MAYO CLINIC LABORATORIES

Test Definition: CARF

Carbamazepine, Free, Serum

Overview

Useful For

Monitoring unbound or free carbamazepine levels in patients where the total carbamazepine result is within the therapeutic range, but the patient is experiencing side effects

Monitoring carbamazepine (free) therapy in patients who are uremic

Method Name

Ultrafiltration followed by Homogeneous Microparticle Agglutination Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Collection Container/Tube: Red top (serum gel/SST are **not acceptable**)
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial within 2 hours of collection.

Forms

If not ordering electronically, complete, print, and send a Therapeutics Test Request (T831) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	7 days	
	Ambient	48 hours	

	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Carbamazepine (Tegretol) is an effective treatment for complex partial seizures, with or without generalization to tonic-clonic seizures.(1) It is frequently administered in conjunction with other antiepileptic agents, such as phenytoin and valproic acid.(2) Under normal circumstances, the carbamazepine that circulates in blood is 70% to 80% protein-bound;(3) only the free drug is able to enter the interstitial space in the brain where the pharmacological effects occur.(4)

Patient management is best guided by monitoring free serum concentrations when protein binding is altered. Altered protein binding occurs in patients with hypoalbuminemia observed during pregnancy, in the malnourished, and liver disease. In patients with kidney disease, uremia may develop whose byproducts can displace bound carbamazepine increasing the unbound fraction. Administration of drugs that can compete for serum protein binding sites may also increase the unbound fraction of carbamazepine. Since neurologic activity and toxicity of carbamazepine are directly related to the circulating free fraction of drug, adjustment of dosage based on knowledge of the free carbamazepine concentration may be more useful in these patient populations.

Reference Values

Therapeutic concentration: 1.0-3.0 mcg/mL
Critical value: > or =4.0 mcg/mL

Interpretation

In patients with normal kidney function, optimal response is often associated with free (unbound) carbamazepine levels above 1.0 mcg/mL, and toxicity may occur when the free carbamazepine is greater than or equal to 4.0 mcg/mL.

Under normal circumstances, 75% of the carbamazepine that circulates in blood is protein-bound. Therapies or conditions such as uremia that displace carbamazepine from protein cause a higher free (unbound) fraction of the drug circulating in blood. In uremia, the free carbamazepine level may be a more useful guide for dosage adjustments than the total level. In patients with severe uremia, subtherapeutic total carbamazepine levels in the range of 1.0 to 2.0 mcg/mL may be associated with therapeutic free carbamazepine levels. Toxicity may occur when the free carbamazepine level is greater than or equal to 4.0 mcg/mL (even though the total carbamazepine concentration is <15.0 mcg/mL).

As with the serum levels of other anticonvulsant drugs, total and free carbamazepine levels should be correlated with the patient's clinical condition. Serum levels are best used as a guide in dose adjustment.

Cautions

Fresh serum with normal protein content is required for optimal analysis.

Specimens subjected to significant heat or other factors that cause protein denaturation may demonstrate an artifactually increased free carbamazepine level.

If hemolysis, lipemia, or icterus exceed the analytical interference threshold, the testing will be canceled.

Clinical Reference

1. Svinarov DA, Pippenger CE. Relationships between carbamazepine-diol, carbamazepine-epoxide, and carbamazepine total and free steady-state concentrations in epileptic patients: the influence of age, sex, and comedication. Ther Drug Monit. 1996;18(6):660-665
2. Bernus I, Dickinson RG, Hooper WD, Eadie MJ. The mechanism of the carbamazepine-valproate interactions in humans. Br J Clin Phamacol. 1997;44(1):21-27
3. Dasgupta A, Volk A. Displacement of valproic acid and carbamazepine from protein binding in normal and uremic sera by tolmetin, ibuprofen, and naproxen: presence of inhibitor in uremic serum that blocks valproic acid-naproxen interactions. Ther Drug Monit. 1996;18(3):284-287
4 Patsalos PN, Berry DJ, Bourgeois BF, et al. Antiepileptic drugs-best practice guidelines for therapeutic drug monitoring: A position paper by the subcommission on therapeutic drug monitoring, ILAE Commission on Therapeutic Strategies. Epilepsia. 2008;49(7):1239-1276
5. Kanner A.M, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs I: Treatment of new-onset epilepsy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2018;91(2):74-81

Performance

Method Description

Free carbamazepine is isolated from serum by ultrafiltration. The ONLINE TDM Carbamazepine Gen.4 assay is a homogeneous microparticle agglutination immunoassay. It is a 2-reagent system used for the detection of carbamazepine in serum. Kinetic interaction of microparticles (KIMS) will be measured using automated analyzers. In this technology, biotinylated drug hapten attached to streptavidin-coated latex beads serves as the binding partner to anti-carbamazepine antibody. A competitive reaction to a limited amount of specific anti-carbamazepine antibody takes place between the latex bound hapten and free carbamazepine in the serum sample. A decrease in the apparent signal is proportional to the amount of drug present in the sample.(Package insert: Carbamazepine reagent. Roche Diagnostics; 06/2024)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

Same day/1 day

Specimen Retention Time

7 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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 has been modified from the manufacturer's instructions. Its performance characteristics were 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

80157

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CARF	Carbamazepine, Free, S	3433-0

Result ID	Test Result Name	Result LOINC® Value
CARF	Carbamazepine, Free, S	3433-0