Amiodarone

General	
• Class of the drug:	Antiarrhythmics
• Synonym(s):	
• Common trade name(s) in Switzerland:	Cordarone®, Escodarone®
• Conversion factors:	Amiodarone: *mg/l x 1.55 = µmol/l* *µmol/l x 0.645 = mg/l* DEA: *mg/l x 1.62 = µmol/l* *µmol/l x 0.617 = mg/l*
Clinical pharmacology	
• Indications for TDM:	Uncertain response or suspected toxicity. Routine monitoring of amiodarone is questioned.
• Protein binding:	96-98% (α_1-acid glycoprotein)
• Elimination half-life:	Amiodarone: 55 (21-78) days DEA: 129 days
• Volume of distribution:	70 l/kg
• Metabolism:	
- Main metabolic pathways:	Via CYP3A4 to desethyl-amiodarone (DEA) and other metabolites
- Active metabolite(s)?	DEA: 2-3 times more potent than amiodarone
- Inhibitor or inductor of the cytochrome P450 system?	Inhibitor of CYP2C9, CYP2D6, CYP3A4
- Other significant pharmacokinetic interactions:	Trimetoprim and ofloxacin decreases renal tubular secretion
• Elimination of parent drug:	Hepatic >98%
• Typical therapeutic range:	0.8-2.6 mg/l (1.2-4.0 µmol/l), not defined for DEA
• Potentially toxic concentration:	>2.6 mg/l (>4.0 µmol/l) for amiodarone >2.0 mg/l (>3.2 µmol/l) for DEA (not well defined)
Pre-analytics	
• Time to steady-state since beginning of treatment or change of posology:	Up to six month (!), faster with a loading dose
• Time for blood sampling:	Before next dose at steady state
• Type(s) of sample:	Serum or plasma

• Stability:	2 days at room temperature; decreases up to 23% within a week (independent of storage temperature); binds to barrier gels in blood collection tubes!
Analytics	
• Position(s) in the analysis list/Method:	8635.02 HPLC/GC 8635.03 LC-MS/GC-MS
Remarks	During therapy the ratio amiodarone to DEA is >1. May be used as index for compliance.
References	• *Natel S et al., Circulation 77 (1988) 200* • *Somani P, J. Clin. Pharmacol. 29 (1998) 405* • *Valdes R et al., Clin. Chem. 44 (1998) 1096* • *Campbell TJ and Williams KM, Br. J. Clin. Pharmacol. 46 (1998) 307* • *Jürgens G et al., Clin. Pharmacokinet. 42 (2003) 647*