G168

IMMUNOSUPPRESSANT DRUG PROFILE 4 (LC-MS / MS)		
Tacrolimus **(**FK-506)	ug/L	
Everolimus	ug/L	(3.00-8.00)

Interpretation

KIDNEY TRANSPLANT	POST TRANSPLANT	THERAPEUTIC RANGE OF TACROLIMUS in ug/L
PEDIATRIC	0-3 months 3 -6 months 6-12 months >12 months	10-12 8-10 6-8 4-7
ADULT	0-6 months 6-12 months >12 months >5 years	8-10 6-8 4-6 3-5
	Toxic range	>20

LIVER TRANSPLANT	POST TRANSPLANT	THERAPEUTIC RANGE OF TACROLIMUS in ug/L
PEDIATRIC	0-3 months 3 -6 months >6 months	10-12 8-10 6-8
ADULT	0-3 months 3-6 months >6 months	10-12 8-10 6-8
	Toxic range	>20

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

Note: 1. Drug 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.

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

3. Test conducted on whole blood

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.

Tacrolimus is a potent immunosuppressant approved for prophylaxis of organ rejection in patients receiving allogeneic liver transplants. It has also been used effectively in other solid organ transplant patients like kidney transplant for prevention of graft versus host disease as well as in pancreatic islet transplantation. It exerts immunosuppressive effect following the formation of a complex with immunophilins. It's absorption from small intestine is highly variable ranging from 4-93% and changes with time following transplant surgery. Even the elimination half life of Tacrolimus is variable being 12 hours in liver transplant patients and 19 hours in renal transplant patients.

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