

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

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)

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

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 1 mL

**Collection Instructions:** Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.

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	
	Ambient	28 days	
	Frozen	28 days	

## Clinical & 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; its metabolites are not active. Essentially 100% of the zonisamide dose is absorbed. Approximately 88% of circulating zonisamide is bound to erythrocytes. The relationship between the serum level and dose is not linear because erythrocyte-bound zonisamide is inactive and binding varies with blood concentration. Time to peak zonisamide concentration is 2 to 6 hours; time to peak is delayed by coadministration with food to 4 to 6 hours. Zonisamide is metabolized by *N*-acetyl transferase (NAT1), cytochrome P450 3A4 (CYP3A4), and uridine diphosphate glucuronosyltransferase (UDPGT). 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 UDPGT 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:

- Patient response correlates with serum level.
- Serum level does not correlate with dose because of concentration-dependent erythrocyte binding.
- Elimination is affected by coadministration of drugs that affect NAT1, CYP3A4, and UDPGT.
- Kidney 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 have zonisamide and rufinamide coadministered may have falsely elevated and uninterpretable zonisamide concentrations reported by this assay.

**Clinical Reference**

1. Milone MC, Shaw LM: Therapeutic drugs and their management. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:420-453
2. Hiemke C, Baumann P, Bergemann N, et al. AGNP consensus guidelines for therapeutic drug monitoring in psychiatry: Update 2011. Pharmacopsychiatry. 2011;44(6):195-235
3. Perucca E. The clinical pharmacokinetics of the new antiepileptic drugs. Epilepsia. 1999;40(Suppl 9):S7-S13. doi: 10.1111/j.1528-1157.1999.tb02088.x
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. doi:10.1016/s0920-1211(01)00287-x
5. Benedetti MS. Enzyme induction and inhibition by new antiepileptic drugs: a review of human studies. Fundam Clin Pharmacol. 2000;14(4):301-319. doi:10.1111/j.1472-8206.2000.tb00411.x
6. Kawada K, Itoh A, Kusaka T, et al. Pharmacokinetics of zonisamide in perinatal period. Brain Dev. 2002;24(2):95-97. doi:10.1016/s0387-7604(01)00407-7

**Performance**

**Method Description**

The serum sample is deproteinated with acetonitrile containing the deuterium labeled internal standard. The protein precipitate is centrifuged, and a portion of the supernatant is diluted with mobile phase for detection by tandem mass spectrometry.(Unpublished Mayo method)

**PDF Report**

No

**Day(s) Performed**

Monday through Saturday

**Report Available**

Same day/1 to 3 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & 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 account representative. 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. It has not been cleared or approved by the US 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