MAYO CLINIC LABORATORIES

Test Definition: LEFLU

Leflunomide Metabolite (Teriflunomide), Serum

Overview

Useful For

Therapeutic monitoring of patients actively taking leflunomide

Assessment of elimination in patients requiring enhanced elimination of the drug

Method Name

High-Turbulence Liquid Chromatography Mass Spectrometry (HTLC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL serum
Collection Instructions:
1. Draw blood no sooner than 12 hours (trough value) after last dose.
2. 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:
-Therapeutics Test Request (T831)
-Neurology Specialty Testing Client Test Request (T732)

Specimen Minimum Volume

Serum: 0.3 mL

Reject Due To

Gross	OK

hemolysis	
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Leflunomide is a disease-modifying antirheumatic drug approved for therapy of rheumatoid arthritis and used off-label to reduce viral nephritis in kidney transplant. It is a prodrug: rapid and complete metabolism converts leflunomide to its active metabolite, teriflunomide (also called A77 1726), which acts by inhibiting pyrimidine synthesis. Teriflunomide has a very long half-life, greater than 2 weeks on average.

There is marked interindividual variability in leflunomide pharmacokinetics, thus therapeutic monitoring of serum teriflunomide concentrations may be helpful in optimizing therapy. Therapeutic targets remain only loosely defined and appear to vary depending on the purpose of therapy, but serum teriflunomide concentrations greater than 40 mcg/mL have been associated with better clinical outcomes. Due to the long half-life, serum specimens for therapeutic monitoring may be collected at any point in the dosing cycle, although trough (immediately before next scheduled dose) sampling is preferred for consistency. Adverse reactions to leflunomide do not correlate well with serum drug concentration but include diarrhea, hypertension, and liver toxicity.

Enhanced elimination of the drug may be required in patients who are or who wish to become pregnant, or who are experiencing toxicity; teriflunomide can persist up to 2 years after ceasing therapy unless elimination is accelerated. This can be accomplished through use of activated charcoal or a bile acid sequestrant such as cholestyramine, reducing the half-life of teriflunomide to approximately 1 day. Serum concentrations less than 0.020 mcg/mL (<20 ng/mL) on 2 independent tests at least 2 weeks apart are preferred for patients anticipating pregnancy to minimize the potential risk of teratogenesis associated with the drug.

Reference Values

Therapeutic: >40 mcg/mL
Elimination: <0.020 mcg/mL

Interpretation

Therapy: clinical targets for serum teriflunomide (leflunomide metabolite) concentrations are still being determined, but levels greater than 40 mcg/mL appear to correlate with better outcome.

Elimination: serum concentrations less than 0.020 mcg/mL (20 ng/mL) on two independent tests at least 2 weeks apart

are preferred to minimize potential teratogenesis for patients considering pregnancy.

Cautions

Leflunomide toxicity does not appear to correlate with teriflunomide concentrations, thus, this assay is unlikely to aid in evaluation of potential adverse drug reactions.

Clinical Reference

1. Cannon GW, Kremer JM. Leflunomide. Rheum Dis Clin North Am. 2004;30(2):295-309
2. Chan V, Charles BG, Tett SE. Population pharmacokinetics and association between A77 1726 plasma concentrations and disease activity measures following administration of leflunomide to people with rheumatoid arthritis. Br J Clin Pharmacol. 2005;60(3):257-264
3. Teschner S, Gerke P, Geyer M, et al. Leflunomide therapy for polyomavirus-induced allograft nephropathy: efficient BK virus elimination without increased risk of rejection. Transplant Proc. 2009;41(6):2533-2538
4. Temprano KK, Bandlamudi R, Moore TL. Antirheumatic drugs in pregnancy and lactation. Semin Arthritis Rheum. 2005;35(2):112-121
5. Hirsch HH, Randhawa PS; AST Infectious Diseases Community of Practice. BK polyomavirus in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13528. doi:10.1111/ctr.13528

Performance

Method Description

Serum samples are diluted in an aqueous solution containing deuterated teriflunomide as an internal standard. This is injected onto a liquid chromatography system with Cohesive turboflow to separate the drug from serum components and analyzed by negative-ion mode tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday, Wednesday, Friday

Report Available

3 to 5 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Test Definition: LEFLU

Leflunomide Metabolite (Teriflunomide), Serum

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

80193

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LEFLU	Leflunomide Metabolite, S	44828-2

Result ID	Test Result Name	Result LOINC® Value
60292	Leflunomide Metabolite, S	44828-2