EVEROLIMUS, WHOLE BLOOD (LC-MS / MS)	**ug/L**	**3.00-8.00**

ORGAN TRANSPLANT	THERAPEUTIC RANGE in ug/L
Kidney (Everolimus in combination with Cyclosporine)	3 -8
Liver (Everolimus in combination with Tacrolimus)	3-8
	Toxic value : > 15

Note: 1. Therapeutic range is based on whole blood specimen drawn 12 hrs post dose or prior to next dose (trough)

2. The recommended concentration is for kidney transplant patients on triple therapy with Cyclosporine, Corticosteroids & Everolimus.

3. Everolimus Whole blood concentrations can be measured by either chromatographic (LC-MS/MS) or immunoassay (CLIA) methodologies. These two techniques are not directly interchangeable and the measured drug level depends on the methodology used. Reference ranges are different for the two methodologies. Generally CLIA has a positive bias as compared with LC-MS/MS due to cross reacting antibodies with the drug metabolites.

Comments

LC-MS/MS is considered the most sensitive, specific and precise technology for monitoring immunosuppressants . Therapeutic drug monitoring (TDM) is commonly used to help maintain drug levels within the concentration range in which the drug exerts its clinical effect with minimal adverse reactions. Everolimus is a synthetically produced derivative of Sirolimus and is a potent immunosuppressive drug specially when used in conjunction with Cyclosporine. It acts by suppressing cytokine driven T lymphocyte proliferation thereby inhibiting progression from G1 to S phase of the cell cycle. It is rapidly absorbed from the GI tract achieving peak concentration in whole blood in about 3 hours. The elimination half life of Everolimus is 24 hours. Cyclosporine inhibits the metabolism of Everolimus, but Everolimus does not affect the metabolism of Cyclosporine. The primary side effect of therapy is hyperlipidemia.

Indications for testing

- Immunosuppressant dose optimization
- Failure to respond to immuosuppressants
- Signs or Symptoms consistent with inadequate or excessive immunosuppression

- Changes to concomitant medications or other variables that affect pharmacokinetics