alpha.\(^{(4)}\)

Urinary LTE4 has also demonstrated significant utility in patients with asthma and respiratory diseases. In a study of adults with mild to moderate asthma on 5-lipoxygenase inhibitors, urine LTE4 concentrations decreased approximately 40% compared with asthma control subjects, suggesting modest decreases in LTE4 production correlates with clinical improvements in asthma severity.

Reference Values

< or =104 pg/mg creatinine

Interpretation

Elevated urinary leukotriene E4 (LTE4) concentrations above 104 pg/mg creatinine are consistent with the diagnosis of systemic mast cell disease when combined with clinical signs and symptoms. Pharmacological treatment with 5-lipoxygenase inhibitors or leukotriene receptor antagonists has been shown to decrease production of LTE4.

Urinary LTE4 may be used together with serum tryptase, urinary 2,3-dinor 11 beta-prostaglandin F2 alpha, and urinary N-methylhistamine.

LTE4 values of 166 pg/mg creatinine were 89% specific for aspirin sensitivity among patients with respiratory diagnoses.

Cautions

Systemic mastocytosis is a heterogenous disease and lack of elevated LTE4 does not exclude the diagnosis of mast cell disease.
Increased excretion of LTE4 has also been reported in the following conditions: asthma, eosinophilic pneumonia, respiratory syncytial virus infection, atopic dermatitis, Crohn disease, and rheumatoid arthritis.

This assay measures both LTE4 and the 11-trans-LTE4 as markers of mast cell release.

**Clinical Reference**

**Performance**

**Method Description**
Leukotriene E4 (LTE4) is quantified in urine by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Deuterium-labeled(d5)-LTE4 internal standard and acetonitrile are added to all standards, controls, and specimens that are then positive pressure filtered to remove salts, particulates, and sediment from the urine. Additional sample clean-up is achieved via a Cyclone MAX mixed mode anion exchange, while a Waters Xbridge C8 analytical column is employed to focus and elute the LTE4 analyte. This eluent is transferred to an API 5000 MS/MS for instrumental analysis. The ratios of the integrated peak areas of LTE4 and its respective deuterium-labeled internal standard are used to calculate the concentration of the analyte.(Unpublished Mayo method)

All LTE4 concentrations are normalized to urine creatinine levels measured using a Roche Cobas enzymatic method.(Package insert: Creatinine plus ver.2 (CREP2), Roche Diagnostics. Indianapolis, IN. 07/2013)

**PDF Report**
No

**Day(s) and Time(s) Test Performed**
Tuesday, Friday; 11 a.m.

**Analytic Time**
2 days

**Maximum Laboratory Time**
6 days

**Specimen Retention Time**
14 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
82542

LOINC® Information

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<th>Order LOINC Value</th>
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<table>
<thead>
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<th>Result LOINC Value</th>
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<tbody>
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<td>62530</td>
<td>Leukotriene E4, U</td>
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