Carbamazepine

General	
• Class of the drug:	Antiepileptics
• Synonym(s):	
• Common trade name(s) in Switzerland:	Neurotop® retard, Tégrétol®, Timonil® retard
• Conversion factors:	*mg/l x 4.23 = µmol/l* *µmol/l x 0.236 = mg/l*
Clinical pharmacology	
• Indications for TDM:	Individual dose adaptation, verification of compliance, side effects, suspicion of toxicity
• Protein binding:	70-80% (mainly to albumin and to a lesser extent to α1-acid glycoprotein)
• Elimination half-life:	- 30 to 45 h during first days of treatment - 20 h on average when auto-induction of metabolism is maximal (achieved after around 4 weeks of treatment) - 10 h on average when given with other inductors (phenytoin, phenobarbital, ...)
• Volume of distribution:	0.8-1.9 l/kg
• Metabolism:	
- Main metabolic pathways:	"10,11-epoxide diol pathway" in the liver : oxydation to carbamazepine 10,11-epoxide mostly by CYP 3A4 followed by almost complete transformation to the transdiol-10,11 derivative (= dihydroxy-10,11-carbamazepine) and its glucuronides
- Active metabolite(s)?	Carbamazepine 10,11-epoxide
- Inhibitor or inductor of the cytochrome P450 system?	Inductor of cytochrome CYP 3A4 (auto-induction!)
- Other significant pharmacokinetic interactions:	Numerous interactions, mostly with inductors and inhibitors of CYP 3A4
• Elimination of parent drug:	Hepatic > 98% Renal < 2%
• Typical therapeutic range:	4 – 10 mg/l (17 – 42 µmol/l)
• Potentially toxic concentration:	> 10 mg/l (>42 µmol/l) (variable)

Pre-analytics	
• Time to steady-state since beginning of treatment or change of posology:	4 weeks (for metabolic induction to be complete)
• 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	For immunoassays, cross-reaction with the active metabolite carbamazepine 10,11-epoxide might occur; the extent of this cross-reaction depends on the method
References	• *Compendium Suisse des Médicaments, Documed, 2005* • *Société suisse de Pharmacologie et de Toxicologie, Bases de la thérapeutique médicamenteuse (15ème éd.), Documed, 2001* • *Barre et al., in Commission Médicaments de la SFBC, Méthodes de dosage et suivi thérapeutique: aminosides, antiépileptiques, hétérosides cardiotoniques, isoniazide, théophylline., Expansion Scientifique Française, 1989, 26-48* • *MacKichan and Kutt, in W. J. Taylor, A. L. Finn, Individualizing Drug Therapy – Practical Applications of Drug Monitoring, Vol. 2, Gross, Townsend, Frank, Inc, New York, 1981, 1-25* • *Regenthal et al., J. Clin. Monit. Comput. 15 (1999) 529* • *Warner et al., Clin. Chem. 44 (1998) 1085.* • *Yukawa, Clin. Pharmacokinet. 31 (1996) 120.*