

Methadone

General	
• Class of the drug:	Analgesics
• Synonym(s):	
• Common trade name(s) in Switzerland:	Ketalgin [®] , Methadon Streuli
• Conversion factors:	$mg/l \times 3.23 = \mu mol/l$ $\mu mol/l \times 0.309 = mg/l$
Clinical pharmacology	
• Indications for TDM:	Individual dose adaptation, verification of compliance, side effects, suspicion of toxicity
• Protein binding:	90%
• Elimination half-life:	15-55 h (depending on urine pH)
• Volume of distribution:	4-5 l/kg
• Metabolism:	
- Main metabolic pathways:	Demethylation to EDDP (Ethyl-dimethyl-diphenylpyrrolidine) and EMDP (Ethyl-methyl-diphenylpyrrolidine) (CYP2D6, CYP3A4), CYP2B6
- Active metabolite(s)?	None
- Inhibitor or inducer of the cytochrome P450 system?	CYP3A4, CYP2D6 inhibitor
- Other significant pharmacokinetic interactions:	No
• Elimination of parent drug:	Hepatic 75% Renal 25%
• Typical therapeutic range:	Substitution: 0.01-0.80 mg/l (0.032– 2.58 $\mu mol/l$) Pain treatment: 0.02-0.09 mg/l (0.064 – 0.29 $\mu mol/l$)
• Potentially toxic concentration:	Inexperienced patients: toxic > 0.5 mg/l (1.61 $\mu mol/l$), coma: > 1.0 mg/l (3.23 $\mu mol/l$)
Pre-analytics	
• Time to steady-state since beginning of treatment or change of posology:	3-6 days
• Time for blood sampling:	Before next dose at steady state or 12-16h after last dose
• Type(s) of sample:	Serum or plasma
• Stability:	7 days at 4°C

Analytics	
<ul style="list-style-type: none"> Position(s) in the analysis list/Method: 	8627.02 HPLC/GC 8627.03 LC-MS/GC-MS
Remarks	<ul style="list-style-type: none"> Chiral drug Enantiomers differ by their metabolism and pharmacology R-enantiomer is active
References	<ul style="list-style-type: none"> <i>Arzneimittelkompendium Schweiz, Documed, 2005</i> <i>Baselt, Disposition of Toxic Drugs and Chemicals in Men, 6th edition, Biomedical Publications, 2002</i> <i>Iten, Fahren unter Drogen- oder Medikamenteneinfluss, Forensische Interpretation und Begutachtung, Institut für Rechtsmedizin der Universität Zürich, 1994</i> <i>Grundlagen der Arzneimitteltherapie, Documed AG, 2005</i>