# Clozapine

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| **General** | |
| • Class of the drug: | Antipsychotics |
| • Synonym(s): | |
| • Common trade name(s) in Switzerland: | Leponex® |
| • Conversion factors: | *Clozapine:* *µg/l x 0.0031 = µmol/l*<br>*µmol/l x 327 = µg/l*<br>*Norclozapine:* *µg/l x 0.0032 = µmol/l*<br>*µmol/l x 313 = µg/l* |
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| **Clinical pharmacology** | |
| • Indications for TDM: | Individual dose adaptation, verification of compliance, side effects, suspicion of toxicity |
| • Protein binding: | 95% ($\alpha_1$-acid glycoprotein) |
| • Elimination half-life: | 6 - 26 h |
| • Volume of distribution: | 1.6 l/kg |
| - Metabolism: | |
| - Main metabolic pathways: | CYP1A2 (Norclozapine), CYP3A4 (Clozapine-N-oxide), CYP2D6 |
| - Active metabolite(s)? | Norclozapine (partial activity) (is determined) |
| - Inhibitor or inductor of the cytochrome P450 system? | Not yet found |
| - Other significant pharmacokinetic interactions: | Cigarette smoking decreases clozapine serum levels |
| - Elimination of parent drug: | Hepatic >30%<br>Renal > 50% |
| - Indicative therapeutic range: | 350 – 810 µg/l (1.07 – 2.48 µmol/l) (Clozapine) |
| - Indicative toxic concentration: | > 1000 µg/l (3.1 µmol/l) (Clozapine) |
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| **Pre-analytics** | |
| - Time to steady-state since beginning of treatment or change of posology: | 3-5 days |
| - Time for blood sampling: | Before next dose at steady state |
| - Type(s) of sample: | Serum or plasma |

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| - Stability: | At 4°C several days in serum |
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| **Analytics** | |
| - Position(s) in the analysis list/Method: | 8636.02 HPLC/GC<br>8636.03 LC-MS/GC-MS |
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| **Remarks** | Plasma levels are 10% higher (clozapine) and 16% higher (norclozapine) than serum levels. |
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| **References** | • *Arzneimittelkompendium Schweiz, 2005*<br>• *R.C. Baselt, Disposition of Toxic Drugs and Chemicals in Man, 6th edition, 2002, Biomedical Publikations, Foster City, USA*<br>• *Kaladjian A et al, Therap Drug Monit 21 (1999) 327*<br>• *Mitchell P, Br J Clin Pharmacol 52 (2001) 45S*<br>• *Baumann P et al., Pharmacopsychiatry 37 (2004) 243* |