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MAYO CLINIC LABORATORIES

Test Definition: SIIRO

Sirolimus, Whole Blood

Overview

Useful For

Monitoring whole blood sirolimus concentration during therapy, particularly in individuals coadministered cytochrome P450 (CYP) 3A4 substrates, inhibitors, or inducers

Adjusting dose to optimize immunosuppression while minimizing toxicity

Evaluating patient compliance

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:

1. Draw blood immediately before a scheduled dose.

2. Do not centrifuge.

3. Send whole blood specimen in original tube. **Do not aliquot.**

Additional Information: Therapeutic range applies to trough specimen collected immediately prior to a.m. dose.

Forms

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

-Therapeutics Test Request (T831)

-Kidney Transplant Test Request

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	OK

Gross lipemia	OK
Gross icterus	OK
Clotted specimens	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated (preferred)	28 days	
	Ambient	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Sirolimus is a macrolide antibiotic, isolated from *Streptomyces hygroscopicus*, with potent effects, including suppression of T- and B-cell proliferation and antineoplastic and antifungal activity. It inhibits the protein kinase mTOR (mechanistic target of rapamycin) to arrest the cell cycle; it has no effects on calcineurin and, therefore, can either be used in addition to cyclosporine or tacrolimus or as a substitute in patients intolerant to these drugs.

Sirolimus is metabolized by cytochrome P450 (CYP) 3A4; thus, blood concentrations are affected by drugs that inhibit or induce this enzyme. The pharmacokinetic interaction between sirolimus and cyclosporine or tacrolimus increases both therapeutic immunosuppression and the toxicity of these agents; lower doses are required with combined use. Adverse effects of sirolimus are generally concentration dependent, making therapeutic drug monitoring essential.

The frequency of monitoring trough concentrations varies on the indication. For example, for kidney transplant recipients, sirolimus is commonly measured at least 3 to 4 days after a loading dose or, if the kidney transplant recipient is receiving cyclosporin, between 5 to 7 days after initiation. Target concentrations vary depending on concomitant therapy, time posttransplant, the desired degree of immunosuppression, and adverse effects. When given with cyclosporine or tacrolimus, the therapeutic range for sirolimus is generally between 4 and 12 ng/mL with minimal added benefit for concentrations greater than10 ng/mL. When sirolimus is given without calcineurin inhibitors, higher trough levels are needed, usually 12 to 20 ng/mL but occasionally up to 20 to 30 ng/mL.

Reference Values

4-20 ng/mL (Trough)

Target steady-state trough concentrations vary depending on the type of transplant, concomitant immunosuppression, clinical/institutional protocols, and time post-transplant. Results should be interpreted in conjunction with this clinical information and any physical signs/symptoms of rejection/toxicity.

Interpretation

Most individuals display optimal response to sirolimus with trough whole blood levels 4 to 20 ng/mL. Preferred therapeutic ranges may vary by transplant type, protocol, and comedications.

Therapeutic ranges are based on specimens collected at trough (ie, immediately before a scheduled dose). Higher results will be obtained when the blood is collected at other times.

The assay is specific for sirolimus; it does not cross-react with cyclosporine, cyclosporine metabolites, tacrolimus, tacrolimus metabolites, or sirolimus metabolites. Results by liquid chromatography with detection by tandem mass spectrometry are approximately 30% less than by immunoassay.

Cautions

The recommended therapeutic range applies to trough specimens collected immediately before a dose. Blood drawn at other times will yield higher results.

Clinical Reference

1. Milone MC, Shaw LM: Therapeutic drugs and their management. In: Rifai N, Chiu RWK, Young I, Burnham CAD, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:420-453
2. Kahan BD. Ten years of mTOR inhibitor therapy. Transplant Proc. 2003;35(3A):3S-240S
3. Yakupoglu YK, Kahan BD. Sirolimus: a current perspective. Exp Clin Transplant 2003;1(1):8-18
4. Groth CG, Backman L, Morales JM, et al. Sirolimus (rapamycin)-based therapy in human renal transplantation: similar efficacy and different toxicity compared with cyclosporine. Sirolimus European Renal Transplant Study Group. Transplantation. 1999;67(7):1036-1042

Performance

Method Description

Blood specimens are subjected to protein precipitation. The resulting supernatant is analyzed by liquid chromatography tandem mass spectrometry.(Pablo AH, Breaud AR, Clarke W. Analysis of immunosuppressant drugs in whole blood by liquid chromatography-tandem mass spectrometry [LC-MS/MS]. Curr Protoc Toxicol. 2020;84(1):e92. doi:10.1002/cptx.92)

PDF Report

No

Day(s) Performed

Monday through Sunday

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

80195

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SIIRO	Sirolimus, B	29247-4

Result ID	Test Result Name	Result LOINC® Value
35144	Sirolimus, B	29247-4