Overview

Useful For
Monitoring zonisamide therapy; recommended for all patients to ensure appropriate dosing
Assessing medication compliance

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

NY State Available
Yes

Specimen

Specimen Type
Serum Red

Specimen Required
Container/Tube: Red top

Specimen Volume: 1 mL

Collection Instructions: Sample must be centrifuged and serum aliquoted off within 2 hours of draw.

Forms
If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume
0.5 mL

Reject Due To

<table>
<thead>
<tr>
<th></th>
<th>Mild OK; Gross OK</th>
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<tbody>
<tr>
<td>Hemolysis</td>
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<tr>
<td>Lipemia</td>
<td></td>
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<tr>
<td>Icterus</td>
<td></td>
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<tr>
<td>Other</td>
<td>Serum Gel, SST</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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<tbody>
<tr>
<td>Serum Red</td>
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<td>28 days</td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>28 days</td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
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Clinical and Interpretive

Clinical Information

Zonisamide (Zonegran) is approved as adjunctive therapy for partial seizures refractory to therapy with traditional anticonvulsants. Zonisamide is the pharmacologically active agent; metabolites are not active. Essentially 100% of the zonisamide dose is absorbed. Zonisamide binds to erythrocytes; approximately 88% of circulating zonisamide is bound in erythrocytes. Because the erythrocyte-bound zonisamide is inactive, and binding varies with blood concentration, the relationship between serum level and dose is not linear. Time to peak zonisamide concentration is 2 to 4 hours; time to peak is delayed by co-administration with food to 4 to 6 hours. Zonisamide is metabolized by N-acetyl transferase (NAT1), cytochrome P4503A4 (CyP3A4), and uridine diphosphate glucuronidation (UDPG). Zonisamide is eliminated in the urine predominantly as the parent drug (35%), N-acetyl zonisamide (15%), and as the glucuronide ester of reduced zonisamide (50%). Co-administration of drugs that affect NAT1, CyP3A4, and UDPG activity, such as phenytoin and carbamazepine, will decrease zonisamide concentration.

A typical zonisamide dose administered to an adult is 400 to 600 mg/day, administered in 2 divided doses. The apparent volume of distribution of zonisamide is 1.5 L/kg. Approximately 40% of the zonisamide circulating in the serum is bound to proteins. Zonisamide protein binding is unaffected by other common anticonvulsant drugs. The elimination half-life from plasma is 50 to 60 hours; the elimination half-life from erythrocytes is >100 hours. Since zonisamide is cleared predominantly by the kidney, the daily dosage of zonisamide given to patients with creatinine clearance <20 mL/min should be reduced.(1,2)

Serum level monitoring is recommended for all patients to ensure appropriate dosing because: 1) patient response correlates with serum level, 2) serum level does not correlate with dose because of concentration-dependent erythrocyte binding, 3) elimination is affected by co-administration of drugs that affect NAT1, CyP3A4, and UDPG, and 4) renal function affects elimination.

The most common toxicity associated with excessive serum level is drowsiness. Adverse effects not related to serum level include rash, increased serum creatinine and alkaline phosphatase, kidney stone formation, and bruising.

Reference Values

10-40 mcg/mL

Interpretation

Steady-state zonisamide concentration in a trough specimen drawn just before next dose correlates with patient response, but not with dose. Optimal response to zonisamide occurs when trough zonisamide concentration is in the range of 10 to 40 mcg/mL. Peak serum concentration for zonisamide occurs 2 to 6 hours after dose, and time to peak is affected by food intake.

Because carbamazepine activates glucuronidation, patients taking carbamazepine concomitantly with zonisamide have significantly lower zonisamide concentrations compared to patients on the same dose not receiving carbamazepine.

Cautions

Rufinamide is a known interference of this assay. Patients who are coadministered zonisamide and rufinamide may have falsely elevated and uninterpretable zonisamide concentrations reported by this assay.

Serum zonisamide will be increased with hemolysis.

Clinical Reference

Test Definition: ZONI
Zonisamide, S


Performance

Method Description
Samples are extracted with analyte detection by mass spectrometry. (Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Saturday

Analytic Time
Same day/1 day

Maximum Laboratory Time
5 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.
## Test Definition: ZONI
Zonisamide, S

### CPT Code Information
80203

### LOINC® Information

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