Guide to Interpretation of Clozapine Plasma Levels

'Trough' clozapine (mg/L)	Clinical response	Comment
<0.01 **'not detected'**	Any	Clozapine is unlikely to have been taken for at least a week before sampling except perhaps in the very early stages of dose escalation (dose 100mg/day or less).
<0.35	Good	Consider repeating assay at 6 months, then annually unless response deteriorates or side-effects become troublesome.
	Poor/ incomplete	If poor adherence is suspected, consider psychoeducation or supervised administration. Please note if a suspension of crushed clozapine tablets is prepared care must be taken to ensure that the bottle is shaken well before administering the suspension to the patient. Review patient and repeat assay after adherence intervention. Consider cautious dose increase (especial caution if dose already 450 mg/d or above due to increased risk of side-effects, in particular seizures). Monitor mental state and side-effects. Review patient again and repeat assay after at least 1 week on new dose.
0.35-0.50	Good	Consider repeating assay at 6 months, then annually unless response deteriorates or side-effects are troublesome. If side-effects are persistent/serious consider cautious dose reduction (e.g. 25 mg/d in week 1, further 25 mg/d in week 2, etc.), but bear in mind possible loss of response.
	Poor/ incomplete	If clozapine treatment has continued at least 3-6 months at current dose, consider psychosocial intervention. Augmentation with other psychoactive drugs to be of benefit, although this is not recommended in the SPC. It is important any such attempts should be carefully considered with respect to side-effects (including the risk of neutropenia) and possible interactions. Clozapine should not be used with drugs known to have a substantial potential for causing agranulocytosis.

'Trough' clozapine (mg/L)	Clinical response	Comment
0.51-0.99	Good – no clinical features of toxicity	Review. Consider a cautious dose reduction (e.g. 25 mg/d in week 1, further 25 mg/d in week 2, etc.), but balance against risk of diminishing the response to clozapine. Consider using an anticonvulsant (not carbamazepine) as prophylaxis against seizures, if dose reduction thought inadvisable. Monitor mental state. Repeat assay after at least 1 week on a new dose, otherwise 3-monthly.
	Poor/ incomplete/ reduced and/or clinical features of toxicity	Cautious dose reduction (see above) to bring plasma clozapine below 0.6 mg/L. Monitor mental state. Repeat assay after at least 1 week on a new dose.
1.0-1.9	Good – no clinical features of toxicity	Review. Consider a cautious dose reduction (e.g. 25 mg/d in week 1, further 25 mg/d in week 2, etc.) to bring plasma clozapine below 1.0 and possibly below 0.6 mg/L, but balance against risk of diminishing the response to clozapine. Consider using anticonvulsant prophylaxis (not carbamazepine). Monitor mental state. Repeat assay after at least 1 week on a new dose, otherwise 3-monthly. Plasma clozapine may continue to rise in the short term even after the dose has been reduced.
	Poor, incomplete or reduced and/ or clinical features of toxicity	Cautious dose reduction (see above) to bring plasma clozapine below 1.0 and possibly below 0.6 mg/L. Monitor mental state. Repeat assay after at least 1 week on a new dose. Plasma clozapine may continue to rise in the short term even after the dose has been reduced.
2 and above	Good – no clinical features of toxicity	Urgent review. Consider cautious dose reduction (e.g. 25 mg/d in week 1, further 25 mg/d in week 2, etc.) to bring plasma clozapine below 1.0 mg/L, and possibly below 0.6 mg/L. Consider anticonvulsant prophylaxis (not carbamazepine). Monitor mental state. Repeat assay after at least 1 week on a new dose. Plasma clozapine may continue to rise in the short term even after the dose has been reduced.
	Poor, incomplete or reduced and/or clinical features of toxicity	Urgent review. If patient is in the community, consider admitting for observation. Withhold Clozapine for 24 h and re-start at 75 % of last dose, thereafter reduce dose slowly (e.g. 25 mg/d in week 1, further 25 mg/d in week 2, etc.) to bring plasma clozapine below 1.0 mg/L, and possibly below 0.6 mg/L. Consider anticonvulsant prophylaxis (not carbamazepine). Monitor mental state. Repeat assay after at least 1 week on a new dose. Plasma clozapine may continue to rise in the short term even after the dose has been reduced.

References

Adapted from: Bazire S. Psychotropic Drug Directory 2018 pp 147 (original reference RJ Flanagan (2010) A practical approach to clozapine therapeutic drug monitoring. CMHP Bulletin Issue 2: 4-5)
Taylor DM, Barnes TRE, Young AH. The Maudsley Prescribing Guidelines in Psychiatry. 13th Edition.