Sussex Partnership NHS
NHS Foundation Trust

Procedure and Guidance for the use of Clozapine

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This document has superseded the policy for management of clozapine in the acute adult in-patient service (Brighton & Hove only) and the guidelines for the community initiation of clozapine (Sussex Partnership Trust)

If you require this document in an alternative format, i.e. easy read, large text, audio, Braille or a community language please contact the Pharmacy Team on 01243 623349 (Text Relay calls welcome).

Procedure and Guidance for the use of Clozapine

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Appendices

The documentation listed below may be printed off from the medication related charts and forms section of the Trust website:

http://www.sussexpartnership.nhs.uk/charts-and-forms

1. Introduction

1.1 Purpose of these guidelines

This document sets out the practice criteria to be followed by Sussex Partnership NHS Foundation Trust (SPFT) healthcare professionals for the prescribing, administration and monitoring of clozapine. The aim of this document is to enable the safe and effective use of clozapine in SPFT in the treatment of mental illness.

1.2 Scope of these guidelines

- These guidelines are intended to be used in all situations where treatment with clozapine is either initiated on an in-patient ward or in a community setting. This policy is for all mental health workers who are involved in any aspect of prescribing, supplying or administering clozapine.
- The decision to initiate clozapine must be made after consultation with the Assessment and Treatment Centres (ATC's), Assessment and Treatment Teams (ATT's) or the Assertive Outreach teams (AOT's), Crisis Resolution and Home Treatment Teams (CRHTs), Early Interventions Services (EIS), other professionals, patient and carers, but the responsibility rests with the Resident Medical Officer (RMO).
- Community initiation of clozapine may be considered if the patient is in good physical health and home treatment is deemed as an alternative to inpatient or day hospital treatment. Community initiation must be conducted with appropriate support for the patient consisting of information and essential monitoring. Clozapine initiated in the community can provide effective treatment and allow patients to be treated in the environment most appropriate for them.
- The most significant risks to consider include severe hypotension with cardiovascular collapse, myocarditis or cardiomyopathy, severe hyperthermia, neutropenia, seizures and gastro-intestinal obstruction. Interactions with other prescribed medication, especially other antipsychotics, benzodiazepines and cardiac medication must also be considered.
- Written information must be given to the patient and their carers about the risks associated with treatment with clozapine. These risks must be fully explained and discussed with the patient.

1.3 Background

Clozapine is an atypical antipsychotic licensed for treatment resistant schizophrenia. The Medicine and Healthcare Products Regulatory Authority (MHRA) has restrictions on its prescribing, which includes extensive monitoring (especially white blood cell [WBC] counts). Failing to follow correct procedure could result in harm to patients.

1.4. Definitions

CPMS
Clozaril Patient Monitoring Service. Telephone number: 0845 769 8269. Website: www.clozaril.co.uk

Named Supply
Dispensed from pharmacy with the individual patient's name on it. Administration of clozapine must be from the named supply. It is a serious medication error to dispense from another patient's supply.

Green Result
WBC more than $3.5x10^9$/L and neutrophils more than $2.0 x10^9$/L and no decreases of more than 10% or repeatedly decreasing values in the previous test(s).
Clozapine may be prescribed and dispensed.

Amber Result
WBC 3.0-3.5 $x10^9$/L and/or neutrophils 1.5-2.0 $x10^9$/L.

If the patient's medical condition is satisfactory, clozapine treatment may continue. The CPMS will telephone the hospital and pharmacy and request twice-weekly samples until counts stabilise or increase.

Red Result
WBC less than 3.0 $x10^9$/L and/or neutrophils less than 1.5 $x10^9$/L and/or platelets less than 50 $x10^9$/L.
Clozapine treatment must be stopped immediately and **all supplies of clozapine removed from the patient.** CPMS will telephone the hospital and the pharmacist to inform them of this, and to request that a further blood sample is taken urgently and analysed locally. The patient should be monitored for signs of infection and further blood tests will need to be taken daily until a green result has been achieved. A red blood test is taken to be confirmed if either of the blood tests on the following 2 days after the initial red blood test produce a further red result. The patient should not routinely be re-exposed to clozapine.

2. Standards for Prescribing

2.1 Indications

The licensed indications for clozapine are:

- Treatment resistant schizophrenia in people whose illness has not responded adequately to treatment, despite the sequential use of adequate doses of at least 2 different antipsychotic drugs. At least 1 of the drugs should be a non-clozapine second-generation antipsychotic. (NICE 2014)
- Service users who have severe, untreatable neurological adverse reactions to other antipsychotics including at least one atypical antipsychotic.
- Psychotic disorders occurring during the course of Parkinson's disease when standard treatment has failed.
- When other antipsychotic drugs have proved ineffective or intolerable.

2.2 Prescribing

The initiation of clozapine in SPFT is restricted to consultant psychiatrists registered with the CPMS. Nominated pharmacists and service users must also be registered. CPMS can be accessed via www.clozaril.co.uk. This is a secure website which requires a user name and a password. Please refer to section 6.3 and 6.4 for contraindications and special precautions in the use of clozapine.

2.3 Consent

Clozapine treatment is usually given after informed consent has been obtained. Prior to the commencement of clozapine therapy, agreement must be reached with the service user to comply with the treatment and blood monitoring regime as clinically indicated. This also applies to those detained under the Mental Health Act. Detained service users who have given informed consent to clozapine treatment must then have a form T2 completed, under section 58 of the Mental Health Act. This must be completed just before the end of 3 months of detention. For patients who lack capacity to consent to clozapine, but who are judged by the RMO to benefit from clozapine therapy this can be included on a T3 form.

3. Healthcare Professional Duties

3.1 Doctors Responsibilities

The RMO who is looking after the patient's care must ensure:

- That it is in the patient's best interests to initiate clozapine.

- That in addition to the standard process the RMO is satisfied that the patient has given valid consent to commencing treatment. (See section 2.3 above).

- Consent is valid when the patient has been given **information** about the treatment in a form that can be understood including information about possible side effects, the likely consequences of not having the proposed treatment and the pros and cons of any alternative treatment.
    - The patient has the **capacity** to make the decision about their treatment.
    - The patient has the **freedom** to make a choice.
    - An entry in the patient's **record** confirming this has been carried out.

- A doctor from the prescribing team is readily available to give advice to the staff.

- The patients existing medication is reviewed by a pharmacist. Some drugs will need to be discontinued e.g. carbamazepine and antipsychotic depot injections.

- Consultant must be registered with CPMS.

3.2 Clinical Team: Nurse Responsibilities

3.2.1 Key Duties

- Checking that there are resources available (particularly feasibility of out-patient initiation and availability of staff to follow up the patient in the community) to provide safe clozapine treatment, e.g. through discussion at team meetings.

- Co-ordination of patient care, including additional support required for clozapine monitoring.

- Checking that processes are operating effectively and efficiently e.g. that monitoring, prescribing and administration (by patients and where appropriate by carers) are taking place according to procedure and guidance.

- Keeping patient records accurately and up-to-date to enable the whole team to provide support in the absence of the care co-ordinator.

- Maintaining knowledge on the potential risks and benefits of clozapine, to enable accurate advice to be provided to patients as part of patient follow-up.

- Ensuring patients understand the practical aspects of blood tests and possible restrictions on holiday arrangements etc.

3.2.2 Patient support and information

- Co-ordinate patient care to help avoid adverse drug reactions, and unplanned or inappropriate omissions of dose administration wherever possible: communicate and maintain contact with each patient and their carers, key-workers, and with in-patient units, CPMS, pharmacy, medical staff, GP's and the local pathology lab, as necessary.

- Ensure that when a patient has missed more than 2 days of treatment, the doctor writes a new prescription, and pharmacy provides an appropriately labelled named-patient supply of tablets to enable the patient to re-titrate their dose as per trust policy, to avoid potentially serious adverse effects. (See section 5.4).

- Confirm with patient and carer that they have received written information about clozapine and ask whether they have any more questions. Respond to these questions where possible or refer back to the psychiatrist or specialist pharmacist.

- Organise with the client how he/she is to receive the medication.

- Organise with the client when and where he/she is to attend for regular blood sampling

- If pharmacy or another named provider contacts the nurse to say that a service user has not attended for blood tests or collection of supplies, the nurse must ensure arrangements are made for immediate contact of care co-ordinator to ensure patient has emergency blood test or supply of medication. Pharmacy should contact the RMO and care co-ordinator if a blood sample has been missed.

- Monitor for and advise patients and carers on the side effects of clozapine and on the effects smoking can have on clozapine treatment.

- Liaise with the consultant or nominated deputy when concerned about the patient's mental health. Concerns about physical health should be addressed to the GP but brought to the attention of the responsible doctor who can then decide whether the problem may be linked to the clozapine treatment.

3.2.3 Record Keeping and Monitoring

- Issue next appointment to client, record the time and date both in the client's notes and appointment diary.

- Unless using point-of-care (clinic) testing, ensure that arrangements are in place for a blood sample to be taken, packaged and collected by the courier or posted, as appropriate, at required times.

- If a client plans to go on holiday, inform the issuing pharmacy and refer to the CPMS website for the Clozaril® Travel Pack and travel guidelines.

- Ensure supplies are collected and follow up if not.

- Inform CPMS and pharmacy of any changes in patient details, e.g. change of consultant etc.

- Ensure patient has weight, height, blood glucose levels and other tests specified in section 5.2 monitored according to schedule.

3.3 Pharmacy's Responsibilities

To ensure the safety of patients clozapine can only be supplied from pharmacies (usually hospital pharmacies) registered with CPMS, under the supervision of a named pharmacist, for patients registered with CPMS who are under the clinical care of a consultant psychiatrist who is registered with CPMS.

The pharmacy service is dependent upon blood samples being taken on time and prescriptions being written in a timely manner to be able to provide supplies for patients, because of the particular risks associated with this treatment, and the special restrictions on monitoring, supply and prescribing imposed by the UK Medicines Control Agency.

3.3.1 Key Duties

- To provide support and advise other healthcare professionals on pharmaceutical matters that need to be taken into account when prescribing, monitoring or administering clozapine.

- To assist and advise on the development of policies and procedures to ensure safe, appropriate and timely patient selection, prescribing, monitoring, administration and supply of clozapine.

- To check that suitable blood results are available before supplies of clozapine are made.

- To arrange delivery/collection of dispensed supplies according to each individual patient's schedule.

- To provide a medicines information service for professionals, patients and carers.

- To liaise with manufacturers and national medicines safety agencies to maintain a sound knowledge base on the use of clozapine for patients cared for by the Trust.

3.3.2 Record keeping and monitoring

- Review registration details. Complete pharmacy record sheets with relevant information to enable the supply of clozapine.

- Check computer database (www.clozaril.co.uk) is updated with details (including frequency of bloods and dispensing).

- Where appropriate utilise Point of Care Blood Analysis (PoCBA) testing in clozapine clinics (Please see **PROTOCOL FOR POINT OF CARE BLOOD ANALYSIS (POCBA) IN CLOZAPINE CLINICS AND THE SUPPLY of CLOZAPINE (July 2011).**

- Add client's name to dispensing rota.

- Liaise with clinical team and where necessary the consultant or nominated deputy regarding any local tests necessary before dispensing for client who did not attend blood test appointment.

- Inform the consultant or nominated deputy, ward or clinic staff of amber and red results as a backup to CPMS.

NB: CPMS should be the first to contact the medical staff about such results as they indicate the need to urgently adjust or stop treatment.

3.3.3 Dispensing and supply

- On receipt of initial green result from the CPMS, receive prescription in pharmacy to confirm dose of clozapine to be commenced.

- For each client, compare blood test results on e-CPMS or via telephone contact with CPMS with dispensing rota held at the pharmacy (and any non-attendance information passed on by nursing staff).

- Liaise with nursing staff when notified by CPMS of change of monitoring frequency. (This will dictate both blood-taking and dispensing weeks.)

- Dispense appropriately labelled supply of drug to cover period authorised by receipt of blood test, for clients with green or amber results.

- Liaise with nursing staff to plan arrangements for blood sampling and collection on bank holidays.

- Ensure contingency plans are in place for access to clozapine for patients in emergency situations. For example disruption to transport networks by adverse weather and out of hours supply situations.

- Work with the Care Co-ordinator/ Team Manager to ensure supplies of clozapine and routine blood testing during service user's holidays.

- Ensure that issues of risk management are highlighted and discussed with the Chief Pharmacist.

4. Service User Information

- Prior to initiation, service users and where appropriate their family/carers, must have a full discussion with their clinicians regarding the risks and benefits of clozapine treatment and the need for lifestyle changes, e.g. avoidance of alcohol and activities such as driving or operating machinery, especially during the initial weeks of treatment.

- Advice must also be given on smoking and smoking cessation. Explain that hydrocarbons in the smoke affect the levels and not e-cigarettes or Nicotine Replacement Therapy.

- The range of common side effects and potential medical complications should be discussed, including the need for regular contact with their clinicians.

- There should be an entry made in the service user's record about the form (written and/or verbal) in which this information was shared.

- Clinicians must ensure that service users and their family/carers are familiar with the local "out- of-hours" arrangements.

- Patient Information Leaflets are available from Novartis (CPMS) at www.clozaril.co.uk and also from SPT at www.sussexpartnership.nhs.uk

- The Summary of Product Characteristics (SPC) for Clozaril® contains a comprehensive list of cautions and contraindications. This should be available in all relevant units and to prescribing doctors involved in the care of service users on clozapine. The SPC for Clozaril® is available from www.clozaril.co.uk or www.medicines.org.uk.

- Leaflets and other educational material about mental illness and its treatment should be available in all relevant units. For example information provided by an external link to www.choiceandmedication.org/sussex can be found on the Sussex partnership trust website.

- The treatment, care, and information service users are given should meet the individual's communication needs and take into consideration the individual's cultural needs. For example, people with additional needs such as physical, sensory or learning disabilities and people who do not speak or read English.

- Clinicians must discuss with service users any cultural constraints that might affect their treatment with clozapine.

5. In-patient Initiation and Monitoring of Clozapine Treatment

Appendix 1 shows the SPFT in-patient clozapine process flow chart.

Normal titration chart

- Gradual titration and a divided dosage regime for clozapine initiation are necessary to minimize the risks of hypotension, seizure, and sedation. The SPFT titration chart for in-

patient clozapine initiation is shown in appendix 2 with an initial daily dose of 12.5mg. The usual minimum effective clozapine dose is around 300mg, which is normally reached two to three weeks after starting.

Slow titration chart

- When patient has other medical conditions e.g. cardiac, hepatic or renal impairment consider the slow titration chart.
- If problematic side effects occur, consider slower dose titration or decreasing dose to one previously tolerated or use the slow titration chart (appendix 3)

Quick titration chart

- When a patient has previously been on clozapine and tolerated a normal titration a quick titration sheet can be used (appendix 4). This must not be used for patients with other medical conditions that may result in an increase in side effects e.g. cardiac, renal impairment.

5.1 Routine baseline assessment for initiation

- Full psychiatric and medical history.
- Completion of the appropriate risk assessment.
- Blood tests - Full blood count
  Fasting glucose (Random blood glucose if fasting not possible)
  Liver Function Tests (LFTs)
  Urea and Electrolytes (Including creatinine or eGFR)
  Blood lipids – cholesterol and triglycerides (Fasting if possible)
  Creatinine Phosphokinase (CPK).
  Prolactin

Electrocardiogram (ECG) if clinically indicated.

Weight, height and measure of obesity - Body Mass Index (BMI) or other obesity measure e.g. waist circumference or waist-hip ratio (WHR) if possible.

Blood pressure and pulse.

5.2 Maintenance monitoring for follow up

Monitoring Parameter	**Continuation**
Full Blood Count	As per maintenance guidelines
Blood Glucose	3-6 monthly then annually
BP & pulse (as per monitoring chart)	Frequently during titration, repeated at intervals during the first 6-months of treatment
CPK	If NMS suspected
ECG	At end of dose titration, and following significant dose increases
EEG	If seizures occur or suspected
LFTs	Annually or before if clinically indicated
U&Es	Annually
Weight (inc. waist size/BMI if possible)	Frequently during first 3-months, then annually
Blood lipids (cholesterol and triglycerides)	At 3-months then annually. Consider more frequently where other CV risk factors are present
Prolactin	At 6-months then annually
Baseline assessment of mental state using an approved rating scale	And when therapeutic dose is reached

Patients must be monitored at specified intervals for Full Blood Count (FBC), monitoring of routine health parameters and side effects, as set out in the SPC. Pharmacy will not dispense clozapine unless there is a valid blood test result. The named consultant is responsible for ensuring that all required physical health checks and side effect monitoring is carried out at initiation. Monitoring after this (for outpatients) should be conducted in primary care by the GP. At every annual review, the care co-ordinator must confirm that health checks are being done by the GP, or where not, that robust alternative arrangements are in place and all parties are aware of them.

An annual physical health check must be completed to determine the risk of metabolic syndrome as clozapine patients are at an increased risk of both cardiovascular disease and diabetes. Unless specifically agreed otherwise, this should be carried out by the GP. It must include the relevant annual blood tests and measurement of blood pressure and weight. Smoking status, alcohol and illicit drug use must be established and relevant health promotion advice offered. Lifestyle factors contributing to overall health such as diet and exercise should be considered and relevant advice given and documented. Results of assessments must be forwarded to the SPT consultant.

5.3 Discontinuing clozapine therapy

Clozapine should be discontinued if the patient has a blood dyscrasia, intolerable side effects and/or a failure to respond. CPMS and the supplying pharmacy must be notified.

The dose should be reduced gradually over at least a 1 to 2 week period unless abrupt discontinuation is necessary e.g. red blood result. If abrupt discontinuation is necessary observe the patient carefully for return of psychotic symptoms & symptoms related to cholinergic rebound (profuse sweating, headache, nausea, vomiting and diarrhoea).

Follow-up blood samples must be taken for four weeks after cessation of treatment with clozapine. This means sample once more for four weekly monitoring, twice for fortnightly monitoring and four times for weekly monitoring. See Section 6.1.

If clozapine therapy has been discontinued for any reason, all stock held by the patient should be removed in order to prevent any unauthorised re-initiation by the patient.

Removal should be undertaken even if the intention is to re-titrate in the near future.

5.4 Re-initiation of therapy

5.4.1 Following non compliance

Following a break in treatment CPMS must be contacted to clarify the necessary monitoring requirements. The supplying pharmacy should also be informed prior to restarting clozapine.

Clozapine plasma level once the drug has been discontinued drops quickly. Based on an average half life of between 7 and 14 hours, after 35-70 hours (5 times the half life) there will be no detectable clozapine remaining. Along with the rapid decline in plasma levels the tolerability to the adverse effects rapidly declines. Patient's who have not had clozapine for more than 48 hours (taken from the last dose given) should be retitrated from 12.5mg per day, with a maximum dose titration possible of 50mg/day. The speed of the titration depends on the original acceptance and tolerability of clozapine, however it should be noted that a slower titration (appendix 3) is preferable to prevent adverse reactions. Hypotension, tachycardia and seizures are risks when re-starting clozapine.

When a patient has previously been on clozapine and they tolerated the standard titration, a quick titration sheet can be used (appendix 4). This must not be used for patients with other medical conditions that may result in an increase in side effects e.g. cardiac, renal impairment.

CPMS On/Off treatment assessment guidelines
The last dose administered is considered the time off clozapine.

Monitoring Frequency	Time Off clozapine ≤ 48 hours	Time Off clozapine >48 hours BUT <7 days	Time Off clozapine >7 days
Weekly	No change to monitoring frequency	No change to monitoring frequency. Retitration dose as per initial titration	Restart at 18 weeks of weekly monitoring. Retitration dose as per initial titration

Monitoring Frequency	Time Off clozapine ≤ 48 hours	Time Off clozapine >48 hours BUT <4 days (96 hrs)	Time Off clozapine >4 days (96 hrs) BUT <28 days	Time Off clozapine >28 days
Fortnightly & Monthly	No change to monitoring frequency	No change to monitoring frequency. Retitration dose as per initial titration	**Treatment Break** Weekly for 6 weeks and then return to previous monitoring frequency	Restart 18 weeks of weekly monitoring

5.4.2 Following Red blood result

Consideration of re-initiation of clozapine is only appropriate in specific circumstances. The risks and benefits of rechallenge of clozapine therapy need to be considered by the whole MDT. Neutropenia during clozapine therapy needs to be assessed for the likelihood of being directly attributable to clozapine and not from any other cause, such as concomitant myelosuppressive drugs (eg. carbamazepine) and underlying physical conditions (e.g. benign ethnic neutropenia). Determination if neutropenia is due to clozapine or another cause cannot be made with certainty. Risk factors for true clozapine induced neutropenia are a low baseline WBC, Afro-Caribbean ethnicity and young age. True clozapine induced neutropenia usually develops early in treatment e.g. in the first 18 weeks decreasing rapidly over 1-2 weeks, with a slow return to normal levels.

The final decision for rechallenge of clozapine therapy rests with the named consultant and should be initiated on a named-patient basis with completion and filing in the patients notes of a new consent form as in such circumstances use will be 'off-licence'. (See appendix 5). The service user and family/carers where appropriate must have a fully documented discussion with the clinician regarding the risks associated with a rechallenge of clozapine.

If there is sufficient strong evidence that true clozapine induced neutropenia has not occurred and that the neutropenia was caused by another factor then lithium therapy may be considered to elevate WBC levels. Consideration of concomitant lithium therapy must be made with specialist pharmacy advice. Lithium will not elevate WBC's if a true clozapine induced neutropenia has occurred.
Initiation of lithium therapy requires baseline U&Es, TFTs and FBC with initial prescribing of 400mg nocte and a target plasma level of >0.4mmol/L for 1-2 weeks, with WBC checked after this trial period. If there is sufficient elevation of WBC's then re-initiation of clozapine if thought to be of sufficient clinical benefit can be considered, with appropriate blood monitoring[1].

N.B. Clozapine and lithium combination can increase the risk of neuroleptic malignant syndrome

Lithium therapy for raising WBC's should not be considered when a patient is high risk:

1. Severe neutropenia/agranulocytosis – (In such cases granulocyte colony-stimulating factor (G-CSF) could be considered following specialist advice).
2. Blood dyscrasia occurred in the first 18 weeks
3. Red WBC result was inconsistent with previous WBC results
4. A prolonged neutropenia

6. Risk Management

6.1 Blood Monitoring

The relevant doctor is responsible for reviewing results of routine monitoring on an ongoing basis and transmitting this information to the GP for any necessary action.

Clozapine can cause a reduction in the number of white blood cells in a minority of people and regular blood sampling is required as set out in the SPC. (For further information refer to section 6.6 (Serious Adverse Events).

An **orange blood pack** (FBC) should be used for blood samples that are sent to CPMS for full blood count analysis (routine blood monitoring). This blood pack can be ordered via CPMS Customer Services (Tel. 0845 769 8269). The pack contains a Clozaril request form which must be completed and sent together with the sample. Access to the CPMS website can be granted to SPFT staff, as long as the relevant forms available from CPMS website are completed. The website user access form is available to download from www.clozaril.co.uk.

The CPMS provides an alert system which gives guidance on the suitability of each service user's blood result for dispensing by assigning a traffic light alert colour scheme. These are as follows:

Green – OK to dispense and administer.
Amber - Dispense and administer with caution. Repeat bloods twice a week until either green or red. Review trends.
Red – Do not dispense or administer. STOP clozapine and contact CPMS immediately**.** This must be strenuously followed.

6.1.1 Blood monitoring Frequency

In the UK, a white cell count with a differential count must be monitored:

- At least weekly for the first 18 weeks of treatment
- At least fortnightly between weeks 18 and 52
- After 1 year of treatment with stable neutrophil counts, patients may be monitored at 4 week intervals
- Monitoring must continue during treatment and for at least 4 weeks after stopping as specified in section 5.3

Patients who have been on clozapine for more than 18 weeks and have had their treatment interrupted for more than 4 days but less than 28 days should have their WBC count and absolute neutrophil count (ANC) monitored weekly for an additional 6 weeks. If no haematological abnormality occurs, monitoring at intervals not exceeding 4 weeks may be resumed. If clozapine treatment has been interrupted for 4 weeks or longer, weekly monitoring is required for the next 18 weeks of treatment and the dose should be re-titrated. (See section 5.4.1).

6.1.2 Missed/Emergency Bloods

If a patient has missed the regular day for their blood test and is close to becoming prohibited, a sample must be sent urgently to a local acute hospital trust pathology department. It is the responsibility of the ward or community staff to arrange this.

A Full Blood Count must be requested on a haematology form. Details of the patient must be fully completed also including:

1. Urgent
2. Please phone/fax through to CPMS
3. Patient on clozapine

CPMS will require the following to provide a result:

1. Patient Name
2. Date of Birth
3. CPMS Number
4. Sample Date
5. White blood cell count
6. Platelet count
7. Neutrophil count
8. Daily dose (optional)

The ward will need to inform pharmacy that the blood is being tested locally. The blood test results should be either entered by ward staff with access to the CPMS website or communicated to pharmacy for entering. Once a green result has been given, pharmacy can dispense the medication. The patient goes back to the regular blood tests.

If a blood test has been missed, pharmacy, under the advice of CPMS, may be able to supply a few days' supply of clozapine, providing there is a valid green result, but not on the initial supply.

6.2 Therapeutic drug monitoring

Routine monitoring of plasma levels (clozapine & norclozapine) is generally not appropriate but may be useful;

- When non-compliance is suspected
- When response to an adequate dose seems poor
- When high doses are being used
- If the patient is on concomitant hepatic enzyme inducing medications or changes smoking habits. Plasma levels of clozapine may rise by up to 70% if a patient stops smoking. This is because the induction of hepatic enzyme caused by hydrocarbons in the smoke is no longer present. The levels will rise when a patient swops smoking for e cigarettes or Nicotine Replacement therapy as these agents do not contain hydrocarbons.

Higher plasma levels increase the risk of seizures and other adverse drug reactions (>0.6mg/l is associated with an increased risk of seizures), though there is a great deal of individual variability. The usual indicated therapeutic range is 0.35 – 0.6mg/l, with values >1mg/l requiring consideration of cautious dose reduction and LFT measurement.

Clozapine plasma levels can be checked via the Plasma Clozapine Assay Service, TDM section, Toxicology Unit, Bessemer Wing, Kings College Hospital. Tel: 020 3299 5881. A **yellow blood pack** (plasma) should be used for taking blood that is to be sent to Viapath for clozapine plasma level analysis. This blood pack can be ordered via CPMS. The pack contains a Viapath request form as shown in appendix 15, which must be completed and sent together with the sample. Viapath is totally independent from CPMS and yellow blood packs must not be sent to CPMS. A plasma clozapine assay request form can also be downloaded from the Viapath website: www.viapath.co.uk

The blood sample must be at least 2mls collected in to an EDTA tube. The sample must be taken before a morning dose or in the morning after an evening dose (trough sample). Sampling less than 6 hours post-dose would make the results difficult to interpret and compare with previous results. Clinicians can register to access results on line.

6.2.1 Clozapine: Norclozapine levels

A clozapine: norclozapine ratio should normally be on average approximately 1.5, (clozapine 1: 0.66 norclozapine). Factors affecting this ratio are poor compliance, fast or slow clozapine metabolism, incorrect sampling and concomitant hepatic enzyme inducing drugs. Recent partial non compliance within the last day or two can be indicated by a low clozapine level and a clozapine: norclozapine ratio which differs greatly from the normal expected value quoted above.

If the ratio value is closer to 1 (clozapine 1: >0.66 norclozapine) then as well as poor compliance being a potential cause the patient could be a fast metaboliser of clozapine or on concurrent hepatic enzyme inducing medication or tobacco smoking.

A ratio value closer to 2 (clozapine 1: <0.66 norclozapine) can indicate that either the patient has only been partially compliant in the last few days, or they are a slow metaboliser of clozapine, or that saturation of clozapine metabolism is present or that a true 'trough' sample has not been taken.

6.3 Contraindications to use of clozapine

The following contraindications are taken from the Clozaril® SPC:

- Hypersensitivity to the active substance or to any of the excipients.
- Patients unable to undergo regular blood tests.
- History of toxic or idiosyncratic granulocytopenia/agranulocytosis (with the exception of granulocytopenia/agranulocytosis from previous chemotherapy).
- History of clozapine induced agranulocytosis.
- Impaired bone marrow function.
- Uncontrolled epilepsy.
- Alcoholic and other toxic psychoses, drug intoxication, comatose conditions.
- Circulatory collapse and/or CNS depression of any cause.
- Severe renal or cardiac disorders (e.g. myocarditis).
- Active liver disease associated with nausea, anorexia or jaundice; progressive liver disease, hepatic failure.
- Paralytic ileus.
- Clozapine treatment must not be started concurrently with substances known to have a substantial potential for causing agranulocytosis; concomitant use of depot antipsychotics is to be discouraged.

6.4 Special precautions for the use of clozapine

Refer to the Clozaril® SPC for a full set of special precautions in the use of clozapine.

- The SPC states that "for clozapine, there are only limited clinical data on exposed pregnancies. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women." Consultants should make decisions with the service user regarding the appropriate course of treatment.

- Since clozapine is excreted in breast milk, mothers receiving clozapine should not breast feed.

- In women of child-bearing potential a return to normal menstruation may occur as a result of switching from other antipsychotics to clozapine. Adequate contraceptive measures must therefore be advised in women of childbearing potential.

- Use in the elderly requires a lower dose at initiation of treatment, and the dose titrated up more slowly as the elderly are more susceptible to side effects.

- When using clozapine in people with learning disability, consideration should be given to any medical condition which may affect their tolerability to clozapine.

- Patients who have a low WBC because of benign ethnic neutropenia should be given special consideration and should only be started on clozapine with the agreement of a haematologist

- Owing to the ability of clozapine to cause sedation and lower the seizure threshold, activities such as driving or operating machinery should be avoided especially during the initial weeks of treatment.

6.5 Interactions with clozapine

Refer to the Clozaril® SPC for an exhaustive list of interactions with clozapine. All healthcare professionals responsible for prescribing medication to clozapine treated service users should be aware of potential drug interactions. The major interactions are outlined below:

6.5.1 Contraindication of concomitant use with clozapine

Drugs such as depot antipsychotics and also drugs that are myelosuppressive such as carbamazepine and hence potentiate the risk of agranulocytosis are contraindicated with clozapine.

Some antipsychotic drugs may increase the risk of sudden cardiac death by causing QTc interval prolongation. All depot antipsychotics, sertindole, pimozide, and thioridazine should be stopped before clozapine is started.

Alcohol should not be used concomitantly with clozapine due to possible potentiation of sedation

6.5.2 Precautions for use with clozapine

Concomitant administration of drugs that induce or inhibit cytochrome P450 isoenzymes may affect plasma levels of clozapine. The major isoenzyme involved in the metabolism of clozapine is CYP1A2, with CYP2D6 and CYP3A4 to a lesser extent. Clozapine is principally metabolised through the CYP1A2 enzyme. In tobacco smokers, metabolism of clozapine is increased by hydrocarbons and so plasma clozapine levels are reduced. On cessation of smoking, reversal of the induction of CYP1A2 occurs resulting in the plasma clozapine levels rising. Steady state occurs approximately 7-10 days after smoking cessation. E-cigatettes and NRT will not affect the metabolism, so swopping to these will still increase the levels of clozapine

The plasma concentration of clozapine is increased by caffeine intake and can decrease significantly during an unusual caffeine-free period. Dosage changes of clozapine may be necessary when there is a significant change in caffeine-drinking habit.

SSRI antidepressants such as fluoxetine and paroxetine can affect the metabolism of clozapine via inhibition of CYP2D6 and thereby alter plasma clozapine levels. Some antibiotics such as erythromycin and ciprofloxacin can also elevate clozapine levels.

Other CNS active drugs known to precipitate neuroleptic malignant syndrome (NMS) e.g. lithium may increase the likelihood of NMS developing.

6.6 Serious adverse events

Any drug may produce unwanted or unexpected adverse reactions. Detection and recording of these is important. Adverse reactions should be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA). Doctors, pharmacists, nurses and service users are all eligible to report. Pre-paid yellow cards for reporting can be found at the back of the British National Formulary or electronic submissions made at: www.yellowcard.gov.uk

The major groups of side effects are detailed below:

6.6.1. Neutropenia/agranulocytosis

- Clozapine can cause neutropenia and in severe cases agranulocytosis.
- Particular attention must be paid to flu-like symptoms such as sore throat and pyrexia which may be indicative of neutropenia.
- CPMS provides guidance on procedures to be followed in the event of neutropenia or agranulocytosis developing.

6.6.2. Pyrexia

- During clozapine therapy, approximately 5% of patients experience transient temperature elevations above 38°C, with the peak incidence within the first 3 weeks of treatment.
- If a patient develops pyrexia and a flu-like illness, a medical examination and full blood count should be performed as soon as possible.
- In the presence of a high fever, the possibility of neuroleptic malignant syndrome (NMS) must be considered.

6.6.3. Seizures

- Clozapine lowers the seizure threshold and patients may develop a seizure disorder especially on high doses of clozapine.
- The minimum effective dose should be prescribed.
- Those patients requiring doses of clozapine that are at risk of causing seizures may be concomitantly prescribed an anticonvulsant that is not associated with bone marrow suppression.
- Prophylactic sodium valproate should be considered for patients who are at high risk of clozapine induced seizures e.g. those on clozapine doses of 600mg daily and above.

6.6.4. Cardiovascular events

- Clozapine patients may have an increased risk of pulmonary embolism and sudden death.
- Cardiomyopathy and fatal myocarditis has been associated with clozapine use with the risk of myocarditis greatest during the first 2 months of treatment.
- Cardiac complications should be suspected if patients experience persistent tachycardia at rest, palpitations, arrhythmias, chest pain or heart failure develops. In these cases clozapine should be immediately reviewed, and the patient referred to a cardiologist by their psychiatrist. Where clozapine is discontinued due to cardiac complicatins, such patients should not be re-exposed to clozapine.
- Consultants should consider performing a baseline ECG before clozapine treatment is initiated and again when the maintenance dose is reached. This is not currently an absolute requirement, however the decision should be a clinical judgment based on an assessment of risk factors.
- The risk of orthostatic hypotension can be minimised by slowly titrating the dose and spreading doses through the day.
- Any contributing factors e.g. raised BP and/or a history of diabetes should be drawn to the attention of the GP for further investigation.

6.6.5. Acute intestinal obstruction

- Clozapine can cause constipation due to slowing of intestinal peristalsis and hence can cause obstruction, and a paralytic ileus which may be fatal.
- Acute obstruction is a medical emergency. Symptoms include abdominal distension, pain and vomiting. When suspected the medical team must be alerted and a surgical referral initiated if appropriate.

6.6.6. Diabetes and impaired glucose tolerance

- Clozapine has been strongly linked to hyperglycaemia, impaired glucose tolerance and diabetic ketoacidosis.
- Up to one third of clozapine patients develop diabetes after 5 years of treatment, the majority of these within the first 6 months. Patients and carers should be aware of the symptoms of diabetes and be encouraged to report these if present.
- Routine baseline screening in the early months of treatment should detect evidence of glucose dysregulation, however if there is suspicion of abnormal glucose metabolism, a

random blood glucose measurement should be undertaken. If this is abnormal, a fasting specimen should be obtained.

6.7 Common side effects

The most common side effects include:
Constipation, tachycardia and ECG changes, drowsiness and sedation, blurred vision, headache, tremor, rigidity, akathisia, convulsions, extrapyramidal side-effects, nausea, vomiting, anorexia, dry mouth, urinary incontinence or retention, weight gain, hypertension, postural hypotension, syncope, disturbance in temperature regulation, sweating, fatigue, fever, elevated LFTs, and dysarthria.

Please note this list is not exhaustive. For further details on side-effects, please refer to Clozaril® SPC.

A GASS clozapine form (Appendix 16) should be complete prior to starting treatment and at regular intervals to assess patient's side effects.

Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately.

6.8 Management of Adverse effects

Adverse Effect	Time course	Action
Sedation	First 4 weeks. May persist but usually wears off.	Give smaller dose in the mornings. Some patients can only cope with single night-time dosing. Reduce dose if necessary. Consider plasma level monitoring.
Hypersalivation	First few months. May persist but usually wears off. Often very troublesome at night.	Give hyoscine 300mcg (Kwells) **sucked** and swallowed at night. Hyoscine patches may be considered as an alternative. Pirenzepine (not licensed in U.K) up to 100mg/day may be tried. Check whether troublesome to patient - treatment not always required. **Beware of increased risk of constipation**.
Constipation	Usually persists	Recommend high fibre diet. Bulk forming laxatives (Fybogel) +/- stimulants may be used.
Hypotension	First 4 weeks	Advise patient to take time standing up. Reduce dose or slow down rate of increase.
Hypertension	First 4 weeks, sometimes longer	Monitor closely and increase dose as slowly as is necessary. Consider antihypertensive therapy if suitable
Tachycardia	First 4 weeks, but often persists	Often occurs if dose escalation is too rapid. Inform patient that it is not usually dangerous. Give small dose of beta blockers if necessary e.g. atenolol. If pulse is persistently above 100bpm, consider cardiology referral. If persistent at rest, associated with fever, hypotension or chest pain may indicate myocarditis – seek cardiology referral. If accompanied by chest pain or shortness of breath. Seek immediate medical assessment.
Weight gain	Usually during first year of treatment	Weight gain is common and often profound (5kg+) Dietary counseling is essential. Advice may be more effective if given before weight gain occurs.
Fever	First 3 weeks	Give antipyretic but check FBC. **N.B.** This fever is not usually related to blood dyscrasias. If persists above 38.5C withhold clozapine and contact CPMS. Consider myocarditis.

Seizures	Dose dependent. Incidence rises at doses > 600mg / day or plasma level >0.6mg/l	Consider prophylactic sodium valproate (1-2g/day or 50-100mg/l) if on high dose (>600mg/day or plasma level of >0.5mg/l). After a seizure – withhold clozapine for one day. Restart at reduced dose and give sodium valproate. (**Avoid carbamazepine**)
Nausea	First 6 weeks	May give anti-emetic.(Avoid prochlorperazine and metoclopramide if history of EPSE)
Nocturnal enuresis	May occur at any time	Try manipulating dose schedule. No fluids at bedtime. In severe cases, desmopressin is usually effective. Consider risk of hyponatraemia.
Neutropenia / Agranulocytosis	Mostly in first 18 weeks but can occur at any time	**STOP CLOZAPINE**, repeat bloods the next day and every day until Green result obtained. Agranulocytosis will require hospital admission.
Hyperglycaemia	Any time. Usually known risk factors	Use oral hypoglycaemics or insulin.

7. Supporting References

1. Blier P et al. Lithium and clozapine-induced neutropenia/agranulocytosis. International Clinical Psychopharmacology 1998; 13:137-140

Further Information

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Novartis Pharmaceuticals UK Ltd. Clozaril 25mg and 100mg tablets Summary of Product Characteristics. Accessed via www.medicines.org.uk

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D. Taylor, C. Paton, S.Kapur. The Maudsley Prescribing Guidelines. 11th Edition. The South London and Maudsley NHS Foundation Trust Oxleas NHS Foundation Trust. London 2010

Bazire S, Psychotropic Drug Directory. 2014 edition. Lloyd-Reinhold Communications LLP

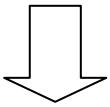
Mental Health Act 1983 and 2007 legislation

Flanagan RJ. Therapeutic monitoring of antipsychotics. CPD Clin Biochem 2006; 7: 3 -18.

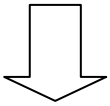
Appendix 1

Clozapine Process Flow Chart

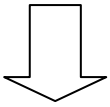
Obtain a Full Blood Count (baseline).



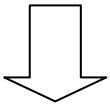
Register patient with CPMS.



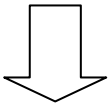
Baseline observations (Temperature, pulse and BP)



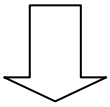
Doctor to prescribe clozapine on drug chart (appendix 2, 3 or 4).



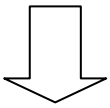
Ward to fax chart to Pharmacy



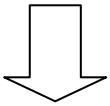
Pharmacy to supply clozapine



Administer clozapine (must use named supply).

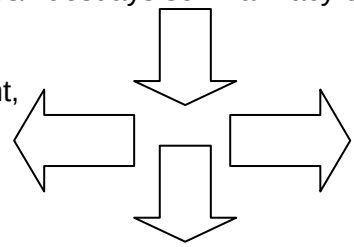


Monitor BP, pulse and temp (Monitor as per Inpatient and out patient policy, see appendices 2 & 12).



Take Full Blood Count weekly/two weekly/four weekly as required.
(Take bloods on Mondays/Tuesdays so Pharmacy can dispense Wednesdays/Thursdays)

Amber Result
Continue clozapine treatment, sample blood twice weekly until counts stabilise or increase.



Red Result
STOP immediately.
Sample blood daily until a green result is achieved. Monitor for signs of infection.

Green result

Continue clozapine

Appendix 2

CLOZAPINE TITRATION PRESCRIPTION CHART – Normal titration

This chart must be attached to the standard prescription chart, which must be endorsed with **'Clozapine as per titration chart'**

If problematic side effects occur, consider slower dose titration or decreasing dose to one previously tolerated.

Ward		Hospital/Unit	
Patient Name		CPMS Number	
Consultant		Hospital No.	
Allergies		Date of Birth	

If clozapine is omitted for greater than 48hrs it is essential to restart clozapine from initial starting doses. However, according to tolerance, upward dose titration may be faster than on first trial.

If previously on clozapine, date stopped :

DAY	DATE	DRUG	MORNING DOSE Time:	GIVEN BY	EVENING DOSE Time:	GIVEN BY
1		CLOZAPINE			12.5mg	
2		CLOZAPINE	12.5mg		12.5mg	
3		CLOZAPINE	25mg		25mg	
4		CLOZAPINE	25mg		25mg	
5		CLOZAPINE	25mg		50mg	
6		CLOZAPINE	25mg		50mg	
7		CLOZAPINE	50mg		50mg	
8		CLOZAPINE	50mg		75mg	
9		CLOZAPINE	75mg		75mg	
10		CLOZAPINE	75mg		100mg	
11		CLOZAPINE	100mg		100mg	
12		CLOZAPINE	100mg		125mg	
13		CLOZAPINE	100mg		150mg	
14		CLOZAPINE	100mg		175mg	
15	**Prescribe the dose on prescription chart.** Generally this dose is 100mg OM and 200mg ON.					

Should a higher dose than 300mg daily be required, increments are 50-100mg per week. Therefore from day 18 aim for 100mg OM & 250mg ON, day 21 100mg OM & 300mg ON and day 28 100mg OM & 350mg ON.

Target doses female non-smoker = 250mg/day (day 13), Male non-smoker = 350mg/day, Female smoker = 450mg/day and Male smoker = 550mg/day. According to plasma levels, consider taking after day 15.

PRESCRIBER'S SIGNATURE		DATE	

MULTIPURPOSE MONITORING CHART FOR CLOZAPINE PATIENTS

	Date																
	Time																
°Celsius	Blood Pressure Lying/Standing	Pre L S	1st hr L S	2nd hr L S	3rd hr L S	4th hr L S	5th hr L S	6th hr L S	Day 2 AM L S	Day 2 PM L S	Day 3 AM L S	Day 3 PM L S	Day 4 AM L S	Day 4 PM L S	Day 5 AM L S	Day 5 PM L S	
41 T	250																
40.5 E	240																
40 M	230																
39.5 P	220																
39 E	210																
38.5 R	200																
38 A	190																
37.5 T	180																
37 U	170																
36.5 R	160																
36 E	150																
	140																
	130																
	120																
	110																
	100																
P	90																
U	80																
L	70																
S	60																
E	50																
Nausea																	
Drowsiness																	
Dizziness																	
Bowels opened																	
Hyper salivation																	
Urinary problems																	
Sweats																	
Extrapyramidal S/E																	

Seek medical advice if there is, a drop in blood pressure >20mmHg (diastolic or systolic), pulse over 100 beats per minute or pyrexia (temperature in excess of 38.5°C).

Side effects should be recorded using the code 0=nil, 1=mild, 2=severe, 3=extreme.

Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately.

Appendix 3

CLOZAPINE TITRATION PRESCRIPTION CHART – Slow titration

This chart must be attached to the standard prescription chart, which must be endorsed with **'Clozapine as per titration chart'**

Consider for patients with other medical conditions e.g. cardiac, hepatic or renal impairment.

If problematic side effects occur, consider slower dose titration or decreasing dose to one previously tolerated.

Ward		Hospital/Unit	
Patient Name		CPMS Number	
Consultant		Hospital No.	
Allergies		Date of Birth	

If clozapine is omitted for greater than 48hrs it is essential to restart clozapine from initial starting doses. However, according to tolerance, upward dose titration may be faster than on first trial.

If previously on clozapine, date stopped :

DAY	DATE	DRUG	MORNING DOSE Time:	GIVEN BY	EVENING DOSE Time:	GIVEN BY
1		CLOZAPINE			12.5mg	
2		CLOZAPINE			12.5mg	
3		CLOZAPINE	12.5mg		12.5mg	
4		CLOZAPINE	12.5mg		12.5mg	
5		CLOZAPINE	25mg		25mg	
6		CLOZAPINE	25mg		25mg	
7		CLOZAPINE	25mg		25mg	
8		CLOZAPINE	25mg		25mg	
9		CLOZAPINE	25mg		50mg	
10		CLOZAPINE	25mg		50mg	
11		CLOZAPINE	25mg		50mg	
12		CLOZAPINE	25mg		50mg	
13		CLOZAPINE	50mg		50mg	
14		CLOZAPINE	50mg		50mg	
15	**Prescribe the dose on prescription chart or 2nd sheet.**					

Should a higher dose be required, increments are 50-100mg per week, as the patient tolerates.

Target doses female non-smoker = 250mg/day, Male non-smoker = 350mg/day, Female smoker = 450mg/day and Male smoker = 550mg/day. According to plasma levels.

PRESCRIBER'S SIGNATURE		DATE	

MULTIPURPOSE MONITORING CHART FOR CLOZAPINE PATIENTS

°Celsius		Pre L S	1st hr L S	2nd hr L S	3rd hr L S	4th hr L S	5th hr L S	6th hr L S	Day 2 AM L L	Day 2 PM S L	Day 3 AM S L	Day 3 PM S L	Day 4 AM S L	Day 4 PM S L	Day 5 AM S L	Day 5 PM S L	
	Date																
	Time																
	Blood Pressure Lying/Standing																
41	T	250															
40.5	E	240															
40	M	230															
39.5	P	220															
39	E	210															
38.5	R	200															
38	A	190															
37.5	T	180															
37	U	170															
36.5	R	160															
36	E	150															
		140															
		130															
		120															
		110															
		100															
	P	90															
	U	80															
	L	70															
	S	60															
	E	50															
Nausea																	
Drowsiness																	
Dizziness																	
Bowels opened																	
Hyper salivation																	
Urinary problems																	
Sweats																	
Extrapyramidal S/E																	

Seek medical advice if there is, a drop in blood pressure >20mmHg (diastolic or systolic), pulse over 100 beats per minute or pyrexia (temperature in excess of 38.5°C).

Side effects should be recorded using the code 0=nil, 1=mild, 2=severe, 3=extreme.

Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately**.**

Appendix 4

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CLOZAPINE TITRATION PRESCRIPTION CHART – Quick titration

When a patient has previously been on clozapine and they tolerated the titration. NOT for patients with other medical conditions that may result in an increase in side effects e.g. cardiac, renal impairment.

This chart must be attached to the standard prescription chart, which must be endorsed with
'Clozapine as per titration chart'

If problematic side effects occur, consider slower dose titration or decreasing dose to one previously tolerated.

Ward		Hospital/Unit	
Patient Name		CPMS Number	
Consultant		Hospital No.	
Allergies		Date of Birth	

If clozapine is omitted for greater than 48hrs it is essential to restart clozapine from initial starting doses. However, according to tolerance, upward dose titration may be faster than on first trial.

If previously on clozapine, date stopped :

DAY	DATE	DRUG	MORNING DOSE Time:	GIVEN BY	EVENING DOSE Time:	GIVEN BY
1		CLOZAPINE	[redacted]		12.5mg	
2		CLOZAPINE	12.5mg		12.5mg	
2		CLOZAPINE	25mg		25mg	
3		CLOZAPINE	25mg		50mg	
4		CLOZAPINE	50mg		50mg	
5		CLOZAPINE	75mg		75mg	
6		CLOZAPINE	100mg		100mg	
7		CLOZAPINE	100mg		100mg	
8		CLOZAPINE	100mg		150mg	
9		CLOZAPINE	100mg		150mg	
10		CLOZAPINE	100mg		200mg	
11		CLOZAPINE	100mg		200mg	
12		CLOZAPINE	100mg		250mg	
13		CLOZAPINE	100mg		250mg	
14		CLOZAPINE	100mg		300mg	
15	**Prescribe the dose on prescription chart.** **Consider the dose the patient was previously on.**					

Target doses female non-smoker = 250mg/day (day 9), Male non-smoker = 350mg/day (day 13), Female smoker = 450mg/day and Male smoker = 550mg/day. According to plasma levels.

PRESCRIBER'S SIGNATURE		DATE	

MULTIPURPOSE MONITORING CHART FOR CLOZAPINE PATIENTS

°Celsius		Pre L S	1st hr L S	2nd hr L S	3rd hr L S	4th hr L S	5th hr L S	6th hr L S	Day 2 AM L L	Day 2 PM S L	Day 3 AM S L	Day 3 PM S L	Day 4 AM S L	Day 4 PM S L	Day 5 AM S L	Day 5 PM S L	
	Date																
	Time																
	Blood Pressure Lying/Standing																
41	T	250															
40.5	E	240															
40	M	230															
39.5	P	220															
39	E	210															
38.5	R	200															
38	A	190															
37.5	T	180															
37	U	170															
36.5	R	160															
36	E	150															
		140															
		130															
		120															
		110															
		100															
	P	90															
	U	80															
	L	70															
	S	60															
	E	50															
Nausea																	
Drowsiness																	
Dizziness																	
Bowels opened																	
Hyper salivation																	
Urinary problems																	
Sweats																	
Extrapyramidal S/E																	

Seek medical advice if there is, a drop in blood pressure >20mmHg (diastolic or systolic), pulse over 100 beats per minute or pyrexia (temperature in excess of 38.5°C).

Side effects should be recorded using the code 0=nil, 1=mild, 2=severe, 3=extreme.

Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately.

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Mental Health Services - Clozapine Consent Form

(Patient Version)

Tick each box if you agree with the statement.

I confirm that:

☐ Doctor ……. has explained the benefits and possible side-effects of using clozapine to treat …….. (diagnosis) and I have understood the explanation.

☐ I have been given a patient medication leaflet.

☐ I consent to the mandatory regular blood tests required with clozapine therapy.

☐ Doctor ……. has discussed treatment options with me, and also the consequences of not using this medication.

Treatment options discussed include:

1. ……
2. ……
3. ……

☐ I have had enough time to consider my decision and to ask questions.

☐ I understand that this medication is being prescribed *within its licence but is contraindicated for me/outside its licensed indication/is an unlicensed medicine*.*

☐ I consent to being treated with the above medication.

☐ I understand I can withdraw my consent at any time and I will inform the prescribing doctor.

Signed: ……. (patient) …….. (printed name)

Date: ……

Signed: ……. (doctor) ……. (printed name)

Date: ……. ……. (title)

**Delete as appropriate*

Updated March 2011

Sussex Partnership NHS
NHS Foundation Trust

Patient Name | Address

Date of birth

Important information about clozapine and potentially fatal side effects

Dear Dr

Two potentially serious side effects of clozapine that are sometimes overlooked are constipation and bowel obstruction (occasionally fatal).

The above patient is to be started on **clozapine** at home on_____ under the supervision of _____ team.

All patients initiated on clozapine will be given information about following a high fibre diet and advised to seek help from their G.P or pharmacist if they become constipated.

If the patient presents to you with symptoms of constipation please ensure:

- Regular laxatives are prescribed. A bulk forming laxative (Fybogel) and, if necessary a stimulant laxative (senna) are advised.
- The mental health team are informed if constipation persists.
- Prescribing of any other medication that may cause constipation as a side effect, (e.g. antimuscarinic medicines) is avoided.

Certain medicines are contra-indicated with the use of clozapine; a table of those more commonly prescribed can be found on the reverse of this letter. The manufacturer's Summary of Product Characteristics for clozapine at www.medicines.org.uk should be referred to for a full list of contraindicated medication and additional cautions.

If this patient either starts smoking or decides to stop, please inform the mental health team. When smoking status changes, this can very significantly affect plasma levels of clozapine and clozapine plasma level monitoring may be needed to ascertain if any changes to the dose are required. Dose increases for smokers of up to 70% are sometimes needed, whilst the average patient who stops smoking needs to reduce their dose by at least one quarter to avoid serious side-effects developing.

Whilst clozapine is being titrated the patient will be supervised closely at home. They have been given an emergency number to contact out-of-hours and at weekends if they have any side-effects or feel unwell.

Please update your records, including the prescribing system, even though secondary care will do all the prescribing, to indicate that this patient has started clozapine and to monitor for constipation. We will keep you informed of their progress. Once the patient is stabilised, if appropriate, (and with the agreement of your practice), ongoing clozapine blood tests may be undertaken at your surgery. In this event, we will advise you how this may be facilitated.

Yours sincerely,

The most common drug interactions with clozapine

Drug	Interactions	Comments
Bone marrow suppressants (e.g. carbamazapine, chloramphenicol), sulphonamides (e.g. co-trimoxazole), pyrazolone analgesics (e.g. phenylbutazone), penicillamine, cytotoxic agents and long-acting depot injections of antipsychotics	Interact to increase the risk and/or severity of bone marrow suppression.	Clozapine **must not be used** concomitantly with other agents having a well known potential to suppress bone marrow function.
Benzodiazepines	Concomitant use may increase risk of circulatory collapse, which may lead to cardiac and/or respiratory arrest.	Caution advised if using together. Respiratory depression and collapse more likely to occur at start of this combination or when clozapine is added to an established benzodiazepine regimen.
Anticholinergics	Clozapine potentiates action of these agents through additive anticholinergic activity.	Observe patients for anticholinergic side-effects, e.g. constipation, especially when using to help control hypersalivation.
Antihypertensives	Clozapine can potentiate hypotensive effects of these agents due to sympathomimetic antagonistic effects.	Caution is advised. Patients should be advised of the risk of hypotension, especially during the period of initial dose titration.
Alcohol, MAOIs, CNS depressants, including narcotics and benzodiazepines	Enhanced central effects. Additive CNS depression and cognitive and motor performance interference when used in combination with these substances.	Caution is advised if clozapine is used concomitantly with other CNS active agents. Advise patients of the possible additive sedative effects and caution them not to drive or operate machinery.
Highly protein bound substances (e.g. warfarin and digoxin)	Clozapine may cause increase in plasma concentration of these substances due to displacement from plasma proteins.	Patients should be monitored for the occurrence of side effects associated with these substances, and doses of the protein bound substance adjusted, if necessary.
Phenytoin	Addition of phenytoin to clozapine regimen may cause a decrease in the clozapine plasma concentrations.	If phenytoin must be used, the patient should be monitored closely for a worsening or recurrence of psychotic symptoms.
Lithium	Concomitant use can increase the risk of development of neuroleptic malignant syndrome (NMS).	Observe for signs and symptoms of NMS.
CYP1A2 inducing substances (e.g. omeprazole)	Concomitant use may decrease clozapine levels	Potential for reduced efficacy of clozapine should be considered.
CYP1A2 inhibiting substances (e.g. fluvoxamine, caffeine, ciprofloxacin)	Concomitant use may increase clozapine levels	Potential for increase in adverse effects. Care is also required upon cessation of concomitant CYP1A2 inhibiting medications as there will be a decrease in clozapine levels.

Taken and abridged from SPC for Clozaril 25/07/2013

Appendix 7

Outpatient initiation of Clozapine

PRESCRIBER'S ADDITIONAL RESPONSIBILITIES For outpatient initiation
Clozapine should only be prescribed under the supervision of a consultant registered with the CPMS. The doctor's responsibilities are the same as those for inpatient initiated patients with the following additional responsibilities.

Key Duties:

- **All the doctor's responsibilities described in the clozapine policy and operating procedure apply.**
- Checking that there are family/carer network resources available – ideally someone to stay overnight for the first 3 days to provide safe clozapine treatment, e.g. through discussion at team meetings
- Informing the full clinical team and the appropriate hospital pharmacy.
- Ensuring that the initial prescription is signed and sent to pharmacy.
- Where possible, scheduling treatment to commence at the beginning of the week and to follow a standard increasing regime.
- Ensuring the patients GP is informed of clozapine prescribing, (see appendix 6), and that arrangements are agreed for annual physical health checks to be carried out.

Monitoring:
The doctor must see the patient regularly and at a minimum once every week during the initiation phase. The doctor must assess the patient in the same way to that which would be carried out if the patient was an in-patient (see appendix 8). These appointments must be booked before the patient starts treatment.

In cases where clozapine prescribing is stopped, the patient must continue with blood tests and results monitoring for four weeks after the last dose has been administered (see section 5.3).

Prescribing as per main policy document but also:
Ensure that the initial prescription is sent to pharmacy one week prior to the planned commencement of therapy.

Ensure that any alterations needing to be made to initiation regime following review of patients are communicated to pharmacy immediately.

Ensure valid prescriptions are supplied to the appropriate hospital pharmacy before the initiation prescription expires.

GUIDELINES FOR NURSING STAFF ON OUT-PATIENT INITIATION OF CLOZAPINE PRESCRIBING

Initiation of clozapine must be carried out through upward titration of the dose under supervision to minimise adverse effects.

Key Duties

- Checking that there are resources available (particularly staff to follow up the patient in the community) to provide safe clozapine treatment.

- Ensuring baseline bloods and ECG have been conducted before referral to the community team.

- Co-ordinating patient care, including additional support required for clozapine monitoring, during initial period.

- Checking that processes are operating effectively and efficiently e.g. monitoring, prescribing and administration are taking place according to procedure and guidance.

- Keeping patient records accurately and up-to-date to enable the whole team to provide support to the patient and carer, using a folder kept at the patient's home which stores monitoring records for physical observations and side effects, a copy of the titration schedule and relevant contact numbers.

- Maintaining own knowledge on the potential risks and benefits of clozapine, to enable accurate advice to be provided to patients and carers as part of patient initiation/treatment.

- Ensuring each patient has a baseline weight and blood glucose level measured prior to initiation. Refer to section 5.1 and 5.2 re' baseline and maintenance monitoring.

Administration and monitoring (observations)
Record baseline observations of pulse, temperature, weight, blood pressure and glucose (see Appendix 8).

The focus of nursing observation during the initial seventy-two (72) hour period is to monitor for hypotension, excessive drowsiness, tachycardia and hyperthermia. The most likely time for this to occur is during the first six hours after the initial dose. **It is crucial that the patient be closely observed throughout this initial six-hour period, by a nurse staying with them or by hourly visits, and following any subsequent increase in dosage.**

Should the patient experience any of the above symptoms:

1. Initiate first aid measures,

2. Record vital signs; pulse, respiration, temperature and blood pressure.

3. Contact medical staff to discuss management.

If out of hours, contact the duty psychiatrist for advice. Undertake routine observations; following baseline observations, the patient should have blood pressure pulse and temperature monitored at intervals during the day as described in the initiation programme.

Discuss side effects with medical staff (and if appropriate with pharmacy) to enable dose adjustments to be made where necessary for individual patients.

Communication

- Liaise with carers and other agencies with regard to follow up by community staff.

- Forward all information related to the clozapine initiation to the clinical team where the patient will be monitored.

- Liaise closely with pharmacy regarding any changes in dose.

- Ensure prescriptions are rewritten when required so that treatment is not disrupted.

- Ensure arrangements are in place with clinical team for blood tests, supply, collection, etc on completion of initiation.

Plan for initiating clozapine

Clozapine treatment will begin on a Monday (day 1), but not a Bank Holiday and follow the community titration protocol shown in appendix 10.

The patient will either attend a day hospital or clinic or be visited at home by a healthcare professional every weekday ideally for the first 2 weeks but as a minimum for 1 week. The length of attendance will be subject to medical review. At each attendance the patient must be asked whether he/she has experienced any adverse reactions/side effects.

Monitoring parameters and side-effects must be recorded on the multipurpose monitoring chart (see appendix 12).

If at any stage the patient/healthcare professional is concerned about the patient's physical health then medical advice must be sought without delay.

A staff grade doctor, associate specialist or consultant psychiatrist will visit the patient twice a week for the first 2 weeks to assess their progress, assess for side-effects, manage any antipsychotic cross titration and confirm the rate of clozapine titration. The specific visit times will be determined by the treating team.

There will be no dose increases on weekends or Bank Holidays.

1. **Day 1 (Monday)** – Patient will be seen either at home or in a day care setting and will have pulse, temperature and lying/standing blood pressure (BP) taken prior to administering first clozapine dose. If these measurements are within outlined parameters (see appendix 13) then the prescribed clozapine dose will be administered. A designated worker will then remain with the patient for 6 hours or hourly visits can be made checking temperature, pulse and BP every hour. This can be done in a shift pattern.

2. **Day 2 (Tuesday) and Day 3 (Wednesday)** – The patient will be seen either at home or in day care setting and the patient's temperature, pulse and lying/standing BP recorded. If within the designated parameters, the prescribed dose of clozapine will be administered. The temperature, pulse and lying/standing BP will be performed at two hourly intervals for 6 hours on day 2 and at three hourly intervals for 6 hours on day 3. During this time staff can discuss with the patient other side effects as listed on the bottom of the multipurpose monitoring form (appendix 12) and complete a clozapine GASS form (appendix 16). If the observations are within the designated parameters, the prescribed evening dose of clozapine will be left with the patient or arrangements made for staff to re-visit. The patient will have a full blood count performed and this will be sent to CPMS or to local pathology lab according to local protocol.

3. **Day 4 and onwards for 2 weeks** – Observations should be conducted at least once a day. A designated worker will attend the patient's home at an agreed time in the morning and take the patient's temperature, pulse and lying/standing BP. If within the designated parameters, the prescribed dose of clozapine will be administered. The worker will assess the patient and ask specifically about possible side-effects completing the multipurpose monitoring form (appendix 12) and completing the clozapine GASS form (appendix 16). If the observations are within the designated parameters, the prescribed evening dose of clozapine will be left with the patient or arrangements made for staff to re-visit.

3. **Day 9**- A full blood count will be performed and sent to CPMS or a local pathology lab.

4. **After 2 weeks**-The patient will be re-assessed and it will be decided if the patients care is to remain with the team initiating clozapine or handed back to the sector team. Physical monitoring can be decreased to alternative days.

At this stage the clozapine dose will need to be reviewed and clozapine prescribed on a SPFT outpatient prescription (Appendix 14). Frequency of further medical reviews will also be decided at this stage.

Arrangements for further weekly blood tests will need to be confirmed at this stage. It should be noted that at any stage during titration the process can be performed at a slower rate if medical staff deem necessary. A bespoke community initiation/re-start prescription chart can be used. (Appendix 11)

If at any time during the first two weeks the doctor reviews a patient and their prescription changes, the team must contact pharmacy immediately to find a practical solution for arranging the new supply, and ensure that all records of the titration regimen are changed.

After the first two weeks' treatment the patient will routinely have their blood tests and medication supplies as per local procedure.

When to refer to the prescriber

- Any intolerable adverse effects
- Patient is clearly over sedated
- Temperature rises above 38°C
- Pulse >100bpm
- Postural blood pressure drop of >30mmHg

Plan for re-titration of clozapine

For patients who have stopped their clozapine for more than 48 hours re-titration is necessary. Re-titration can be performed at a faster rate than if the patient was commencing clozapine for the first time. All monitoring requirements will remain in place, as detailed above (see section 5.4 for further details).

Appendix 8

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Clozapine Community Initiation Pre-assessment Record

Check that a full medical and medication history are in the notes and if not these need undertaking.

Mental State Examination

Appearance & Behaviour:

Speech:

Mood

Thought Content:

Perception:

Insight:

Risk Issues:

Other:

Physical Examination

Weight: Height:

Pulse:

Temp:

BP: / Lying: / Standing: /

Results

ECG

Chest x-ray

FBC

LFTs

Blood glucose Lipids

PERSON COMPLETING THIS RECORD
Name/ Position:
Signature:
Date:

Appendix 9

Sussex Partnership NHS
NHS Foundation Trust

CLOZAPINE ASSESSMENT APPOINTMENT CHECKLIST

Patient name: Date:

DOB:

Clozaril® (CPMS) patient No:

Address:

Telephone number:

Consultant Psychiatrist:

Care-Coordinator:

Current Medication	
Name	Dose

CHECKLIST

Full medical history in notes **Date**
Medication history in notes **Date**
FBC sent to Clozaril® Monitoring Service **Date**
Baseline LFTs/ blood glucose/lipids **Date**
ECG **Date**
Chest x-ray (if applicable) **Date**
Baseline mental state examination **Date**
Physical examination to include;

- Weight/height **Date**
- Pulse **Date**
- Temperature **Date**
- Lying/ standing BP **Date**

GP informed of clozapine start date and possible side-effects **Date**
Clozapine drug information and side-effect profile given **Date**
Emergency contact number given (including out of hours) **Date**

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Appendix 10

CLOZAPINE STANDARD COMMUNITY INITIATION PRESCRIPTION

To be used in conjunction with clozapine procedure and guidance, and in particular Appendix 7

Patient Name		CPMS Number	
Address		Hospital No.	
		CMHC/Team	
Date of Birth		Consultant	

DATES	DRUG	MORNING DOSE Time:	GIVEN BY	EVENING DOSE Time:	GIVEN BY
Monday	CLOZAPINE	12.5mg		[redacted]	
Tuesday	CLOZAPINE	12.5mg		12.5mg	
Wednes..	CLOZAPINE	25mg		25mg	
Thursday	CLOZAPINE	25mg		25mg	
Friday	CLOZAPINE	25mg		50mg	
Saturday	CLOZAPINE	25mg		50mg	
Sunday	CLOZAPINE	25mg		50mg	
Monday	CLOZAPINE	50mg (end of initial supply)		50mg	
PRESCRIBER'S SIGNATURE			DATE		
Tuesday	CLOZAPINE	50mg		75mg	
Wednes.	CLOZAPINE	75mg		75mg	
Thursday	CLOZAPINE	75mg		100mg	
Friday	CLOZAPINE	100mg		100mg	
Saturday	CLOZAPINE	100mg		100mg	
Sunday	CLOZAPINE	100mg		100mg	
Monday	CLOZAPINE	100mg (end of 2nd supply)		125mg	
PRESCRIBER'S SIGNATURE			DATE		
Tuesday	CLOZAPINE	125mg		125mg	
Wednes.	CLOZAPINE	125mg		125mg	
Thursday	CLOZAPINE	125mg		Prescribe on out-patient chart	
PRESCRIBER'S SIGNATURE			DATE		

If problematic side effects, consider **SLOWER** dose titration

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Appendix 11

CLOZAPINE COMMUNITY BESPOKE INITIATION/RE-START PRESCRIPTION

Patient Name		CPMS Number	
Address		Hospital No.	
		CMHC/Team	
Date of Birth		Consultant	

IF PATIENT PREVIOUSLY ON CLOZAPINE DATE STOPPED

RE-TITRATION IS NECESSARY IF CLOZAPINE OMITTED FOR > 48 HOURS

DOSE RE-TITRATION RATE IS DEPENDENT ON PATIENT TOLERABILITY

DATES	DRUG	MORNING DOSE Time:	GIVEN BY	EVENING DOSE Time:	GIVEN BY
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
PRESCRIBER'S SIGNATURE			DATE		
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE				
PRESCRIBER'S SIGNATURE			DATE		
	CLOZAPINE				
	CLOZAPINE				
	CLOZAPINE			Prescribe on out-patient chart	
PRESCRIBER'S SIGNATURE			DATE		

If problematic side effects, consider **SLOWER** dose titration

Appendix 12

MULTIPURPOSE MONITORING CHART FOR COMMUNITY CLOZAPINE PATIENTS - WEEK 1

Temp °C		Date (day)	(1)							(2)				(3)			(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
		Time																						
		BP	Pre	1hr	2hr	3hr	4hr	5hr	6hr	Pre	2hr	4hr	6hr	Pre	3hr	6hr	Daily	Daily	Daily	Daily	Daily	Daily	Daily	Daily
			L S	L S	L S	L S	L S	L S	L S	LS	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S
42	B	240																						
41.5	L	230																						
41	O	220																						
40.5	O	210																						
40	D	200																						
39.5		190																						
39	P	180																						
38.5	R	170																						
38	E	160																						
37.5	S	150																						
37	S	140																						
36.5	U	130																						
36	R	120																						
35.5	E	110																						
35		100																						
		90																						
	P	80																						
	U	70																						
	L	60																						
	S	50																						
	E	40																						
Nausea																								
Drowsiness																								
Dizziness																								
Constipation																								
Hyper salivation																								
Urinary problems																								
Sweats																								
Extrapyramidal S/E																								

Seek medical advice if there is, a drop in blood pressure >30mmHg (diastolic or systolic),
L = lying BP S = standing BP Pulse over 100 beats per minute or Pyrexia (temperature in excess of 38°C).
Side effects may be recorded using the code 0=nil, 1=mild, 2=severe, 3=extreme
Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately.

MULTIPURPOSE MONITORING CHART FOR CLOZAPINE PATIENTS - WEEK 2

Temp °C		Date (day)	(12)	(13)	(14)											
		Time														
		BP	Daily	Daily	Daily											
			L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S	L S
42	B	240														
41.5	L	230														
41	O	220														
40.5	O	210														
40	D	200														
39.5		190														
39	P	180														
38.5	R	170														
38	E	160														
37.5	S	150														
37	S	140														
36.5	U	130														
36	R	120														
35.5	E	110														
35		100														
		90														
	P	80														
	U	70														
	L	60														
	S	50														
	E	40														
Nausea																
Drowsiness																
Dizziness																
Constipation																
Hyper salivation																
Urinary problems																
Sweats																
Extrapyramidal S/E																

Seek medical advice if there is, a drop in blood pressure >30mmHg (diastolic or systolic),
L = lying BP S = standing BP Pulse over 100 beats per minute or Pyrexia (temperature in excess of 38°C).
Side effects may be recorded using the code 0=nil, 1=mild, 2=severe, 3=extreme.
Some of the side-effects above may also be caused by other prescribed medication the patient may be on (e.g. lithium, anticholinergics). Ensure this is considered and managed appropriately.

Appendix 13

Parameters of Pulse, BP and Temperature (MEWS)

Pulse; More than 60bpm and less than 100 bpm (beats per minute)

Blood Pressure, Systolic/ Diastolic:
Diastolic: - more than 60mmHg and less than 90mmHg.
Systolic: - more than 100mmHg and less than 140mmHg

Lying/standing BP: The postural drop must be no greater than 30mmHg from previous readings

Temp: More than 35^{o}C and less than 37.5^{o}C

If the patient parameters fall outside any of the above, repeat again after 15 mins. If the recordings still fall outside of these parameters please contact the Staff Grade/Associate Specialist/Consultant Psychiatrist.

Do not give the dose of clozapine until measurements lie within these parameters or when the doctor advises you to go ahead.

Appendix 14

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Clozapine Patient Prescription and Dispensing Record

Name	**Consultant**
Address	Care Co-ordinator
Tel:	Ward/Team
Date of Birth:	Hypersensitivity / Allergies:

Date		***Medication***	**Dose**	**Form**	***Directions***	**Prescriber's signature**	**Duration** *Maximum of six dispensings*
	A						
	B						
	C						
	D						
	E						

Blood test frequency:	Weekly		2 weekly		4 weekly			
Dispensing frequency:	Weekly		2 weekly		4 weekly			

CPMS No: **JAC No:** **Delivery method:**

Dispensing Record: Rx checked:

Date blood taken	**Results of blood test**	**Seen by** (initial)	**Date dispensed**	**Medication** (Dose & frequency indicated by letters above)	**Dispensing details clozapine**	**Dispensing details other medication**	**CPMS entered** (initial)	**Dispenser** (initial)	**Checker** (initial)
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				
					x 25mg x 100mg				

Appendix 15

Viapath Plasma Clozapine Assay Request Form

PLASMA CLOZAPINE ASSAY REQUEST FORM

Please send the completed form with a blood sample (at least 2 mL, collect into EDTA tube) to:

Prof RJ Flanagan, Toxicology Unit, Bessemer Wing, King's College Hospital, Denmark Hill, London SE5 9RS

Tel: 020 3299 5881, Fax: 020 3299 5888, e-mail: *kch-tr.toxicology@nhs.net*

***** Pack safely to Post Office regulations - Do not send with courier for FBC *****

- Take the sample **before** a morning dose or in the morning after an evening dose ("trough sample"). **Sampling < 6 h post-dose may make the results difficult to interpret/compare with previous results**
- Serum can be analysed although plasma is preferred. **Addresses to which the report and the invoice are to be sent must be supplied.**
- Cost: £25 per sample
- The **report will be sent to the consultant**, unless other arrangements are specified or in place.
- Assay results will be available within 2 working days of sample receipt ***(log on to http://www.kingspath.co.uk/results.php to register with our free, secure Results On-Line service).***

Patient

Last name
First name(s)
Clozapine Monitoring Service No
Hospital or NHS no

Date of birth	*Sex* M / F	*Weight (kg)*

Date of sample?	*Time of sample?*
Date of last clozapine dose?	*Time of last clozapine dose?*
Clozapine dose (mg/d)?	*Smoker?* YES/NO

Reason for request:

- ☐ Baseline value?
- ☐ Poor / non-compliance?
- ☐ Dose correct?
- ☐ Drug interaction?
- ☐ Adverse reaction?
- ☐ Other (please give details)?

Report and invoice

Assay requested by
Phone / bleep no
E-mail address
Consultant
**Address for report & invoice (if invoice address is different, use space below)*
Postcode
**Address for invoice (& cost centre if needed)*
Postcode
** Invoice details may be omitted if invoice address/cost centre already notified for this patient*

This form may be photocopied or downloaded (http://www.kingspath.co.uk) RF-CB-TOX-CLOZ v2.0

Appendix 16

GASS monitoring form for clozapine

GASS for Clozapine

Name: _____ Current Medications: _____

Date: _____ _____

Caffeine intake: .....cups/day _____ _____

Smoker: Y / N .....cigarettes/day _____ _____

Has there been a recent change in your smoking habit?: Increase/Decrease by.....cigarettes/day

This questionnaire is being used to determine if you are suffering from excessive side effects from your medication.
Please put a tick in the column which best indicates how often or how severely you have experienced the following side effects.

Over the past week:		Never	Once	A few times	Everyday	Tick if severe or distressing
1	I felt sleepy during the day					
2	I felt drugged or like a zombie					
3	I felt dizzy when I stood up or have fainted					
4	I have felt my heart beating irregularly or unusually fast					
5	I have experienced jerking limbs or muscles					
6	I have been drooling					
7	My vision has been blurry					
8	My mouth has been dry					
9	I have felt sick (nauseous) or have vomited					
10	I have felt gastric reflux or heartburn					
11	I have had problems opening my bowels (constipation)					
12	I have wet the bed					
13	I have been passing urine more often					
14	I have been thirsty					
15	I have felt more hungry than usual or have gained weight					
16	I have been having sexual problems					

I have also experienced: (please write down any other side effects **OR PHYSICAL PROBLEMS OR COMPLAINTS** that you may have experienced over the past week)	
17	
18	
19	
20	

Adapted from the Glasgow Antipsychotic Side-effect Scale© 2007 by St. John of God Hospital and South London and Maudsley Trust

Waddell, Taylor and Hynes 2012
DT,FG,AA, PH, RD comments

Staff Information

1. Allow the service user to fill in the side-effects scale themselves. All questions relate to the previous week.

2. **Scoring**

0 Points	"Never"
1 point	"Once"
2 points	"A few times"
3 points	"Everyday"

3. **Results**

0-16	absent/mild side-effects
17-32	moderate side-effects
33-48	severe side-effects

4. **Side-effects covered include:**

1-2	Drowsiness and sedation
3	Postural hypotension
4	Tachycardia
5	Myoclonus
6	Hypersalivation
7-8	Anticholinergic side-effects
9-10	Gastrointestinal side-effects
11	Constipation
12	Nocturnal enuresis
13-14	Screening for diabetes mellitus
15	Weight gain
16	Sexual dysfunction

5. The column relating to the severity/distress experienced with a particular side effect is not scored, but is intended to inform the clinician of the service user's views and condition.

6. Questions 17 to 20 invite the service user to report any other side-effects or problems not already mentioned. These questions should not be scored but may instigate a discussion with the service user if clinically appropriate.

Adapted from the Glasgow Antipsychotic Side-effect Scale© 2007 by St. John of God Hospital and South London and Maudsley Trust

Waddell, Taylor and Hynes 2012
DT,FG,AA, PH, RD comments