Overview

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

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

Highlights
Urinary leukotriene (LTE4) is elevated in the urine of patients with systemic mastocytosis (SM).
When this test is used in combination with 2,3-dinor-11beta-prostaglandin F2 alpha (2,3 BPG) and N-methyl histamine analyses, the sensitivity for SM detection increases to 90% with a specificity above 60%.

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

Supplies: 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

Supplies: Plastic, 5-mL tube (T465)
Test Definition: LTE4
Leukotriene E4, U

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

<table>
<thead>
<tr>
<th>Preservative</th>
<th>Status</th>
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<tbody>
<tr>
<td>Ambient</td>
<td>OK</td>
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<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>
<td>No</td>
</tr>
<tr>
<td>6M Nitric Acid</td>
<td>No</td>
</tr>
<tr>
<td>Sodium Carbonate</td>
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</tr>
<tr>
<td>Thymol</td>
<td>No</td>
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<tr>
<td>Toluene</td>
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</table>

Reject Due To

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

Specimen Minimum Volume

1 mL

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>
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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 genetic alteration at codon 816 in the KIT gene
3. CD2 and/or CD25 expression in mast cells
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 11beta-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 mixed mode anion exchange. The LC-MS/MS performs the instrumental analysis. The ratios of the integrated peak areas of LTE4 and its respective 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. The enzymatic method is based on the determination of sarcosine from creatinine with the aid of creatininase, creatinase, and sarcosine oxidase. The liberated hydrogen peroxide is measured via a modified Trinder reaction using a colorimetric indicator. Optimization of the buffer system and the colorimetric indicator enables the creatinine concentration to be quantified both precisely and specifically. (Package insert: Creatinine plus ver 2. Roche Diagnostics; V15.0 03/2019)

**PDF Report**
No

**Specimen Retention Time**
14 days

**Performing Laboratory Location**
Rochester

**Fees & Codes**

**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 US Food and Drug Administration.

**CPT Code Information**
82542

**LOINC® Information**

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<td>62530</td>
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