MAYO CLINIC LABORATORIES

Test Definition: VALPG

Valproic Acid, Free and Total, Serum

Overview

Useful For

Monitoring both total and free valproic acid levels in therapy

Assessing compliance

Evaluating potential toxicity

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
VALPF	Valproic Acid, Free, S	Yes	Yes
VALPA	Valproic Acid, Tot, S	Yes	Yes

Method Name

VALPA: Enzyme Immunoassay (EIA)
VALPF: Ultrafiltration followed by Enzyme Immunoassay (EIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions:
1. Serum gel tubes should be centrifuged within 2 hours of collection.
2. Red-top tubes should be centrifuged, and the serum aliquoted 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	Refrigerated (preferred)	14 days	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Valproic acid (valproate, Depakote, or Depakene) is an effective medication for absence seizures, generalized tonic-clonic seizures, and partial seizures, when administered alone or in conjunction with other antiepileptic agents.

The valproic acid that circulates in blood is 85% to 90% protein-bound under normal circumstances. In uremia or during concomitant therapy with other drugs that are highly protein-bound (such as phenytoin), valproic acid is displaced from protein, resulting in a higher free fraction of the drug circulating in blood.

Since neurologic activity and toxicity of valproic acid are directly related to the unbound fraction of drug, adjustment of dosage based on knowledge of the free valproic acid concentration may be useful in the following: concomitant use of highly protein-bound drugs (usually >80% bound), hypoalbuminemia, pregnancy, kidney or liver failure, and in older adults. In these situations, the total valproic acid concentration in the blood may underestimate the disproportionately higher free valproic acid fraction.

Reference Values

VALPROIC ACID, TOTAL
Therapeutic: 50 (trough)-125 (peak) mcg/mL
Critical value: > or =151 mcg/mL

VALPROIC ACID, FREE
Therapeutic: 5-25 mcg/mL
Critical value: >30 mcg/mL

Interpretation

The generally acceptable range for total valproic acid used as a reference to guide therapy is 50 to 125 mcg/mL. The corresponding range of free valproic acid concentration for clinical reference is 5 to 25 mcg/mL.

Low free valproic acid concentration relative to these ranges may suggest inadequate dosing, whereas a high free

valproic acid concentration may be associated with toxic effects.

Because the concentration of valproic acid fluctuates considerably depending on the time from last dose, interpretation of the clinical significance of the valproic acid concentration must take into consideration the timing of the blood specimen. For this reason, 2 collections are sometimes made to assess the trough and peak concentrations.

Cautions

Specimens subjected to significant heat or other factors that could cause protein denaturation would demonstrate an artificially increased free valproic acid.

Clinical Reference

1. Cloyd JC, Fischer JH, Kriel RL, Kraus DM: Valproic acid pharmacokinetics in children: Effects of age and antiepileptic drugs on protein binding and intrinsic clearance. Clin Pharmacol Ther. 1993;53:22-29
2. Wagner ML, Graves NM, Leppik IE, et al: The effect of felbamate on valproic acid disposition. Clin Pharmacol Ther. 1994;56:494-502
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;18:284-287
4. Moyer TP: Therapeutic drug monitoring. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 4th ed. WB Saunders Company; 2005:1237-1285
5. Patsalos PN, Spencer EP, Berry DJ: Therapeutic drug monitoring of antiepileptic drugs in epilepsy: A 2018 update. Ther Drug Monit. 2018 Oct;40(5):526-548. doi: 10.1097/FTD.0000000000000546

Performance

Method Description

The assay is based on a homogeneous enzyme immunoassay technique used for the quantitative analysis of valproic acid (free and protein-bound) in human serum or plasma. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PD) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD[+]) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PD does not interfere because the coenzyme functions only with the bacterial (*Leuconostoc mesenteroides*) enzyme employed in the assay.(Package insert: ONLINE TDM Valproic Acid. Roche Diagnostics; 02/2024)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

Same day/1 day

Specimen Retention Time

1 week

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

VALPA-80164
VALPF-80165

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VALPG	Valproic Acid, Free and Total, S	57775-9

Result ID	Test Result Name	Result LOINC® Value
VALPA	Valproic Acid, Tot, S	4086-5
VALPF	Valproic Acid, Free, S	4087-3