

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

Collection Container/Tube: Red top (serum gel/SST is **not** acceptable)

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-[Neurology Specialty Testing Client Test Request](#) (T732)

-[Therapeutics Test Request](#) (T831)

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	28 days	

Specimen Type	Temperature	Time	Special Container
	Ambient	28 days	
	Frozen	28 days	

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 P450 3A4 (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%). Coadministration 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 over 100 hours. Since zonisamide is cleared predominantly by the kidney, the daily dosage of zonisamide given to patients with a creatinine clearance below 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 collected 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

1. Hiemke C, Baumann P, Bergemann N, et al: AGNP consensus guidelines for therapeutic drug monitoring in psychiatry: Update 2011. *Pharmacopsychiatry*. 2011 Sep;44(6):195-235
2. Rifai N, Horwath AR, Wittwer CT, eds. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 6th ed. Elsevier; 2018
3. Perucca E: The clinical pharmacokinetics of the new antiepileptic drugs. *Epilepsia*. 1999;40(Suppl 9):S7-S13
4. Marson AG, Hutton JL, Leach JP, et al: Levetiracetam, oxcarbazepine, remacemide and zonisamide for drug resistant localization-related epilepsy: a systematic review. *Epilepsy Res*. 2001;46(3):259-270
5. Benedetti MS: Enzyme introduction and inhibition by new antiepileptic drugs: a review of human studies. *Fundam Clin Pharmacol*. 2000 Jul-Aug;14(4):301-319
6. Kawada K, Itoh A, Kusaka T, et al: Pharmacokinetics of zonisamide in perinatal period. *Brain Dev*. 2002 Mar;24(2):95-97

Performance**Method Description**

The serum sample is crashed with acetonitrile containing the deuterium labeled internal standard. The protein precipitate is centrifuged, and a portion of the supernatant is diluted with mobile phase 1 for detection by tandem mass spectrometry (MS/MS).(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**

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- 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

80203

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
ZONI	Zonisamide, S	29620-2

Result ID	Test Result Name	Result LOINC Value
83685	Zonisamide, S	29620-2