Clozaril® Patient Monitoring System™

Protocol

June 2023



Clozaril®
clozapine
SEE BOXED WARNING

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June 2023 CLZ-2021-0002

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VIATRIS

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1 About CPMS

1.1 Introduction

In order to optimise the management of patients on Clozaril® (clozapine), a Clozaril® Patient Monitoring System (CPMS) was developed and implemented from the time of the drug's introduction in Australia. This protocol refers to the blood monitoring requirements for patients treated with Clozaril®. For further product information please refer to the full TGA-approved Clozaril® Prescribing Information.

Clozaril® is an atypical antipsychotic of the dibenzodiazepine class of compounds, indicated for the management of schizophrenia patients who have had inadequate responses to other antipsychotic medications[1]. It is chemically and pharmacologically distinct from standard antipsychotic drugs and has been shown to improve both positive and negative psychotic symptoms while producing minimal extrapyramidal side effects [2,3].

In keeping with Viatris' commitment to responsible health practice and TGA regulations, Clozaril® in Australia can only be accessed through the CPMS. This protocol provides an in-depth overview of this distribution system for Clozaril® in Australia.

1.1.1 Aims

The aims of the CPMS are to:

- Optimise the management of patients with schizophrenia on Clozaril® in Australia.
- Minimise the risk of any patients on Clozaril® developing agranulocytosis or neutropenia by monitoring their white blood cells regularly.
- Ensure that patients previously discontinued from Clozaril® due to neutropenia or agranulocytosis are not re-exposed.
- Provide advice to centres on Clozaril® protocol-related matters.

1.1.2 Development

The CPMS was developed by Novartis to ensure maximum safety standards for patients receiving Clozaril® treatment and to meet TGA regulations for clozapine usage in Australia. The system and protocol were developed in close consultation with a multidisciplinary Clozaril® Advisory Board.

The Clozaril® Advisory Board comprises members from the Royal Australian and New Zealand College of Psychiatrists, a hospital pharmacist and a consultant haematologist.

In February 2018, the CPMS was acquired by and transferred to Mylan Health Pty Ltd (**Mylan**), which was subsequently renamed to Viatris Health Pty Ltd (**Viatris**) in November 2020. Currently, advice on matters relating to the use of Clozaril®, amendments to this protocol and action required in respect to breaches of compliance within this protocol, are provided to Viatris by the Quality Assurance Committee (see Section 1.1.5).

1.1.3 The system – an overview

The role of the CPMS office is to maintain the operation of the CPMS database according to the CPMS protocol. The CPMS protocol is defined as this document and its amendments (see Section 1.1.7).

The CPMS requires that all patients, Medical Officers and health care professionals (including those prescribing, or assessing patients' results and physical health status to assist prescribers ascertaining suitability for ongoing Clozaril® treatment), pharmacies, pharmacists (whether dispensing or involved in distribution direct to patients), centre coordinators and assistants, and treating centres involved with the distribution of Clozaril® to be registered with the CPMS (see Sections 2.2 & 2.3).

Before patients can be deemed suitable to receive Clozaril® treatment, they are required to have their total white blood cell count (WBC) and neutrophil count (NC) assessed. Subsequently, weekly monitoring for 18 weeks is required from the start of treatment, then at least every 28 days while on therapy. After cessation of treatment, further blood monitoring is also required (see Section 6.2). Further blood monitoring is required in other situations as described in Sections 5.1 and 6.2 of this protocol.

All patients' WBC and NC must be sent to the CPMS database electronically, via email or fax.

These results are monitored to determine:

- Missing or unusual haematological data.
- Potentially dangerous haematological trends.
- Unusual or missing dosage information.

1.1.4 Online convenience

eCPMS is the web-based database used to monitor all Clozaril® patients.
The following can be completed or requested online via eCPMS:

- Patient registrations
- Blood result data entry
- Patient reports
- Patient transfers
- Dispensations

The eCPMS website also generates daily alerts that are electronic duplications of the faxes or emails sent to centre personnel. Non-primary centre coordinators can elect to only receive alerts via the web in eCPMS.

The following forms need to be faxed or emailed to the CPMS:

- CPMS centre registration
- Centre coordinator registration
- Medical Officer registration
- Pharmacy and pharmacist registration
- Laboratory registration
- Patient Health Information Collection and Storage Consent
- Patient or multiple patients registration when switching brands
- Dispensation (if greater than pre-approved limits - see Section 8)
- Discontinuation of therapy

1.1.4.1 Patient and Healthcare Professional Privacy and Consent

Patient consent to the collection and storage of their health information in the CPMS database must be submitted to CPMS with patient registration requests and retained in the patient's notes. Registering to participate in this program constitutes agreement for all information submitted about patients and registered health care professionals to be stored on the CPMS database and shared as required in accordance with this program.

This protocol and its contents can be obtained and printed from the website:
https://www.ecpms.com.au
For any website issues, refer to the eCPMS website manual (via the Help menu) or contact the CPMS on 1800 501 768.

1.1.5 Quality and safety

In order to maximise patient safety, a Quality Assurance Committee (QAC) oversees issues of non-compliance with the CPMS protocol, in addition to general safety matters relating to the use of Clozaril® and the running of the CPMS. The QAC consists of independent psychiatrists, a haematologist, medical advisors and Viatris representatives.

The QAC meets regularly to review safety issues, although ad hoc meetings can be conducted to resolve urgent safety issues. The role of the committee is to provide recommendations to Viatris and CPMS users, particularly on action to be taken in the event of breaches of compliance with the CPMS protocol.

1.1.6 Breaches of compliance

Breaches of compliance with the CPMS protocol may be brought to the attention of the QAC by Viatris or the CPMS office.

Such matters can include isolated but serious breaches such as the prescribing of Clozaril® to unregistered patients or apparently minor, but still potentially dangerous, protocol breaches such as consistent overdue counts, signing of blank Blood Count forms or the completion of Blood Count forms by non-registered personnel, or unauthorised access of patient or healthcare professional personal information.

Viatris may contact centres directly to ascertain the reasons for breaches.

While every effort will be made to maintain the treatment of patients who are deriving benefit from Clozaril®, in the interests of the safety of these patients, the continued registration of centre personnel and/or centres who are unwilling or unable to comply with this protocol cannot be supported.

Action taken in the event of breaches of compliance may include the following:

- Warning letter from the QAC.
- Contact with centre personnel by the CPMS office or Viatris management (as recommended by the QAC) in order to determine the reasons for non-compliance.
- Moratorium on the enrolment of new patients.
- De-registration of individual centre personnel.
- De-registration of individual centres.

Failure of a centre to comply with the CPMS Protocol may prevent further Clozaril® supplies from being dispatched to that centre.

1.1.7 Protocol amendments

Viatris may amend this protocol at any time by notice to the CPMS office and each primary centre coordinator who will inform each member of their centre of the protocol update.

There may be situations in which the QAC recommends a departure from the protocol in a specific instance. If accepted by Viatris, the relevant centre(s) and the CPMS office will be notified of this in writing. Such recommendations will then be considered to be part of the protocol for that particular patient or circumstance. All amendments will take effect from the date specified in the notice.

1.1.7.1 Changes to this version of the CPMS Protocol and eCPMS

This version of the CPMS protocol contains updates reflecting the company name change from Mylan to Viatris and the consequent update to the privacy policy (see Section 1.1.8), update to the minimum Product Information (PI) including the boxed warning, the cardiac monitoring recommendations (page 21) and editorial changes.

Approved PI is available at https://medsinfo.com.au/product-information/document/Clozaril_PI.

For more information or assistance please call 1800 501 768.

1.1.8 Privacy

The Viatris group companies in Australia (consisting of Viatris Health Pty Limited and its related bodies corporate) (**Viatris**) are bound by and comply with the Privacy Act 1988 (Cth) and applicable health records laws. Viatris collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program for participating patients on the CPMS. Access to CPMS data is restricted to registered CPMS personnel, Viatris staff or Viatris con tractors (such as the CPMS) and regulatory agencies (such as the TGA) for the sole purpose of monitoring patients on Clozaril® and/or to ensure the proper operation of the CPMS and access or use of CPMS data is strictly prohibited unless the need is central to the purpose and operation of the CPMS.

The Viatris privacy policy explains how Viatris handles personal (including health) information we collect and hold, how individuals can request access to and correction of the personal information we hold about them, how to make a privacy complaint and how Viatris deals with privacy complaints. Anyone can request a copy of our Privacy Policy by contacting our Privacy Officer at Viatris Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

Viatris is committed to patient safety. In accordance with regulatory obligations, it has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris). All information forwarded to the Viatris drug safety department is treated in accordance with local privacy laws and may be captured and processed in countries outside of Australia, and shared with health authorities or other pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris drug safety department may contact the patient's healthcare professional in order to collect further information on the adverse event.

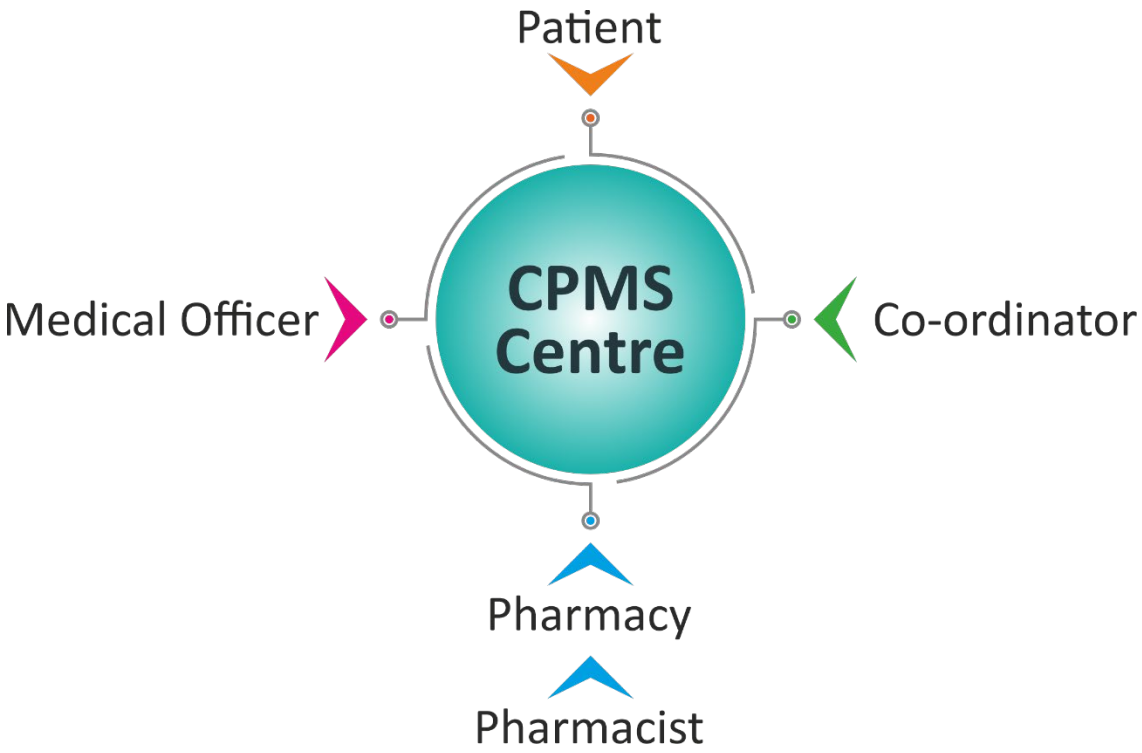
1.1.9 CPMS Structure

A CPMS centre links patients to Medical Officers, pharmacies and pharmacists.

- Each centre has one or many coordinators (centre contacts).
- A patient is linked to only one centre.
- A Medical Officer can be linked to one or many centres.
- Pharmacies can be linked directly to one or many centres or unlinked.
- Pharmacists are linked to one or many pharmacies.

To access a patient's blood sample results,

- A Medical Officer and the patient must be linked to the same centre.
- Pharmacists can access all maintenance patient results nationally or be linked via a pharmacy to a centre to access non-maintenance patient results.
- A Medical Officer must check a recent blood result before prescribing and a pharmacist must double check that blood result before dispensing.



2 Registering a centre

Patients are grouped into centres. A hospital, clinic or single treating clinician can be registered as a centre, there are no size restrictions. A hospital may be one or many centres depending on local needs. A patient can belong to only one centre; healthcare professionals and pharmacies can be linked to many centres.

In order for Clozaril® to be dispensed to a non-maintenance patient, a centre must be linked to a CPMS-registered pharmacy. Any CPMS-registered pharmacy can dispense to any maintenance patient. In Australia, Viatris will only allow distribution of Clozaril® to those pharmacies registered with the CPMS database.

Viatris will provide education to centres, pharmacies and personnel concerning the CPMS protocol.

2.1 Personnel and service requirements

- As a minimum, a centre can be one Medical Officer who also acts as coordinator.
- At least one centre coordinator must be identified for each centre. It is preferable that a centre coordinator be a full-time staff member for larger centres. Any CPMS-registered user (e.g. nurse, Medical Officer or pharmacist) can be registered as a coordinator.
- In order for a CPMS pharmacy to dispense Clozaril® for a non-maintenance patient, it must be linked to the patient's centre.
- Each centre must have access to a haematology laboratory which can process and report on Clozaril® patient samples within 24 hours of the time the samples were taken.

An independent consultant haematologist is available to give advice and assist with the care of patients as required (see Section 4.3).

2.2 Simple registration

1. To register as a centre, simply complete the centre registration form [10.4.1] located either (1) in Appendix of this document or (2) print a form from the website.

2. Complete the centre coordinator registration form [10.4.2] and at least one Medical Officer registration form [10.4.3].

3. If you intend to manage non-maintenance patients, identify a CPMS-registered pharmacy to be linked to your centre, or provide pharmacy and pharmacist registration forms [10.4.4 and 10.4.5, respectively] to register a new CPMS pharmacy.

4. All forms must be signed and forwarded to the CPMS office either by fax or email (see Section 9 - important contacts).

2.3 Registering further personnel or pharmacies to the centre

When new Medical Officers or additional coordinators are registered and linked to a centre, an eCPMS notification will be sent to the existing coordinators. Coordinators can request deregistration of Medical Officers and coordinators linked to their centre in error.

2.3.1 Adding Medical Officers

The Medical Officer registration form [10.4.3] is available in the Appendix (Section 10) and on the eCPMS website. Medical Officers can be linked to multiple centres. When registering initially, please include all centres for which you require registration. If this is not known initially, additional registration forms will need to be completed and submitted to CPMS to link to other centres.

Upon permanent relocation to another centre, registration under the CPMS for the initial centre will lapse and re-registration at the new centre will be necessary. Medical Officers must notify the CPMS and primary centre coordinator if they are no longer active at a centre.

2.3.2 Adding pharmacies and pharmacists

The pharmacy and pharmacist registration forms [10.4.4 and 10.4.5, respectively] are available in the Appendix (section 10) and on the eCPMS website. Pharmacists can be linked to any number of pharmacies, and pharmacies can be linked to many centres.

CPMS-registered pharmacies may dispense medication to any maintenance patient without requiring being linked to the patient's centre; however, in order to dispense for a non-maintenance patient, the pharmacy must be directly linked to the patient's centre.

If the pharmacist works at more than one CPMS-registered pharmacy, in the initial registration all CPMS pharmacies should be recorded. If this is not known initially, additional registration forms will need to be completed and submitted to CPMS to link to other pharmacies.

Pharmacists must notify the CPMS upon resignation/permanent relocation from a pharmacy.

2.4 Personnel responsibilities

2.4.1 The centre coordinator

A centre may have multiple coordinators and coordinators may be registered to multiple centres. At centres with more than one coordinator, a primary coordinator must be elected as the CPMS primary contact. Centre coordinators facilitate the smooth running of the CPMS centre and ensure it complies with the CPMS protocol.

The role of the centre coordinator is to:

- Ensure necessary blood tests are performed, reviewed and acted upon accordingly.
- Ensure the centre communicates all required registrations, patient information and blood results from their centre to the CPMS office.
- Ensure that the centre complies with the CPMS protocol.
- Ensure that any Medical Officer or GP involved in checking patient blood results or physically assessing patients as part of the CPMS process are registered with the CPMS.
- Ensure that any pharmacies and pharmacists involved in checking patient blood results, dispensing or supplying medication to registered non-maintenance patients as part of the CPMS process are registered with the CPMS.
- Distribute all necessary communication with respect to patient monitoring to registered centre staff (e.g. Medical Officers, and pharmacies supplying non-maintenance patients).
- Keep a log of all active personnel and pharmacies supplying non-maintenance patients at your centre(s).
- Maintain and distribute to any registered centre staff a list of all patient names and CPNs registered to your centre(s) to ensure any fax or email alert identifying a patient by their CPN, can be acted on promptly.
- Notify CPMS if any personnel need to be deregistered from your centre.

All CPMS communication from a centre should include notification to the primary centre coordinator.

If a Medical Officer, coordinator, pharmacy supplying non-maintenance patients or a patient relocates, a centre coordinator should communicate this information to the CPMS office. If the primary centre coordinator resigns, the centre must nominate another coordinator to take on the responsibility.

2.4.2 The Medical Officer

Clozaril® may only be initiated or discontinued by a specialist psychiatrist and prescribed by a CPMS-registered Medical Officer or GP for CPMS-registered patients. A CPMS Medical Officer includes psychiatrists, and appropriately qualified hospital medical officers and registrars. A general practitioner may assist a psychiatrist in the care of Clozaril® patients.

The Medical Officer and GP must gain approval from the centre coordinator before registering with CPMS and linking to a centre.

Dosage changes may only occur under the guidance of the treating psychiatrist. Patients should be seen by their psychiatrist for a mental health review at least once every 6 months.

All GPs who are involved in shared care or co-management of Clozaril® patients and who are responsible for checking CPMS blood results must be registered with the CPMS.

The role of the Medical Officer and general practitioner is to:

- Prescribe Clozaril® in accordance with the TGA-approved Product Information.

The prescription of Clozaril® must not occur until a satisfactory WBC and NC has been reviewed by the Medical Officer or GP. Each prescription for Clozaril® in the initial 18 weeks must not exceed 7 days' supply, and after 18 weeks no more than 28 days' supply (unless dispensation has been approved, see Section 8.1) providing that the patient's blood counts are within the Green range (see Sections 3.2 and 10.3).

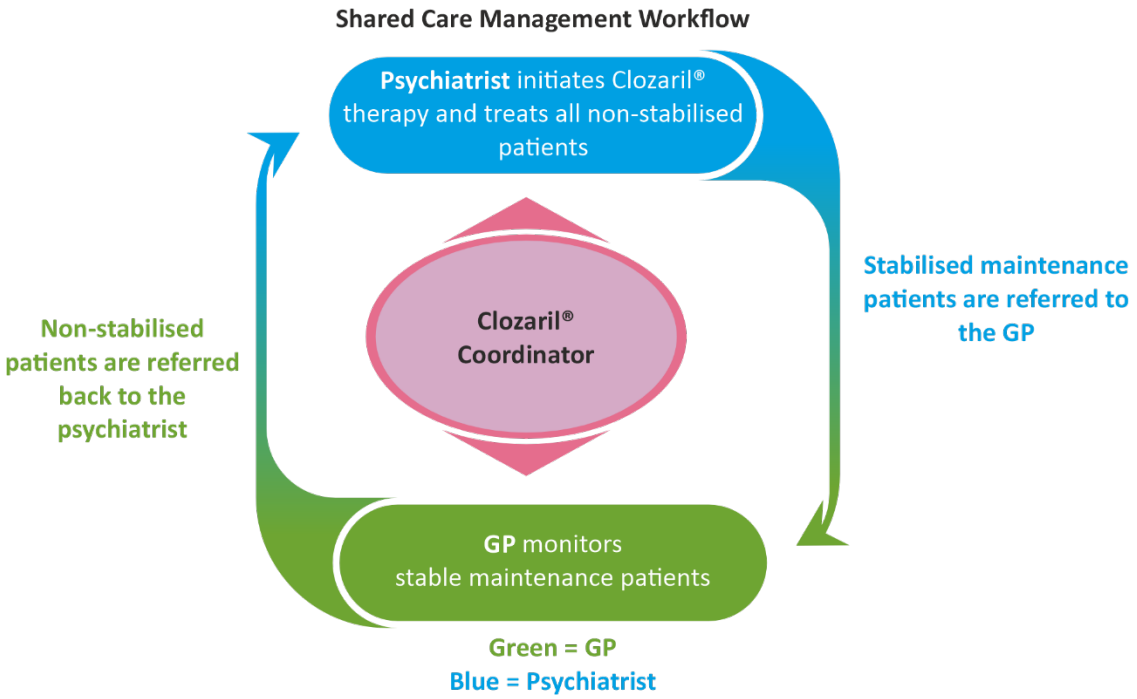
- Ensure that each patient is monitored in accordance with the requirements stipulated in this protocol.
- Ensure that each WBC and NC result is forwarded to the CPMS-registered pharmacist on a completed blood count form along with the next prescription for review by the pharmacist prior to dispensing. Alternatively, the blood results can be entered directly into the eCPMS website.
- Inform all patients, and relevant carers and relatives of the symptoms which may occur with white cell deficiency or myocarditis/cardiomyopathy and to instruct them to contact their Medical Officer if symptoms appear.
- Notify CPMS and the centre coordinator within 24 hours when you no longer require registration at a centre.

2.4.3 The role of the GP

The general practitioner plays a vital role in the care of a stabilised maintenance patient on Clozaril®, ensuring compliance with the CPMS protocol. Once stabilised, a treating psychiatrist may engage a GP in co-management of the CPMS blood monitoring and clinical management of maintenance patients to assist in their recovery. The GP's involvement not only provides improved convenience for the patient, it ensures all members of the medical care team are informed and aware of the requirements for clinical management of Clozaril® and the associated CPMS blood tests.

In addition to the duties outlined in 2.4.2 above, the role of GPs may include;

- General health assessment.
- Management of comorbidities.
- Educating the patient as to the signs and symptoms of infection.
- Ordering and monitoring pathology tests for haematological, cardiovascular and other medical investigations.
- Prescribing concomitant medications.
- Identifying and managing any adverse drug interactions.
- Participation in optimal holistic care and engaging the patient in healthy living choices.
- Identifying and treating medication side effects.
- Managing medication and blood test compliance.



2.4.4 The role of the nominee pharmacist and other pharmacists

Clozaril® may only be supplied, distributed or dispensed from a CPMS-registered pharmacy by a CPMS-registered pharmacist to a CPMS-registered patient. Each pharmacy will have a nominated contact, preferably the owner, who is designated as the nominee pharmacist. Dispensing must be confirmed online in eCPMS or by fax to CPMS. Please note that when supply is staged, only the first occasion of dispensing after each blood test requires confirmation of dispensing.

CPMS registration of a pharmacy is a statement of intent by the nominee pharmacist and pharmacy staff to participate in the distribution of Clozaril® in association with the CPMS. The nominee pharmacist is responsible for ensuring any pharmacist who distributes or dispenses Clozaril® to patients at their pharmacy complies with the CPMS protocol.

To distribute or dispense Clozaril®, the prescription must be written by a CPMS-registered Medical Officer within the last 48 hours and accompanied by either a blood count form [10.4.8] signed by the CPMS-registered Medical Officer, or entered electronically on the eCPMS website.

Medication dispensed for the initial week of active treatment can be confirmed by searching for the Clozaril® Patient Number (CPN) in eCPMS and identifying the initial blood result is less than 10 days old. Pharmacist confirmation is not required in eCPMS for the initial treatment week.

The pharmacist, upon confirming blood results are acceptable, may supply or dispense after either signing a CPMS paper blood count form [10.4.8] and faxing to CPMS, or signing electronically by confirming dispensing via the eCPMS website. A pharmacist may arrange with a centre to enter the blood results and confirmation of dispensing.

How much can the pharmacist supply?

The total amount dispensed is equal to one blood test cycle. Each prescription for Clozaril® in the initial 18 weeks of treatment must not exceed 7 days' supply and after 18 weeks each Clozaril® prescription must not exceed 28 days' supply unless dispensation has been approved (see section 8.1) providing the patient's results are within the Green range (see Sections 3.2 and 4.3).

There is a 48-hour window within which a patient must have a blood test taken, reviewed and medication dispensed (see Section 4.2, a repeat blood test is required > 48 hours). Thus, a blood test cycle, and the amount of medication dispensed for a weekly patient could include testing on Monday, 7 days' supply dispensed on Wednesday, with the next test due the next Monday, and dispensing again the next Wednesday.

In any event, the amount of medication supplied should only last the patient up to 48 hours after the next due blood test to ensure continuity.

What should the pharmacist do if the dose needs to be increased between blood tests?

If an increase in dose is required in the period between blood tests, the doctor may prescribe, and the pharmacist may dispense or supply, sufficient medication to account for the dose change until the end of the current blood test period.

3 Registering a patient

3.1 4-step registration

1. Gain patient consent to collect and store health information in CPMS

To register with CPMS, the Patient Health Information Collection and Storage Consent form [10.4.6] must be signed and sent to CPMS with the registration details.

The Patient Health Information Collection and Storage Consent form must be signed by a CPMS-registered Medical Officer and either the patient or an authorised person on behalf of the patient (which includes the registered Medical Officer), after appropriate discussion with the patient of the risks and benefits of treatment with Clozaril® and the requirements of the CPMS. This consent allows for patient data to be entered by CPMS users and held on the CPMS and associated databases. **It does not constitute consent to treatment.**

The Patient Health Information Collection and Storage Consent form highlights to the patient that their CPMS data may be used for future research or publication. Patient names are not mandatory for registration. Including patient names facilitates improved communication between CPMS and CPMS users, and assists the important task of uniquely identifying the patient to ensure they have not previously received a Red result on clozapine.

The Patient Health Information Collection and Storage Consent form is to be maintained in the patient's file and is required to be sent to the CPMS office to complete patient registration.

2. Obtain pre-treatment result

A baseline WBC and NC must be performed and reviewed no more than 10 days prior to commencing Clozaril®. The results must be entered on the registration form (or entered in eCPMS). For centres requesting an online patient registration, the pre-treatment results can be entered into the patient profile screen on eCPMS at the time of the online patient registration request.

3. Complete patient profile/registration form

Once a psychiatrist has decided to register a patient on the CPMS, a CPMS coordinator or Medical Officer from the patient's centre should either complete the patient registration in eCPMS or fax a patient registration form [10.4.7.1] to the CPMS office.

Before a patient can be started on Clozaril® therapy, the Medical Officer must determine whether the patient has been previously discontinued from any brand of clozapine due to neutropenia or agranulocytosis, or has a history of drug-induced neutropenia or bone marrow disorders. The Medical Officer must also determine if the patient is unsuitable for treatment with Clozaril® due to other reasons.

A Benign Ethnic Neutropenia (BEN) patient has a lower range of acceptable parameters for CPMS blood results. If the patient has a diagnosis of BEN, the consultant should submit confirmation in writing to the CPMS haematologist including adequate history, preferably referencing haematology diagnosis and details for diagnostic confirmation to complete registration.

Personal and health information to be entered on the patient registration form [10.4.7.1] include:

- Patient name (optional)
- Patient initials
- Date of birth
- Sex
- Blood group
- Consent form completed? (Y/N)
- Previously treated with clozapine (Clozaril®)? (Y/N)
- History of drug-induced neutropenia? (Y/N)
- History of any bone marrow disorders? (Y/N)
- Does the patient have a diagnosis of Benign Ethnic Neutropenia? (Y/N)
- Name of Medical Officer (must be registered with the CPMS)
- Name of responsible pharmacy (must be registered with the CPMS)
- Baseline/pre-treatment blood results and date.
- Proposed date of treatment commencement.

If any of the above information changes after submitting a registration application, including the commencement date, you must inform CPMS in writing promptly (by email or fax).

4. Database cross-check CPN allocation (by CPMS)

The CPMS staff cross-check the patient details with the CPMS database and with other clozapine databases, to determine if the patient has previously discontinued clozapine due to neutropenia or agranulocytosis. Due to the high risk of the reoccurrence of agranulocytosis on re-exposure to clozapine, these patients will be ineligible to re-register with the CPMS or receive clozapine in the future (unless QAC-approved, see Section 4.5).

If the cross-check reveals no history of neutropenia/agranulocytosis, and the blood cell count is within appropriate ranges (see Section 3.2) a CPN will be allocated for the patient. This patient identification number will be used for all further correspondence with the CPMS office and will not change even if the patient name changes.

i.e. Clozaril® PATIENT NUMBER (CPN) XX/YYYYY
Where 'XX' = patient initials and 'YYYYY' = next available number, e.g. 00001

3.2 Guidelines for evaluating the baseline WBC and NC results

WBC AND NC RESULTS	RANGE	ACTION
WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L	GREEN	Clozaril® therapy may be commenced subject to assessment by the treating Medical Officer and successful registration.
WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L	AMBER	Repeat Blood Count after one week. If still within same range, Clozaril® therapy may commence subject to assessment by the treating Medical Officer and successful registration.
WBC < 3.0 x 10^9/L and/or NC < 1.5 x 10^9/L	RED	CLOZARIL® THERAPY MUST NEVER BE STARTED

3.3 Commencing Clozaril®

3.3.1 Initial blood results

The pre-treatment/initial results can be used to initiate a patient (the pre-treatment test should be no more than 10 days old). A further blood test should be performed no longer than 7 days after commencement. (This constitutes the end of week 1).

3.3.2 Initial dosage

Dosage of Clozaril® should be individualised on clinical assessment. For each patient, the lowest effective dose should be used. In the elderly or underweight patients, or those suffering from renal, hepatic or cardiovascular disorders, cerebral vascular insufficiency or cerebral sclerosis, the initial dose should be low and any dose increase should be gradual.

To commence Clozaril®, start with 12.5 mg (half of a 25 mg tablet) once or twice daily on the first day, followed by one or two 25 mg tablets on the second day. If well tolerated, the dosage may be increased in daily increments of 25 - 50 mg, achieving a dose level of up to 300 mg per day within 2 to 3 weeks. Thereafter, if required, the daily dose may be further increased in increments of 50 - 100 mg at half-weekly or, preferably, weekly intervals.

Dose titration schedule example [1]

Day	Day 1	Day 3	Day 5	Day 7	Day 8	Day 9	Day 11	Day 13	Day 15	Day 17	Day 19	Day 21	Day 28+
Dose	12.5	50	75	100	125	150	175	200	225	250	275	300	Or after 300 mg
am	12.5	25	25	25	25	50	50	50	50	75	75	100	Increase 50-100 mg at weekly intervals
pm		25	50	75	100	100	125	150	175	175	200	200	

Each prescription for Clozaril® in the initial 18 weeks of treatment must not exceed 7 days' supply and after 18 weeks each Clozaril® prescription must not exceed 28 days' supply if blood results are within the Green range (unless dispensation has been approved see section 8.1).

During the titration phase, the dosage recorded on the blood count form [10.4.8] should reflect the highest potential dose that the patient received in any single day over the week.

3.3.3 Therapeutic dose range

In most patients, antipsychotic efficacy can be expected with 200 - 450 mg per day in divided doses. The total daily dose may be divided unevenly, with the larger portion at bedtime.

Because of the significant risk of agranulocytosis and seizure, events which both present a continuing risk over time, the extended treatment of patients failing to show an acceptable level of clinical response should ordinarily be avoided.

3.3.4 Maximum dose

For most patients, the usual recommended maximum dose is 600 mg/day. However, a few patients may require larger doses to obtain the maximum therapeutic benefit, in which case increments of not more than 100 mg are permissible up to a maximum dose of 900 mg/day.

3.3.5 Maintenance treatment

After the maximum therapeutic benefit has been achieved, the minimum effective dosage should be used to maintain clinical remission.

3.3.6 Monitoring vital signs

In order to detect if there are any adverse effects after the first Clozaril® dose, all patients should be kept under close medical supervision with monitoring of vital and neurological signs for a period of about 6 hours. During this period, the blood monitoring procedure and visit schedule must be effectively communicated to each patient. Viatris may provide assistance to support commencing patients in a community setting. To request a copy of the community assistance request form please call CPMS.

3.3.7 Cardiac monitoring

Cases of myocarditis, some of which have been fatal, and cardiomyopathy have been reported in patients on clozapine[1]. If myocarditis is confirmed, Clozaril® should be discontinued and the patient immediately referred to a cardiologist. Patients who develop clozapine-induced myocarditis or cardiomyopathy should not be re-exposed to Clozaril® unless assessed to be appropriate by a cardiologist, following a complete cardiac evaluation, and under close monitoring. Generally, patients with a history of clozapine-associated myocarditis or cardiomyopathy should not be rechallenged with Clozaril®. However, as clozapine is often a 3rd- or 4th-line treatment, withdrawing it may adversely affect the patient's mental and physical health as well as their risk for suicide. If the benefit of Clozaril® treatment is judged to outweigh the potential risks of recurrent myocarditis or

cardiomyopathy, the clinician may consider rechallenge with Clozaril® in consultation with a psychiatrist and cardiologist, after a complete cardiac evaluation and under close monitoring or in an inpatient setting.

The Clozaril® (clozapine) and myocarditis clinical monitoring guidelines were drafted by an expert panel of cardiologists, psychiatrists and other medical advisors with expert clinical opinion contributed by the Clozaril® Cardiovascular Advisory Board. It is recommended, though not mandatory, that all patients undergo cardiac assessment during initiation of Clozaril® and periodically thereafter.

For cardiovascular referrals, please contact CPMS Medical Information (Section 9).

Baseline	**Prior to Clozaril® therapy**	**Troponin T or I**	High sensitivity test preferred.	Not all pre-existing cardiac abnormalities preclude Clozaril® treatment. Consult a cardiologist if abnormalities are detected.
		CRP	High sensitivity c-reactive protein test preferred.	
		Echocardiography	Highly desirable.	
		ECG		
During Clozaril® therapy	**First 28 days**	**At all times**	Educate patients 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.	
		Weekly (days 7, 14, 21 and 28)	Troponin T or I, CRP, pulse, blood pressure, respiratory rate.	
	If at any time	**Temperature >38°C or flu-like symptoms**	Immediate CRP and troponin.	Continue Clozaril® at current dose. Do not escalate until features normalise.
		Troponin > 2 ULN and CRP elevated	**Urgent cardiology consultation. Urgent echocardiography.**	Withhold Clozaril®.
		Troponin > 2 ULN and normal CRP	Urgent cardiology consultation – query ACS (acute coronary syndrome).	Continue Clozaril® at current dose. Do not escalate until features normalise.
		Troponin 1-2 ULN and elevated CRP	Assess troponin, CRP and symptoms daily until features normalise. If no progressive elevation, consider differential diagnosis and cardiology consult.	Continue Clozaril® at current dose. Do not escalate until features normalise.
	Every 1-2 years (in absence of symptoms)	**Echocardiography**		

4 Maintaining a patient on Clozaril®

4.1 Clinical assessment

Patients on Clozaril® require regular clinical assessment involving taking a patient history and physical examination to identify signs and symptoms of infection and to review blood test results. At each review, the patient should receive education as to the signs and symptoms of infection and instructed to notify their treating doctor should symptoms present between consultations.

During the initial 18 weeks of treatment, clinical assessment should be conducted by a CPMS-registered Medical Officer. If a patient has successfully completed the initial 18 weeks of weekly monitoring under normal CPMS protocol guidelines, clinical assessment of the patient may be undertaken by a suitably qualified healthcare professional under the guidance of the responsible Medical Officer prior to Clozaril® being dispensed.

An appropriately qualified health professional includes a CPMS-registered psychiatrist or general practitioner, registered nurse or remote area nurse / nurse practitioner. The CPMS-registered Medical Officer remains responsible for ensuring appropriate examination has occurred and to have cited blood test results before prescribing Clozaril®. If the treating psychiatrist deems the patient is suitable for co-management by extended medical team members and suitably qualified healthcare professionals, a clinical assessment and psychiatric review of the patient should be carried out by the treating psychiatrist at least once every 6 months.

4.2 Blood test monitoring

It is imperative that the Medical Officer reviews the WBC and NC and ensures the patient has been clinically assessed before writing the next Clozaril® prescription. Blood results are required weekly for the initial 18 weeks (126 days) and then every 28 days thereafter, providing blood results remain in the green range (WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L).

The following must be completed within a 48-hour period commencing the morning of when the blood sample is due:

- A blood sample taken.
- Haematology examination performed by the laboratory.
- Clinical assessment of the patient for signs of infection.
- Review of blood results by the Medical Officer and new prescription written.
- Results entered into eCPMS by centre personnel or onto a paper blood count form [10.4.8] which is forwarded to the pharmacy supplying the patient.
- Medication dispensed after a pharmacist reviews blood results and prescription.
- If applicable, a completed paper blood count form [10.4.8] should be faxed to CPMS.

What happens if a blood count is not received ≤ 48 hours after the due date?
An alert will be generated by eCPMS and an appropriate letter emailed or faxed to the centre coordinator and the Medical Officer who signed the most recent blood count form.*
If the patient has absconded or refused to have further blood tests, written notification should be faxed or emailed to CPMS.

What happens if medication is not dispensed ≤ 48 hours after the blood test?
An alert is generated by eCPMS for the Medical Officer and coordinator 3 days after entering a blood result if dispensing confirmation has not occurred in eCPMS. A repeat blood test should be issued.

* Note that alerts such as overdue notices in eCPMS will be sent to the primary coordinator plus either an email or fax, however other CPMS personnel may elect to switch external notifications off (i.e. email and fax alerts).

4.3 Assessment of results

WBC AND NC RESULTS	RANGE	ACTION
WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L	GREEN	Continue with Clozaril® treatment
WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L	AMBER	Increase monitoring to twice weekly
WBC < 3.0 x 109/L and/or NC < 1.5 x 10^9/L	RED	STOP immediately and repeat test in 24 hours

4.4 Monitoring Frequency

The time interval after which a patient must have blood tests performed, and whether they are allowed to receive Clozaril® treatment, is determined by their status and monitoring frequency.

Awaiting registration

When a patient is first registered and before an initial green result has been entered. At this time, the patient cannot receive Clozaril®. Once a green result has been entered the patient becomes active.

Active

An active patient has had their blood monitored on an ongoing basis and may receive Clozaril® as per their monitoring regimen.

Clozaril® Prohibited

After a given period following the due date for a blood test, if a result has not been entered, a patient is deemed to have had a treatment interruption and should not receive Clozaril®. This status is called Clozaril® Prohibited. If a green or amber blood result is received for an overdue patient who is Clozaril® Prohibited, they will return to Active status. An overdue patient who is Clozaril® Prohibited for a specific period of time becomes deregistered.

Discontinued

When a decision is made to stop treatment on Clozaril®, or a red result occurs, a patient is discontinued. The patient cannot receive further Clozaril®, however blood results are still required for one month. After this time, they are deregistered.

Deregistered

A deregistered patient cannot receive Clozaril®, they are no longer monitored and no blood results are taken.

Monitoring sub-status

The higher order status for an Active patient is to require weekly or 28-day monitoring. If a patient is required to have more frequent monitoring due to the occurrence of an amber or red result, due to the presence of symptoms of infection or when a treatment break has occurred, they will have a 'Sub-status' denoting the requirement for extra blood tests.

Special monitoring

In special circumstances the CPMS haematologist may indicate that a patient's regimen involves special ranges and frequencies for blood test results, and specially defined ranges for red, amber and green results. Special monitoring instructions will apply and the patient may be manually monitored.

Automatic Frequency Hold

Under certain circumstances the automatic CPMS process for being promoted from weekly to 28-day monitoring may be suspended pending special monitoring requirements. CPMS will activate the Automatic Frequency Hold and manually promote the patient after specific blood test requirements have been fulfilled.

Notification days and patient status

MONITORING FREQUENCY	SAMPLE DUE DAY	OVERDUE NOTIFICATION	CLOZARIL® PROHIBITED	PATIENT DEREGISTERED
Weekly	7	9	10	21
4-Weekly	28	35	42	56
Status on screen	Active	Active / Overdue	Clozaril® Prohibited	Deregistered

Frequency and dispensing

MONITORING FREQUENCY	DISPENSING AMOUNT
Weekly	7 days
4-Weekly	28 days
Twice Weekly	3-4 days
Daily	1 day

4.5 Blood monitoring key recommendations

What if the results are in the amber range?

- The monitoring sub-status changes to twice weekly. The patient may be maintained on Clozaril®, but clinical and haematology reviews should be increased to twice weekly. Continue twice-weekly reviews until WBC and NC increase beyond 3.5 x 10^9/L and 2.0 x 10^9/L, respectively.
- Once this has occurred, return to weekly or 28-day monitoring depending on the patient's previous higher order monitoring status.

No more than 3 – 4 days of medication should be dispensed when patients have blood results in the amber range.

What if the results are in the red range?

- STOP CLOZARIL® IMMEDIATELY (see Section 6.1 on ceasing Clozaril® abruptly).
- Within 24 hours, forward the red result to the CPMS office immediately and perform a second blood count.
- Call 0404 451 327 on receipt of first red result.
- Upon receipt of the second blood count result contact the CPMS haematologist, and forward results to CPMS office immediately.

For a rapid response, inform the CPMS haematologist that your contact is relating to a red result.
PH: 0404 451 327

- If the second test result is in the red range, perform WBC and NC daily until results are in the amber range, then twice weekly until in the green range. Once back into the green range, perform WBC and NC weekly for 4 weeks.
- Monitor patients for symptoms of infection.
- If levels fall further after discontinuation of Clozaril®, to WBC < 2.0 x 10^9/L and/or neutrophils < 1.0 x 10^9/L, management must be guided by a clinical haematologist. It is important that the treating haematologist contact the CPMS consultant haematologist. In the absence of a nominated centre haematologist please contact the CPMS haematologist. If possible, the patient should be referred to a specialised haematological unit, where protective isolation may be indicated.

Can a patient who has had a red result recommence treatment?

A patient who has had a red result with clozapine, providing the neutropenia/agranulocytosis could be attributed to a cause other than clozapine therapy, may be considered for rechallenge by the CPMS consultant haematologist and the CPMS QAC. Please consult the nominated centre haematologist for review, but ensure that the patient is not re-exposed without the advice of the CPMS haematologist. **If it is likely that the patient has had a red result due to clozapine, they cannot be recommenced on Clozaril®**. Applications for QAC review of discontinued patients can be organised via the CPMS. Clinicians must adhere strictly to any QAC rechallenge instructions including any special monitoring conditions.

What should you do if the patient shows physical signs of infection?

If at any time symptoms indicate possible infection e.g. fever, sore throat, mouth ulcers or flu-like symptoms, patients may be maintained on Clozaril®, however a WBC or NC should be performed immediately. If the results are normal, clinical and haematological reviews should continue twice weekly until symptoms resolve.

What if the patient develops eosinophilia?

It is recommended to discontinue Clozaril® if the eosinophil count rises above 3.0 x 10^9/L, and to restart therapy only after the eosinophil count has fallen below 1.0 x 10^9/L.

What if the patient develops thrombocytopenia?

In the event of thrombocytopenia, it is recommended to discontinue Clozaril® if the platelet count falls below 50 x 10^9/L.

Why do some patients take over 18 weeks to reach the 4-weekly promotion date?

For clarity, 18 weeks on treatment equates to 126 days on active treatment.

If there have been treatment breaks these periods are subtracted from the days on treatment and do not count toward the 126 days required before a patient can promote to 4-weekly tests. A treatment break includes time as 'Clozaril® Prohibited' where a patient was overdue and assumed to have missed taking medication. In principle, a patient remains on weekly tests for 18 weeks and is then placed on the 4-weekly tests, although the details depend on whether or not that patient has had time periods where it is assumed medication was not taken. For clarity, the existence of amber blood results within the 18-week period does not extend the 126 days required.

6-Week rule – Please note that if a treatment break occurred during weekly therapy and the therapy interruption 6-week rule extends beyond the end of the 18 weeks, the end of the 6-week rule is used as opposed to the 18-week period to complete weekly monitoring.

How much medication is dispensed if a patient presents late at pharmacy, but there has not been a break in active treatment?

The amount of medication dispensed should only be enough to last up to 48 hours past the next due blood test.

4.6 Reporting adverse events

Any person who becomes aware of a serious or non-serious adverse event (AE) that occurs in a patient being treated with a Viatris drug, including Clozaril®, should report the AE to Viatris Drug Safety within 24 hours via:

Viatris Drug Safety
Phone: 1800 931 383
Fax: +61 2 9298 3992
Email: pv.australia@viatris.com

When reporting an AE, please try to provide the following information (if available): exact event terms reported, whether or not the event(s) is related to the Viatris drug, patient details (initials, date of birth, gender), event onset date, reporter contact details and whether there is consent to contact the reporter for follow up.

The Viatris Drug Safety team ensures that the AE(s) are reported to the relevant Health Authorities, as per local regulations.

The Medical Officer is also encouraged to report Adverse Drug Reactions (ADRs) related to Clozaril® or a non-Viatris drug to the local Health Authority, the Therapeutic Goods Administration (TGA), via:

Online form: https://aems.tga.gov.au
Email: adr.reports@tga.gov.au
Fax: +61 2 6232 8392

Adverse event definition: An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, that does not necessarily have a causal relationship with this treatment.

An AE can therefore be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal product.

Medical conditions/diseases present before commencing Clozaril® are only considered adverse events if they worsen after Clozaril® was started.

In addition, the following scenarios are also classified as reportable:

- Pregnancy cases (via the mother or father) and drug use during lactation
- Withdrawal reaction/syndrome and rebound effects, with or without clinical symptoms
- Lack of efficacy, with or without clinical symptoms
- Overdose, with or without clinical symptoms
- Intentional drug misuse/abuse with or without clinical symptoms
- Drug dependence/addiction with or without clinical symptoms
- Medication errors, including maladministration, occupational/accidental exposures and dispensing/prescribing errors with or without clinical symptoms
- Drug-drug, drug-food interactions with or without clinical symptoms
- Disease progression and aggravation, with or without clinical symptoms
- Off-label use including paediatric exposure, with or without clinical symptoms
- Treatment non-compliance with clinical symptoms
- Unexpected beneficial effects

A **serious adverse event** (SAE) is defined as an event which:

- is fatal or life-threatening.
- results in persistent or significant disability/incapacity.
- constitutes a congenital anomaly/birth defect.
- requires inpatient hospitalisation or prolongation of existing hospitalisation, unless hospitalisation is for:
  - routine treatment or monitoring of Clozaril® therapy, not associated with any deterioration in condition.
  - elective or pre-planned treatment for a pre-existing condition that is unrelated to Clozaril therapy and has not worsened since the commencement of Clozaril.
  - treatment on an emergency outpatient basis for an event not fulfilling any of the definitions of a SAE given above and not resulting in hospital admission.
  - social reasons and respite care in the absence of any deterioration in the patient's general condition.
- is medically significant, i.e. defined as an event that jeopardizes the patient or may require medical or surgical intervention to prevent one of the outcomes listed above. Note, transmission of infectious agent via medicinal product is always considered medically significant.

If an AE is identified (as per the definition above) during interactions between the CPMS team and Medical Officers, pharmacists, Clozaril® coordinators or any other personnel, the AE will be reported to Viatris Drug Safety by the CPMS team. Viatris Drug Safety collects and databases the AEs and conducts AE follow up with the reporting HCP (healthcare professional) or relevant HCP, as per local and global requirements. If you are contacted by Viatris Drug Safety for additional information regarding an AE, it is expected that the additional information would be provided, if available.

5 Recommencing therapy after an interruption

5.1 Step one: Identifying changes to dosage and monitoring

Depending on the interval since the last dose was taken, a patient may require changes to dosage and blood monitoring frequency.

What dosage should you select and how frequently should you monitor?

Period of interruption (time since last dose taken)	Dosage / monitoring requirements
≤ 48 hours	No change to dosage or monitoring.
> 48 hours and ≤ 72 hours	Start on 12.5 mg and titrate up. No additional monitoring requirements.
> 72 hours and < 28 days	Start on 12.5 mg and titrate up. The 6-week rule applies. For 4-weekly patients: weekly monitoring for 6 weeks. If no abnormality, resume 4-weekly monitoring. For weekly patients: weekly monitoring for 6 weeks or as long as needed to reach 126 days (18 weeks accumulated active treatment), whichever is the greatest.
≥ 28 days	Restart patient with a new patient registration form [10.4.7.1]. New pre-treatment result and monitoring. Dosage recommenced at 12.5 mg and titrated up. As per new patient, 126 days/18 weeks weekly monitoring No initial 6-hour vital sign monitoring required.

5.2 Step two: re-registration following >4 weeks off medication

A patient who has not had active treatment for more than 4 weeks is classified as discontinued. The patient will need to be re-registered to restart active treatment:

- A new patient registration form [10.4.7.1] should be completed if the patient has been off Clozaril® treatment > 4 weeks.
- A new pre-treatment blood test is necessary.
- A patient cannot be re-registered if they have previously had a blood dyscrasia related to clozapine.
- Dose recommences at 12.5 mg and is titrated up.
- Recommencement does not require initial 6-hour vital sign monitoring.

6 Discontinuing therapy

6.1 Discontinuing dosage

If Clozaril® therapy needs to be stopped, reducing the dose gradually over one to two weeks is recommended where possible.

If abrupt discontinuation is necessary, the patient should be carefully observed for rebound exacerbation of their psychotic symptoms. The patient should also be carefully observed for symptoms related to cholinergic rebound such as headache, nausea, vomiting and diarrhoea. The use of other antipsychotics such as olanzapine, risperidone or quetiapine may be considered to prevent emergence of psychotic symptoms.

If abrupt discontinuation is required, an anticholinergic agent may be started to prevent cholinergic rebound symptoms.

6.2 Blood test monitoring

Centre personnel must inform the CPMS office of each patient discontinuation within 24 hours by indicating 'post treatment' on the Blood Count Form [10.4.8] that therapy has discontinued, and by filling out a Discontinuation of Therapy Form [10.4.9]. A pharmacist's name is not required with blood results if no medication is dispensed. Following discontinuation of Clozaril®, full haematological evaluation must be continued for at least 4 weeks or until full recovery has occurred (whichever is greater).

6.2.1 Post-monitoring for weekly patients

For patients on weekly blood test monitoring, a WBC and NC should be performed at least weekly for 4 weeks after discontinuing due to non-haematological reasons.

6.2.2 Post-monitoring for 4-weekly patients

For patients on 4-weekly blood test monitoring, one further blood count should be performed one month after ceasing due to non-haematological reasons. The result must be green. The intention of this is that the patient has a blood test as close as possible to the time of discontinuation and then a follow up count 4 weeks later.

If a patient was to discontinue close to the time of their next blood test and no test was done until 4 weeks later; it would be nearly 8 weeks between blood tests, which would be too long.

6.2.3 For patients on more frequent monitoring

Patients who are on increased monitoring due to symptoms of infection and/or an amber result (WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L) at the time of cessation are required to be tested at least twice weekly until the WBC > 3.5 x 10^9/L, neutrophil count is > 2.0 x 10^9/L and/or symptoms of infection have resolved. Once back in the green range, perform WBC and NC weekly for 4 weeks.

Patients who have been discontinued due to a red result must continue to have daily blood count monitoring until WBC/NC have returned to the green or amber range. Once back in the green range, perform WBC and NC weekly for 4 weeks.

7 Transferring a patient

7.1 Within Australia

A centre coordinator wishing to transfer a patient must first contact the coordinator at the receiving centre by phone to ensure that centre accepts responsibility for the monitoring of the patient.

A patient transfer can be processed using the eCPMS website. The date of transfer must not be more than 30 days in the future and must not be in the past. Once a transfer is accepted by the receiving centre, the patient is the responsibility of the receiving centre and their blood history will appear on their patient data.

Alternatively, you can complete the Patient Transfer form [10.4.10] and fax to the CPMS office and the receiving centre. If requested, CPMS can assist by sending a blood history to the coordinator at the receiving CPMS centre.

7.2 Overseas travel

For patients intending to travel overseas, Viatris may be able to assist with arrangements for monitoring, provided adequate notice is given (approximately 6 weeks prior to travelling).

A dispensation should be arranged to cover the patient for the time outside Australia (see Dispensation to Supply Additional Medications, Section 8.1). You must advise the CPMS office if travel is going to exceed the Dispensation period as the automatic Overdue, Clozaril® Prohibited and Deregistered faxes will be sent as appropriate. You may be instructed by CPMS to ignore these and to act on them when the patient returns.

Should the patient's status change to deregistered while outside Australia, the Medical Officer will need to complete a registration form when the patient returns and if applicable to send CPMS confirmation that there has been no break in treatment. To ensure the patient can continue on 4-weekly blood test monitoring on their return, copies of blood results will need to be forwarded to CPMS. CPMS can assist by back-entering the results in the CPMS system.

Any patient returning without blood test results may be required to undergo 6 weeks of weekly blood testing on return or re-register and complete another 18 weeks of weekly monitoring.

Patients are encouraged to bring back to Australia the results of any blood tests performed overseas (as required by CPMS) to ensure that the patient can continue on 4-weekly blood test monitoring on his/her return.

7.3 From a generic clozapine

For a patient switching from a generic clozapine to Clozaril®, a registration form for patients switching brands [10.4.7.2] must be completed and faxed or emailed to the CPMS office, along with a complete blood history from the generic blood monitoring service.

If the patient being treated with the generic clozapine preparation was receiving 4-weekly blood monitoring, they will be placed on weekly monitoring on commencement of Clozaril® unless an adequate blood history can be provided. Unless approved by the CPMS haematologist, patients can only be switched to Clozaril® from a generic clozapine if they have not experienced agranulocytosis, neutropenia or leucopenia previously whilst on the generic clozapine.

7.4 To a generic clozapine

If a patient is switching from Clozaril® to a generic clozapine, the CPMS should be notified in writing as soon as the patient has transferred to a generic clozapine centre, or commenced on the generic form. Where required, Clozaril® coordinators are encouraged to forward a complete Clozaril® blood history to the generic clozapine coordinator, in order to help facilitate the transfer.

8 Dispensation for supply of additional medication

8.1 Dispensation to supply additional medications

Under special circumstances Viatris may approve a dispensation allowing the dispensing of additional medication for a patient and therefore an extension of their blood test period.

Approval to extend the blood test interval and supply additional medication does not extend to patients with current blood test results in the amber range or to patients showing any signs of infection.

Dispensation requests can be made at any time online via eCPMS for up to two days for weekly patients or two weeks for 4-weekly patients. Approval is automatic if blood results are up to date and in the green range.

Dispensations for longer periods of time must be approved by the CPMS consultant haematologist and must be organised through the CPMS.

9 Important contacts

For further clarification and other queries, please contact the CPMS office.

9.1 CPMS office

(To provide advice on protocol related matters to centres on request)

Free call: 1800 501 768
Free fax: 1800 550 150
Email: cpms@cpharm.com.au

The hours of operation of the CPMS office are 9am to 5pm (Australian EST), Monday to Friday. For urgent CPMS matters outside these hours, the usual CPMS phone number should be called to obtain the after-hours number and your call will be dealt with by after-hours staff.

9.2 CPMS Medical Information

(For questions relating to the efficacy and safety of Clozaril® and cardiovascular referrals)

Phone: 1800 931 383
Fax: +61 2 9298 3992
Email: medinfo_anz@viatris.com

9.3 Adverse reaction reporting (Viatris Drug Safety)

Phone: 1800 931 383
Fax: +61 2 9298 3992
Email: pv.australia@viatris.com

9.4 CPMS consultant haematologist

(To discuss haematological problems related to Clozaril® or report red patients)

Mobile: 0404 451 327

9.5 After-hours contacts

Haematologist: 0404 451 327
CPMS phone: 1800 501 768

9.6 Quality Assurance Committee

Post: CPMS Manager
Viatris
Level 1, 30-34 Hickson Rd
Millers Point NSW 2000

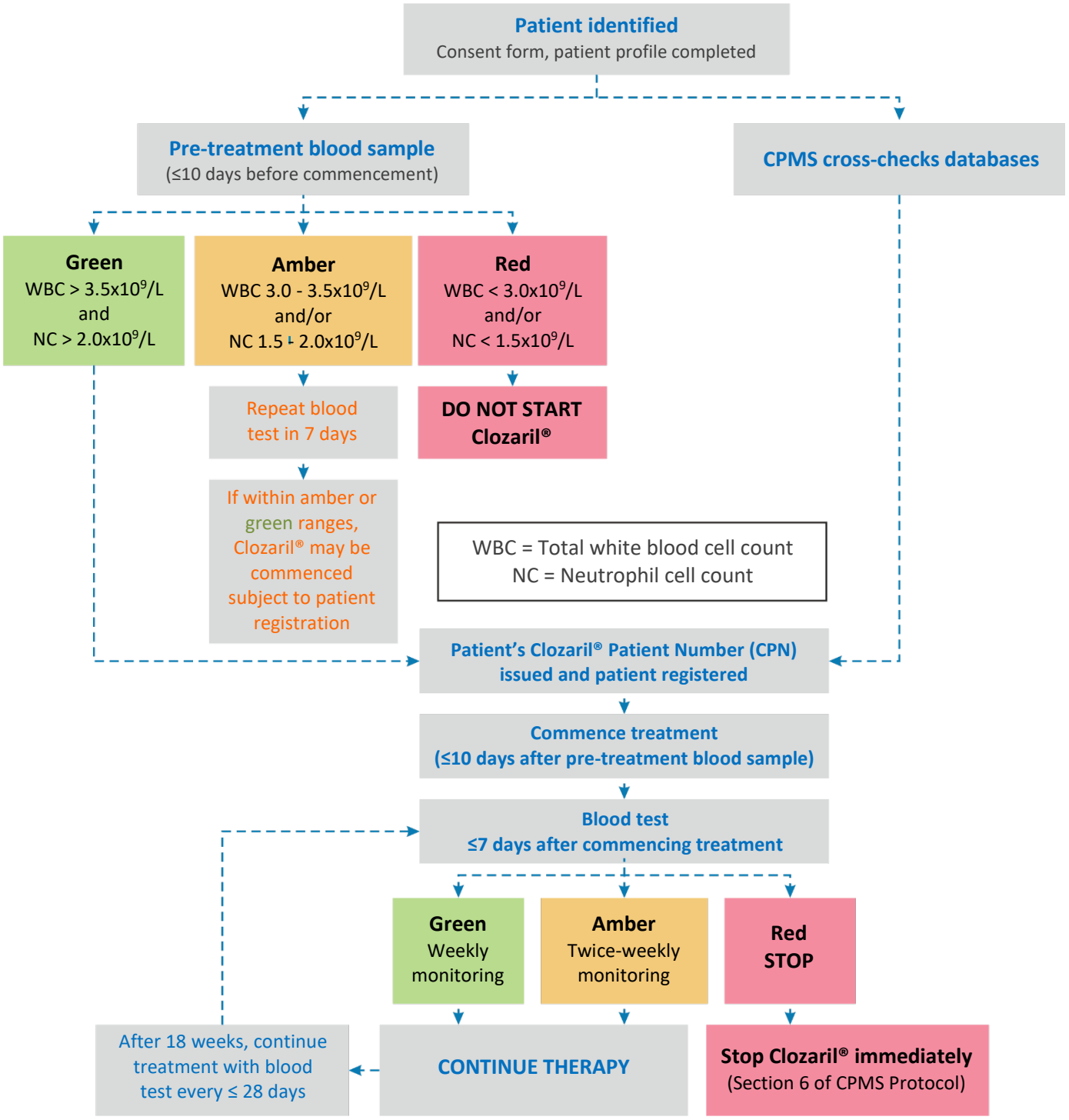
10 Appendices

10.1 Glossary

Agranulocytosis	Agranulocytosis is an acute condition in which there is a severe reduction in the number of neutrophils (defined as a neutrophil count of less than 0.5 x 10^9/L)
Clozapine	Generic name for Clozaril®
Clozaril®	Viatris trade name for clozapine in Australia
Clozaril® Patient Monitoring System (CPMS)	System devised to monitor patients while taking Clozaril®
CPMS protocol	Guidelines for the use of Clozaril® with the CPMS
Eosinophilia	Presence of increased number of eosinophils in the blood
HCP	Health care professional
Leucopenia	Decrease in the total WBC to below 3.0 x 10^9/L*
Thrombocytopenia	Decrease in the platelet count below 150 x 10^9/L*
Neutropenia	Decrease in the blood neutrophil count to below 1.5 x 10^9/L*
Neutrophil count (NC)	Measurement of the number of neutrophils in a blood sample
Total white blood cell count (WBC)	Measurement of concentration of white cells in a blood sample

*These levels are stated for purposes of the CPMS protocol.

10.2 How to initiate a patient on Clozaril® (flow chart)



10.3 Important Tables

Dose titration schedule example [1]

Day	Day 1	Day 3	Day 5	Day 7	Day 8	Day 9	Day 11	Day 13	Day 15	Day 17	Day 19	Day 21	Day 28+
Dose	12.5	50	75	100	125	150	175	200	225	250	275	300	Or after 300 mg
am	12.5	25	25	25	25	50	50	50	50	75	75	100	Increase 50-100 mg at weekly intervals
pm		25	50	75	100	100	125	150	175	175	200	200	

Guidelines for evaluating the baseline WBC and NC results

WBC AND NC RESULTS	RANGE	ACTION
WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L	GREEN	Clozaril® therapy may be commenced subject to assessment by the treating Medical Officer and successful registration.
WBC 3.0-3.5 x 10^9/L and/or NC 1.5-2.0 x 10^9/L	AMBER	Repeat blood count after one week. If still within same range, Clozaril® therapy may commence subject to assessment by the treating Medical Officer and successful registration.
WBC < 3.0 x 10^9/L and/or NC < 1.5 x 10^9/L	RED	CLOZARIL® THERAPY MUST NEVER BE STARTED

Assessment of results for patient maintenance

WBC AND NC RESULTS	RANGE	ACTION
WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L	GREEN	Continue with Clozaril® treatment
WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L	AMBER	Increase monitoring to twice-weekly
WBC < 3.0 x 109/L and/or NC < 1.5 x 10^9/L	RED	STOP immediately and repeat test in 24 hours

10.4 List of CPMS forms (also available on the eCPMS website)

10.4.1	CENTRE REGISTRATION
10.4.2	COORDINATOR REGISTRATION
10.4.3	MEDICAL OFFICER REGISTRATION
10.4.4	PHARMACY REGISTRATION
10.4.5	PHARMACIST REGISTRATION
10.4.6	PATIENT HEALTH INFORMATION COLLECTION AND STORAGE CONSENT
10.4.7.1	PATIENT REGISTRATION FORM
10.4.7.2	REGISTRATION FORM FOR PATIENTS SWITCHING BRANDS
10.4.7.3	MULTIPLE PATIENTS SWITCHING REGISTRATION FORM
10.4.8	BLOOD COUNT FORM
10.4.9	DISCONTINUATION OF THERAPY FORM
10.4.10	PATIENT TRANSFER TO ANOTHER CPMS CENTRE
10.4.11	DISPENSATION FORM
10.4.12	LABORATORY REGISTRATION FORM

10.4.1 CENTRE REGISTRATION

Please complete all mandatory sections of this form.*

This document is a statement of intent from the centre, the Medical Officer and Clozaril® (clozapine) Co-ordinator to participate in the distribution of Clozaril® in association with the Clozaril® Patient Monitoring System (CPMS).

Signing of this form constitutes a commitment on the part of the centre and the undersigned to adhere to the CPMS Protocol, and to ensure that additional CPMS users registered to this centre with the CPMS, comply with the Protocol.

- As a minimum, a centre must have one Medical Officer.
- At least one Centre Co-ordinator must be identified for each centre. It is preferable that a Centre Co-ordinator be a full-time staff member. Any CPMS registered user (e.g. nurse, Medical Officer, pharmacist) can be registered as a Co-ordinator.
- A CPMS Pharmacy needs to be linked to your centre to dispense Clozaril® to non-maintenance patients.
- Each centre must have access to a haematology laboratory which can process and report on Clozaril® patient samples within 24 hours of the time the samples were taken.
- It is recommended that each centre have access to a Clinical Haematologist to oversee the management of any patient who develops agranulocytosis.

CENTRE REGISTRATION DETAILS

Centre Name:*			
Postcode:*			
Sub Building or Clinic Name:			
Building or Hospital Name:			
Address Line 1:*			
Address Line 2:			
Suburb:*		State:*	
Phone:*	( )	Fax:	( )
Pharmacy Name (Optional):			
Laboratory Name (Optional):			

Before prescribing or dispensing Clozaril®, please review the Australian Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/ and the CPMS Protocol available from the eCPMS Information page.

I understand and agree to the conditions for the prescription of Clozaril® as detailed in the CPMS Protocol, which I have read. I undertake to be bound by the obligations set out in the CPMS Protocol.

As a healthcare professional participating in this activity sponsored by Viatris, I have read and understood the enclosed privacy statement and I agree with it. I understand that information relating to an adverse event with a Viatris product that is identified during this activity will be forwarded to Viatris drug safety department, and possibly to health authorities when required. I understand that my participation in this activity indicates my consent for Viatris' drug safety department to contact me for further information regarding any adverse event identified as part of this activity. If the activity also involves patients, I acknowledge that I must check with my patient before providing the requested follow-up information.

Please see overleaf for further important information about the collection of you and your patient's personal and health information.

VIATRIS

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

10.4.1 CENTRE REGISTRATION cont.

NOMINATED MEDICAL OFFICER

Name:*				
Signature:*		Date:*	Are you currently registered with CPMS?:*	☐ Yes ☐ No

NOMINATED PRIMARY CENTRE CO-ORDINATOR

Name:*				
Signature:*		Date:*	Are you currently registered with CPMS?:*	☐ Yes ☐ No

*To complete registration:**

1. Attach a completed Medical Officer Registration Form.
2. Attach a completed Centre Co-ordinator Registration Form.
3. Email or fax all signed forms to CPMS at cpms@cpharm.com.au / 1800 550 150.

The CPMS will confirm your centre registration with the nominated Centre Co-ordinator.

Privacy Collection Notice:

Viatris Inc. its subsidiaries and affiliates ('Viatris') collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program ('Program') for participating patients on the Clozaril® eCPMS database ('Database'). This includes registering health care professionals ('HCPs') and patients on the Database, storing patients' blood tests, monitoring patients' use of the products, communicating with HCPs and patients about the products to support the administration and use of the products, complying with regulatory obligations (including the reporting and processing of adverse events patients may experience) and sending invitations to participate or arranging for participation in activities managed by or on behalf of Viatris. Viatris may need to disclose this personal information to its third- party services providers, who may be located overseas, for these purposes and personal information in the Database is held on Viatris' behalf in servers located overseas in the UK and/or Ireland. By providing your personal information to Viatris, you agree that you understand this Privacy Statement. By providing your personal information (and/or if you are an HCP, the health information of a patient) to Viatris, you consent (and/or confirm that you are authorised by or on behalf of the patient), to Viatris collecting and holding, using and disclosing that personal information for these purposes.

Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

All information forwarded to the Viatris drug safety department is handled in accordance with local privacy laws and may be captured and processed in countries outside of the jurisdiction in which it was collected, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris' drug safety department may contact the patient's HCP to collect further information on the adverse event.

You are not obliged to provide personal information. However, if you do not provide the information, you may not, for example, be able to participate fully in activities managed by us.

You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.2 CENTRE CO-ORDINATOR REGISTRATION

Please complete all mandatory sections of this form.*

This document is my statement of intent to participate in the distribution of Clozaril® (clozapine) in association with the Clozaril® Patient Monitoring System (CPMS). Signing of this form constitutes commitment on my part to adhere to the CPMS Protocol.

PRESCRIBING REMINDERS

1. Clozaril® may only be prescribed for patients who are registered with the CPMS.
2. No more than one week's supply of Clozaril® may be prescribed for the initial 18 weeks, and thereafter, no more than 28 days' supply. The prescription of Clozaril® is dependent on the review of the patient's current haematological profile.
3. All prescriptions for Clozaril® must be accompanied by a completed and signed Blood Count form unless entered into eCPMS online.

PRIMARY CENTRE CO-ORDINATOR RESPONSIBILITIES

1. Ensure the necessary blood tests are performed, reviewed and acted upon accordingly.
2. Advise centre personnel to communicate all registrations, patient information and blood results to the CPMS.
3. Ensure that the centre and registered personnel comply with the CPMS Protocol.
4. Distribute all necessary communication with respect to patient monitoring to registered centre staff.
5. Keep a log of all personnel registrations.
6. Maintain a list of all patient names and their Clozaril® Patient Numbers (CPNs) registered to your centre(s).
7. Notify CPMS if any personnel need to be deregistered or Pharmacies de-linked from your centre.

CENTRE CO-ORDINATOR REGISTRATION DETAILS

Have you been registered with CPMS previously? ☐ Yes ☐ No

Title: | First Name:* | Last Name:*

Position: *(e.g. pharmacist, doctor, nurse, assistant):*

MODE OF COMMUNICATION FOR ALERTS* Selecting Fax/Email means you will receive alerts both within eCPMS and externally. Selecting Web Alerts only means you will only receive alerts within eCPMS. Please note, the Primary Centre Co-ordinator must receive both.

Selection:* (please tick) ☐ Fax/Email ☐ Web Alerts

DESIGNATED PRIMARY CONTACT METHOD* Please provide email and/or fax. If you do not provide email you must provide a fax no.

Email: | Fax:

Work Phone:* | Mobile:

Centre Name:*

Other Centre Co-ordinators will be advised of your registration. For assistance with centre names call CPMS.

Sub Building or Clinic Name:

Building or Hospital Name:

Address Line 1:

Address Line 2:

Suburb:

State: | Postcode:

Please see overleaf for further important information about the collection of you and your patient's personal and health information.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

JAN 2023
CLZ-2018-0004

10.4.2 CENTRE CO-ORDINATOR REGISTRATION cont.

Are you to be the Primary Co-ordinator for this Centre?* ☐ Yes ☐ No

Are you currently registered to another CPMS Centre?* ☐ Yes ☐ No

If so, to which Centre?*

Do you wish to be deregistered from the above Centre?* ☐ Yes ☐ No

If registering for more than one centre, please add centre names below.

Additional Centre 1:

Additional Centre 2:

Additional Centre 3:

Additional Centre 4:

Before prescribing or dispensing Clozaril® please review the Australian Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/ and the CPMS Protocol available from the eCPMS Information page.

I understand and agree to the conditions for the supply of Clozaril® as detailed in the CPMS Protocol, which I have read. I undertake to be bound by the obligations of a Co-ordinator set out in the CPMS Protocol.

As a healthcare professional participating in this activity sponsored by Viatris, I have read and understood the enclosed privacy statement and I agree with it. I understand that information relating to an adverse event with a Viatris product that is identified during this activity will be forwarded to Viatris' drug safety department, and possibly to health authorities when required. I understand that my participation in this activity indicates my consent for Viatris' drug safety department to contact me for further information regarding any adverse event identified as part of this activity. If the activity also involves patients, I acknowledge that I must check with my patient before providing the requested follow-up information.

Signature:*

Name:* Please print

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150. CPMS will confirm registration via your designated contact method.

Privacy Collection Notice:

Viatris Inc. its subsidiaries and affiliates ('Viatris') collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program ('Program') for participating patients on the Clozaril® eCPMS database ('Database'). This includes registering health care professionals ('HCPs') and patients on the Database, storing patients' blood tests, monitoring patients' use of the products, communicating with HCPs and patients about the products to support the administration and use of the products, complying with regulatory obligations (including the reporting and processing of adverse events patients may experience) and sending invitations to participate or arranging for participation in activities managed by or on behalf of Viatris. Viatris may need to disclose this personal information to its third- party services providers, who may be located overseas, for these purposes and personal information in the Database is held on Viatris' behalf in servers located overseas in the UK and/or Ireland. By providing your personal information to Viatris, you agree that you understand this Privacy Statement. By providing your personal information (and/or if you are an HCP, the health information of a patient) to Viatris, you consent (and/or confirm that you are authorised by or on behalf of the patient), to Viatris collecting and holding, using and disclosing that personal information for these purposes.

Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

All information forwarded to the Viatris drug safety department is handled in accordance with local privacy laws and may be captured and processed in countries outside of the jurisdiction in which it was collected, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris' drug safety department may contact the patient's HCP to collect further information on the adverse event.

You are not obliged to provide personal information. However, if you do not provide the information, you may not, for example, be able to participate fully in activities managed by us.

You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.3 MEDICAL OFFICER REGISTRATION

Please complete all mandatory sections of this form.*

This document is my statement of intent to participate in the distribution of Clozaril® (clozapine) in association with the Clozaril® Patient Monitoring System (CPMS). Signing of this form constitutes commitment on my part to adhere to the CPMS Protocol.

I undertake to be bound by the obligations of a Medical Officer set out in the CPMS Protocol and understand that notwithstanding these obligations, management of patients for whom I have prescribed Clozaril® remains my sole responsibility.

PRESCRIBING REMINDERS

1. Clozaril® may only be prescribed for patients who are registered with the CPMS.
2. No more than one week's supply of Clozaril® may be prescribed for the initial 18 weeks, and thereafter, no more than 28 days' supply. The prescription of Clozaril® is dependent on the review of the patient's current haematological profile.
3. All prescriptions for Clozaril® must be accompanied by a completed and signed Blood Count form unless entered online in eCPMS.

MEDICAL OFFICER REGISTRATION DETAILS

Have you been registered with CPMS previously? ☐ Yes ☐ No

Title: ☐ First Name:* ☐ Last Name:* ☐

Position:* (please tick) ☐ Consultant ☐ RMO/HMO ☐ Associate Specialist ☐ Registrar ☐ GP

MODE OF COMMUNICATION FOR ALERTS* Selecting Fax/Email means you will receive alerts both within eCPMS and externally. Selecting Web Alerts only means you will only receive alerts within eCPMS.

Selection:* (please tick one) ☐ Fax/Email ☐ Web Alerts

DESIGNATED PRIMARY CONTACT METHOD* Please provide email and/or fax. If you do not provide email you must provide a fax no.

Email: ☐ Fax: ☐

Office Phone:* ☐ Mobile: ☐

CPMS centre you are registering to join:* ☐

The Centre Co-ordinator will be advised of your registration. For assistance with centre names call CPMS.

Sub Building or Practice Name: ☐

Building or Hospital Name: ☐

Address Line 1:* ☐

Address Line 2: ☐

Suburb: ☐

State: ☐ Postcode: ☐☐☐☐

Please see overleaf for further important information about the collection of you and your patient's personal and health information.

10.4.3 MEDICAL OFFICER REGISTRATION cont.

Are you currently registered in CPMS at another Centre?* ☐ Yes ☐ No

If so, to which Centre?*

Do you wish to be deregistered from the above Centre?* ☐ Yes ☐ No

If registering to join more than one Centre, please enter additional Centre Names below.

The Centre Co-ordinator will be advised of your registration. For assistance with Centre Names call CPMS.

Additional Centre 1:

Additional Centre 2:

Additional Centre 3:

Do you have AHPRA registration?* ☐ Yes ☐ No Registration number:

Before prescribing or dispensing Clozaril® please review the Australian Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/ and the CPMS Protocol available from the eCPMS Information page.

I understand and agree to the conditions for the prescription of Clozaril® as detailed in the CPMS Protocol, which I have read. I undertake to be bound by the obligations of a Medical Officer set out in the CPMS Protocol.

I acknowledge that I have provided the patient a copy of the Privacy Collection Notice and I also confirm that the patient understands the Privacy Collection Notice, including with respect to the overseas transfer of such information.

Signature:*

Name:* Please print

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150. CPMS will confirm registration via your designated contact method.

Privacy Collection Notice:

Viatris Inc. its subsidiaries and affiliates ('Viatris') collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program ('Program') for participating patients on the Clozaril® eCPMS database ('Database'). This includes registering health care professionals ('HCPs') and patients on the Database, storing patients' blood tests, monitoring patients' use of the products, communicating with HCPs and patients about the products to support the administration and use of the products, complying with regulatory obligations (including the reporting and processing of adverse events patients may experience) and sending invitations to participate or arranging for participation in activities managed by or on behalf of Viatris. Viatris may need to disclose this personal information to its third- party services providers, who may be located overseas, for these purposes and personal information in the Database is held on Viatris' behalf in servers located overseas in the UK and/or Ireland. By providing your personal information to Viatris, you agree that you understand this Privacy Statement. By providing your personal information (and/or if you are an HCP, the health information of a patient) to Viatris, you consent (and/or confirm that you are authorised by or on behalf of the patient), to Viatris collecting and holding, using and disclosing that personal information for these purposes.

Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

All information forwarded to the Viatris drug safety department is handled in accordance with local privacy laws and may be captured and processed in countries outside of the jurisdiction in which it was collected, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris' drug safety department may contact the patient's HCP to collect further information on the adverse event.

You are not obliged to provide personal information. However, if you do not provide the information, you may not, for example, be able to participate fully in activities managed by us.

You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.4 PHARMACY REGISTRATION

Please complete all mandatory sections of this form.*

This document is a statement of intent by the Nominee Pharmacist and Pharmacy staff to participate in the distribution of Clozaril® (clozapine) in association with the Clozaril® Patient Monitoring System (CPMS).

Signing of this form constitutes a commitment on the part of the Pharmacy and the undersigned to adhere to the CPMS Protocol, and to ensure that pharmacists at the Pharmacy who dispense Clozaril® are registered with the CPMS, and where applicable, comply with the Protocol.

PHARMACY REGISTRATION DETAILS

Pharmacy Type: ☐ Hospital Pharmacy ☐ Community Pharmacy

Pharmacy Name:*

Clozaril® Centre to link to:

Pharmacies linked to a Centre can access patient results and dispense for non-maintenance and maintenance patients.
Non Centre-linked pharmacies can only access results and dispense for maintenance patients.

Phone:* **Fax:**

Postcode:*

Sub Building Name:*
e.g. Pharmacy Name

Building Name:

Address Line 1:*

Address Line 2:

Suburb:*

State:*

If linking to more than one CPMS centre, please add centre names below.

Additional Centre 1:

Additional Centre 2:

Additional Centre 3:

Additional Centre 4:

Additional Centre 5:

Additional Centre 6:

Additional Centre 7:

Additional Centre 8:

Additional Centre 9:

Please see overleaf for further important information about the collection of you and your patient's personal and health information.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

10.4.4 PHARMACY REGISTRATION cont.

Clozaril® purchasing from wholesalers is restricted to CPMS registered Pharmacies. If you require clearance to purchase from wholesalers please include your details below:

Wholesaler	Account Name	Account Number	State

Pharmacy Email:

Before prescribing or dispensing Clozaril® please review the Australian Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/ and the CPMS Protocol available from the eCPMS Information page.

I understand and agree to the conditions for the dispensing of Clozaril® as detailed in the CPMS Protocol, which I have read. I undertake to be bound by the obligations of a Nominee Pharmacist set out in the CPMS Protocol.

As a healthcare professional participating in this activity sponsored by Viatris, I have read and understood the enclosed privacy statement and I agree with it. I understand that information relating to an adverse event with a Viatris product that is identified during this activity will be forwarded to Viatris drug safety department, and possibly to health authorities when required. I understand that my participation in this activity indicates my consent for Viatris' drug safety department to contact me for further information regarding any adverse event identified as part of this activity. If the activity also involves patients, I acknowledge that I must check with my patient before providing the requested follow-up information.

Nominee Pharmacist

Signature:*

Name:* Please print

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150. CPMS will confirm registration via your designated contact method.

Privacy Collection Notice:

Viatris Inc. its subsidiaries and affiliates ('Viatris') collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program ('Program') for participating patients on the Clozaril® eCPMS database ('Database'). This includes registering health care professionals ('HCPs') and patients on the Database, storing patients' blood tests, monitoring patients' use of the products, communicating with HCPs and patients about the products to support the administration and use of the products, complying with regulatory obligations (including the reporting and processing of adverse events patients may experience) and sending invitations to participate or arranging for participation in activities managed by or on behalf of Viatris. Viatris may need to disclose this personal information to its third- party services providers, who may be located overseas, for these purposes and personal information in the Database is held on Viatris' behalf in servers located overseas in the UK and/or Ireland. By providing your personal information to Viatris, you agree that you understand this Privacy Statement. By providing your personal information (and/or if you are an HCP, the health information of a patient) to Viatris, you consent (and/or confirm that you are authorised by or on behalf of the patient), to Viatris collecting and holding, using and disclosing that personal information for these purposes.

Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

All information forwarded to the Viatris drug safety department is handled in accordance with local privacy laws and may be captured and processed in countries outside of the jurisdiction in which it was collected, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris' drug safety department may contact the patient's HCP to collect further information on the adverse event.

You are not obliged to provide personal information. However, if you do not provide the information, you may not, for example, be able to participate fully in activities managed by us.

You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.5 PHARMACIST REGISTRATION

Please complete all mandatory sections of this form.*

This document is my statement of intent to participate in the distribution of Clozaril® in association with the Clozaril® Patient Monitoring System (CPMS). Signing of this form constitutes commitment on my part to adhere to the CPMS Protocol.

I undertake to be bound by the obligations of a pharmacist set out in the CPMS Protocol and understand that notwithstanding these obligations, management of patients for whom I have dispensed Clozaril® remains my sole responsibility.

Make sure you have approval from the Nominee Pharmacist at the CPMS Pharmacy you are registering to join.

DISPENSING REMINDERS

1. Clozaril® may only be dispensed by a CPMS registered pharmacist to a CPMS registered patient.
2. The amount of Clozaril® dispensed must not exceed 7 days for the initial 18 weeks of therapy after which each prescription may be on a 28 day basis (unless the patient has special dispensation).
3. The amount of Clozaril® dispensed is dependent on the pharmacist's review of the patient's current haematological profile. Patients with symptoms of infection or **AMBER** results may only receive up to 4 days medication. Clozaril® must not be dispensed to patients with **RED** results.
4. All prescriptions for Clozaril® must only be filled when either accompanied by a Blood Count Form signed by a CPMS registered doctor, or when results are checked online in eCPMS.
5. Following dispensing, a pharmacist **must** confirm dispensing by signing and faxing a completed Blood Count Form to CPMS or by entering confirmation of dispensing in eCPMS.

PHARMACIST REGISTRATION DETAILS

Have you been registered with CPMS previously? ☐ Yes ☐ No

Title: ☐ First Name:* ☐ Last Name:* ☐

Are you the nominee pharmacist for your Pharmacy?* ☐ Yes ☐ No

CPMS Pharmacy Name:* ☐ Postcode:* ☐☐☐☐

MODE OF COMMUNICATION FOR ALERTS* Selecting Fax/Email means you will receive alerts both within eCPMS and externally. Selecting Web Alerts only means you will only receive alerts within eCPMS.

Selection:* (please tick one) ☐ Fax/Email ☐ Web Alerts

DESIGNATED PRIMARY CONTACT METHOD* Please provide email and/or fax. If you do not provide email you must provide a fax no.

☐ Fax: ☐

Work Phone:* ☐ Mobile: ☐

Email: ☐

Do you have AHPRA registration?* ☐ Yes ☐ No Registration number: ☐

Are you currently registered with CPMS?* ☐ Yes ☐ No

If so, to which Pharmacy?* ☐

Your Postal Address details:

Sub Building Name: ☐

Building Name: ☐

Address Line 1: ☐

Suburb: ☐ State: ☐

Please see overleaf for further important information about the collection of you and your patient's personal and health information.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

10.4.5 PHARMACIST REGISTRATION cont.

FOR REGISTRATION AT ADDITIONAL PHARMACIES COMPLETE THE DETAILS BELOW

2. Pharmacy Name:
   Phone: Fax:
3. Pharmacy Name:
   Phone: Fax:
4. Pharmacy Name:
   Phone: Fax:
5. Pharmacy Name:
   Phone: Fax:

Before prescribing or dispensing Clozaril® please review the Australian Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/ and the CPMS Protocol available from the eCPMS Information page.

I understand and agree to the conditions for the dispensing of Clozaril® as detailed in the CPMS Protocol, which I have read. I undertake to be bound by the obligations of a pharmacist set out in the CPMS Protocol.

As a healthcare professional participating in this activity sponsored by Viatris, I have read and understood the enclosed privacy statement and I agree with it. I understand that information relating to an adverse event with a Viatris product that is identified during this activity will be forwarded to Viatris drug safety department, and possibly to health authorities when required. I understand that my participation in this activity indicates my consent for Viatris' drug safety department to contact me for further information regarding any adverse event identified as part of this activity. If the activity also involves patients, I acknowledge that I must check with my patient before providing the requested follow-up information.

Signature:* Name:* Please print

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150. CPMS will confirm registration via your designated contact method.

Privacy Collection Notice:

Viatris Inc. its subsidiaries and affiliates ('Viatris') collects and holds, uses and discloses personal information, including health information of patients, for the purposes of operating and administering the Clozaril® patient blood monitoring program ('Program') for participating patients on the Clozaril® eCPMS database ('Database'). This includes registering health care professionals ('HCPs') and patients on the Database, storing patients' blood tests, monitoring patients' use of the products, communicating with HCPs and patients about the products to support the administration and use of the products, complying with regulatory obligations (including the reporting and processing of adverse events patients may experience) and sending invitations to participate or arranging for participation in activities managed by or on behalf of Viatris. Viatris may need to disclose this personal information to its third- party services providers, who may be located overseas, for these purposes and personal information in the Database is held on Viatris' behalf in servers located overseas in the UK and/or Ireland. By providing your personal information to Viatris, you agree that you understand this Privacy Statement. By providing your personal information (and/or if you are an HCP, the health information of a patient) to Viatris, you consent (and/or confirm that you are authorised by or on behalf of the patient), to Viatris collecting and holding, using and disclosing that personal information for these purposes.

Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

All information forwarded to the Viatris drug safety department is handled in accordance with local privacy laws and may be captured and processed in countries outside of the jurisdiction in which it was collected, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. Viatris' drug safety department may contact the patient's HCP to collect further information on the adverse event.

You are not obliged to provide personal information. However, if you do not provide the information, you may not, for example, be able to participate fully in activities managed by us.

You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.6 PATIENT HEALTH INFORMATION COLLECTION AND STORAGE CONSENT

Please complete all mandatory sections of this form.*

I have been informed by my medical practitioner about the nature of Clozaril® (clozapine) and the Clozaril® Patient Monitoring System **(CPMS)** procedures associated with its use and provided with a copy of the Clozaril® Consumer Medicine Information leaflet **(CMI)** and the Privacy Collection Notice. I have been given the opportunity to ask my medical practitioner questions about Clozaril® and the CPMS and I understand and am satisfied with the responses that I have received. I understand that, as part of my treatment on Clozaril®, I must have regular blood tests and the results of those blood tests will be monitored via the CPMS. I consent to my personal information (including my name, DOB, sex and blood type) and health information (including blood test results) being collected by Viatris Health Pty Ltd **(Viatris)** and stored in the CPMS database to monitor my blood counts in line with the Privacy Collection Notice. I consent to my information in the CPMS being accessed, used by and disclosed to: the hosts and administrators of the CPMS database as contracted by Viatris, including CPharm Pty Ltd which operates the CPMS, my medical practitioner and his/her staff, the CPMS Quality Assurance Committee, Viatris staff and its authorised contractors, and drug regulatory authorities (together, **CPMS Users**). I acknowledge that the CPMS Users require access to the CPMS to monitor patients on Clozaril® and/or to ensure the proper operation of the CPMS. I understand that CPMS Users may share my information with other CPMS Users, in accordance with the CPMS protocol and in line with the Privacy Collection Notice. I also consent to my information being used in scientific research, which may result in publications or presentations, provided I will in no way be identified through such research.

I understand that all information in the CPMS (including my information) will be cross-checked against third party databases of patients who are receiving (or have received) clozapine under other brand names or from other suppliers and the combined clozapine exclusion database **(CED)** in order to ensure that I, or other patients who have discontinued clozapine treatment on the basis of blood test results, do not recommence treatment.

I understand that my information in the CPMS database may be stored on third party servers located in jurisdictions outside of Australia, such as the United Kingdom and Ireland. I understand that some of those countries may not offer the same level of privacy protection as in Australia. However, I understand that Viatris has agreements with its third party service providers to protect my privacy and keep my information secure.

I understand that Viatris' Privacy Policy (a copy of which is on Viatris' website at https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or available by requesting a copy using the details explained below), explains how to request access to and correction of my personal information in CPMS, how to make a privacy complaint and how my complaint will be dealt with. I understand that I can request access to or correction or updates to my personal information in the CPMS by Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com. I understand that if I transfer to another medical practitioner/centre during my treatment, arrangements must be made to provide my new medical practitioner/centre with access to my information in CPMS to ensure continuity of my care. I understand that if I do not provide my information, my ability to be treated with Clozaril®, and/or the safety and efficacy of such treatment, will be impacted. Viatris is committed to patient safety.

In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris). All information forwarded to the Viatris drug safety department is treated in accordance with local privacy laws and may be captured and processed in countries outside of Australia, and shared with health authorities or other Pharmaceutical companies with whom Viatris has a license agreement, for the purpose of meeting the regulatory requirements for reporting safety information on Viatris products. The Viatris drug safety department may contact a patient's healthcare professional in order to collect further information on the adverse event. I understand that information relating to an adverse event with a Viatris product that is identified during this activity will be forwarded to the Viatris drug safety department, and possibly to health authorities when required. I understand that my participation in this program indicates consent for Viatris' drug safety department to contact my healthcare professional for further information regarding any adverse event identified as part of this activity.

Please see Privacy Collection Notice overleaf.

10.4.6 PATIENT HEALTH INFORMATION COLLECTION AND STORAGE CONSENT cont.

Signature of Patient or Authorised Representative:*		**Date:***	
Name of Patient:*			
Name of Authorised Representative where applicable:*			

*Authorised representative must be legally authorised to act as a Personal Representative of the Patient.

CPMS Centre:*	
Patient Date of Birth:*	

I, being the medical practitioner of the patient referred to above, confirm that I have read the consent, provided the patient with a copy of the Patient Collection Notice and fully explained to the patient the nature, and purpose, of Clozaril® treatment and the associated blood tests, examinations and monitoring described above and I have provided the patient with the Clozaril® CMI leaflet. I understand the nature of the CPMS and I consent to my name and contact information being collected and stored in the CPMS as a treating doctor. I acknowledge that CPMS Users (as defined above) require access to my information to ensure the proper operation of the CPMS.

Signature of Medical Practitioner:*		**Date:***	
Name of Medical Practitioner:*			

Before prescribing please review the CPMS Protocol available from the eCPMS Information page and the Approved Clozaril® Product Information available from https://www.ebs.tga.gov.au/

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Viatris is committed to patient safety. In accordance with regulatory obligations, Viatris has a systematic process in place to collect, store and process reports of adverse events experienced by patients taking a Viatris product, when identified by a Viatris representative (or by a third party acting on behalf of Viatris).

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You have the right to access, update or correct your personal information and/or decline to receive communications from Viatris. To find out how, please refer to our: Privacy Policy https://www.viatris.com/en-AU/lm/countryhome/Privacy-Policy or contact our Head of Global Privacy at, 1000 Mylan Boulevard, Canonsburg, PA 15317, United States, or at, Mylan Health Pty Ltd, PO Box R1462, Royal Exchange Post Office, NSW 1225. Ph: 02 9298 3999. Email: dataprivacy@Viatris.com.

10.4.7.1 PATIENT REGISTRATION FORM

Please complete all mandatory sections of this form.*

PATIENT REGISTRATION DETAILS

PATIENT NAME: (optional)

First Name: | Last Name:

Patient Initials:* | Date of Birth:*

Blood Group:* | Sex:*

1. Has the patient previously received clozapine?* ☐ Yes ☐ No
2. Has the patient ever had an episode of drug-induced neutropenia?* ☐ Yes ☐ No
3. Has the patient ever had a bone marrow disorder?* ☐ Yes ☐ No
4. Has the patient/authorised representative signed the consent form?* ☐ Yes ☐ No

   The Patient Health Information Collection and Storage Consent Form must be submitted to CPMS with this registration form.
5. Does the patient have a diagnosis of benign ethnic neutropenia?* ☐ Yes ☐ No

   If 'Yes', requires assessment by the CPMS consultant haematologist.

If Question 2 or 3 are YES, CPMS haematologist approval to commence is required.
If the response to Question 4 is NO, this patient cannot be commenced on Clozaril® (clozapine).

Has the patient been registered with CPMS previously? ☐ Yes ☐ No

If known, please provide the patient's CPN:

Proposed date of commencement:*

Pre treatment WBC: x 10^9/L Tick box if result is not yet available: ☐

Pre treatment NC: x 10^9/L

Date of blood sample result:

The pre-treatment WBC and NC must be from a blood sample taken ≤ 10 days before starting treatment.
Registration can only be completed after a suitable pre-treatment sample is provided.

Centre Name:*

Centre Co-ordinator:*
Please print

General Practitioner:*
Please print

Pharmacy:*
Please print

Medical Officer:*
Please print

Signature:* | Position:*

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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10.4.7.2 REGISTRATION FORM FOR PATIENT SWITCHING BRANDS

Please complete all mandatory sections of this form.*

First Name: | Last Name:

Patient initials:* | Date of Birth:*

Blood Group:* | Sex:*

1. Has the patient previously received clozapine?* ☐ Yes ☐ No
   If 'No', please complete Patient Registration Form 10.4.7.1
2. Has the patient ever had an episode of drug-induced neutropenia?* ☐ Yes ☐ No
3. Has the patient ever had a bone marrow disorder?* ☐ Yes ☐ No
4. Has the patient/authorised representative signed the consent form?* ☐ Yes ☐ No
   The Patient Health Information Collection and Storage Consent Form must be submitted to CPMS with this registration form.
5. Does the patient have a diagnosis of benign ethnic neutropenia?* ☐ Yes ☐ No
   If 'Yes', requires assessment by the CPMS consultant haematologist.

If Question 2 or 3 are YES, CPMS haematologist approval to commence is required.
If the response to Question 4 is NO, this patient cannot be commenced on Clozaril® (clozapine).

Select one:* ☐ Non-Maintenance Patient ☐ Maintenance Patient

Has the patient been registered with CPMS previously? ☐ Yes ☐ No

If known, please provide the patient's CPN:

Proposed date to start Clozaril® treatment:*

Date the patient initially commenced Clozapine:

Date of last blood:* | WBC: x 10^9/L | NC: x 10^9/L

Monitoring frequency (e.g. weekly, 4-weekly, twice weekly):*

Has there been any therapy interruption in the last 3 months? ☐ Yes ☐ No

If yes, date therapy stopped: | Date restarted:

CPMS Centre:*

Medical Officer:* Please print

General Practitioner:* Please print

Pharmacy:* Please print (For a non-maintenance patient):

Centre Co-ordinator:* Please print

Signature:* | Position:*

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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10.4.7.3 MULTIPLE PATIENTS SWITCHING REGISTRATION FORM

This form is only to be used for multiple patients who are on active clozapine treatment switching to a CPMS Clozaril® (clozapine) Centre and commencing Clozaril® treatment.

Q		1	2	3	4	5
1	Patient's First Name (optional)					
2	Patient's Last Name (optional)					
3	Patient's Initials					
4	Date of Birth					
5	Sex					
6	Blood Group					
7	Has the patient ever had an episode of drug induced neutropenia?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
8	Has the patient ever had a bone marrow disorder?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
9	Has CPMS Consent Form 10.4.6 been signed and attached?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
10	Does the patient have a diagnosis of BEN?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
11	Proposed Clozaril® start date					
12	Date clozapine started initially					
13	Date of last blood test					
14	Last WBC x 10^9/L					
15	Last NC x 10^9/L					
16	Monitoring status (wkly, mthly, amber)					
17	Has there been any therapy interruption in last 3 months?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
18	If YES to Q 17 Interruption Start Date					
19	If YES to Q 17 Interruption End Date					
20	Generic Monitoring Code e.g. AB/12345					
21	CPMS CPN if known e.g. AB/12345					
22	Maintenance Patient	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

If Question 7, 8 or 10 are YES, CPMS haematologist approval to commence is required.
If the response to Question 9 is NO, this patient cannot be commenced on Clozaril®.

Centre:*

Medical Officer:*

Pharmacy:* (For a non-maintenance patient):

Centre Co-ordinator:*

Signature:*

Position:*

Date:*

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150.

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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CLZ-2018-0010

10.4.8 BLOOD COUNT FORM V3

*You **MUST** complete all mandatory* sections when using this form.*

This form can be used to convey results between the doctor, pharmacy and CPMS.

To assist the supplying pharmacy, please indicate if this result has been faxed to CPMS or entered into eCPMS prior to the patient presenting to pharmacy: ☐ Yes ☐ No

First Name:		Last Name:	
CPN:*			
Patient Initials:		Date of Birth:	
Date of blood test:*		Total / highest daily dose (mg):*	

Patient Status	Tick Selection
Initiation Therapy	☐
Maintenance Therapy	☐
Post Treatment	☐

Therapy Interruption	
Number of days	
Date from:	
Date to:	

Patient CPMS Centre:

Days indicated below equals the amount of medication the pharmacy will supply the patient

Next blood test due in: 28 days: ☐ 7 days: ☐ **Or other (state no. of days):**

White cell count (WBC):* x 10^9/L Neutrophil count (NC):* x 10^9/L

Medical Officer Name:*
Please print

Medical Officer Signature:*

If the CPMS haematologist has approved a "Special Range" for this patient's result, please enter the range in the table below for use by the supplying pharmacist.

Name of Laboratory:

PHARMACIST SECTION (not required for post-treatment results)

- Complete all areas & fax form to CPMS OR enter dispensing in eCPMS.
- Before supply, you must confirm acceptable WBC & NC taken within 48 hrs.

Has the prescription been dispensed?* ☐ Yes ☐ No

Pharmacist Name:*
Please print

Pharmacist Signature:*

Date of dispensing:*

Pharmacy:*

WBC and NC results	Range	Action	Special Range
WBC > 3.5 x 10^9/L and NC > 2.0 x 10^9/L	GREEN	Continue with Clozaril® (clozapine) treatment	
WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L	AMBER	Increase monitoring to twice-weekly	
WBC < 3.0 x 10^9/L and/or NC < 1.5 x 10^9/L	RED	STOP immediately and repeat test in 24 hrs	

To submit this form, email to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150.

VIATRIS
Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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CLZ-2018-0011

10.4.9 DISCONTINUATION OF THERAPY FORM

If you are not the Primary Centre Co-ordinator, please ensure they are notified of this request.

POST-TREATMENT MONITORING

For patients on weekly blood test monitoring, a WBC and NC should be performed at least weekly for 4 weeks after discontinuing due to non-haematological reasons.

For patients on 4-weekly blood test monitoring, one further blood count should be performed 28 days after ceasing due to non-haematological reasons. The intention of this is that the patient has a blood test as close as possible to the time of discontinuation and then a follow up count 4 weeks later.

Patients who are on increased monitoring due to symptoms of infection and/or an **AMBER** result (WBC 3.0 - 3.5 x 10^9/L and/or NC 1.5 - 2.0 x 10^9/L) at the time of cessation are required to be tested at least twice weekly until the WBC > 3.5 x 10^9/L, NC is > 2.0 x 10^9/L and/or symptoms of infection have resolved. Once back in the **GREEN** range, perform WBC and NC weekly for 4 weeks.

Patients who have been discontinued due to a **RED** result must continue to have daily blood count monitoring until WBC/NC have returned to the **GREEN** or **AMBER** range. Once back in the **GREEN** range, perform WBC and NC weekly for 4 weeks.

Blood Count forms submitted to CPMS post-treatment do not require a pharmacist's signature.

Patient names are optional, please complete all other sections of this form.

PATIENT NAME: (optional)

First Name: Last Name:

Clozaril® (clozapine) Patient Number (CPN):

Request date:

Transfer to generic? ☐ Yes ☐ No

Patient's CPMS Centre Name:

Primary Centre Co-ordinator:

Co-ordinator Phone Number:

Person completing this form:

Your Phone Number:

Date of last blood test recorded in CPMS:

The last date the patient did or will take Clozaril®:

DUE TO REGULATORY REQUIREMENTS FOR ADVERSE EVENT REPORTING
CPMS MAY CONTACT YOU AFTER SUBMITTING THIS FORM

VIATRIS
Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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10.4.10 PATIENT TRANSFER TO ANOTHER CPMS CENTRE

Please complete all mandatory sections of this form.*

If you do not know the name and contact details for the receiving or sending centre, call CPMS.

Completed by: ☐ Patient's current Centre ☐ Patient's new Centre

PATIENT NAME: (optional)

First Name:		Last Name:	
Clozaril® (clozapine) Patient Number (CPN):*			
Sex:*		Date of Birth:*	
Initials:*		Blood Type:*	
Monitoring frequency:*			

Transfer From

Centre Name:*	
Centre Co-ordinator:*	
Phone Number:*	

Transfer To

Centre Name:*	
Centre Co-ordinator:*	
Phone Number:*	
Receiving Psychiatrist:*	
Receiving Pharmacy:*	
Date of last blood test:*	
WBC count:*	
Neutrophil count:*	
Date next test is due:*	
Clozaril® daily dose:*	
Date to present at new Centre:*	

ONCE COMPLETE, FAX THIS FORM TO THE CPMS

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

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CLZ-2018-0013

10.4.11 DISPENSATION FORM

Under special circumstances Viatris may approve the dispensation of additional medication for a patient and therefore an extension of their blood test period.

Approval of additional medication does not extend to patients with current blood test results in the **AMBER** range or to patients showing any signs of infection.

Dispensation requests can be made online at any time or by fax or email to the CPMS office using this form. Weekly patients can be given up to two days dispensation and 4-weekly patients up to two weeks. Approval is automatic if blood results are up to date and in the **GREEN** range.

If you have already requested a dispensation for this patient and are requesting a further extension, approval by the CPMS haematologist will be required.

Dispensations for longer periods of time must be approved by the CPMS Consultant Haematologist and must be organised through the CPMS.

Patient names are optional, please complete all other sections of this form.

PATIENT NAME: (optional)

First Name:		Last Name:	
Clozaril® (clozapine) Patient Number (CPN):*			
Request date:*			
Number of days requested:*			
Patient status:*			
Centre Name:*			
Person completing this form:*			
Your Phone Number:*			
Date of the last blood test recorded in CPMS:*			
Date next test due before dispensation:*			
Date blood test due after dispensation:*			

Email: cpms@cpharm.com.au
Address: Level 1, 30 – 34 Hickson Rd, Millers Point NSW 2000
Telephone: 1800 501 768
Fax: 1800 550 150

10.4.12 LABORATORY REGISTRATION FORM

Please complete all mandatory sections of this form.*

This document enables registration of a Laboratory to process blood samples of patients treated with Clozaril® (clozapine) in association with the Clozaril® Patient Monitoring System (CPMS).

Laboratory Name:*		**Postcode:***	
Sub Building Name:			
Building Name:			
Address Line 1:*			
Address Line 2:			
Suburb:*		**State:***	
Phone:*		**Fax:**	
Local Laboratory Code:			
CENTRE TO LINK TO THIS LAB:			
OTHER CPMS CENTRES TO BE LINKED TO THIS LABORATORY:			
Centre Name 2:			
Centre Name 3:			
Centre Co-ordinator completing this form:			

To complete registration, email this form to CPMS at cpms@cpharm.com.au or via Fax 1800 550 150.

Privacy Collection Notice:

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10.5 FAQ Regarding 1st July 2015 PBS Changes

The Commonwealth Government introduced changes to the PBS Section 100 for Clozaril from 1st July 2015. These changes aim to provide equitable access to medicines for stable patients.

What are the changes?

- New prescriber codes define patients as maintenance or non-maintenance.
- The same existing procedures apply for non-maintenance patients.
- Maintenance patients are now able to have scripts filled at the pharmacy of their choice.
- Private psychiatrists not affiliated with HSD facilities are now able to manage maintenance patients.

What are the criteria for identifying a patient as maintenance?

If the treating psychiatrist makes a clinical assessment that the patient's mental health status is stable, and they have completed the initial 18 weeks of weekly blood tests they may be identified as maintenance. Other factors the clinician may consider include stable dosage and the individual response to medication. The patient must be treated by a psychiatrist or by an authorised medical practitioner, with the agreement of the treating psychiatrist and must be under the supervision and direction of a psychiatrist reviewing the patient at regular intervals.

How do community pharmacies participate in the CPMS program?

Contact CPMS on 1800 501 768 to receive a copy of the CPMS protocol and registration forms. Community pharmacies not linked specifically to CPMS centres can dispense for maintenance patients. The role of a pharmacist is to check the patient's blood result accompanying the script, and if appropriate, to dispense the amount of medication required to last the patient until their next presentation at a pharmacy after their next blood test (usually 28 days). Confirmation of dispensing must either be entered into eCPMS or a completed blood count form faxed to CPMS.

What do pharmacists do if patients present late to pick up medication?

A prescription should be dispensed and supplied within 48 hours of a blood test. If a patient is late presenting to pharmacy to receive medication, the amount dispensed should be altered so that only enough medication is dispensed to last the patient until their next presentation at a pharmacy after their next blood test (usually 28 days). The confirmation date for dispensing in eCPMS should be the supply date. You should also advise the prescriber if the patient has presented late as they may require a repeat blood test or have had a treatment break and require re-titration.

What do pharmacists do if a non-maintenance patient presents from a Centre you are not connected to?

If a non-maintenance patient presents at your pharmacy from a CPMS centre you are not connected to, call CPMS on 1800 501 768 and they will assist with contact details for the patient's centre. Your pharmacy can be linked to the Centre if requested by the hospital pharmacy, Medical Officer or a centre coordinator.

How do pharmacists check results and communicate dispensing to CPMS?

Any CPMS-registered pharmacist can search for a patient's profile using their CPN and enter results or confirm dispensing online via eCPMS. Alternatively, if the patient presents using paper blood count forms the pharmacist can simply fax the completed form with their signature to CPMS.

How will health care staff know where to direct patients for dispensing?

Use eCPMS search to find pharmacies by post code and locate pharmacies on the Google Maps feature. The eCPMS Pharmacies report lists all registered pharmacies nationally so you can direct patients to approved pharmacies.

Is brand substitution permitted?

Patients must be registered to the blood monitoring service for the brand they are taking, so in order to change brands the clinician and patient would have to be transferred and registered with the alternative service first. There are significant drug safety issues if a patient were to have a neutropenia episode requiring urgent medical management by the company responsible (the brand consumed) and that company did not have registration and blood history details on the patient.

What other prescriber instructions are recommended to assist pharmacists?

Pharmacists are required to log dispensing against a specific blood result with CPMS. Prescribers assist pharmacists by either writing the patient's CPN on prescriptions or by attaching a CPMS Blood Count form [10.4.8] to a prescription. Using a CPN is the easiest way for the pharmacist to search for blood results in eCPMS (search is also possible with initials and date of birth). Ensure blood results are entered into CPMS before the patient presents at a pharmacy. This facilitates the pharmacist finding the correct result online against which to confirm dispensing. Alternatively, use CPMS blood count forms [10.4.8].

How do the changes affect co-management and prescribing by GPs?

Existing state and territory authorisations for shared care arrangements apply (some states and territories require special authorisation). In order to check blood results or to complete prescriptions for Clozaril®, GPs must be registered in the CPMS system and connected in CPMS to the patient's centre.

GPs already registered with CPMS as Medical Officers should contact CPMS to request their profile be changed to indicate they are a GP.

In summary,

- From 1st July 2015 clinicians can identify stable patients as 'maintenance'.
- Maintenance patients are able to have their prescriptions filled at the CPMS-registered pharmacy of their choice.
- eCPMS assists healthcare staff managing maintenance patients by providing reports and Google map features in search to identify CPMS registered pharmacy locations.

For further information please call CPMS on 1800 501 768.

10.6 FAQ Regarding Patient Consent

Is this consent to treatment or for storing information?

This is only consent for Viatris to collect and store the patient's health information, such as blood test results and patient identification. Clinicians have separate legislative obligations such as local jurisdiction mental health acts which outline the responsibilities for fully informing patients or their legal representatives regarding the risks and benefits of treatment.

Who has access to the information?

Access to health information collected and stored in CPMS is strictly controlled by privacy and health records laws and reinforced by Viatris' Privacy Collection Notice, Patient Consent and Privacy Policy. Access to information is only provided where the purpose relates to either a regulatory obligation, or for the principal purpose for which the database exists i.e. to meet TGA drug safety requirements ensuring adequate blood monitoring of patients on Clozaril®.

Who can sign the form and who is an authorised representative?

If the clinical judgement of the clinician instigating treatment is that the patient is suitably capable of understanding the requirements of the consent process, then the patient should sign the form. If the clinical opinion is that the patient is not able to understand and appreciate the reason why Viatris is required to collect and store health information to enable blood monitoring, then a legally authorised person can sign on their behalf. An authorised person could include a legal guardian, parent, or in some cases the medical specialist who has decided to instigate Clozaril® treatment.

Why would treatment be impacted if consent was not provided?

Viatris is bound by legal requirements to ensure the patient's rights are protected. Save in certain exceptional circumstances permitted by applicable privacy and health records laws, if consent to collect and store the required information in CPMS is not given, Viatris is not permitted to do so.

Why does Viatris need a copy of this consent?

By securely storing the health information consent forms with patient registration, Viatris can meet its regulatory obligations to government authorities and evidence that the information in CPMS was collected in a manner consistent with the privacy laws and health records laws which protect the patient's rights.

Why are patient names stored in the database?

The accurate identification of individual patients in CPMS is critical to ensure patient safety. As the number of patients in the database grows, the ability to correctly individualise each person becomes more difficult. Adding patient names strengthens our ability to ensure correct patient identification.

10.7 References

1. Clozaril (clozapine) Australian TGA approved Product Information.
2. Casey D.E., 'Clozapine: neuroleptic-induced EPS and tardive dyskinesia.' *Psychopharmacology* (Berl.) 99: S47-S53.
3. Fitton A. and Heel R., 'Clozapine. A review of its pharmacological properties, and therapeutic use in schizophrenia.' *Drugs* 1990; 40: 722-747.

WARNING

Clozapine induced gastrointestinal hypomotility

Clozapine induced gastrointestinal hypomotility: Severe gastrointestinal adverse reactions have occurred with the use of clozapine resulting in potential outcomes of hospitalisation, surgery and death (see Section 4.4 Special warnings and precautions for use, and Section 4.8 Adverse effects (undesirable effects)). Prior to initiating and during treatment with CLOZARIL, screen for constipation and if necessary, manage as per current clinical guidelines.

Myocarditis

Cases of myocarditis, some of which have been fatal, and cardiomyopathy have been reported in patients on clozapine (see "4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE" and "4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)"). If myocarditis or cardiomyopathy is suspected, Clozaril treatment should be stopped and the patient immediately referred to a cardiologist. Generally, patients with a history of clozapine-associated myocarditis or cardiomyopathy should not be rechallenged with Clozaril.

PBS Information: This product is listed on the PBS as a Section 100 item.
Refer to PBS Schedule for full authority information.

Please review the full Product Information (PI) before prescribing, available at https://medsinfo.com.au/product-information/document/Clozaril_PI or on request by calling 1800 931 383.

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