PROFORMA 523: CLOZAPINE SERVICE SUMMARY

SAMPLE COLLECTION/TIMING

The method is validated for the analysis of human plasma samples, harvested from whole blood collected into ETDA (red, purple, or pink-topped) blood tubes. Haemolysed blood samples (which may arise due to a delay in the whole blood sample reaching the laboratory) will be analysed, but interpretation of clozapine and norclozapine concentrations is based on plasma concentrations and so repeat sampling may be advised. Serum collected into gel separator tubes may also be analysed, but adsorption of clozapine and/or norclozapine into the gel has not been assessed during our method validation, and so these samples are best avoided. Samples should be collected pre-dose ('trough'), i.e. at least 6 hours after the last dose of clozapine. The minimum acceptable sample volume for analysis is 0.5 mL whole blood.

ANALYTICAL METHOD SUMMARY

Samples are analysed by an ISO/IEC 17025 (Testing) validated method using liquid chromatography with tandem mass spectrometric detection (LC-MS or LC-MS/MS). Samples are analysed in batches, which are calibrated using clozapine and norclozapine reference standards, using isotopically-labelled internal standards for both analytes to produce calibration curves. The assay has been validated over the range 0.01 to 3.00 mg/L for both clozapine and norclozapine. Three levels of quality control (QC) sample are analysed within each batch, including one at the threshold for therapeutic response for clozapine of 0.35 mg/L. Uncertainty of measurement (k = 2) was assessed during method validation using QC level 0.35mg/L [clozapine (± 0.032 mg/L) and norclozapine (± 0.036 mg/L)] and is monitored ongoing to ensure assay performance. All concentrations will be reported to 2 decimal places (to the nearest 0.01 mg/L). For samples where either, or both, clozapine and norclozapine are below 0.01 mg/L, the results will be reported as '<0.01 mg/L'. Samples with concentrations exceeding 3.00 mg/L will be diluted and re-analysed to produce an accurate quantitative result.

ASI CLOZAPINE ASSAY SERVICE

Samples will be analysed and reported within 72 hours (3 working days) upon receipt in the laboratory. All samples require a completed clozapine assay request from (downloadable from the ASI Laboratory Portal website, www.asilab.co.uk). Completed request form details must match those of the labelled blood tube for the sample to be accepted for analysis.

Following analysis, all samples will be reported via the ASI Laboratory Portal for registered users. All results with a clozapine concentration greater than 2.00 mg/L will be telephoned through to the requestor/consultant urgently. Blood samples will be centrifuged to yield plasma on the day of receipt. Remaining blood cells will be stored refrigerated in the primary tubes for 5 working days following receipt. Plasma samples will be stored refrigerated (2 to 8 degrees C) prior to analysis, and for 2 months following analysis.

CONTACT DETAILS

Laboratory address: Analytical Services International, City St Georges – University of London, Cranmer Terrace, London, SW17 0RE **Website:** www.asilab.co.uk (ASI Laboratory Portal) **Email:** info@asilab.co.uk

Telephone: +44(0)20 8725 2405, +44(0)20 8725 5345.

UKAS Accreditation:

https://www.ukas.com/wp-content/uploads/schedule_uploads/00002/7641Testing-Single.pdf

FURTHER READING AND USEFUL REFERENCES

Taylor DM, Barnes TRE, Young AH. The Maudsley Prescribing Guidelines in Psychiatry, 15th Ed. Wiley-Blackwell, May 2025.

Couchman L, Morgan PE, Spencer EP, Flanagan RJ. Plasma clozapine, norclozapine, and the clozapine:norclozapine ratio in relation to prescribed dose and other factors: data from a therapeutic drug monitoring service, 1993-2007. *Ther Drug Monit* 2010; **32**: 438-47.