Test Definition: SIIRO

Sirolimus, B

Overview

Useful For

Monitoring whole blood sirolimus concentration during therapy, particularly in individuals coadministered CYP3A4 substrates, inhibitors, or inducers

Adjusting dose to optimize immunosuppression while minimizing toxicity

Evaluating patient compliance

Method Name

High-Performance Liquid Chromatography-Tandem Mass Spectrometry (HPLC-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 specimen in original tube.

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

Forms

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

-Renal Diagnostics Test Request (T830)

-Therapeutics Test Request (T831)

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK

Gross icterus	OK

Specimen Stability Information

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

Clinical and 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 to arrest the cell cycle; it has no effects on calcineurin and, therefore, can be used in addition to cyclosporine or tacrolimus, or as a substitute in patients intolerant to these drugs. Sirolimus is metabolized by CYP3A4, 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.

Trough sirolimus concentrations are generally measured every 5 days. 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 >10 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 drawn at trough (ie, immediately before a scheduled dose). Blood drawn at other times will yield higher results.

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 liquid chromatography-tandem mass spectrometry are approximately 30% less than by immunoassay.

Cautions

The recommended therapeutic range applies to trough specimens drawn immediately before a dose. Blood drawn at

other times will yield higher results.

Clinical Reference

1. Kahan BD: Ten years of mTOR inhibitor therapy. Transplant Proc 2003;35(3A):3S-240S

2. Yakupoglu YK, Kahan BD: Sirolimus: a current perspective. Exp Clin Transplant 2003;1:8-18

3. 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 April;67(7):1036-1042

Performance

Method Description

Blood samples are subjected to protein precipitation. The resulting supernatant is analyzed by liquid chromatography-tandem mass spectrometry.(Charlson JC, Moyer TP: Therapeutic drug monitoring. In Tietz Textbook of Clinical Chemistry. Fourth edition. Edited by CA Burtis, ER Ashwood, DE Bruns. New York, WB Saunders Company, 2004)

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

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

80195

LOINC® Information

Test Definition: SIIRO

Sirolimus, B

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