



LABORATORY ALLIANCE

of Central New York, LLC

Sirolimus by Tandem Mass Spectrometry

Effective January 19, 2009, Laboratory Alliance of Central New York will begin testing for whole blood Sirolimus (Rapamune®; Rapamycin) levels by liquid chromatography/tandem mass spectrometry (LC/MS/MS). The LC/MS/MS assay utilizes the Waters Mass Trak Immunosuppressants XE RUO Kit and is performed on an Alliance 2795 HPLC coupled to a Quattro micro tandem mass spectrometer. This method shows greater specificity for the parent drug of sirolimus than enzyme immunoassay methods, resulting in a more accurate determination of sirolimus concentration.

Clinical Significance:

Sirolimus (Rapamune®; rapamycin) is a potent immunosuppressive drug used to prevent rejection following organ transplantation. Sirolimus blocks activation of T- and B- cells by inhibiting the response of these cells to Interleukin-2. The mechanism of action of sirolimus differs from other immunosuppressive drugs, the calcineurin inhibitors (tacrolimus and cyclosporin A), which exert their immunosuppressive effects by inhibiting the production of IL-2. Because of different mechanisms of action, sirolimus can act synergistically with tacrolimus or cyclosporine A and is often administered in combination with these drugs.

Therapeutic drug monitoring of sirolimus is necessary to insure an adequate blood concentration to effectively reduce organ rejection, but not so high as to produce side effects such as thrombocytopenia or hypercholesterolemia.

Whole blood is the recommended sample matrix for therapeutic drug monitoring because sirolimus is largely sequestered within erythrocytes.

There are a number of sirolimus metabolites that can complicate therapeutic drug monitoring. A study of pediatric patients found 13 metabolites in blood samples comprised mainly of hydroxylated or demethylated derivatives of the parent drug. This study found a large variability in the metabolite profiles between individuals. Furthermore the metabolite profile is influenced by the age of the patient. For example, 39-O-desmethyl sirolimus is the most prevalent metabolite in adults, but represents less than 10% of the metabolites in pediatric patients.

The metabolites display varying degrees of immunosuppressive activity. For example the 39-O-desmethylosirolimus retains 10% of the immunosuppressive activity of the parent drug, and 12-hydroxysirolimus (a metabolite prominent in pediatric patients) retains 7% of the activity of sirolimus.

The sirolimus metabolites can cross react with sirolimus immunoassays and thereby contribute to the apparent sirolimus concentration. The variability of the metabolite profiles between individuals will therefore have a significant impact on the sirolimus concentrations derived by clinical immunoassay.

Test Code: SIRO

Method: LC/MS/MS

Specimen Requirements: 3.0 mL EDTA whole blood (1.0 mL minimum)
Specimen should be drawn 12 hours post-dose or prior to next dose (trough sample).

Unacceptable Conditions: Clotted specimens or specimens stored at ambient temperature for greater than 24 hours.

Stability: 24 hours ambient, 7 days refrigerated

Schedule of testing: Tuesday, Friday

CPT Code: 80195

Billing Code: 1010409

Storage and Transport: Refrigerated

For More Information:

References are available upon request. For questions or concerns regarding this new test service, please contact Ms. Cheryl Haskins, Chemistry Manager, at 410-7014.

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