Valproic Acid

General	
• Class of the drug:	Antiepileptics
• Synonym(s):	Valproate
• Common trade name(s) in Switzerland:	Convulex®, Depakine®, Orfiril®
• Conversion factors:	*mg/l x 6.93 = µmol/l* *µmol/l x 0.144 = mg/l*
Clinical pharmacology	
• Indications for TDM:	Individual dose adaptation, verification of compliance, side effects, suspicion of toxicity
• Protein binding:	85 à 95% at low concentration, decreases to 70% with higher dosing (mainly to albumin)
• Elimination half-life:	5 – 20 h
• Volume of distribution:	0.13 - 0.15 l/kg
• Metabolism:	
- Main metabolic pathways:	Glucuroconjugation by uridine diphosphate glucuronosyltransferases (~50%), mitochondrial β-oxydation (~40%) and P-450 oxidation (~10%)
- Active metabolite(s)?	Present but not clinically relevant
- Inhibitor or inducer of the cytochrome P450 system?	Inhibitor of cytochromes CYP2C9 and CYP3A4
- Other significant pharmacokinetic interactions:	Numerous interactions, in particular with other antiepileptics (e.g. phenytoin, lamotrigine, phenobarbital)
• Elimination of parent drug:	Hepatic > 95% Renal < 3%
• Typical therapeutic range:	50 – 100 mg/l (347 – 693 µmol/l)
• Potentially toxic concentration:	> 120 to 150 mg/l (> 832 to 1'040 µmol/l)
Pre-analytics	
• Time to steady-state since beginning of treatment or change of posology:	2 - 4 days
• Time for blood sampling:	Before next dose at steady state
• Type(s) of sample:	Serum or plasma

• Stability:	48 h at 4°C (for longer conservation, freeze at –20°C)
Analytics	
• Position(s) in the analysis list/Method:	8630.01 Immunoassay 8630.02 HPLC/GC
Remarks	In patients with renal insufficiency the free valproic acid concentration should be determined due to reduced protein binding.
References	• *Compendium Suisse des Médicaments 2005* • *Société suisse de Pharmacologie et de Toxicologie, Bases de la thérapeutique médicamenteuse (16ème éd.), Documed, 2005* • *DeVane, Psychopharmacol. Bull. 37 Suppl 2 (2003) 25* • *Regenthal et al., J. Clin. Monit. Comput. 15 (1999) 529* • *Warner et al., Clin. Chem. 44 (1998) 1085*