Sirolimus

General	
• Class of the drug:	Immunosuppressants
• Synonym(s):	Rapamycine
• Common trade name(s) in Switzerland:	Rapamune®
• Conversion factors:	*µg/l x 1.09 = nmol/l* *nmol/l x 0.91 = µg/l*
Clinical pharmacology	
• Indications for TDM:	Individual dose adaptation, symptoms of rejection or toxicity, CYP3A4 genetic deficiency
• Protein binding:	95 – 97 % localized in erythrocytes; in plasma 92 % bound to albumin
• Elimination half-life:	46 - 78 h
• Volume of distribution:	5 – 19 l/kg
• Metabolism:	
- Main metabolic pathways:	Liver, mainly through CYP3A4
- Active metabolite(s)?	Desmethylmetabolites + hydroxymetabolites represent a maximum of 30 % of sirolimus activity
- Inhibitor or inductor of the cytochrome P450 system?	Inductor of CYP3A4
- Other significant pharmacokinetic interactions:	PGP substrate and inhibitor
• Elimination of parent drug:	Hepatic > 90% Renal < 3 %
• Typical therapeutic range:	Dependent on combination therapy and indication
• Potentially toxic concentration:	> 30 µg/l
Pre-analytics	
• Time to steady-state since beginning of treatment or change of posology:	~ 4 days
• Time for blood sampling:	Before next dose at steady state
• Type(s) of sample:	Whole blood on EDTA
• Stability:	1 day at 25°C, 2-3 days at 4°C, for longer conservation freeze at -20°C

Analytics	
• Position(s) in the analysis list/Method:	8634.01 Immunoassay 8634.03 LC-MS
Remarks	Samples should be shipped frozen
References	•*Compendium suisse des médicaments, 2005* •*Napoli KL, Taylor PJ;Therap Drug Monit 23 (2001) 559* •*Macphee IAM et al., Transplantation 74 (2002) 1486* •*Ingle Gret al, Ann Pharmacother 34 (2000) 1044* • *Marzolini C, et al, Clin Pharmacol Ther 75 (2004) 13*