SA Health

Clozapine Management Clinical Guideline

Version 2.0

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Government of South Australia
SA Health

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Clozapine Management Clinical Guideline

2. Introduction

Clozapine, available as Clozaril®, Clopine® and Clozitor® brand, is a medication regulated by the Therapeutic Goods Administration (TGA), subsidised under the Pharmaceutical Benefits Scheme - Highly Specialised Drugs Program Section 100 (PBS S100). It is indicated as a third line treatment in the management of schizophrenia for participants who are non-responsive to, or intolerant of other antipsychotic medications. Participants may only be prescribed clozapine when mandatory blood testing, regular administration and other monitoring requirements can be achieved.

3. Background

Clozapine is associated with a number of adverse effects; many of which are dose-dependent and associated with speed of titration, and others (although rare) can be serious and fatal. Once commenced, doses must be carefully titrated to achieve symptom control, whilst minimising the severity of adverse effects. The Northern Adelaide Local Health Network (NALHN), Central Adelaide Local Health Network (CALHN) and Southern Adelaide Local Health Network (SALHN) mental health services provide care for community-based clozapine participants through Clozapine Clinics, each managed by designated Clozapine Coordinators, including shared care with general practice. The Women's and Children's Health Network (WCHN) co-ordinates community clozapine management through Mallee Ward, located at the Women's and Children's Hospital. The SA Regional Local Health Networks comprising of, Barossa Hills Fleurieu LHN, Eyre and Far North LHN, Flinders and Upper North LHN, Limestone Coast LHN, Riverland Mallee Coorong LHN and Yorke and Northern LHN (Regional LHNs) mental health service provides care for community based clozapine participants in shared care arrangements with general practice (GP) and designated Clozapine Coordinators. Headspace youth services (operated by Sonder) provide community clozapine services to youth 16-25 years. Clozapine is also prescribed to participants in bedded services, managed within each LHN ward area. There are no exemptions to the monitoring criteria or other care components outlined in this document.

This guideline is to be used for the initial treatment (commencement), continued treatment (ongoing participant management) of clozapine participants and management of recommencement/treatment interruption and tobacco cessation.

This guideline has been developed inclusive of the TGA endorsed Clozaril ® Patient Monitoring System™ Protocol Sept 2019 version 5(CPMS).

Clozaril® is the preferred brand of clozapine on the SA Medicines formulary. This document will refer to the accompanying Clozaril Patient Monitoring System (CPMS) throughout.

Any service using the alternative clozapine brands Clopine® or Clozitor® will be required to use the ClopineCentral™ or Juno Connected™ monitoring systems accordingly.

For further information, copies of related documents and forms refer to the SA Health Clozapine Webpage www.sahealth.sa.gov.au/clozapine

4. Definitions/Acronyms/Therapeutic Reference Ranges

SA Health Mental Health Services (MHS)

Clozaril® Patient Monitoring System (CPMS) – the System developed to optimise the management of patients taking Clozaril®

Hospital Clozapine Centre Coordinators – A person who is registered as the centre coordinator with CPMS to ensure that the hospital clozapine centre runs smoothly in accordance with the requirements of the CPMS protocol.

Community Clozapine Centre Coordinators – A Registered Nurse who is registered with CPMS, as the centre coordinator responsible for ensuring that the MHS community clozapine centre runs smoothly in accordance with the requirements of the CPMS protocol and who is responsible for the coordination of clozapine care for participants registered to the MHS community clozapine centre.

Neutropenia - a blood disorder characterized by an abnormally low number of neutrophils circulating in the blood (usually defined as a neutrophil count of less than 1.8 x 109/L). Neutrophils are the type of white blood cell most significant in the immune response to infection.

Agranulocytosis, also known as **agranulosis**,- is an acute condition involving a severe and dangerous leukopenia (lowered white blood cell count), most commonly of neutrophils, causing a neutropenia in the circulating blood.[1][2] It represents a severe lack of one major class of infection-fighting white blood cells. People with this condition are at very high risk of serious infections due to their suppressed immune system.

Normal reference range (as per SA Pathology):

- white cell count: 4.0 – 11.0 (x 109/L)
- neutrophil count: 1.8 - 7.5 (x 109/L)
- Fasting glucose: 3.2 – 5.5 mmol/L
- Total cholesterol: <5.5 mmol/L
- Troponin T: <13 ng/L for females, <17ng/L for males
- C-Reactive Protein: 0.0 - 8.0mg/L
- High sensitivity C-Reactive Protein: low <1.0mg/L
intermediate 1.0 – 3.0mg/L
high >3.0mg/L

- NB: with the change to a more sensitive troponin T assay range (13ng/L for females and 17ng/L for males) consideration as to whether cases of myocarditis would be missed has been given. SA Pathology still consider that a troponin T >30ng/L is appropriate for an action point for a value 1-2 times the upper level of normal and troponin T >60ng/L is appropriate for an action point for a value 2 times the upper level of normal.

- NB: high sensitivity C-Reactive Protein levels, it is recommended interpretation be based on changes with serial CRP values and in conjunction with other prognostic / risk factors. Result >10: A raised high sensitivity CRP level is a non-specific finding in acute inflammatory states.

White Cells: made up of the following cell types at the level indicated:

- Neutrophils: 1.8-7.5 x 109/L SA Pathology reference
- Eosinophils: 0.02-0.5 x 109/L SA Pathology reference
- Basophils: 0-0.1 x 109/L SA Pathology reference
- Monocytes: 0.2-0.8 x 109/L SA Pathology reference
- Lymphocytes: 1.5-3.5 x 109/L SA Pathology reference.

Therapeutic serum clozapine range (as per SA Pathology) - 350-600 ug/L – blood plasma/serum concentration usually expected to prevent relapse of schizophrenia, and limit toxic/adverse effects. With some participants requiring a range below this or up to 1000 ug/L for beneficial therapy, determined by clinical response.

QT interval -The QT interval is the time from the start of the Q wave to the end of the T wave on an electrocardiograph (ECG).

Corrected QT interval (QTc) – the QT interval corrected for a standard heart rate of 60 bpm. A normal QTc interval is 400- 440 milliseconds (ms). Abnormal for males is >440 ms and >460 ms for females, >500ms is life threatening.

Smoking – any reference to smoking in this guideline refers to the smoking of tobacco unless otherwise specified.

Bedded Services – any reference to bedded services in this guideline refers to all services where a participant is admitted into a health service that provides 24 hour care or supervision.

5. Governance and Quality Improvement

Local Health Networks (LHN) through the Mental Health Clinical Leads for Medicine and Nursing or equivalent and their quality and governance processes are responsible for implementation, monitoring and evaluation of clozapine guidelines.

The SA Health Psychotropic Drugs Committee (PDC) through the Clozapine Strategic Management Group (CSMG) is responsible for the oversight of Clozapine Centres to ensure compliance with this guideline including monitoring of performance indicators and protocol compliance through annual clinical audit in June/July and annual supplementary clinical audit in Feb/March for Clozapine Centres that achieve <80% compliance.
Within SA Health the Viatris brand of clozapine (Clozaril®) is listed as the preferred brand on the SA Medicines Formulary to be used for initiating treatment. The other brands of clozapine available in SA are the Pfizer Australia brand, Clopine®. Pfizer Australia has its own monitoring system ClopineCentral™ and the Pharmacor Pty Ltd brand, Clozitor®, administered by Juno Pharmaceuticals. Juno Pharmaceuticals has its own monitoring system Juno Connected™. From here on in the guideline will refer to the Viatris CPMS as the default clozapine monitoring system. Clozapine may only be commenced by a Consultant Psychiatrist who is a Staff Specialist or Visiting Medical Officeraffiliated with the public hospital at or from which the participant is receiving treatment. After the first 18 weeks of initial treatment, clozapine participants may be managed under continuing* treatment criteria if the dose is considered stable and the treatment remains under the supervision and direction of a psychiatrist reviewing the participant at regular intervals.

The Viatris eCPMS is a web-based database (governed by Viatris Health Pty Ltd), where all participant white cell and neutrophil count blood test results and relevant information is stored. Blood count, dose and dispensing data can be accessed and entered by registered personnel enabling them to check compliance with the monitoring requirements. If a participant or organisation does not adhere to monitoring requirements, the information in the eCPMS database will be incomplete and dispensing and dosing of the medication should cease until the required monitoring is completed as indicated by the CPMS protocol and in this clinical guideline.

Once initiated, stabilised and managed under continuing treatment by the Consultant Psychiatrist in a specialist setting, the participant will be encouraged to move to a shared care arrangement with a General Practitioner (GP), provided the prescriber is under the supervision of a Consultant Psychiatrist while remaining registered to a SA Health Clozapine Centre (see Section 10.1). There is an option for the participant to be transferred to a private centre that agrees to take over the full care (see Section 12.1).

*see PBS Authority Required continuing treatment criteria www.pbs.gov.au

6 Areas of Responsibility

Medical and Nursing Clinical Leads or equivalent of Mental Health Services (MHS) are responsible for ensuring that all staff comply with the responsibilities and requirements outlined in this guideline.

All staff involved in the management of clozapine are required to comply with TGA and PBS requirements, and relevant SA Health guidelines.

SA Health currently uses the Clozaril brand in conjunction with the Clozaril Patient Monitoring System (CPMS). Where protocol compliance is breached, or adverse events are reported or evident the first responding staff member is responsible for making the formal notification on the SA Health Safety Learning System (SLS) website.

All participants, Medical Officers, health care professionals (including those prescribing or assessing participant results and physical health status), pharmacies, pharmacists, centre co-ordinators and assistants, and treating centres or clinics involved with the distribution of clozapine must be registered with the relevant clozapine patient monitoring program.

Each Centre must have at least one Centre Coordinator, and consideration should be given to having Assistant Coordinators where required for continuity of service. A patient can belong to only one centre;

healthcare professionals and pharmacies can be linked to many centres. In selected circumstances major tertiary SA Hospital Pharmacies may be registered to dispense all clozapine brands.

Each community nurse-led clozapine clinic requires the nomination of a Consultant Psychiatrist to act as the nurse-led clinic sponsor to support that clinic and ensure that conditions exist at each site to allow the application of these clinical guidelines. Regional LHN Clozapine Centres are supported by visiting and distance consultancy services.

Medical Officers prescribing clozapine must know the indications, contra-indications, adverse effects, treatment options for these adverse effects and reporting requirements. Medical Officers must be registered to prescribe clozapine with the CPMS and must ensure that each participant commenced on clozapine meets CPMS criteria for the prescription and supply of clozapine including participant CPMS registration and referral to the relevant community Clozapine Centre for ongoing management. Medical Officers are also responsible for ensuring the required screening and monitoring tests are ordered at appropriate intervals, that CPMS documentation and relevant forms are completed providing evidence of review and that prescriptions meet TGA and PBS S100 standards.

Nursing staff who administer clozapine must know the indications, safe use and screening processes for clozapine and data entry requirements. Nurses must be aware of the presentations of common and life-threatening adverse effects and their management, and all other protocol and care requirements for a participant prescribed clozapine.

It is recommended that all SA Health staff, involved in the prescription, management and dispensing of clozapine, complete the Clozapine- High Risk Medications online training module as a minimum requirement.

Clozapine Centre Coordinators and Assistant Coordinators are responsible for facilitating the smooth running of the centre as follows:

- Ensuring centre compliance with the relevant monitoring system, SA Health guidelines, TGA and PBS Section 100 requirements;
- Registering new staff and participants with CPMS and ensuring information recorded is accurate and current;
- Education of Medical Officers, other clinical staff, participants and relevant other stakeholders on specific clozapine monitoring and documentation (electronic and paper-based) requirements;
- Monitoring weekday email alerts and running the Open Architecture Clinical Information System (OACIS) and Sunrise EMR & PAS (Sunrise) clozapine report each morning to identify any participants admitted to an emergency department or hospital ward and contacting the hospital treating team when appropriate to support the safe continuity of clozapine treatment;
- Ensuring necessary bloods and assessments are performed, reviewed and acted upon accordingly and in a timely manner;
- Liaising with hospitals, health services and pharmacies to ensure continuity of medication management at transitions of care;
- Monitoring the appropriate initiation, maintenance and cessation of clozapine alerts in OACIS/ Sunrise, Client Based Information System (CBIS) and Country Consolidated CME (CCC) as appropriate; and
- All Clozapine Centre Coordinators are responsible for providing regular feedback on centre workload, performance and outcomes as required by the SA Health Psychotropic Drugs Committee and for supporting 6 and/or 12 monthly audits of the processes outlined in these guidelines.

Safety Quality and Risk Managers are responsible for ensuring that 6 and / or 12 monthly audits of each community nurse-led clozapine clinic are completed in June/July and if required February/March by suitably qualified nursing or medical staff using the approved audit tools.

Public hospital Mental Health Liaison Teams (Psychiatric Consultation Liaison) are responsible for monitoring weekday email alerts or running the OACIS and Sunrise Clozapine report each morning to identify all new local clozapine admissions. Liaison teams must notify the appropriate Community Clozapine Centre of the admission and ensure that the inpatient treating team has sufficient understanding of the risks of prescribing clozapine and their responsibilities under PBS Section 100, CPMS, and SA Health guidelines and provide adequate support for the safe management of clozapine treatment. Liaison teams must ensure safe transfer of care including the completion of required documentation, Medical Record (MR) forms and electronic databases and alerts (OACIS, CBIS, CCC, ATS and Sunrise).

SA Health Directors of Pharmacy are responsible for facilitating the smooth running of CPMS registered hospital pharmacies and ensuring all hospital pharmacy staff comply with clozapine protocols, the SA Health guidelines, and SA Pharmacy business rules.

Smooth running of a CPMS registered pharmacy involves:

- Ensuring centre compliance with the Clozaril® CPMS, SA Health Guideline, TGA and PBS Section 100 requirements
- Ensuring all pharmacists are CPMS-registered and that information recorded is up to date
- Ensuring all pharmacists are familiar with the CPMS protocol, SA Health guideline and PBS Section 100 Highly Specialised Drugs criteria
- Ensuring all pharmacists are trained in the process of dispensing clozapine
- Liaising with the community pharmacy and clinical pharmacist directly involved in the inpatient care as needed
- Liaising with hospitals, community pharmacies, community mental health teams and/or Clozapine Coordinators at the point of transfer of care to ensure continuity of medication management
- Liaising with community pharmacies, community mental health teams and/or Clozapine Coordinators for arrangement of clozapine dispensing for those consumers in the initial 18 weeks of clozapine treatment (including courier arrangements where necessary)

Pharmacists involved in the care of consumers on clozapine and dispensing of clozapine are responsible for:

- Compliance with the PBS and CPMS protocol, including assessment of blood test results, dispensing accordingly, and entering dispensing data; dose and quantity of tablets into eCPMS
- Consumer counselling prior to discharge from hospital
- Reporting of clozapine-related adverse events
- Arranging supply of clozapine from a SA Hospital Pharmacy during the initial 18 weeks of clozapine treatment
- Liaising with the community mental health team, GP, patient and/or carer for continued supply if needed
- Liaising with community mental health Clozapine Coordinator for early medical review if issues with noncompliance or significant adverse effect occurs
- Supporting Medical Officers in the prescription of clozapine

7 Protocols

7.1 Commencing Clozapine

The SA Health MR74D clozapine commencement form (or electronic equivalent where available i.e. Sunrise), is the required documentation for all clozapine commencements at bedded services or community based sites. It has been designed to meet the checks and observational needs of the participant during the first 18 weeks of treatment. The full completion of the form is a minimum requirement and is a multidisciplinary responsibility within each team/unit. It must be completed if clozapine is commenced for the first time or recommenced after more than a 28 day break in treatment. Where CBIS and CCCME Clozapine Review and Physical Health Assessment screens are available, clozapine reviews and physical observations are to be recorded electronically and treatment details reflected in the service plan.

7.2 Pre–commencement: Consent and Registration

Prior to the first commencement of clozapine, the participant will have had an adequate trial of at least two other antipsychotic drugs, with documented assessment demonstrating there has been insufficient response, or unacceptable adverse effects. The participant's ability to comply is assessed and documented through a clinical review process including the participant, carers and treating community team.

The commencing team is to:

Communicate directly with the community team who would be assuming the care of the person to ensure there is capacity for the team including;

- The community Consultant Psychiatrist agrees with the proposed commencement
- The community Clozapine Coordinator has been consulted regarding the proposed commencement
- The community team has capacity to provide the necessary follow up for the consumer to ensure safe and effective care.

Documentation of this discussion with the community team Consultant Psychiatrist is to be documented under 1st stage: pre-commencement on the MR74D clozapine commencement form. It is necessary to ensure that adequate compliance with oral administration and monitoring of medication can be achieved in the community.

Where there is disagreement regarding the commencement of clozapine between treating teams, the issue should be resolved utilising the LHNs established dispute resolution processes.

Informed consent process: The participant and family where appropriate must be provided with verbal and written information specific to clozapine, including benefits, alternatives, required monitoring, side effects and their management. Participant and carer information related to clozapine is available on the Choice and Medications site and **Appendix 1a** SA Health Clozapine Participant Information and **Appendix 1b** Clozapine Information for Carers and Support Persons This process and the participant's decision should be documented on the MR74D clozapine commencement form (or electronic equivalent) and in the CBIS & CCCME record.

The participant must be registered with CPMS prior to commencing clozapine. Registration requires the completion of the CPMS patient registration and the patient health information storage consent forms, which must be faxed or emailed to CPMS. The participant is required to sign the patient health information storage consent form. If a participant is involuntary and does not have capacity to give consent, then the doctor concerned may sign on the participant's behalf following the Local Health Network (LHN) procedure for consent to treatment. In this case it is important that the participant is later informed of the ongoing collection of data and commitment to privacy. The participant must not be commenced before confirmation of registration from CPMS including the patient Clozaril® Patient Number (CPN) is received by fax or email.

7.3 Pre-commencement: Baseline Assessment

A thorough search of the participant's medical history is required to ensure that they do not have a prior history of drug induced neutropenia or bone marrow disorder before deciding to commence clozapine. A physical examination should be performed to identify other comorbidity that may contra indicate clozapine prescription. Other medication should be reviewed, and consideration should be given to discontinuation or tapering where there may be significant interactions.

Particular attention should be paid to the participant's bowel habits. Clozapine must not be started in people who are constipated or at risk of bowel obstruction until such issues have been appropriately investigated and resolved. Psychoeducation about clozapine and constipation is to be provided including the use of a stool chart as indicated. **Appendix 2** See Psychotropic Induced Constipation Guideline and Choice and Medications Clozapine and constipation fact sheet

If the participant is pregnant further consideration and discussion with the participant and their family is required. This is due to the potential of currently unknown effects on the foetus with only limited data available.

Clozapine is contraindicated in breastfeeding therefore it is important to ensure that the participant is not breastfeeding prior to the initiation of clozapine.

A baseline white cell and neutrophil count is required, meeting the 'green range' of the guidelines (WCC >3.5 x 109/L, Neutrophils >2.0 x 109/L) – this sample must have been obtained within 10 days of the proposed start date. If the blood picture is not within this range and meets the criteria for the 'amber range' (WCC 3.0 - 3.5 x 109/L, Neutrophils 1.5 -2.0 x 109/L), a repeat blood test and medical review is required. Stability in the white cell and neutrophil count must be achieved prior to commencing clozapine. Blood results are to be recorded on the SA Health MR75D clozapine investigation review and prescription record form where this is in use (or electronic equivalent).

Viatris has access to a consultant haematologist specialising in clozapine management, who can be consulted for advice in difficult cases (tel: 0404 451 327).

Due to diurnal variation and white cell count being lowest in the morning, taking blood late in the day may avoid a false low being recorded that could prevent the participant from starting (or continuing) clozapine. The decision for afternoon blood testing will be based on the participant's individual response. Baseline fasting lipids, fasting glucose, liver and renal function and electrolyte tests prior to commencement of the medication are required, usually at the same time as the pre- treatment white cell and neutrophil tests to ensure there are no underlying comorbidities that may be exacerbated by clozapine. Baseline results are to be recorded on the SA Health MR75D clozapine investigation review and prescription record form where this is in use (or electronic equivalent) and the date of the observations recorded on the SA Health MR74D clozapine commencement form (or electronic equivalent).

The participant will have a cardiac assessment, including:

- Electrocardiograph (ECG), troponin level and high sensitivity c-reactive protein (hs-CRP) blood tests prior to commencement of the medication;
- Where possible an echocardiogram is to be performed prior to clozapine commencement;
- If there is no history or evidence of cardiac disease and the participant is to be commenced in bedded services, the echocardiogram must be completed within six months of commencement;
- The echocardiogram should always be completed prior to commencement if there is a prior cardiac history, current cardiac symptoms or the participant is being considered for a community start; and
- Echocardiograms are required annually after commencement.

Viatris has a cardiology and medical information service accessible on 1800 931 383.
Evidence of compliance with the cardiac monitoring protocol must be accessible in the participant's medical record. Cardiac monitoring results are to be recorded on the SA Health MR74D clozapine commencement form (or electronic equivalent). Where it is in use, the SA Health MR75D clozapine investigation review and prescription record form (or electronic equivalent) can also be used to record cardiac pathology test results.

A full medication management plan must be completed that considers potential drug interactions and resulting effects on clozapine levels, adverse effects, and efficacy (see **Appendix 3** Clozapine Toxicity and Therapeutic Drug Monitoring). This includes assessment of current smoking, caffeine, alcohol, illicit drugs and over the counter medications. Potential interactions and their risks should be discussed with the participant.

7.4 First Time Commencement

Once a participant has been registered but prior to commencement the initiating team must enter clozapine alerts on the appropriate clinical information systems including: CBIS (Metro LHNs, CAMHS), OACIS, CCCME (Regional LHN), the iPharmacy dispensing system, Sunrise and the medical record. Information should include the Clozaril® Patient Number (CPN). If at any time clozapine needs to be ceased, the status of these alerts must be updated (including a reason for cessation) on the clinical information systems by the team who ceased the medication.

For bedded services the clozapine titration doses are to be recorded on the appropriate National Inpatient Medication Chart or SA Health equivalent or electronic equivalent. All other clozapine assessment recording is to be completed on the SA Health clozapine protocol forms (or electronic equivalent).

The rate of clozapine titration will depend on symptom response, tolerability, gender, body mass index (BMI) and serum clozapine levels. Standard titration protocols are provided on the SA Health MR74D clozapine commencement form, in the CPMS protocol and in this Clinical Guideline (see **Table 1 Normal Dose Titration** and **Table 2 Rapid Dose Titration**). Consistent with TGA endorsed guidelines, it is recommended that the maximum dose should not exceed 900 mg per day.

Table 1: Normal Dose Titration Example

	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Dose (mg)	12.5	-	25	-	25	-	25	25	25	25	25	50	25	75

	Day 8		Day 9		Day 10		Day 11		Day 12		Day 13		Day 14	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Dose (mg)	25	100	50	100	50	100	50	125	50	125	50	125	50	150

The above table shows the recommended dose titration for those commencing clozapine for the first time. From day 14 the dose can be increased in 50mg intervals every two to three days depending on efficacy and side effects. Maximum dose is 900mg per day. Clozapine levels should be assessed as per commencement protocol, or if side effects are apparent; there is evidence of infection; there are changes in medications that interact with clozapine and or changes in the use of drugs such as tobacco smoking (**see section 8.3 Tobacco Use in Community Settings**) and caffeine.

Table 2: Rapid Dose Titration Example

	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Dose (mg)	12.5	-	25	-	25	25	25	50	25	75	25	75	25	100

	Day 8		Day 9		Day 10		Day 11		Day 12		Day 13		Day 14	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
Dose (mg)	50	100	50	125	50	150	50	175	75	175	100	175	100	200

Rapid titration is optional for participants with good tolerance to previous clozapine treatment (See table 2 above). From day 14 the dose can be increased in 50mg intervals every two to three days depending on efficacy and side effects. Maximum dose is 900mg per day. Clozapine levels should be assessed as per commencement protocol, or if clinically indicated by side effects; evidence of infection; there are changes in medications that interact with clozapine and or changes in the use of drugs such as tobacco smoking and caffeine.

When commencing clozapine for the first time the participant will require monitoring for a period of six hours after the first dose, including vital and neurological signs as detailed on the SA Health MR74D clozapine commencement form (or electronic equivalent). When commenced in a community based setting a nurse special is required. All observations are to be recorded on the SA Health MR74D clozapine commencement form (or electronic equivalent). If there are any changes in vital signs i.e. blood pressure drop of 20mmHg systolic, increase in pulse above120 beats per minute (bpm) or pulse irregularity, chest pain, shortness of breath, syncope or altered conscious state the participant should be transported to the nearest emergency department for medical review and/or a code blue called. The Medical Officer responsible for commencement of the medication is to be notified.

Vital signs of participants in a bedded unit following day one of commencement are continued as per local monitoring procedures incorporating daily temperature for first 28 days or as clinically indicated. For participants discharged before the 28 days of temperature monitoring is completed or participants commenced in the community, the participant is to be given a thermometer, a participant temperature monitoring chart (**Appendix 4**) to complete and the appropriate education to record their own temperature and when to seek assistance.

Subsequent monitoring: Following commencement participants must have weekly monitoring including a Complete Blood Examination (CBE) and physical health assessment for the first 18 weeks of treatment. Following the first 18 weeks of continuous treatment with clozapine the participant may be eligible to move to a maintenance schedule of four weekly monitoring for long term management.

7.5 Commencing Clozapine in Older Persons

Following commencement at 12.5mg it is recommended that subsequent dose increments are restricted to 25mg/day. Noting that there is no specific titration regimen suggested for older persons it is considered that clozapine titration may be significantly slower than titration regimens in younger participants. The minimum effective dose may also be significantly lower than the dose used in younger people.

Older persons may be more susceptible to the potential side effects of orthostatic hypotension and tachycardia especially for those with compromised cardiovascular function. Older persons may also be more susceptible to the anticholinergic effects of clozapine such as constipation and urinary retention.

It is recommended that a baseline of comorbid medical problems is clearly documented to determine if any side effects experienced are attributable to clozapine use.

It is recommended that a comprehensive medication review is completed prior to clozapine commencement.

7.6 Interruption to Clozapine Therapy and Recommencement

If clozapine is stopped for more than 48 hours and then recommenced at full dosage there is a significant risk of severe side-effects similar to those that occur at initial titration including severe sedation, cardiovascular adverse effects and seizures. The CPMS protocol for recommencement of clozapine and associated monitoring requirements must be followed.

Table 3 outlines clozapine dosage requirements for recommencement after greater than 48 hours but less than or equal to a 28 day break in treatment. Monitoring should be documented on the MR78D clozapine recommencement form (or electronic equivalent). When the break in treatment is longer than 28 days the full pre-commencement work up must be repeated in accordance with CPMS guidelines.

To avoid adverse events related to recommencement at full dose after a period of non- adherence, concerns regarding adherence should be discussed with the treating Medical Officer/ Consultant Psychiatrist prior to dosing. Where a participant has been admitted to a non-psychiatric ward the treating team should always consult with the participant's Clozapine Coordinator or the hospital's Psychiatry Consultation Liaison team before continuing clozapine treatment. Outside of office hours the on-call psychiatry registrar should be contacted. Additional monitoring requirements may be required depending on the period of interruption (**See Table 3**).

Participants who experience an interruption in therapy are at risk of severe rebound psychosis. Treating teams should provide close monitoring of mental state during this period and consider the use of an alternative antipsychotic to control psychotic symptoms, the reason and period of interruption is to be established during the assessment process to ensure a safe treatment plan. The hospital Psychiatry Consultation Liaison team must be contacted by non-psychiatric hospital units for advice on the management of participants following an interruption in therapy.

Table 3: Dosage and Monitoring Requirements Following Treatment Interruption

Period of interruption (time since last dose was taken)	Dosage / Monitoring Requirements
≤ 48 hours	No change to dosage or monitoring
> 48 hours to ≤ 72 hours	Start on 12.5mg and titrate up No additional monitoring requirements
> 72 hours to ≤ 28 days	Start on 12.5mg and titrate up For 4 weekly participants: Weekly monitoring for 6 weeks. If no abnormality resume 4 weekly monitoring For weekly participants: Weekly monitoring for 6 weeks or as long as needed to reach 18 weeks (126 days) (whichever is the greatest).
> 28 days	New participant registration form New pre-treatment result and monitoring same as new commencement (18 weeks): Start on 12.5mg and titrate up.

7.7 Discontinuing Therapy

If a decision has been made to cease treatment it is recommended that it occur over a period of one to two weeks with an introduction of an alternative antipsychotic if clinically indicated.

If an abrupt cessation is required or occurs the participant should be monitored for rebound psychosis and cholinergic rebound; headache, nausea, vomiting and diarrhoea with consideration for use of an anticholinergic agent.
Blood test monitoring requirement:

- Notify the monitoring provider within 24 hours via phone, fax or email using the Discontinuation of Therapy Form, available in the CPMS protocol;
- Participants on weekly monitoring: weekly for four weeks after cessation; and
- Participants on 4 weekly monitoring: one blood test four weeks after cessation.

Participants who are being monitored due to an amber or red result with subsequent cessation may need additional monitoring as per clinical need or CPMS haematology advice.

If clozapine is discontinued for a red range result, CPMS requires further weekly blood tests for a total of four weeks once the blood readings have returned to the green range. In this case recommencement of clozapine can only be considered after discussion with the CPMS haematologist. There must be clear evidence that clozapine did not cause the low white cell count, that is, another probable cause is identified. Due to the risk of severe infection secondary to very low neutrophil counts (febrile neutropenia), the participant must be monitored for signs and symptoms of infection. If they have an infection such as a sore throat, a further complete blood examination (CBE) must occur.

8 Ongoing Participant Monitoring

Following the commencement of clozapine, mandatory participant monitoring includes assessment of test results, physical health, mental state and function. The goal of these monitoring processes is to identify problems with efficacy, adverse events or comorbidity and intervene early to prevent further complications. Monitoring should be documented on the MR77D Clozapine patient protocol four weekly form (or electronic equivalent).

8.1 White Cell Count Monitoring

Neutropenia occurs in 2-3% of participants treated with clozapine. It should be noted that 85% of neutropenia cases occur during the first 18 weeks of treatment. Blood tests for white cell count and neutrophil counts are taken at least each seven days for the first 18 weeks and then every 28 days if there are no complications during the initiation period. **Table 4** shows that white cells and neutrophils are stratified into ranges indicating level of risk to the participant.

Table 4: White Cell Count Monitoring Ranges

White Blood Cell (WBC) & Neutrophil Count (NC) Results	Range	Action
WBC >3·5 x10^9/L and NC >2·0 x10^9/L	**Green**	Clozapine therapy can continue or be titrated upwards as required
WBC 3·0 - 3·5 x10^9/L and/or NC 1·5 - 2·0 x10^9/L	**Amber**	Requires increasing frequency of monitoring, to twice weekly
WBC <3·0 x10^9/L and/or NC <1·5 x10^9/L	**Red**	STOP clozapine immediately and repeat blood test within 24 hours. Contact Consultant Psychiatrist and arrange urgent medical review

When in the **amber range** blood tests must be completed twice weekly until the participant blood result returns to the green range. Once in the green range regular monitoring is recommenced. During the time the participant is in the amber range only three-four days of medication can be provided at a time.

When in the **red range**, clozapine must be ceased and telephone contact with the CPMS haematologist (Tel: 0404 451 327) is mandatory. Contact the Consultant Psychiatrist and arrange an urgent medical review. Blood tests need to be repeated daily until out of the red range, then twice weekly until back into the normal (green) range. Once back into the green range blood tests, WCC and NC are to continue weekly for four weeks.

NOTE: If the participant is in the amber or red range, immediately contact a senior psychiatrist with experience in the use of clozapine to discuss a management plan.

8.2 Clozapine Level Monitoring

During commencement, blood testing for serum clozapine levels will occur at least on week four, week nine, and prior to discharge from hospital. Once the participant has moved to four weekly monitoring, levels are recommended at least six monthly. More regular levels may be indicated if there are concerns regarding efficacy, compliance, changes in concomitant medications or substance use (e.g. tobacco). Clozapine level testing on admission should be considered as part of the assessment.

If efficacy is incomplete and there are no significant side effects, then levels should be titrated above 350 ug/L (literature evidence of best efficacy). Clozapine levels above 600 ug/L are associated with an increased risk of severe side effects including seizures and sedation. Where possible participants should be maintained at levels below 600 ug/L, however a percentage of participants will respond only at higher levels. Participants requiring above 600 ug/L require close monitoring for concentration dependent side effects (sedation, hypotension and adverse neurological effects including myoclonus and seizure)
The consensus maximum serum level is 1000 ug/L. Where participants record serum levels above 1000 ug/L or above 600 ug/L where response is known below this value, a review of treatment should occur, to identify drug interactions, changes in substance use (e.g. tobacco), timing of clozapine level in respect to dose, or comorbid infection, liver or renal dysfunction.

The rate of dose reduction will depend on the risk as determined by the clozapine level, the presence of dose related side effects, the stability of the participant, the clozapine level at which the participant is known to respond and the management of the cause of the level increase (e.g. drug interaction). Where risk is high due to severe side effects and/or very high levels, the dose can be held for up to 48 hours without interruption of therapy (see section 7.6, and CPMS guidelines). If there are no contraindications, recommencement at a reduced dose should be considered before 48 hours to avoid an interruption in therapy. Where interruption in therapy is unavoidable, CPMS guidelines for recommencement must be followed (see section 7.6).

Where the risk from clozapine levels or side effects is low, then a gradual down titration at 25-50mg increments until a safe tolerable level is achieved will reduce the risk of relapse. Mental state should be monitored as clinically indicated during this period and clozapine levels can be reviewed from five days after the adjustment in dose.

Participants whose clozapine level provides adequate therapeutic effect below 350 ug/L or above 600 ug/L should have this reflected in the care plan documentation.

If a level less than 50 ug/L is recorded it indicates a break in therapy which is likely to be longer than 48 hours. An urgent assessment of compliance is required to determine the likely length of non-compliance. Recommencement at full dose may result in severe sedation, cardiovascular adverse effects and seizures, and contra-indicated. CPMS recommencement guidelines must be followed (see section 7.6).
A serum clozapine level should be taken on hospital admission as a part of routine participant assessment.

NOTE: Blood testing samples for serum trough levels should be taken 12 hours after the last dose

8.2.1 Clozapine Levels During Infection

There is evidence that a normal response to infection inhibits cytochrome P450 enzymes resulting in significantly elevated serum clozapine concentration which can lead to increased side effects including sedation and seizure activity. If there is evidence of an infection, the participant should be assessed for signs of clozapine toxicity and if indicated a serum clozapine concentration taken and reviewed by a Medical Officer. In the event of a raised serum clozapine concentration or clinical signs of clozapine toxicity then a medical review is required with consideration given to dose reduction if indicated. If the serum clozapine concentration is raised, consideration should be given to monitoring the serum clozapine concentration weekly during the period of infection. Treatment with antibiotics that inhibit CYP enzymes associated with clozapine metabolism (e.g. CYP 1A2 - quinolones such as ciprofloxacin) will also increase the risk of toxicity (see Clozapine Toxicity and Therapeutic Drug Monitoring **Appendix 3**)

8.2.2 Clozapine Levels: Tobacco and Caffeine Use During Clozapine Treatment

Changes in tobacco use can affect clozapine concentrations. Commencement of tobacco smoking (or an increase in smoking) may reduce clozapine concentration, while tobacco smoking cessation may increase serum clozapine concentration, with potential for clozapine toxicity and its associated adverse effects, including death.

Polycyclic aromatic hydrocarbons in tobacco smoke induce the CYP1A2 enzyme responsible for clozapine metabolism. On cessation of smoking, serum clozapine concentration may rise significantly over the next seven-10 days, regardless of the use of nicotine replacement therapy.

The potential for increased serum concentration of clozapine is NOT a reason to discourage participants from stopping smoking, as smoking is one of the most serious risk factors for poor physical health and reduced life expectancy among people living with mental illness.

Factors to consider when determining impact of smoking cessation and caffeine intake on clozapine levels include:

1. How much a person smokes: light (5-12 cigarettes per day); moderate (13-24 cigarettes per day), heavy (≥ 25 cigarettes per day);
2. The expected change in smoking on admission (e.g. complete cessation on closed wards) and on discharge (e.g. return to pre-admission levels, an increase from baseline);
3. The participant's normal compliance with clozapine preadmission;
4. The participant's rate of clozapine metabolism, as measured by dose versus serum clozapine concentration;
5. History of side effects on clozapine and the approximate serum clozapine concentration at which these occurred; and
6. Changes in caffeine intake, an increase in caffeine can result in increasing serum clozapine concentrations.

Participants should be encouraged to reduce their caffeine intake when stopping smoking. Caffeine toxicity may result as caffeine is also a substrate for CYP1A2. Caffeine toxicity may cause agitation, sleep disturbance and gastrointestinal symptoms all of which may be misinterpreted as nicotine withdrawal. It must be noted that nicotine replacement therapy (NRT) will not mitigate these effects.

8.3 Tobacco Use in Community Settings

The participant's smoking habits are to be recorded at each clozapine review. Participants should be actively encouraged to cease smoking and advise staff (prior if possible) if they do cease, reduce, or otherwise change their smoking habit. See SA Health Smoke-free Policy. The potential effects of smoking and smoking cessation are to be explained to the participant and their carer's.

If a participant reports the commencement/recommencement of regular smoking for longer than one week then a clozapine level should be considered, particularly for participants with break through symptoms, unstable illness or those with dosing adjusted close to threshold of efficacy. Where clozapine levels are significantly reduced, then upward titration of dose should be considered to return to therapeutic levels. This can occur at 25 to 50mg increments depending on the severity of illness and drop in clozapine level.

When the participant has made the decision to stop smoking where possible, measure serum clozapine concentration prior to smoking cessation.

Consider the participant's likely adherence to smoking cessation, establishing good communication to ensure that, if the Quit program fails the clozapine dose is adequate to maintain therapeutic serum clozapine concentration for that participant. Participants with irregular smoking patterns will require closer monitoring of their serum clozapine concentrations.

It is recommended that serum clozapine concentration following smoking cessation or reduction is taken at day seven, day 14, day 21 and day 28 or until stable. Ensure the test includes time of last dose and the time that the blood is taken. An early morning blood sample 12 hours after the last dose is required (this can be synchronised with routine blood tests).

An action management plan is to be documented in the medical record to ensure the participant receives appropriate smoking cessation assistance and counselling. The plan is to include a timeline for blood monitoring, the education required to ensure that the participant/carer has an ongoing understanding of symptoms that may indicate clozapine toxicity and the contact details for medical support.

All participants that cease smoking should be monitored closely for clinical side effects of raised serum clozapine concentration. The risk of sedation, hypotension and adverse neurological effects including myoclonus and seizures will be greater when serum clozapine concentrations are higher; however, the occurrence of clozapine-induced agranulocytosis and many other adverse effects are not dose dependent.

The clozapine dose may need to be reduced if the serum clozapine concentration rises outside of the participant's base range, or above 1000 ug/L, during smoking cessation.

8.3.1 Tobacco Use in Bedded Services

Participants who are admitted to a non-smoking bedded service are to have their serum clozapine concentration taken as soon as possible following admission.

It is recommended that serum clozapine concentrations are taken at day one, day seven then weekly for the duration of the admission or until stable and then on discharge. Ensure the test includes time of last dose and the time that the blood is taken. An early morning fasting blood sample, 12 hours after the last dose, is required (this can be synchronised with routine blood picture tests).

All participants should be monitored closely for clinical side effects of raised serum clozapine concentration and have their dose adjusted accordingly as per the management described for community teams as described above.

The participant's smoking status should be assessed on a regular basis and education provided to the participant regarding notifying staff of any change in their smoking status.

On discharge from a bedded service the Transfer of Care (MR76D) form is to be completed with the current serum clozapine concentration and documentation of the participant's smoking status and smoking plans post-discharge.

8.3.2 E- Cigarettes

The effect of e-cigarettes and vaping on clozapine levels is not well known. There is little information currently on the level of polycyclic aromatic hydrocarbons present in e-cigarettes or vaping 'juice'.

It is recommended that the same protocol for tobacco cessation is followed to assess the effect of moving to or ceasing E-cigarettes.

An assessment of the type of e-cigarette or vaping juice is required including whether there is the addition of nicotine, the e-liquid strength, vial quantity (ml) and number of vials consumed over a time frame. This information is to be recorded on the clozapine monitoring forms.

8.4 Cardiac Monitoring

Cardiac monitoring is designed to assess for complications such as arrhythmias, long QT interval, myocarditis and cardiomyopathy. Required investigations include ECG, Troponin and high sensitivity CRP (hsCRP) (also known in SA Pathology as ICRP) and echocardiogram.

Week 1 (day 7) - ECG, Troponin and hsCRP blood tests
Week 2 (day 14) - ECG, Troponin and hsCRP blood tests
Week 3 (day 21) - Troponin and hsCRP blood tests
Week 4 (day 28) - ECG, Troponin and hsCRP blood tests
Week 12 - ECG, Troponin and hsCRP blood tests
Annual: - ECG, Troponin and hsCRP blood tests, echocardiogram

NB: the Viatris cardiac guidelines recommend a hsCRP for all cardiac pathology screenings, they have removed the requirement for annual ECG. SA Health has maintained the annual ECG requirement at this time.
It is preferable that all ECG's, CRP, and Troponin assays are completed by SA Pathology. This will enable the implementation of cardiac decision support through a proposed statewide network.

8.4.1 Myocarditis

- Myocarditis is most common in the first month of clozapine treatment and is associated with fever, flu-like illness, gastrointestinal and cardiorespiratory symptoms.
- Participants and their carers should be encouraged to report flu-like symptoms, GI upsets, dizziness or chest pain to their treating team.
- Body temperature should be monitored daily (at the same time) to assess for fever. A temperature above 38 degrees centigrade may indicate the onset of myocarditis or of febrile neutropenia, requiring urgent medical intervention.
- To support daily monitoring during the first 28 days, thermometers will be supplied to participants commencing clozapine. Participants should be trained in the use of thermometers and should understand the urgency of seeking medical intervention in the event of a febrile reading.
- If at any time participants report a flu-like illness or a fever of 38 degrees centigrade or greater then clozapine may continue but an urgent Troponin and hsCRP and CBE measurement is required in accordance with CPMS guidelines.

8.4.2 Troponin

- If Troponin is more than two times the upper level of normal (ULN) (using the values 30ng/L as one times ULN and 60ng/L as two times ULN) and hsCRP is elevated, then an urgent echocardiogram and cardiology review is required to assess for myocarditis and the clozapine should be withheld. Participants should be transported to the nearest emergency department.
- If Troponin is more than two times the upper level of normal (60ng/L) and hsCRP is normal, then an urgent cardiology review is required to exclude an acute coronary syndrome/ myocardial infarction and consideration should be given to withholding the clozapine. Participants should be transported to the nearest emergency department.
- If Troponin is one-two times the upper level of normal (30-60ng/L) then clozapine treatment can continue but a cardiology consult should be obtained and daily assessment of Troponin, hsCRP and symptoms are indicated to assess for progressive elevation. This may involve transfer to a local emergency department. See **Appendix 5** Clozapine Cardiac Guidelines

8.4.3 Abnormal Echocardiogram & Echocardiography

Abnormal ECGs or echocardiography should be discussed with a cardiologist. Any evidence of acute myocardial infarction, severe heart failure or significant arrhythmia should be referred for urgent medical review. When this occurs as an outpatient, urgent transport to an Emergency Department is required. Clozapine has the potential to increase QT interval and increase the risk of arrhythmia. A finding of abnormal QT interval on ECG should be discussed with a cardiologist. QTc is prolonged if > 440ms in men or > 460ms in women. QTc> 500 is associated with increased risk of life-threatening arrhythmias (torsades de pointes). QTc is abnormally short if < 350ms.

8.5 Annual Blood Pathology Review

At yearly intervals following transition to four weekly monitoring as indicated on the SA Health MR77D Clozapine patient four weekly protocol form (or electronic equivalent), the following blood testing will occur in addition to the CBE:

- Clozapine level
- Fasting blood glucose level
- Fasting full lipid studies
- Electrolytes / Liver function test
- High Sensitivity C - reactive protein (hsCRP)
- Troponin I or T

All results will be documented on the SA Health MR75D clozapine investigation review and prescription record form (or electronic equivalent) where this is in use. Abnormal clozapine levels or cardiac blood test results must be managed by Medical Officers according to guidelines. Abnormal glucose, lipids and electrolyte /liver function tests should be reviewed and managed by Medical Officers. Where appropriate this may involve liaison with GP shared care or may involve the use of emergency medical services.

8.6 Six Monthly Pathology Review

This will be conducted as noted on the SA Health MR77D Clozapine patient four weekly protocol form. The review will consist of the usual physical health assessment and complete pathology testing as indicated on the annual review minus the cardiac screening which occurs annually. All results will be documented on the SA Health MR75D clozapine investigation review and prescription record form (or electronic equivalent) where this is in use. Abnormal clozapine levels must be managed by Medical Officers according to guidelines. Abnormal glucose, lipids, and electrolyte / liver function tests should be reviewed and managed by Medical Officers. Where appropriate, this may involve liaison with GP shared care or may involve the use of emergency medical services.

8.7 The Physical Health Assessment

All reviews are to be conducted face to face within 48 hours of the CBE blood test and include:

1. Physical health assessment:
    - Weight
    - Waist measurement;
    - Body Mass Index (BMI);
    - Blood pressure;
    - Temperature;
    - Manual Pulse;
    - Number of cigarettes smoked per day; and
    - Recording of any other relevant clinical information as indicated by review of the self-report questionnaire (**Appendix 6**) including surplus tablets from the last cycle of care.
2. Clinical response to the medication;
3. Review for constipation; see **Appendix 2** Psychotropic Induced Constipation flow chart and Choice and Medications Clozapine and constipation fact sheet.
4. Review for sialorrhea (hypersalivation)

5. Review for signs of toxicity (including seizure activity that may be related to clozapine serum levels);
6. Chest pain, palpitations
7. An assessment for signs and symptoms of infection;
8. Review of the CBE result by a medical officer;
9. Finger prick random blood glucose level (three monthly) to monitor for type two diabetes mellitus and hyperglycaemia;
10. Assessment of changes in medications: Drugs that inhibit or enhance clozapine metabolism may affect serum clozapine levels and either decrease efficacy or increase risk of clozapine toxicity. Changes in medications can exacerbate known side effects e.g. sedation, agranulocytosis, and constipation; and
11. Participants are encouraged to actively participate in the clozapine review by completing the self-report participant questionnaire and discussing clozapine adherence, response and side effects. This assessment will also cover changes in concurrent medications, smoking habit, caffeine consumption, and illicit drug use.

All observations will be recorded by the person completing the assessment on the clinically indicated form (or electronic equivalent):

- SA Health MR74D Clozapine commencement form or the
- SA Health MR78D Clozapine recommencement form or the
- SA Health MR77D Clozapine patient four weekly protocol form

Clozapine reviews and physical observations are to be recorded electronically into the CBIS, CCCME and Sunrise physical health and clozapine-specific screens where available.

8.7.1 Constipation

A potential severe gastrointestinal adverse effect of clozapine treatment is clozapine induced gastrointestinal hypomotility (CIGH), commonly referred to as 'slow gut' which may result in severe constipation, ileus, bowel obstruction, bowel ischaemia, gastrointestinal necrosis, toxic megacolon and death.

CIGH is significantly more common than blood dyscrasias and has a reported higher mortality rate.

During all stages of clozapine assessment for commencement, re commencement and maintenance thorough and complete history of bowel hygiene and habits needs to be documented.

A physical review of the participant should be completed prior to clozapine commencement to rule out pre-existing constipation and or impacted bowels.

Ongoing review utilising the participant questionnaire **Appendix 6** with particular emphasis on the bowel hygiene questions is to be completed at every assessment. Intervention to ensure adequate bowel evacuation is to be considered and highly recommended, utilisation of the antipsychotic constipation guideline **Appendix 2** will assist.

8.7.2 Sialorrhea (hypersalivation)

Sialorrhea is a common side effect of clozapine treatment. The active metabolite norclozapine is a muscarinic M1 agonist which is believed to be responsible for the drooling or hypersalivation.

Clozapine participants often refer to hypersalivation as their most annoying side effect causing embarrassment in public and potential aspiration causing pneumonia during sleep. These issues have led participants to cease clozapine. Conservative treatments are advocated, the use of pillow protectors and chewing gum to encourage swallowing during the day.

Pharmacological interventions in the past have included the use of atropine eye drops. Following the 2014 Coroners investigation recommendations, **SA Health do not recommend atropine for use to treat clozapine induced hypersalivation.** Atropine eye drops are not approved by the TGA for use sublingually to treat hypersalivation and are only listed on the SA Health Medicines Formulary for use in eye

examinations and procedures. Refer to **Appendix 7** Off label Use of Atropine Eye Drops for Clozapine-Induced Hypersalivation.

Alternative treatment options, Hyoscine Hydrobromide 300 microgram tablets, recommended dose 300microgram tablet sucked or chewed, up to three times a day, listed in the SA Health formulary for clozapine patients with hypersalivation, are available with support from SA Health where possible for subsidised SA Health hospital pharmacy prescriptions.

8.7.3 Abnormal Physical Findings

Abnormal physical findings should be referred for medical review and this process should be documented in the participant's record/care plan. In some cases, the care process will involve liaison with the participant's GP or medical specialists. Cardiometabolic syndrome and related physical health issues can be managed using the Positive Cardiometabolic Algorithm **Appendix 8**: or the Adolescent version **Appendix 9**

Clozapine treatment is associated with an increased risk of pneumonia. Due to clozapine's effect on the immune system pneumonia may not present with an elevated WCC and there may be an absence of classical clinical signs and symptoms. Due to elevated clozapine levels during infection consumers treated with clozapine may be sedated and confused and therefore present late for treatment with worse prognosis. Respiratory infection should be considered in consumers with high white cell counts. Where respiratory infection is suspected then an appropriate physical exam must be performed. When this exam is abnormal (i.e. abnormal findings on auscultation, reduced oxygen saturation, increased confusion) there should be a low threshold for urgent chest X-ray examination to identify possible pneumonia. Urgent antibiotic treatment may prevent further deterioration and risk of mortality. Please note there is a potential for interactions between clozapine treatment and antibiotics. For more information, refer to 'Clozapine levels during infection' section 8.2.1.

Note: These guidelines cover the basic requirement for physical health observations for clozapine management. More thorough general physical and oral health review including annual preventative health screening with a GP and dentist should be arranged and or encouraged for all clozapine participants.

For participants in Shared Care with General Practice or private psychiatrist refer to section 10.

8.8 Frequency and Monitoring Plan

When commencing clozapine for the first time or when recommencing after a break of more than 28 days, weekly for eighteen weeks from commencement, the participant will receive a CBE and physical health assessment within 48 hours by a qualified health practitioner. This will be accompanied by a clozapine review performed by a Medical Officer. Medical reviews during this period may only be completed by a Consultant Psychiatrist or Medical Officer under the direct supervision of a Psychiatrist. In remote Regional LHN areas this can be achieved using Tele-health if face to face appointments are not possible. This is mandatory and in the event of Did Not Attend (DNA) or appointment cancellation, then an appointment will need to be re-allocated for medical review within 48 hours of the CBE. The Medical Officer will only prescribe medication once they have reviewed a satisfactory WCC and NC and performed a medical review. Each prescription for clozapine in the initial eighteen weeks for participants undergoing weekly monitoring must not exceed seven days' supply unless dispensation has been approved by CPMS.

After 18 weeks of continuous weekly monitoring, and if clinically stable, the participant will progress to four weekly monitoring within a community mental health clozapine clinic or in shared care with general practice. The participant will receive a full review that will be considered as the first annual review at transition to four weekly monitoring. There after annual reviews will be conducted at the completion of 12 four weekly review cycles. During these cycles, participants are reviewed by a Medical Officer or a nurse every 28 days within 48 hours of the CBE at a community clozapine clinic or at a GP clinic or by local medical or nursing staff in bedded services. This is mandatory and cannot be cancelled. If the participant cancels, he/she will need to be re-allocated an appointment for clinical review within 48 hours of the CBE.

8.9 Medical / Psychiatric Review

Participants seen within nurse-led clinics or general practice shared care (see section 9 and 10) must have a psychiatric review a minimum of every six months or earlier as clinically indicated. This is facilitated using Tele-health in rural areas if face to face appointments are not possible.

If there are significant concerns during the nurse-led clinic or GP shared care review assessment, a senior Medical Officer is to be contacted to assess the participant. This may occur on the day of the review if urgent or the participant can be scheduled for an early psychiatric review appointment. When the risk is considered to be high, transfer to an emergency department for review should occur.

Metropolitan mental health service participants whose mental state and clozapine management is considered unstable must continue to be seen in public medical clinics.

Regional LHN mental health service participants whose mental state and clozapine management is considered unstable must have a regular psychiatric review as clinically indicated. This is facilitated using Tele-health in rural areas if face to face appointments are not possible.

All prescriptions must be compliant with PBS and CPMS Protocol guidelines and are to be written following Medical Officer review of satisfactory blood results and given to the participant or forwarded to pharmacy following the satisfactory completion of the physical health assessment. It is desirable that the prescription details will be recorded on the SA Health MR75D clozapine investigation review and prescription record (or electronic equivalent) where this is in use, by the Medical Officer writing the prescription for bedded and community services.

NOTE: Medical Officers, General Practitioners and Consultant Psychiatrists directly involved in clozapine management are required to be registered with the relevant CPMS Clozapine Centre.

9 Nurse-led Clinic Model

Nurse-led clinics are to be supported by a designated Consultant Psychiatrist as the clinic sponsor. In Regional LHN this is the Clinical Lead Psychiatrist.

Stable participants requiring four weekly monitoring are seen by nursing staff in the SA Health Nurse-led clinics or in partnership with a GP.

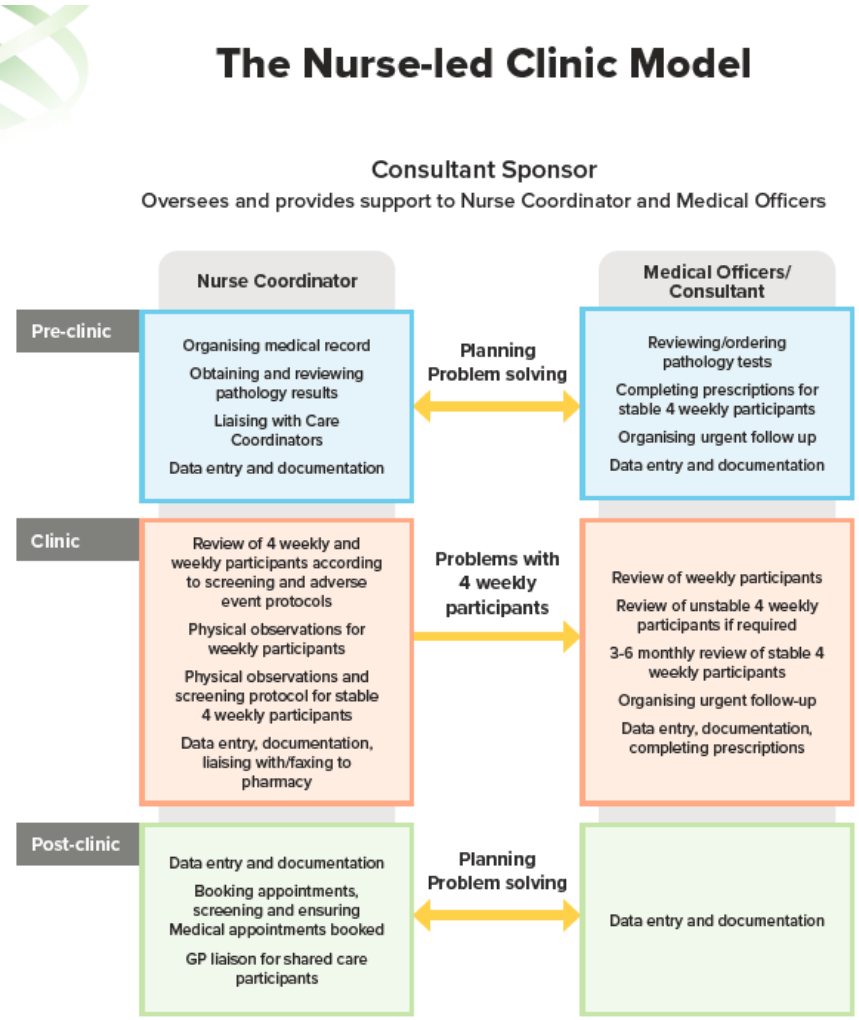
A Medical Officer is to be allocated to review the blood test and write the clozapine prescription within 48 hours of the blood test.

Nurses are to encourage participants to complete a self-report 'Clozapine questionnaire' (see Appendix 6) to assist in the assessment of side effects, compliance, mental state and changes in other medication, tobacco or substance use.

If the nurse has significant concerns, a Medical Officer is to be contacted to discuss the review and if required assess the participant. Otherwise Medical Officers review participants as determined by clinical need or a minimum of six monthly.

If the nurse feels that the community clozapine clinic is unable to meet the requirements of the TGA endorsed CPMS protocol or the SA Health Clinical Guidelines, this should be raised through local management structures and with the consultant sponsor and further to the SA Health Psychotropic Drugs Committee (PDC) via the Clozapine Strategic Management Group (CSMG) if local processes are not able to rectify the situation.

The complete set of nurse-led clinic tools for use including the adverse event protocols can be found on the SA Health Clozapine web page at www.sahealth.sa.gov.au/clozapine



10 Shared Care

10.1 General Practice Shared Care

The SA Health Clozapine Pathways (see **Appendix 10**) are to be followed when managing the care of clozapine participants between SA Heath clozapine clinics and General Practitioners (GPs).

Participants who are considered stable and who are on a maintenance dose of clozapine can be moved into shared care with GPs guided by GP shared care pathways for Green, Amber and Red results **Appendix 11a, 11b, 11c**.

Participants in shared care must be registered to a SA Health clozapine centre and be registered with the SA Health MHS until they are eligible for transfer to a private centre.

GPs registered with CPMS can prescribe maintenance doses of clozapine under the supervision of a Consultant Psychiatrist. Dosage changes may only occur under the guidance of a psychiatrist.

It is recommended that a minimum of two GPs are registered to each practice to cover each other, minimising the risk of interruptions to treatment.

Clozapine participants will attend the GP practice every 28 days for a face to face clozapine review including mental state assessment, physical health assessment (refer to section 8.7 for physical health monitoring requirements), assessment and management of side effects, monitoring of metabolic changes and prescription management. While GPs have their own data record systems it is best practice to use a system of liaison with the Clozapine Coordinator to facilitate review and support. The system of information exchange should be mutually agreed and may include the use of an electronic GP Shared Care form available for selected GP practice software systems at www.sahealth.sa.gov.au/clozapine

SA Health Clozapine Coordinators are to ensure that they review the blood results of participants in shared care.

SA Health Clozapine Coordinators or Pharmacists are to enter the blood results into the eCPMS data base or where other systems are in place, ensure the blood results have been entered in a timely manner (e.g. Regional LHN SA Health Clozapine Coordinators ensure that dispensing pharmacists have entered the blood results and dispensing data into the eCPMS database).

SA Health Clozapine Coordinators are to enter the GP clozapine review into the CBIS or CCCME GP clozapine review screen. SA Health Clozapine Coordinators are to communicate regularly, (minimum of three monthly), with GPs providing shared care. At this time the Clozapine Coordinators are to collect the physical health review information from GPs if it hasn't already been sent to the MHS. The physical health data collected from GPs is to be uploaded into the CBIS service Physical Health Assessment GP Receipt screen. Clozapine Coordinators are to advise the GP of any six monthly or annual testing requirements to ensure the protocols are met. Clozapine Coordinators are to encourage GPs to set up protocol reminders in their data base.

Participants under shared care are to have a psychiatric assessment by a private or public mental health psychiatrist a minimum of every six months or more frequently as clinically required. GPs are to be encouraged to provide a summary of efficacy, side effects and metabolic data when referring participants for assessment.

Participants who return an amber reading can still be maintained in shared care with in-reach and support to the GP from the SA Health Clozapine Coordinator and treating psychiatrist and monitored according to protocol.

The care of participants in shared care who return a red result are to be returned to the public MHS for urgent follow up with a Consultant Psychiatrist and haematologist.

The care of participants in shared care with a significant clinical or functional instability, partial/non-adherence or significant clozapine side effects are to be returned to the public MHS for review and follow up.

10.2 Private Psychiatrist Shared Care

Private psychiatrists participating in shared care with SA Health must be registered with CPMS and the clozapine centre that the participant they care for is registered to.

A private psychiatrist may be registered to multiple centres.

Participants under shared care with a private psychiatrist may also simultaneously be involved in a shared care arrangement with general practice.

The private psychiatrist is responsible for following all requirements of this SA Health Clozapine Management Clinical Guideline. This includes the minimum six monthly psychiatric reviews, clozapine prescription and dose management, and if the participant is not in a GP shared care arrangement, the completing of all physical health assessment criteria as per section 8.7.

A mutually agreeable means of communication of information is to be maintained with the SA Health Clozapine Coordinator, private psychiatrist and GP if applicable.

10.3 Community Mental Health Clozapine Shared Care Data Codes

Within CBIS/CCCME there are team codes available for the recording of clozapine services. For participants in shared care who have no other involvement with the community teams other that the clozapine clinic service, the clozapine team code can be entered in both the primary team and the service grid. By doing this the participant is identified as a clozapine only mental health consumer.

The management of clozapine clinic caseloads is a local health network matter and will not be discussed in this guideline.

11 Prescriptions and Pharmacy

All prescriptions must be written in accordance with PBS and Section 100 requirements and the CPMS Protocol guidelines following the Medical Officer review of satisfactory blood results and given to the participant or forwarded to pharmacy after the satisfactory completion of the physical health assessment.

Prescriptions are to be written on an authority or hospital prescription pad or paper and must contain the following (see Community Clozapine Prescription Guide **Appendix 12**):

- Participant name and address;
- Medicare number;
- PBS box ticked;
- CPN (Clozaril Patient Number) of the participant;
- Hospital provider number of the Consultant Psychiatrist (initiation only prescriptions);
- Must use the brand name “Clozaril” (only private psychiatrists may use Clopine or Clozitor);
- Clozaril tablet strength in mg (a separate script is required for each strength);
- Exact number of tablets;
- Clozaril dose regimen (e.g. 300mg nocte oral);
- Streamlined code for quantities less than 200 tablets/strength or authority approval number for quantities more than 200 tablets/strength;
- White cell count (WCC) and neutrophil count (NC) and the date that the blood test was taken; and
- No brand substitution box must be ticked for all community prescriptions.

A prescription must not be issued if a clinical assessment has not been undertaken. Completed prescription(s) for maintenance treatment can be given to the participant, carer, or support person to take to the community pharmacy.

There are two streamlined codes, one for initiation, being the first 18 weeks of treatment, and one for maintenance therapy, considered to be after the first 18 weeks of treatment. The initiation streamlined code should only be used until the person has completed the first 18 weeks of weekly treatment. If a person on maintenance therapy requires recommencement for periods of less than 28 days interruption, then the maintenance streamlined code is applicable.

The quantity prescribed/dispensed must not exceed three to four days treatment for twice weekly monitored participants, seven days treatment for weekly monitored participants or 28 days treatment for four weekly monitored participants, unless dispensation has been applied for and approved by the CPMS. **NB**. For participants in the community who are on twice weekly monitoring following an amber result, a prescription for the required seven or 28 days may be prescribed and dispensed, as this will reduce additional dispensing costs for the person. However only three to four days of medication should be provided to the person until they receive a green result, at which time the balance can be supplied. The dispensing pharmacy must be notified of the amber result, requirements for the initial reduced quantity of medication to be supplied, and then further notified about subsequent blood tests and medication quantity to be supplied until a green result is received, at which time regular supply can resume.

When a participant is being discharged from a bedded service, if the service is unable to provide enough clozapine medication up until the next scheduled appointment, the participant is to be provided with a prescription for the balance of the 28 day supply. This is to avoid the participant needing to have an unnecessary blood test.

It is desirable that the prescription details are recorded on the SA Health MR75D clozapine investigation review and prescription record (or electronic equivalent) where this is in use, by the Medical Officer writing the prescription for bedded and community services.

During the initiation phase of treatment (i.e. the first 18 weeks), a SA Health hospital pharmacy is required to supply clozapine either directly to the participant or via the participant’s chosen designated community pharmacy, as per the public sector clozapine commencement partnership. This needs to be negotiated via team consultation and specified in the care plan.

To ensure a smooth transition and timely clozapine supply the following information is required to be communicated to both the dispensing hospital pharmacy and the relevant community clozapine clinic:

- Community mental health team responsible for ongoing care
- Community Clozapine Coordinator name
- Community Care Coordinator, if applicable

- Community Consultant Psychiatrist
- Public hospital site commencing clozapine
- Public hospital pharmacy contact, including fax number
- Estimated discharge date
- Intended SA public hospital dispensing pharmacy responsible for the balance of the 18 week initiation supply including contact details and fax number.
- Note it is recommended that the SA public hospital dispensing pharmacy be located as near as practical to the participant's residential address. In most cases for rural LHN participants this will mean a change of hospital from that in which clozapine was initiated.
- Address of clozapine delivery destination (must not be a PO Box)
- Negotiated preferred community pharmacy details (if applicable)
- GP details if a Regional LHN commencement

Communication is to be maintained between the SA Health hospital pharmacy and the Clozapine Coordinator throughout the initiation phase to minimise any possibilities of supply interruption.

12 Transfer of Care

Clear communication of the participant details, CPMS registration, monitoring results and documentation surrounding clozapine treatment progress and any history of adverse events, side effects or risk factors in treatment including compliance is essential to ensure the safe management of clozapine during the transition of care. The transition process is potentially a high risk period for breaks in treatment or other adverse events occurring due to poor communication.
Every transfer between treating sites requires the completed SA Health MR76D *Clozapine transfer of care form* (or electronic equivalent) to be provided to the subsequent treating team as early as possible (must be prior to the first community clozapine assessment appointment for transfer from bedded services) to allow seamless transition of the participant's care. This includes transfer between community sites, transfer from the community to bedded services, transfer between bedded services and transfer from bedded services back into the community.

The transferring team are responsible for ensuring that monitoring requirements can be met during the transition of care through discussion and planning with the participant and receiving team.

If the participant has been commenced on clozapine for the first time then the referring team needs to provide the required information to the hospital pharmacy that will allow for the provision of dispensing services and courier the medicine to the identified community pharmacy as the collection point.

Clozapine Coordinators are to be notified as soon as discharge planning commences from bedded services. Timely information exchange and direct liaison to set up appointments either with the clozapine clinic or GP service within 48 hours of the complete blood examination (CBE) should be reflected in the mental health care plan and electronic clinical review documentation.

The discharge team in collaboration with the receiving team must organise a CBE to occur at the appropriate interval post discharge as per the CPMS protocol (e.g. within a week of the last CBE if weekly monitoring or within four weeks of the last CBE if on maintenance monitoring) and provide the participant with a pathology form and instructions. CPMS may be contacted to provide dispensation to extend the time to the next follow up CBE/assessment if there is a delay in community clozapine clinic appointments (up to two days for weekly participants, up to two weeks for four weekly participants). Alternatively, an early blood test can be performed on discharge to ensure monitoring requirements are met until the next CBE/assessment.

Participants still in the first 28 days of the initiation phase require a thermometer on discharge so they can self-monitor their temperature daily to screen for possible myocarditis or febrile neutropenia. They are to be given instructions on how to monitor temperature and how to respond to an elevated result.

Participant instructions:
- Measure oral temperature under your tongue at the same time every day;
- Do not measure your temperature immediately after hot drinks food or a cigarette;
- If your temperature is above 38 degrees centigrade repeat it after 15 minutes;
- If your temperature remains above 38 degrees centigrade then seek medical review either by contacting your Clozapine Coordinator, care coordinator or visiting your GP or local hospital emergency department; and
- If your fever is persistent you will need blood tests to rule out low white cells or inflammation of the heart (myocarditis), you may require urgent treatment for these conditions.

On discharge from an inpatient service, participants are to be supplied with enough clozapine to last up to their next clozapine review. As long as the participant's last blood test was in the 'green range', CPMS can be contacted for an extra two days dispensation to ensure supply is maintained in the event of a delayed appointment.

Transfer of care paperwork for the receiving clozapine centre and GP, if applicable, should be sent directly to the receiving team and GP. Although sending the information with the participant is person centred the risk of the information not getting to the receiving team is high, so should be avoided. The transfer paperwork typically consists of the following information:

- Original form of the SA Health MR 76D Clozapine Transfer of Care form (or electronic equivalent); a copy of the relevant form is to be made and placed in the medical record.
- Original form of the current SA Health monitoring protocol form (MR74D Clozapine commencement form, MR78D Clozapine recommencement form, MR77D Clozapine patient four weekly protocol form); a copy of the relevant form is to be made and placed in the medical record.
- Original form of the SA Health MR75D Clozapine investigation review and prescription record form (where used and no electronic equivalent is available); a copy of the relevant form is to be made and placed in the medical record.
- A copy of the current medication record (or electronic equivalent);
- A copy of recent blood results, ECGs and echocardiograms; and
- A discharge summary if transferred from a bedded service.

If a participant arrives unexpectedly from out of region or interstate the new treating team should urgently establish the following:

- The contact details of the person's usual prescriber/ Clozapine Coordinator;
- If there been an interruption to treatment;
- How many tablets/ days of clozapine supply does the participant have access to;
- The contact details of their usual dispensing pharmacy;
- When are the next blood results due; and
- Are they taking Clozaril®, Clopine® or Clozitor®?

If a participant is taking Clopine® or Clozitor®, contact should be made with the ClopineCentral™ Team on 1800 656 403 or the Juno Connected™ Team on 1800 271 186 to establish current treatment, blood test monitoring results, and plans for ongoing monitoring and dispensing. If you require further information or support, contact your pharmacy department. If the participant requires long term treatment in the South Australian public health system, consideration should be given to switching to Clozaril and monitoring via the eCPMS system.

While Clozaril® is the formulary-preferred brand of clozapine, SA Health maintains a supply of Clopine® and Clozitor® to public hospitals allowing continuity of monitoring via ClopineCentral™ and Juno Connected™ for patients maintained on Clopine and Clozitor respectively.

NOTE: CPMS and ClopineCentral™ have a memorandum of understanding whereby they exchange the blood test results history and transfer to the current monitoring system, it is expected that Juno Connected™ will also have this provision.

Within South Australia a request should be made to the previous treating team for an SA Health MR76D clozapine transfer of care form. Interstate prescribers should be asked for equivalent information, a copy of the MR76D clozapine transfer of care form can be sent to the interstate team for completion.

12.1 Transfer to a Private Clozapine Centre

Consideration can be given to transferring care to a private clozapine centre if the following has been achieved and a transfer plan has been developed via clinical review involving the participant and their family/ carers, the treating and receiving psychiatrists and the GP service:

- 12 months of maintenance therapy in a public clinic or GP Shared Care with no exacerbations.
- Regular attendance of blood tests and appointments.
- Stable blood test results including therapeutic clozapine levels with no known complications.
- A private psychiatrist has been reviewing the participant's care six monthly and is willing to take over responsibility under their own clozapine centre with a partnership of the GP and nominated pharmacy taking full responsibility for the eCPMS data entry and management.

- A full handover and transfer of care would formalise the closure of the episode with the MHS; and
- Assuring immediate re-entry to the MHS would be facilitated should there be:
    - An exacerbation /relapse or if
    - There are concerns with compliance,
    - Abnormal results or
    - Should any part of the arrangement be unsustainable.

13 Bedded Services Including Non-Mental Health Unit Admissions

All SA Health bedded services need to have a plan for clozapine management supported by their pharmacy department, medical staff and managers. A designated nurse(s) Clozapine Coordinator assists with oversight and liaison with community based Clozapine Coordinators, medical staff, pharmacies, care coordinators and other relevant stakeholders.

13.1 Bedded Services

Ward nursing staff are responsible for the completion or coordination of the following tasks upon admission:

- Request SA Health MR76D Clozapine transfer of care form with referral.
- Select appropriate SA Health forms or admission pack.
- Complete baseline observations and record on appropriate form.
- Utilise the clozapine questionnaire to cover all assessment domains and record in electronic data system checking compliance, efficacy and side-effects.
- Obtain patient's own clozapine supply if possible and contact the relevant pharmacist / pharmacy department for review.
- Check frequency of monitoring and when next blood test due (if this information is not freely available call CPMS on 1800 501 768 for people taking Clozaril or call ClopineCentral™ on 1800 656 403 for people taking Clopine or Juno Connected™ on 1800 271 186 for people taking Clozitor).
- Manage changes to smoking in conjunction with medical staff, including arranging for a clozapine level to provide an assessment of compliance and to exclude high levels associated with infection or inflammation and to identify the need for preventative dose adjustment prior to smoking cessation (see in Section 8.3.1 - Tobacco use in bedded services).
- Notify the hospital pharmacy, community Clozapine Coordinator, GP/psychiatrist of admission.
- Review clozapine alerts and the care plan.
- Ensure blood test and physical health review due dates are added to the local Journey Board system or equivalent.
- Ensure timely liaison with the hospital pharmacy, community Clozapine Coordinators regarding discharge planning, continuity of clozapine monitoring, discharge medications and transfer of care; and the quantity of clozapine provided at discharge must not exceed three to four days treatment for twice weekly monitored participants, seven days treatment for weekly monitored participants or 28 days treatment for four weekly monitored participants, unless dispensation has been applied for and approved by the CPMS. Smaller quantities may be supplied if there is a risk associated with the participant having large quantities, but continuity of supply must be organised in the community.
- If a participant is being discharged from a bedded service and the service is unable to provide enough clozapine medication up until the next scheduled appointment, the participant is to be provided with a prescription for the balance of the 28 day supply. This is to avoid the participant needing to have an unnecessary blood test.

13.2 Psychiatry Consultation Liaison

- Run the OACIS/Sunrise Clozapine report each morning to identify all new local admissions of participants who are treated with clozapine.
- Notify the hospital pharmacy and the appropriate community clozapine centre of the admission.
- Ensure that the inpatient treating team has sufficient understanding of the risks of prescribing clozapine and their responsibilities under PBS, CPMS, and SA Health guidelines and provide adequate support for the safe management of clozapine treatment.
- Assist with safe transfer of care including the completion of required documentation such as MR forms and electronic databases (CBIS, CCCME, Sunrise), timely liaison with the hospital pharmacy, community Clozapine Coordinators regarding discharge planning, continuity of clozapine monitoring and discharge medications, and
- The quantity of clozapine provided at discharge must not exceed three to four days treatment for twice weekly monitored participants, seven days treatment for weekly monitored participants or 28 days

treatment for four weekly monitored participants, unless dispensation has been applied for and approved by the CPMS. Smaller quantities may be supplied if there is a risk associated with the participant having large quantities of medication, but continuity of supply must be organised in the community.

14 COVID-19

For information related to clozapine and COVID-19 refer to the latest interim clozapine COVID-19 guideline and fact sheet available at www.sahealth.sa.gov.au/clozapine

15 Evaluation

Annual audits which monitor the key performance indicators related to compliance with TGA endorsed protocol requirements are mandatory. Each LHN is responsible for administering the audit in June/July, managing these results and providing a quality improvement action plan to the CSMG who will report to the SA Health Psychotropic Drugs Committee (PDC).

A supplementary audit may be required where audit results <80%, this audit will be conducted in Feb/March with subsequent results and action plans reported to the CSMG who will report to the PDC.

Audit of the medical records of participants who have ceased smoking for evidence that serum clozapine concentrations were tested as per procedure, and toxic levels were not reached is encouraged.

Adverse events such as red blood results are reported according to Safety Learning System (SLS) and CPMS notification requirements which are monitored and reviewed by each LHN.
Amber blood results will be managed and reported as per the CPMS increased monitoring protocol and are not required to be reported on the SA Health SLS system.

If a participant dies whilst on clozapine, an SLS notification is required, as well as notifications regarding any breaches in the clozapine protocol.

16 Safety, Quality and Risk Management

The information in this guideline aligns with the Australian Commission on Safety and Quality in Health Care – National Safety and Quality Service Standards: Standard 1 - Governance for Safety and Quality in Health Care and Standard 4 - Medication Safety

Standard 1 Clinical Governance	Standard 2 Partnering with Consumers	I Standard 3 Preventing & Controlling Healthcare - Associated Infection	I Standard 4 Medication Safety	Standard 5 Comprehensive Care	Standard 6 Communicating for Safety	Standard 7 Blood Management	Standard 8 Recognising and Responding to Acute Deterioration	Standards for Mental Health Services
√			√					

17 Appendices

Appendix 1a Clozapine Participant Information
Appendix 1b Clozapine Information for Carers and Support Persons
Appendix 2 Psychotropic Induced Constipation Guideline
Appendix 3 Clozapine Toxicity and Therapeutic Drug Monitoring
Appendix 4 Participant Temperature Monitoring Chart
Appendix 5 Clozapine Cardiac Guidelines
Appendix 6 Clozapine Self-report Questionnaire
Appendix 7 Off Label Use of Atropine Eye Drops for Clozapine Induced Hypersalivation
Appendix 8 Positive Cardiometabolic Algorithm
Appendix 9 Adolescent Positive Cardiometabolic Algorithm
Appendix 10 Clozapine Pathways Community Mental Health
Appendix 11a Clozapine GP Shared Care Pathway – Green
Appendix 11b Clozapine GP Shared Care Pathway – Amber
Appendix 11c Clozapine GP Shared Care Pathway – Red
Appendix 12 Clozapine Prescription Example

18 Associated Policies / Guidelines / Clinical Guidelines / Resources

Clozaril® Patient Monitoring System™ Protocol Version 5 September 2019

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20 Document Ownership and History

Developed by: Office of the Chief Psychiatrist
Contact: Clozapine Strategic Management Group health.ocpsafetyquality@sa.gov.au
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Does this clinical guideline amend or update and existing clinical guideline? **Y**
If so, which version? **Version 1**
Does this clinical guideline replace another clinical guideline with a different title? **N**

Approval Date	Version	Who approved New/Revised Version	Reason for Change
12/07/2022	V2	Domain Custodian, Clinical Governance, Safety and Quality	Reviewed – updated documents and evidence based information
05/09/2017	V1	SA Health Policy Committee	Original approved Policy No: CG260 Objective No: 2017/09582 | A462116

The Big Issue – Side Effects

It is important to discuss side effects at each visit with your doctor and/or Clozapine Coordinator nurse so that they can be addressed straight away. Some of the side effects may decrease over time and others can be managed. If you experience any changes in side effects or your physical health perhaps make a note of these changes by writing them down. That way if they worry you, you can tell your doctor or nurse.

Some common side effects include:

- Tiredness, drowsiness
- Dizziness or light headedness when standing up
- Fast heart rate
- Increase in saliva or dribbling (mostly at night)
- Constipation
- Weight gain

RARE but very important side effects
If these occur seek urgent medical care.

- Fever, sore throat, mouth ulcers or “flu-like” symptoms can be an effect of blood conditions (agranulocytosis or neutropenia)
- Seizures (fits) if blood levels go too high
- Problems controlling or passing urine
- Confusion, muscle stiffness, unsteadiness and collapse
- Severe constipation or diarrhoea if left untreated can lead to bowel blockage
- Chest pain, racing heart beat or shortness of breath

Ask your Clozapine Coordinator about the wallet size **Clozapine Care card**. In emergency situations this can be shown to any hospital staff that may not know you or understand clozapine.

QUESTIONS ABOUT CLOZAPINE?

Ask your doctor, nurse or pharmacist.

This is not intended to replace the Consumer Medicine Information (CMI) for clozapine. Please speak to your pharmacist to get a copy of the CMI and any further information that you require.

Extra fact sheets on clozapine and managing side effects are available through your Clozapine Coordinator and SA Health

sahealth.sa.gov.au/clozapine

Interpreting and Translating Centre
1800 280 203

Emergency contact after hours
13 14 65

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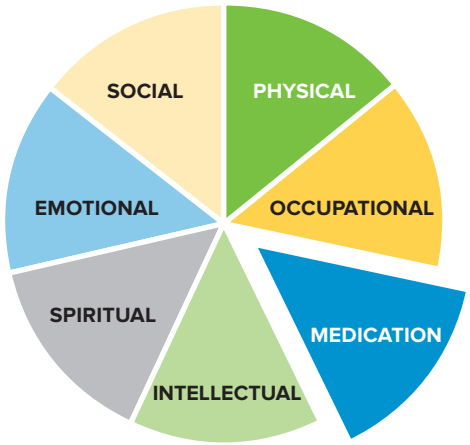
Clozapine Information



Medication can play a significant role in your recovery and wellbeing

Government of South Australia
SA Health

What do I need to know about taking clozapine?

Clozapine (brand names Clozaril® or Clopine®) is a medication that can help treat symptoms of schizophrenia when other medications haven't worked.

Why do I need blood tests?

Blood tests are necessary because in rare cases clozapine has been known to lower the number of white blood cells which are important in fighting infection. They are also done to check your physical health.

When starting clozapine for the first time blood testing is done weekly for the first 18 weeks. You will also need to **check and record your temperature every day for the first 28 days** on the temperature monitoring sheet.	
Every **28** days	A Complete Blood Examination (CBE) is collected in a purple top container. Usually on a Monday or Tuesday **Within 48 hours of the blood test** Attend a regular appointment with your doctor or nurse who will check: • The blood test result • Your wellbeing and ask about any side effects • Blood pressure • Temperature and pulse • Weight and waist measurement • Arrangements for the next prescription • You have a blood form
At least every **6** months	• **Clozapine level** blood test is done 12 hours after the last dose. Medication can then be taken after the blood test. • **Diabetes and cholesterol** blood tests must be done after you have fasted for at least 8 hours from food and fluid (water is OK). • **Liver and kidney blood tests** • **Psychiatric specialist review**
Every **12** months	**Heart check-up** In rare cases clozapine can affect the heart. These tests can help to pick up problems early: • Electrocardiogram (ECG) • Echocardiogram (ECHO)

Decisions regarding your clozapine dose will be made with you and your psychiatrist to individualise a medication regimen to suit your lifestyle. Please ask questions and if required take a support person with you to the appointment.

IMPORTANT INFORMATION

The factors below can affect your clozapine and need to be discussed with your doctor or nurse as the dose may need to be changed.

Starting, stopping or cutting down cigarette and cannabis smoking can significantly change clozapine levels and side effects. You will need to work with your doctor or nurse to safely make the changes you want.

Changing caffeine consumption (coffee, tea, cola, energy and diet drinks) can alter clozapine levels.

Alcohol and Illicit Drugs can make you feel excessively tired and have poor concentration and are not good for your physical health.

Other prescribed and over the counter medicines need to be discussed with your doctor and pharmacist.

If you miss a dose don't panic, make sure you take your next dose as prescribed. Don't ever take a double dose. If you are worried, contact your doctor or nurse for advice. After hours call 13 14 65.

If you have forgotten to take clozapine for more than two days, do not start taking it again before you contact your doctor.

If you feel unwell check your temperature and seek medical care.

Take clozapine as prescribed including when travelling, as changing the dose or times may result in increased side effects or the medication being less effective.

Clozapine should be stored in a safe, dry place, at room temperature, away from direct sunlight and out of the reach of children.

Taking care of your health

It is important to maintain your health by:

- Eating a healthy varied diet
- Drinking plenty of water
- Have good routines for wellbeing and self-care
- Cleaning your teeth morning and night
- Regularly exercising and
- Reducing or quitting smoking. Plan this with your doctor.

Your support team

Your opinion counts, as do those of people that support and care for you. It is important for you:

- to understand why you are being prescribed clozapine and to be actively involved in your recovery.
- to have a **regular GP** who can work with you on your health care plan.
- if needed be referred to a dietician, psychologist, physiotherapist or podiatrist.

Shared Care Your GP can be registered to prescribe clozapine and work with your psychiatrist, pharmacist and Clozapine Coordinator.

"It's easier and more convenient for me to see my local doctor."

"It gives me the opportunity to choose who provides my health care."

"It promotes holistic/complete care."

At least **every six months your psychiatrist** will review the medication and treatment plan with you and let your GP know if anything needs to change.

Your **Clozapine Coordinator nurse and /or GP** will work closely with you to:

- Keep up with a treatment routine and a plan for taking the clozapine at a regular time each day
- Coordinate blood tests and appointments
- Check your physical and mental health
- Provide prescriptions
- Arrange extra tablets if you are planning a holiday or travelling overseas

The Big Issue – Side Effects

It is important to encourage the person to discuss side effects at each visit with their doctor and/or Clozapine Coordinator nurse so that side effects can be addressed straight away. Some of the side effects may decrease over time and others can be managed. If the person experiences any changes in side effects or their physical health that worries you or the person, **tell the doctor or nurse.**

Some common side effects include:

- Tiredness, drowsiness
- Dizziness or light headedness when standing up
- Fast heart rate
- Increase in saliva or dribbling (mostly at night)
- Constipation
- Weight gain

RARE but serious side effects

If these occur the person must seek urgent medical care.

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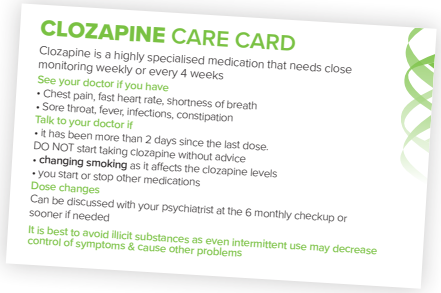
- Seizures (fits) if blood levels go too high
- Problems controlling or passing urine
- Confusion, muscle stiffness, unsteadiness and collapse
- Severe constipation or diarrhoea if left untreated can lead to bowel blockage
- Chest pain, racing heart beat or shortness of breath

A wallet size **Clozapine Care card** is available and can be carried by the person taking clozapine. In emergency situations it can be shown to any hospital staff that may not know the person or be familiar with clozapine.



IF AT ANY TIME YOU HAVE QUESTIONS ABOUT CLOZAPINE?

Ask the doctor, nurse or pharmacist who sees the person you support.

As a carer, it is important to look after your own health and wellbeing too.

If you are seeking support contact the Carer Gateway 1800 422 737

www.carergateway.gov.au

This is not intended to replace the Consumer Medicine Information (CMI) for clozapine. Please speak to the pharmacist who sees the person you support to get a copy of the CMI and any further information that you require.

Extra fact sheets on clozapine and managing side effects are available through the Clozapine Coordinator and SA Health

sahealth.sa.gov.au/clozapine

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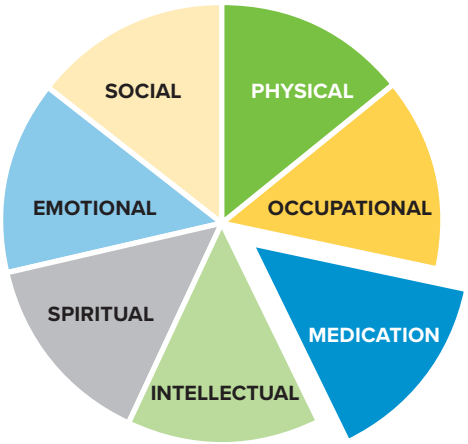
SA Health

Clozapine Information for Carers and Support Persons



Medication can play a significant role in recovery and wellbeing

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What do I need to know about taking clozapine?

Clozapine is a specialized antipsychotic medication that can help treat symptoms of schizophrenia when other medications haven't worked.

It is important for the person that you are supporting who is taking clozapine to have a regular routine for attending to blood tests and appointments and to **book them in advance.** These health check-ups are required to monitor the response to treatment and pickup and manage any abnormal results.

Why are blood tests required?

Blood tests are necessary because in rare cases clozapine has been known to lower the number of white blood cells which are important in fighting infection. They are also done to check physical health.

The Clozapine process

When starting clozapine for the first time blood testing and medical appointments are attended weekly for the first 18 weeks. The person taking clozapine will also need to **check and record their temperature every day for the first 28 days** on the temperature monitoring sheet.	
Every **28** days	A Complete Blood Examination (CBE) is collected in a purple top container. Usually on a Monday or Tuesday
	Within 48 hours of the blood test
	The person **must** attend a regular appointment with the doctor or nurse who will check: • The blood test result • The person's wellbeing and ask about any side effects • Blood pressure • Temperature and pulse • Weight and waist measurement • Arrangements for the next prescription • Give the person a blood form
At least every **6** months	• **Clozapine level** blood test is done 12 hours after the last dose. • Medication can then be taken after the blood test. • **Diabetes and cholesterol** blood tests must be done after the person has fasted for at least 8 hours from food and fluid (water is OK). • **Liver and kidney blood tests** • **Psychiatric specialist review**
Every **12** months	**Heart check-up** In rare cases clozapine can affect the heart. Tests can help to pick up problems early: • Electrocardiograph (ECG) • Echocardiogram (ECHO)

Decisions regarding the clozapine dose will be made with the person and their psychiatrist to create a plan to suit their lifestyle. We encourage the person to ask questions and if required take a support person with them to the appointment particularly in the early weeks of clozapine treatment.

Clozapine must be taken as prescribed including when travelling, as changing the dose or times may result in increased side effects or the medication being less effective.

Clozapine should be stored in a safe, dry place, at room temperature, away from direct sunlight and out of the reach of children.

IMPORTANT INFORMATION

The factors below can affect clozapine and need to be discussed with the doctor or nurse as the dose may need to be changed.

Starting, stopping or cutting down cigarette and cannabis smoking can significantly change clozapine levels and side effects. The person will need to work with the doctor or nurse to safely make the changes that they want.

Caffeine (coffee, tea, cola, energy and diet drinks) can increase clozapine levels.

Alcohol and Illicit Drugs can increase the sedative side effects making the person feel excessively tired and have poor concentration. They are also not good for physical health.

Other prescribed and over the counter medicines need to be discussed with the doctor and pharmacist as they may interact with clozapine.

If the person misses a dose don't panic, make sure they take the next dose as prescribed. The person should never take a double dose. If you or the person is worried, contact the doctor or nurse for advice. After hours call 13 14 65.

If the person has forgotten to take Clozapine for more than two days, they must not start taking it again before the doctor has been contacted.

Don't hesitate to Contact the clozapine coordinator or doctor if:

- The person has a buildup of spare tablets or the person is not taking doses as prescribed.
- There is a noticeable change in the persons mental state, behaviour or physical health
- You have any concerns regarding the persons health and wellbeing

Taking care of health

It is important to maintain health by:

- Eating a healthy varied diet
- Drinking plenty of water
- Have good routines for wellbeing and self-care
- Cleaning teeth morning and night (this also helps keep white cell counts up)
- Regularly exercising and
- Reducing or quitting smoking. Plan this with the doctor.

You as a carer or support person

Your opinion counts, as does that of the person on clozapine. It is important for you:

- To understand why the person is being prescribed clozapine and to be actively involved in their recovery.
- To encourage the person to establish a regular routine of blood test and appointments.
- To encourage the person to have a **regular GP** who can work with them on their health care plan.

Shared Care A GP can be registered to prescribe clozapine and work with the psychiatrist, pharmacist and Clozapine Coordinator.

The GP can also If needed refer to a dietician, psychologist, physiotherapist or podiatrist.

We encourage people who are stable on clozapine to engage with their GP with the plan to establish a shared care arrangement. This provides a consistent and more holistic approach to care

At least every **six months the psychiatrist** will review the medication and treatment plan with the person and where possible carers/support people and let the GP know if anything needs to change.

The **Clozapine Coordinator nurse and /or GP** will work closely with the person and you to:

- Keep up with a treatment routine and a plan for taking the clozapine at a regular time each day
- Coordinate blood tests and appointments
- Check physical and mental health
- Provide prescriptions
- Arrange extra tablets if the person is planning a holiday or travelling overseas.

Psychotropic Induced Constipation Guideline
(Antipsychotic / Clozapine / Depot)

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RED FLAGS
- Moderate to severe abdominal pain

OR
- Any abdominal pain/ discomfort lasting over an hour

AND
One or more of the following:
- abdominal distension
- vomiting
- diarrhoea (esp bloody)
- absent or high pitched bowel sounds
- haemodynamic instability
- signs of sepsis
- leukocytosis

- NIL BY MOUTH
- **EITHER** URGENT MEDICAL REVIEW

  OR
- TRANSFER TO NEAREST TERTIARY CENTRE/ EMERGENCY DEPARTMENT

Prophylaxis: Is the person able to:
- Adequately hydrated 1.5L minimum fluid intake
- Do 20 min light aerobic exercise / day
- Be adherent with bulk forming / stool softening agents (Metamucil, Fybogel, Docusate)
- Make dietary / lifestyle changes
- Use a stool chart

		Low risk pathway less than 3-4 risk factors[1]	High Risk Pathway no or inadequate adherence to conservative measures
BNO 2-3 days	1st line	1 sachet Movicol daily	Docusate + senna 2 tabs daily
BNO 3 days	2nd line	Increase Movicol/Macrogel to 1 sachet twice daily	Increase Docusate + senna to 2 tabs twice daily
BNO 4 days	3rd line	Docusate + senna 2 tabs nocte	Add Movicol/Macrogel 1 sachet twice daily
BNO 5 days	4th line[3]	Lactulose 15ml daily; Enema	Lactulose 15ml daily; Enema

Persisting Constipation

[2]Resolving Constipation

[1]RISK FACTORS

Profile
- age > 65

Lifestyle
- Low fibre
- Lack of exercise/immobility
- Dehydration

Medical
- CNS: Parkinsons, Stroke, MS
- ERS: Hypothyroid, Diabetes
- GIT: IBS, Diverticular disease
- RHEUM: Scleroderma,
- SURG: Previous abdominal surgery

Iatrogenic
- opioids
- anticholinergics
- calcium channel blockers
- antipsychotics
- Supplements, Iron, Calcium

[2]Once resolution of constipation occurs sequentially step back through lines of intervention
[3]Long term use of lactulose has malabsorption risks

Review and reassess as clinically required to achieve successful resolution of constipation: If opening bowels regularly every 3 days or greater despite 3rd and 4th line interventions or regular use of G&O enemas or laxatives like Magnesia San Pellegrino, expedient referral to a specialist gastroenterologist or general physician is required for guidance.

Information for Health Care Professionals

Clozapine Toxicity and Therapeutic Drug Monitoring

Clozapine (Clozaril®) is an atypical antipsychotic medication indicated for treatment resistant schizophrenia (TRS). Although often a highly effective treatment its use is restricted due to the potential for severe and potentially life threatening adverse effects. This information sheet provides an overview of signs and symptoms of clozapine toxicity and outlines when to consider therapeutic drug monitoring. There should be psychiatric involvement in any patient admitted to hospital and on clozapine, with referral to the Consultation Liaison Psychiatry within 24 hours. Clozapine orders need to be reviewed and co-signed by Liaison Psychiatry.

Recognising the signs of clozapine toxicity

Clozapine toxicity can occur when clozapine levels are high and when there are sudden and large increases in clozapine levels.

It may be recognised by the following signs:	Toxicity can cause:
> Excessive sedation	> Seizures
> Confusion	> QTc prolongation
> Delirium	> Cardiac arrhythmia
> Hypersalivation	> Respiratory depression
> Myoclonus	> Sudden Cardiac Death

What causes clozapine toxicity?

Clozapine toxicity can be secondary to a number of factors:

- Intentional or unintentional overdose
- Concurrent prescription of interacting medications
- Changes in tobacco smoking
- Changes in doses
- Concurrent infection or inflammation

Therapeutic Drug Monitoring (TDM)

Clozapine levels are routinely recommended at least 6 monthly during maintenance therapy.

In addition, they should be measured on admission to hospital and when non-compliance is suspected.

The recommended therapeutic range is 350-600 µg/L, however some patients require higher levels; up to a maximum of 1000 µg/L. Levels should be measured 12-hours after the last dose, as the range is based on a 12-hour trough.

It can take up to a week for clozapine levels to be reported. If there is a suspicion of clozapine toxicity, clozapine can be held whilst the Psychiatric Liaison service is consulted.

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Drug interactions

Clozapine is primarily cleared hepatically by CYP1A2, and to a lesser extent by CYP3A4 and CYP2D6.

There are a number of clinically significant drug interactions that prescribers should be aware of (see Box 1).

Addition of strong CYP1A2 inhibitors should be avoided and if required, may necessitate pre-emptive dose reduction of clozapine.

Concurrent infection and inflammation

Evidence suggests that infection and inflammation can inhibit cytochrome P450 enzymes resulting in a significantly elevated serum clozapine concentration.

If an infection is present (e.g. pneumonia, UTIs, abscess), assess for signs of clozapine toxicity and if indicated perform clozapine TDM. Psychiatry involvement in dose changes is crucial.

Note: due to potential delay in reporting of clozapine levels pre-emptive dose reduction may be required based on presentation.

Changes in tobacco smoking

Smoking tobacco is a strong inducer of CYP1A2 and of clozapine metabolism.

Changes in tobacco smoking, i.e. due to intentional cessation or during hospitalisation can have a large effect on clozapine concentrations. This effect can appear within the 3-5 days and tends to be more apparent when smoking is reduced to less than 10 cigarettes per day.

When there is a significant change in smoking, patient awareness and close monitoring for signs of toxicity is important, with clozapine levels taken at day 1, 7, then weekly until stable. Pre-emptive reduction isn't routine.

Contact Psychiatry Liaison for advice in smoking cessation.

Dose changes

Dose changes can result in disproportionate changes in clozapine levels. Clozapine TDM is recommended 5-7 days after a dose change is made.

Re-titrating

The dose may need to be re-titrated to previous levels post resolution (i.e. post infection or after ceasing interacting medication).

Dose changes should be no more than 100mg every 5-7 days. Clozapine can only be re-initiated or re-titrated by Consultation Liaison Psychiatry.

It must not be recommenced at the previous prescribed dose if there has been a break of more than 48 hours.

Box 1: Drug interactions

This list is not exhaustive, and pharmacist or psychiatry advice on management is required.

Potential to Increase Clozapine Levels (enzyme inhibitors)	> Selective serotonin reuptake inhibitor (SSRIs) e.g. fluvoxamine (very large effect), fluoxetine, paroxetine, sertraline (large doses) > Caffeine (3-4 cups/ day, especially in non- smokers) > Some antibiotics such as quinolones i.e. ciprofloxacin (large effect), macrolides (erythromycin) > Oral contraceptives > Ritonavir
Potential to Depress Respiration	> Benzodiazepines (especially large parenteral doses or at start of therapy)
Potential for Anticholinergic Side Effects (e.g. constipation, urinary retention, delirium)	> Anticholinergic tricyclic antidepressants (TCAs) e.g. amitriptyline, dothiepin > Anticholinergic antipsychotics e.g. chlorpromazine, olanzapine > EPSE medication e.g. benztropine
Potential for Hypotension (both postural and non-postural)	> Anti-hypertensives > TCAs

For more information

SA Pharmacy Medicines Information
Telephone: 8222 5546
www.sahealth.sa.gov.au

Public-I1-A1

Clozapine Temperature Monitoring

Important information on how to manage a high temperature or fever during the first 28 days of treatment with clozapine.

Record extra temperature or your notes here:

Start date:						
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
End date:						

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FIS: 200793

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End date:						

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FIS: 200793

Why should I check my temperature?

- A raised temperature is common in the first 28 days of clozapine treatment, and usually means that it is starting to work.
- In rare cases a high temperature or feeling feverish can be signs of a severe blood infection in the body or a heart condition.
- It is important to check your temperature every day to safeguard your wellbeing and help detect problems early on.
- If you don't have your own thermometer, you will be given one like this to keep:

What do I need to do?

- Check your temperature under your tongue or your armpit at approximately the **same time every day, for the first 28 days**
- If placing under your tounge make sure you have not had a hot or cold drink for at least 20 minutes beforehand
- Record your temperature in the table overleaf
- Clean thermometer after each use and store safely
- Note: You can also check your temperature any other time you feel unwell

High temperature instructions

- If your temperature is **38 degrees or more**
  - Check your temperature again after 15 minutes
  - Telephone your GP or Clozapine Coordinator who will advise you what to do
  - If it is a weekend or public holiday go to a hospital Emergency Department. Tell the staff that you are on clozapine, and that your temperature is raised. Some extra blood tests and heart checks may be needed and/or changes in treatment.

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Clozapine Cardiac Guidelines

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Baseline

Prior to Clozapine therapy	Troponin T or I	High sensitivity test preferred	Not all pre-existing cardiac abnormalities preclude clozapine treatment. Consult a cardiologist if abnormalities are detected
	hs-CRP	High sensitivity c-reactive protein test	
	Echocardiography	Highly desirable, Mandatory for community starts	
	ECG		

During Clozapine Therapy

First 28 days	At all times	Educate participants and carers to report flu-like symptoms, GI upsets, dizziness or chest pain	
	Once a day	Measure body temperature at the same time each day	
During Initiation (First 18 weeks)	Days 7, 14, 21 and 28, week 12 then annual review	Troponin T or I, hs-CRP, ECG (except day 21) Pulse, Blood Pressure, Respiratory Rate	
If at any time	Temperature >38°C or flu-like symptoms	Immediate hs-CRP, troponin and CBE.	Continue clozapine at current dose. Do not escalate until features normalise
	Troponin >60ng/L and hs-CRP elevated	**Urgent transfer to Emergency department. Urgent cardiology consultation – query myocarditis.** **Urgent echocardiography.**	**Withhold Clozapine**
	Troponin >60ng/L and normal hs-CRP	Urgent transfer to Emergency Department. Urgent cardiology consultation – query acute coronary syndrome (ACS).	Continue clozapine at current dose. Do not escalate until features normalise
	Troponin 30-60ng/L and elevated hs-CRP	Daily assess troponin, hs-CRP and symptoms until features normalise. If no progressive elevation, consider differential diagnosis and cardiology consultation.	Continue clozapine at current dose. Do not escalate until features normalise
Annually	Troponin T or I	High sensitivity test preferred	
	hs-CRP	High sensitivity c-reactive protein test	
	Echocardiography		
	ECG		

NB: with the change to a more sensitive troponin T assay range (13ng/L for females and 17ng/L for males) consideration as to whether cases of myocarditis would be missed has been given. SA Pathology still consider that a troponin T >30ng/L is appropriate for an action point for a value 1-2 times the upper level of normal and troponin T >60ng/L is appropriate for an action point for a value 2 times the upper level of normal.

Adapted with consent from Clozaril Protocol CPMS- V5 30 Sept 2019

Clozapine Questionnaire

Name:_____ Date:_____/_____/_____

This questionnaire is to be used by anyone taking clozapine or health professionals involved in supporting clozapine care and management. We hope that the last week/month has been a positive one for you.
Please answer honestly, circle yes even if the answer is only sometimes.

	These questions relate to possible side effects or health problems		Please circle	
1	Have your thoughts been as clear as usual this week/month?		Yes	No
	Have you or your carer noticed hallucinations (voices, smells, seeing images)?		Yes	No
	Have you been able to manage your home and/or finances this week/month?		Yes	No
	Have you had any thoughts that have worried you this week/month?		Yes	No
	Have you attended	an emergency department?	Yes	No
		been admitted to hospital?	Yes	No
		had extra visits to your GP or outpatients?	Yes	No

2	Have you increased or decreased how much tobacco you smoke?			Yes	No	Amt/day :
	Do you Vape?	Yes	No	Does your Vape Juice contain nicotine?	Yes	No	Amt/day :

3	What is your dose of clozapine?		mg	What time of day do you take the clozapine?		AM		PM
	Have you missed clozapine doses?						Yes	No
	Have you changed your dose of clozapine?	Yes	No	If yes from	mg	to		mg
	How many tablets / blister packs do you have left at home?						Blister Packs / Tablets	

4	Have you started, stopped or changed any medications including pain relief, medication prescribed by a doctor or anything over the counter from the pharmacy?	Yes	No
	Have you missed, decreased or increased your dose of any other prescribed medications?	Yes	No

5	Do you use any of the following substances?					
	coffee, cola or high energy drinks	Yes	No	alcohol	Yes	No
	other drugs such as meth / cocaine	Yes	No	cannabis	Yes	No
	If Yes has your usage of the substances changed?				Yes	No

6	Have you been physically unwell?	fever or increased sweating?	Yes	No
		cough or cold?	Yes	No
		nausea or vomiting	Yes	No

7	Have you felt dizziness when standing up, chest pain or shortness of breath?	Yes	No
8	Have you noticed any muscle stiffness, jumpy or jerky movements or tremors? (circle)	Yes	No
9	Have you felt more drowsy or sleepy than usual?	Yes	No
	Has your sleep pattern changed or your dreams become upsetting?	Yes	No
10	Have you had an increase or decrease in saliva or dribbling?	Yes	No

Constipation is a major side effect and brings a deal of risk to your general health and wellbeing.
Please turn over for specific bowel hygiene questions.

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11	Have your bowel movements changed?							Yes	No
	When was the last time you used your bowels?		Today	Yesterday	2-3 days ago	4-5 days ago	More than 5 days ago		
	How often do you usually go?								
	Using the **Bristol Stool Chart** below please circle the stool type that best describes your usual bowel motion.								
	Consistency			**Type 4**		Sausage or snake like, smooth and soft			
	Type 1		Separate hard lumps, like nuts (hard to pass)	**Type 5**		Soft blobs with clear-cut edges (easy to pass)			
	Type 2		Sausage-shaped, but lumpy	**Type 6**		Fluffy pieces with ragged edges, mushy			
	Type 3		Like a sausage, but with cracks on its surface	**Type 7**		Watery, no solid pieces (entirely liquid)			
	How do you manage constipation? (circle all applicable)								
	Strain and squeeze	drink more water	eat more fiber	exercise	Use stool softeners/ medications				
	If you use stool softeners/ medications what is the name of them?								
	Do you ever have blood in your stools?							Yes	No
	What describes best how your tummy usually feels?								
	soft	bloated	Occasional cramping	painful					
12	Has there been any change in the frequency in which you pass urine?							Yes	No
13	Have you had any sexual side effects that are bothering you?							Yes	No

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Fact sheet

Off-label Use of Atropine Eye Drops for Clozapine-Induced Hypersalivation

SA Health staff are advised against the use of off-label atropine eye drops for the treatment of clozapine-induced hypersalivation.

A 2014 coroner's investigation into the accidental death of a patient was attributed to accidental ingestion of a toxic quantity of atropine eye drops prescribed off-label for sublingual administration. Expert toxicology opinion determined that the concentration of atropine found in the patient was 50-100 times the expected therapeutic dose. In addition, it was noted that:

- the plastic eye drop bottle was very easy to empty with a gentle squeeze
- the dose taken by the deceased was at least 6-8 mL of the solution
- higher systemic exposure is expected from sublingual administration of atropine eye drops compared with oral administration (tablets) due to bypassing of first-pass metabolism and therefore toxicity is expected to be seen at lower sublingual doses than oral ones

TGA and SA Health Response:

The Therapeutic Goods Administration (TGA) circulated a Medicines Safety Update (Vol 9, number 3, August-September 2018) warning to health professionals to exercise extreme caution when considering off-label prescribing of atropine eye drops for hypersalivation.

Atropine eye drops are not approved by the TGA for use sublingually to treat hypersalivation and are only listed on the SA Health Medicines Formulary for use in eye examinations and procedures.

Use of atropine eye drops for hypersalivation in SA Health public hospitals and health services for an individual patient must therefore be approved by the relevant Local Health Network Quality Use of Medicines or Drug and Therapeutics Committee (individual patient use (IPU) request), prior to commencement.

Alternative Treatment Option(s)

Hyoscine hydrobromide tablets are listed on the SA Medicines Formulary for clozapine patients with hypersalivation which is consistent with The Maudsley Prescribing Guidelines in Psychiatry (available via SALUS).

SA Health will subsidise prescriptions written by SA Health prescribers, dispensed in SA Health hospital pharmacy.

Prescribers are to be mindful of:

- dose: 300 microgram sucked or chewed up to three times a day, when required
- possible anticholinergic/ antimuscarinic side effects including constipation
- potential ongoing cost to consumers as this indication is off-label and therefore not reimbursed under PBS
- ensuring an adequate treatment plan is in place
- other alternatives listed in The Maudsley Prescribing Guidelines that may be considered for individual consumers (will require IPU request)

For more information

SA Pharmacy Medicines Information Service
Telephone: 8161 7555
Email: medinfo@sa.gov.au
www.sahealth.sa.gov.au

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Positive Cardiometabolic Health : an early intervention framework for patients on psychotropic medication

Smoking	Lifestyle	Obesity		Blood Pressure	Fasting Blood Glucose	Fasting Blood Lipids	Polycystic ovary syndrome
		Weight	Waist				
Current Smoker	Poor diet **AND/OR** Sedentary lifestyle	BMI (kg/m^2) > 25 **AND/OR** Weight ↑> 5kg	Male≥94cm* Female≥80cm **AND/OR** Waist ↑> 5cm	>140 systolic **AND/OR** >90 diastolic	> 5.6 mmol/L	>6.5 TChol (>5.5 TChol if diabetic) >2.0 Trig	No periods for 3 months^ Acne Hirsutism

Structured nutritional counseling and modify lifestyle

Consider antipsychotic switching; review medications and rationalize any polypharmacy

Brief individual intervention Smoking cessation program **quitnow.info.au**		Consider metformin	Consider anti-hypertensive	5.6-6.9: at risk Consider metformin ***>7.0 DIABETES*** ***endocrine review; monitor HbA1c 3 monthly***	Consider Statin Fibrate for triglycerides	?Normal prolactin Consider metformin ***(adequate contraception if sexually active)***
Target Smoking cessation	**Target** Improve quality of diet Contain energy intake Daily exercise	**Target** BMI 20-25 and WC <94 males* < 80cm females	**Target** < 140/90 mmHg (< 130/80 if diabetic)	**Target** Fasting glucose ≤5.5 mmol/L If diabetic: HbA1c <7%	**Target** TChol ≤5.5 mmol/L LDL ≤ 4 mmol/L Trig ≤1.6 mmol/L	**Target** Regular menstrual cycle

Curtis J, Newall H, Samaras K. HETI 2011

* for south Asians, Chinese, south and central American and Japanese individuals, recommend WC target < 90cm

^ for premenopausal women

History: smoking, exercise, diet, FHx (diabetes, obesity, CVD), gestational diabetes, ethnicity, Polycystic ovary syndrome

Then at least 3 monthly

Examination: weight, BMI, waist circumference, BP

Investigations: Fasting blood glucose and lipids: total cholesterol (TChol); LDL, HDL, triglycerides (Trig);

Vitamin D (twice per year).

Interventions:

Nutritional counseling: reduce take away and junk food, reduce energy intake to prevent weight gain, stop soft drinks and juices, increase fibre intake.

Physical activity: structured education-lifestyle intervention. Advise daily physical activity: eg 30 minutes of walking.

If unsuccessful after 3 months in reaching targets, then consider switching and medication interventions below

Switching: Consider switching to a more weight neutral medication. Review diagnosis and ensure ongoing need for all psychotropic medications.

Don't just SCREEN → INTERVENE

for all patients in the "red zone"

Screen cardiometabolic risk factors using screening tool (eg Waterreus, et al 2009, Curtis et al 2009 SESLHD); examine and investigate 3 monthly on all clients on psychotropic medications.

NB additional considerations for those on mood stabilizers & clozapine not included here and need to be performed (eg medication plasma levels, TFT's UEC's, ECHO, etc)

Always involve general practitioner, and, where appropriate and possible refer to specialist (eg dietitian/ physician/ diabetic clinic/ exercise physiologist).

NB: Some drugs used in metabolic disease treatment are contraindicated in pregnancy (eg some antihypertensives and lipid lowering drugs). If your patient on any metabolic medications is considering pregnancy, please discuss with their GP

Authors: Curtis J, Newall H, Samaras K.

Specific Pharmacological Interventions:

Consider metformin if:

- impaired glucose
- PCOS
- obesity or rapid weight gain

Metformin therapy: start at 500mg x ½ tablet before breakfast and dinner for two weeks then increase to 500mg bd. Dose can be increased to a maximum of 3 grams daily, though as this is off label treatment, no adverse effects should be tolerated. If side-effects of nausea, abdominal cramping, shift to after meal.

Lipid lowering therapy: (use PBS guidelines)

Statin initiation doses for cholesterol lowering:

simvastatin 10 mg nocte	atorvastatin 10mg nocte
pravastatin 10mg nocte	rosuvastatin 10 mg nocte

Fibrate therapy for triglyceride lowering:

gemfibrozil 600 mg bd	fenofibrate 145 mg mane

Anti hypertensive therapy: Multiple agents are available. Liaise with the GP who can monitor.

Vitamin D:

- <50 nmol/L: replenish stores: cholecalciferol 4,000 IU per day for one month;
- maintenance: 1,000 IU daily. Target >80nmol/L.

References: Alberti K, Zimmet P, Shaw J. "The metabolic syndrome - a new worldwide definition". *Lancet.* 2005; 366: 1059-62. Correll, C. U., P. Manu, et al. "Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents". *JAMA.* 2009; 302: 1765-1773. De Hert M, Dekker JM, Wood D, et al. "Cardiovascular disease and diabetes in people with severe mental illness position statement from the European Psychiatric Association (EPA), supported by the European Association for the Study of Diabetes (EASD) and the European Society of Cardiology (ESC)". *European Psychiatry*. 2009; 24: 412-24. Newall H, Myles N, Ward PB, Samaras K, Shiers D, Curtis J. "Efficacy of metformin for prevention of weight gain in psychiatric populations: a review". *Int Clin Psychopharmacol*. 2012; 27: 69-75. Newcomer JW, Hennekens CH. "Severe Mental Illness and Risk of Cardiovascular Disease". *JAMA*. 2007; 298: 1794-6. Waterreus AJ, Laugharne JD. "Screening for the metabolic syndrome in patients receiving antipsychotic treatment: a proposed algorithm". *MJA*. 2009; 190:185-9. Wu, R. R., J. P. Zhao, et al. "Lifestyle intervention and metformin for treatment of antipsychotic-induced weight gain: a randomized controlled trial". *JAMA.* 2008; 299:185-193.

For online access to this fact sheet, please visit http://www.heti.nsw.gov.au/cmalgorithm

Adolescent Version

Positive Cardiometabolic Health: An early intervention framework for adolescents on psychotropic medication

Adapted from Curtis J, Newall H, Samaras K. ©HETI 2011

Lifestyle			Overweight / Obesity		Blood Pressure	Glucose	Blood Lipids	Polycystic ovary syndrome
Smoking	Diet	Activity	Weight, BMI	Waist				
Lifestyle advice to include diet, physical activity and smoking prevention or cessation								
RED ZONE								
Current Smoker	Poor diet	Sedentary lifestyle	BMI ≥ 85th centile* AND/OR Weight ↑ > 5kg over 3 months	Waist:height ratio ≥ 0.5 AND/OR Waist ↑ > 5cm over 3 months	≥ 90th centile^ systolic AND/OR diastolic (use appropriate cuff size for arm circumference)	FPG ≥ 5.6 mmol/L OR RPG ≥ 11.1 mmol/L AND/OR HbA_{1c} ≥ 42 mmol/mol (≥6%)	Total Chol ≥ 5.2 mmol/L LDL ≥ 3.4 mmol/L HDL < 1.03 mmol/L Trig ≥ 1.7 mmol/L	Delayed menarche, No periods for 3 months, Acne, Hirsutism
Intensify and individualise structured nutritional counseling and lifestyle interventions (consider dietitian and/or exercise professional referral)								
Medication review (consider antipsychotic switching; review medications and rationalize any polypharmacy)								
INTERVENTION								
Individualised Smoking cessation program quitnow.gov.au icanquit.com.au	↓ Energy intake Stop soft drinks / juices ↑ Vegetables & fibre eatforhealth.gov.au	↓ Sedentariness ↓ Screen time ↑ Physical activity exerciseismedicine.org.au	Consider metformin BMI ≥ 95th centile* refer to specialist	≥ 95th centile^ Refer to GP or specialist	At high risk of Diabetes FPG : 5.6-6.9 mmol/L HbA_{1c} 42-47 mmol/mol (6.0-6.4%) OGTT; if abnormal, refer to specialist Consider metformin	Diabetes FPG ≥ 7.0 mmol/L RPG ≥ 11.1 mmol/L HbA_{1c} ≥ 48 mmol/mol (≥6.5%) Endocrine referral	Refer to GP or specialist	Check prolactin Consider metformin (ensure contraception if sexually active)
TARGET								
Smoking prevention or cessation	Improve quality of diet	Physical activity (eg > 60 mins per day) Screen-based activities < 2hrs/day	BMI ≤ 85th centile* Waist:height ratio < 0.5	< 90th centile^	Prevent Diabetes FPG ≤ 5.5 mmol/L HbA_{1c} <42 mmol/mol (<6.0%)	HbA_{1c} 42-53 mmol/mol (6.0-7.0%)	Total Chol < 4.4 mmol/L LDL < 2.85 mmol/L HDL > 1.56 mmol/L Trig < 1.02 mmol/L	Regular menstrual cycle

*BMI sex-specific centile chart, either US-CDC or WHO. Ensure that the same chart is used over time to allow for consistent monitoring of growth ^Pediatrics 2004; 114;555

BMI = Body Mass Index | FPG = Fasting Plasma Glucose | RPG = Random Plasma Glucose | Total Chol = Total Cholesterol | LDL = Low Density Lipoprotein | HDL = High Density Lipoprotein | Trig = Trigylcerides

History & examination following initiation or change of psychotropic medication:

History: Seek history of smoking, poor diet (eg high calorie, high fat/ sugar), physical activity and sedentariness (eg screen time), polycystic ovary syndrome. Ask about family history (diabetes, obesity, early CVD), gestational diabetes. Note ethnicity.

Frequency: As below. Consider more frequently if changing medications, rapid weight gain, abnormal lipids, glucose or blood pressure.

	Baseline	Weekly**	3 months	6 months	9 months	12 months
Personal / FHx	✓					✓
Lifestyle Review*	✓	✓	✓	✓	✓	✓
Weight	✓	✓	✓	✓	✓	✓
Height (BMI)	✓			✓		✓
Waist Circumference	✓		✓	✓	✓	✓
Blood Pressure	✓		✓	✓		✓
FPG/RPG/HbA1c	✓		✓	✓		✓
Lipid Profile^	✓		✓	✓		✓
LFTs	✓			✓		✓
Vitamin D	✓			✓		✓

**Smoking, diet & physical activity*
^Total cholesterol LDL, HDL, triglycerides. If fasting samples are impractical, then non-fasting samples are satisfactory for most measurement, except for triglycerides

**
Weight should be assessed 1- 2 weekly in the first 6 - 8 weeks following initiation or change of medication. Adolescents may be at particular risk of rapid early weight gain and this may predict severe weight gain in the longer term

Other baseline investigations are not included here and need to be performed as clinically required (eg TFTs, UECs, FBC, ECHO). Additional monitoring requirements apply for those on mood stabilizers & clozapine (eg medication plasma levels). Prolactin measurement only recommended if symptomatic. Consider ECG/ cardiology review if concern re QT prolongation or cardiovascular risk factors present.

Ensure adequate contraception and sexual health advice. Some medications used to treat metabolic disorder are contraindicated in pregnancy (eg some antihypertensives and lipid lowering drugs). Other issues such as sleep and substance use have not been included in this resource though are important to discuss with all adolescents.

The general practitioner and psychiatrist/mental health clinician will work together to ensure appropriate monitoring and interventions are provided and communicated

After 12 months, continue to monitor regularly, with increased frequency if abnormality of physical health emerges, which should then prompt appropriate action and/or continuing review at least every 3 months

Don't just screen... INTERVENE for all adolescents in the RED ZONE

Interventions:

Promote benefits of healthy lifestyle to parents and carers

Strategies include: metabolic apps, lifestyle workbook, weblinks.

Review of psychotropic medications: Normally psychiatrist supervised and should involve discussion with adolescent and parents/carer. Choose lower metabolic liability medication first-line where possible. Review diagnosis and ensure ongoing need for all psychotropic medications. Consider switching to a more weight neutral medication where possible. Avoid antipsychotic polypharmacy. Avoid off-label use of antipsychotic medications.

If adolescent has not successfully reached their targets after 3 months, then consider specific pharmacological interventions.

Specific Pharmacological Interventions:

Consider metformin trial if:
- impaired fasting glucose
- polycystic ovary syndrome
- obesity or rapid weight gain

Note that **off-label** use requires documented informed consent

Metformin therapy: start at 250mg before dinner for two weeks, then increase to 250mg bd. Dose can be increased by 500 mg per week to a maximum of 2 grams daily. If side-effects of nausea, abdominal cramping, shift to after meal (or the XR preparation)

Lipid lowering therapy: (use PBS guidelines): consider lipid lowering therapy if severe hyper-lipidemia or with other risk factors with appropriate specialist referral

Anti-hypertensive therapy: refer to specialist paediatrician

Vitamin D:
- <50 nmol/L: replenish stores: cholecalciferol 4,000 IU per day for one month;
- maintenance: 1,000 IU daily. Target 80-140 nmol/L.

Download Adolescent version of Positive Cardiometabolic Health algorithm: www.heti.nsw.gov.au/cmalgorithm

Clozapine Pathways

Community Mental Health Services

Government of South Australia
SA Health

As per TGA endorsed clozapine management protocols the participant is to be seen every 7 or 28 days (depending on whether they are on weekly or 4 weekly monitoring) for clinical assessment of signs and symptoms of infection

Participant attends community pathology collection centre for blood test

Blood results returned to CMHS with copy to nominated GP

Within 48 hrs of blood test

Scheduled appointment at CMHS for review of participant's MSE, BP, weight, BMI, waist circumference, pulse, temperature, plus education & assessment of general tolerance, constipation & side effects of clozapine in addition to management of any other issues.

Face to face review by medical officer if on weekly monitoring

A medical officer reviews the blood test & completes a blood count form where required

An authority prescription is to be written by an authorised clozapine prescriber & annotated with: CPN, streamlined code, exact quantity of tablets & blood results (100mg and 25mg tablets need to be written on separate prescriptions, as per PBS requirements) **Any dose changes MUST be authorised by a Consultant Psychiatrist**

The blood count form (if required) & prescription are forwarded to the registered pharmacy by the Clozapine Coordinator via fax, post or the participant

The registered pharmacist dispenses clozapine according to protocol

Blood results and clozapine dosage are entered into eCPMS data base by the Clozapine Coordinator in metro areas &/or by the registered pharmacist in rural areas

All results including BP, weight, BMI, waist circumference, pulse, temperature and metabolic monitoring are entered onto the standard monitoring chart and electronic data system and managed accordingly

Clozapine Pathways

Clozapine GP Shared Care Arrangements

GREEN Results Pathway

Government of South Australia
SA Health

As per TGA endorsed clozapine management protocols the participant is to be seen every 7 or 28 days (depending on whether they are on weekly or 4 weekly monitoring) for clinic assessment of signs and symptoms of infection

Participant attends community pathology collection centre for blood test

↓

Blood results returned to GP with copy to nominated CMHS: **GREEN Result Noted**

↓

Within 48 hrs of Blood Test

Face to face scheduled appointment with GP:

Physical Health Review:
BP, weight, BMI, pulse, temp, waist measurement, constipation assessment, smoking status

Review:
Blood pathology results, MSE, assessment of general tolerance, effects, side effects and adverse events, any other health issues, review of chronic condition management plan. Provide education as required.

Face to face review by medical officer if on weekly monitoring

Script:
An authority prescription is to be written by an authorised clozapine prescriber & annotated with:
CPN, streamlined code, exact quantity of tablets, blood results and date of blood test*.
100mg and 25mg tablets need to be written on separate prescriptions, as per PBS requirements.
*A blood count form may be completed if this is the preferred notification.
Any dose changes MUST be authorised by a Consultant Psychiatrist

Communication:
GP to contact the Clozapine Coordinator as necessary with concerns or feedback.
Clozapine Coordinator requests and GP provides a copy of the metabolic monitoring every 3 months.
Psychiatric review required every 6 months or more often as clinically indicated

↓

Participant either takes the prescription and the blood count form (if required) or they are faxed to the registered pharmacy by the GP practice.

↓

The registered pharmacist dispenses clozapine according to protocol

↓

Blood results and clozapine dosage are entered into eCPMS data base by the Clozapine Coordinator in metro areas and/or by the registered pharmacist in rural areas

All results including BP, weight, BMI, pulse, temperature, waist measurement and metabolic monitoring are entered onto the standard monitoring chart and electronic data system and managed accordingly

Clozapine Pathways

Clozapine GP Shared Care Arrangements

AMBER Results Pathway

Government of South Australia
SA Health

As per TGA endorsed clozapine management protocols the participant is to be seen every 7 or 28 days (depending on whether they are on weekly or 4 weekly monitoring) for clinical assessment of signs and symptoms of infection

Participant attends community pathology collection centre for blood test

Blood results returned to GP with copy to nominated CMHS **AMBER Result Noted**

Treating psychiatrist notified by Clozapine Coordinator (CC)

CC notifies GP of **AMBER** results and discusses Plan

Participant notified of **AMBER** results, associated risk of infection & need for repeat blood test

GP & psychiatrist discuss management plan

Within 48 hrs of Blood Test

Face to face scheduled appointment with GP:

Physical Health Review:
for evidence of infection including focal signs and symptoms, BP, weight, BMI, pulse, temp, waist measurement, constipation assessment, smoking status. Treat infections as required (note antibiotic interactions)

Review:
Blood pathology results, MSE, assessment of general tolerance, effects, side effects and adverse events, any other health issues. Provide education re low white cell count, increased risk of infection and need for twice weekly monitoring.

Script:
An authority prescription is to be written by an authorised clozapine prescriber & annotated with: CPN, stream-lined code, exact quantity of tablets, blood results & date of blood test*.100mg and 25mg tablets need to be written on separate prescriptions, as per PBS requirements. *A blood count form may be completed if this is the preferred notification.

Any dose changes MUST be authorised by a Consultant Psychiatrist

Participant either takes the prescription & the blood count form (if required) or they are faxed to the registered pharmacy by the GP practice.

The registered pharmacist dispenses no more than 3-4 days of medication at a time until bloods return to **GREEN** range according to protocol

The blood results and clozapine dosage are entered into the eCPMS data base by the Clozapine Coordinator in metro &/or registered pharmacist in rural areas

Increase blood monitoring to twice weekly coordinated by CC in collaboration with GP and psychiatrist

When blood result returns to **GREEN** range, return to regular monitoring according to **GREEN** pathway

Clozapine Pathways

Clozapine GP Shared Care Arrangements

RED Results Pathway

Government of South Australia
SA Health

As per TGA endorsed clozapine management protocols the participant is to be seen every 7 or 28 days (depending on whether they are on weekly or 4 weekly monitoring) for clinical assessment of signs and symptoms of infection

Blood results returned to GP with copy to nominated CMHS **RED** **Result Noted**

Treating psychiatrist notified by Clozapine Coordinator (CC)

CC notifies GP of **RED** results and discusses Plan

Participant notified of **RED** results, advised of increased risk of infection & the need to attend hospital if febrile/unwell. Requested to have repeat blood test within 24hrs and told not to take clozapine

In metro GP returns management to CMHS clinic & treating psychiatrist. Rural GPs continue to manage in conjunction with treating psychiatrist & CC support

CC enters **RED** blood result into eCPMS database

CC & GP notified by automated eCPMS fax

Within 24 Hours – Participant is to have a repeat blood test

If second blood result is **RED,** participant advised of the result & not to take any clozapine. Urgent review appointment is arranged at the CMHS with psychiatrist and CC. In rural / remote areas urgent GP and Telehealth psychiatrist review arranged.

Participant notified of second blood result. Depending on the result return to **AMBER** or **GREEN** pathway

Metro CC / rural GP completes a physical health review including temperature, pulse, BP and signs and symptoms of infection. If evidence of infection present, urgent transfer to ED is required.

MSE of participant by psychiatrist. Participant advised that management will return to the CMHS in conjunction with the GP for rural / remote as increased monitoring is required. Alternative antipsychotic medication is prescribed.
NO CLOZAPINE PRESCRIPTION GIVEN

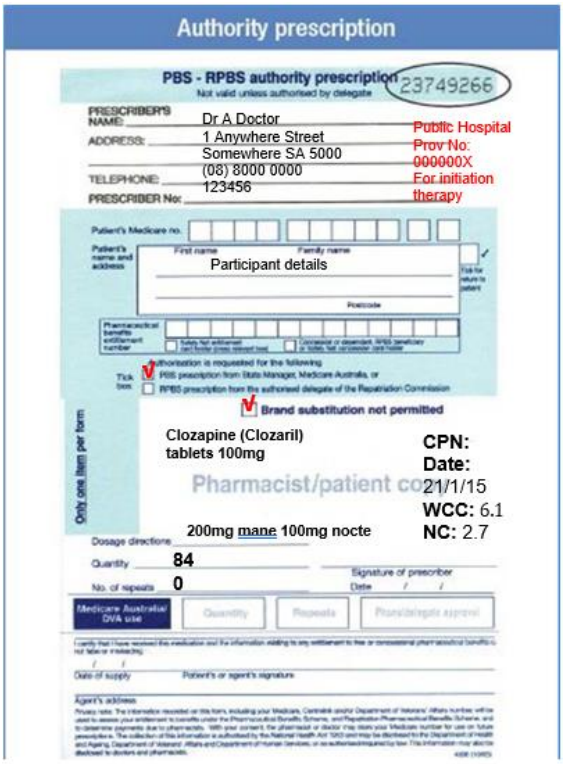
The participant has daily CBE blood testing until results are in the **AMBER** range, then twice weekly until in the **GREEN** range. Once bloods results are back in the **GREEN** range, continue blood monitoring for 4 weeks post-cessation either weekly or 4 weekly depending on monitoring frequency

CC enters all blood result into eCPMS and completes the discontinuation form

Fact Sheet

Community Clozapine Prescription Guide

TABLET CALCULATOR		
28 day supply		
Dose (mgs)	Days	No of tablets
PBS Prescription		
25	28	28
50	28	56
75	28	84
100	28	28
200	28	56
300	28	84
400	28	112
500	28	140
600	28	168
700	28	196
Telephone Authority required		
800	28	224
900	28	252
Limit of prescription		
7 day supply		
Dose (mgs)	Days	No of tablets
PBS Prescription		
25	7	7
50	7	14
75	7	21
100	7	7
200	7	14
300	7	21
400	7	28
500	7	35
600	7	42
700	7	49
800	7	56
900	7	63
Limit of prescription		



PBS and Safety Reminders

- Use an authority pad or paper
- A separate script is required for each strength
- No repeats

Annotate with:

- CPN
- CBE Date & result
- Exact tablet quantity
- √ PBS box and
- √ No brand substitution

- Streamlined Authority Code (SAC):
  5015 initiation
  4998 maintenance
  Or
  Authority Approval No for increased quantities of >200 tabs

For more information

SA Pharmacy Medicines Information

Telephone: 8222 5546
www.sahealth.sa.gov.au

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