Government of **Western Australia**
Department of **Health**

Guidelines for the use of the WA Clozapine Initiation and Titration Chart

Version 08/22 of Chart

Medicines and Technology Unit in collaboration with North Metropolitan Mental Health Service

Contents

Acknowledgements

WA Health acknowledges contributions from North Metropolitan Mental Health Service and Queensland Health Medication Management Services in the development of this chart.

To obtain further information or queries, contact the Medicines and Technology Unit, Patient Safety and Clinical Quality Directorate, Department of Health, Western Australia (DoH.MedicinesandTechnologyUnit@health.wa.gov.au).

In order to maintain the standard safety components and adhere to the underlying principle of standardisation to optimise patient safety, sections of the chart other than the hospital logo and MR number are not to be changed without approval of the Medicines and Technology Unit, Patient Safety and Clinical Quality Directorate, Department of Health.

Recommendations for change to these charts should be lodged to the WA DoH Medicines and Technology Unit. Recommendations for change must be evidence based, with the primary objective of improving patient safety. MTU will screen these requests and escalate to the WA Medication Safety Collaborative where appropriate.

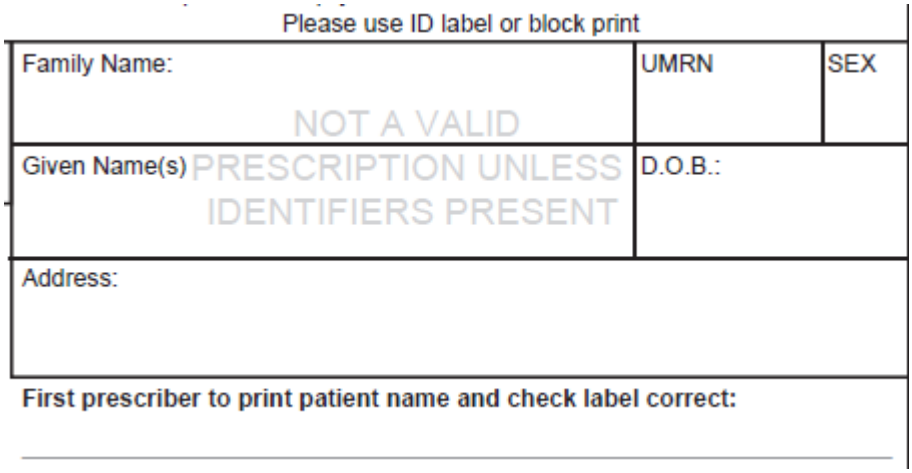
1. GENERAL INSTRUCTIONS

The following are general requirements regarding use of the WA Clozapine Initiation and Titration Chart:

- The use of the WA Clozapine Initiation and Titration Chart is restricted to mental health inpatient units under the supervision of a psychiatrist.
- All prescribers must order clozapine for inpatients in accordance with the WA Poisons Regulations.
- The Clozapine Initiation and Titration Chart should be completed for all inpatients initiated and re-titrated on clozapine.
- The WA HMC medication chart must be annotated clearly to identify when a Clozapine Initiation Chart is in use.
- The Clozapine Initiation Chart must be kept with all the other medication charts.
- All orders are to be written legibly in black ink. Water soluble ink (e.g. fountain pen) should not be used.
- A clozapine order is valid only if the prescriber enters all the required items.
- Only use acceptable abbreviations.
- No erasers or whiteout can be used.

2. FRONT PAGE OF CLOZAPINE INITIATION CHART

2.1 Identification of the patient

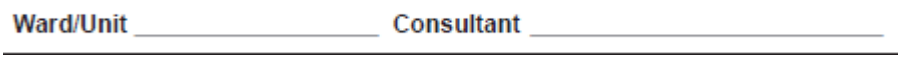


A watermark has been placed on the "Patient Identification Section" as a reminder that a prescription is not valid unless the patient's identifiers are present on pages 1 and 2 of the chart; that is:

- EITHER the current patient identification label
- OR, as a minimum, the patient's name, UMRN number, date of birth and gender written in legible print

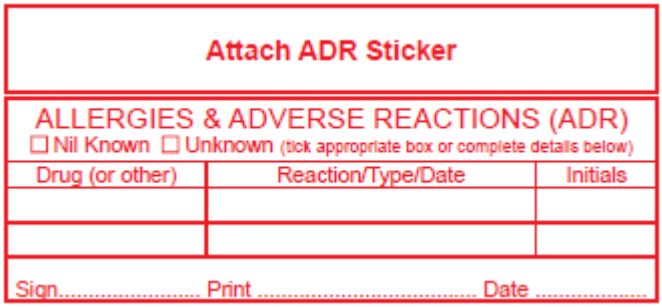
The first prescriber **must handwrite (PRINT)** the patient's name under the addressograph. This will reduce the risk of wrong identification label being placed on the chart and the wrong medication given to a patient.

2.2 Patient Location



The patient's location should be clearly marked on the clozapine initiation chart as well as the treating team or consultant.

2.3 Adverse Drug Reaction Alerts



Attach ADR Sticker		
ALLERGIES & ADVERSE REACTIONS (ADR) ☐ Nil Known ☐ Unknown (tick appropriate box or complete details below)		
Drug (or other)	Reaction/Type/Date	Initials
Sign..... Print ..... Date		

The first prescriber is required to complete the "Allergies and Adverse Drug Reactions (ADR)" details for all patients.

If the patient is not aware of any previous Adverse Drug Reaction, the Nil Known box should be ticked and the person documenting the information must date and sign the entry.

If a patient's Adverse Drug Reaction is unobtainable, the Unknown box should be ticked and the person documenting the information must date and sign the entry.

If a previous ADR exists, then the following must be completed:

a. Document the following information in the space provided on the medication chart:
   - Drug (or other allergen) name
   - Reaction/Type details (e.g. rash, diarrhoea)
   - Date of reaction (or approximate timeframe e.g. 20 years ago)
   - The initials of the person documenting the information
   - Sign entry

   This is the minimum information that should be documented. It is preferable also to document how the reaction was managed (e.g. 'withdraw & avoid offending agent') and the source of the information (e.g. patient self-report, previous documentation in medical notes etc).

b. Affix an ADR alert sticker to the front of the chart in the space provided

2.4 Preparation Prior to Clozapine Initiation

2.4.1 Pre-commencement

It **must** be a Consultant Psychiatrist that authorises the initiation of clozapine treatment.

The treating team **must** document:

- The indication for the use of clozapine (page 2 of chart)
- Whether the patient has any chronic medical condition and if so, document the condition in the space provided
- Whether the patient has a personal or family history of cardiovascular disease and if so, document the history in the space provided
- Whether the patient has a history of epileptic seizures and if so, document the details in the space provided

2.4.2 Before commencing clozapine

All boxes on the checklist **must** be ticked / addressed in the pre-commencement screen before clozapine treatment can be initiated.

The treating team **must** check:

- Whether the patient has been adequately trialled on 2 or more other antipsychotics and were found to be either non-responsive or intolerant to the antipsychotics
- Psychiatrist has completed and returned the 'Clozapine registration form for new patients' to a pharmacist
- Whether the patient meets PBS eligibility
- Continuation of supply at a registered clozapine centre has been considered
- Patient/carer/family has signed the Monitoring System Privacy statement
- Patient/carer/family has been provided with written Medication Information and the treatment explained
- Patient/guardian has given informed consent, or second opinion obtained (if applicable)
- All Pre-Clozapine Baseline Tests have been performed before clozapine commencement
- Full blood picture (FBP), C-Reactive Protein (CRP) and troponin to be performed within 10 days before clozapine commencement.

The Consultant Psychiatrist **must** print name, sign and date that all the checks and documentations have been completed prior to commencing clozapine therapy.

2.5 Observations

Observations during the first 7 days of therapy **MUST** be documented on the front of the WA Clozapine Initiation and Titration Chart **AND** on the Adult Observation and Response Chart used within the organisation.

All observations **must** be reviewed by the treating team.

2.5.1 Baseline Observations

The following baseline observations **must** be conducted prior to administering the first dose of clozapine:

- Temperature
- Pulse
- BP (standing BP and lying down BP)
- Respiratory Rate

The person conducting the baseline observations must record the date, time and observations in the provided space.

Temp- Black Pulse -Red	**Baseline** (Prior to 1st dose): Respiratory Rate____breaths/min Date___/___/___ Time ___:___ Temp ___°C Pulse ____bpm Standing BP____mmHg Lying BP ____mmHg

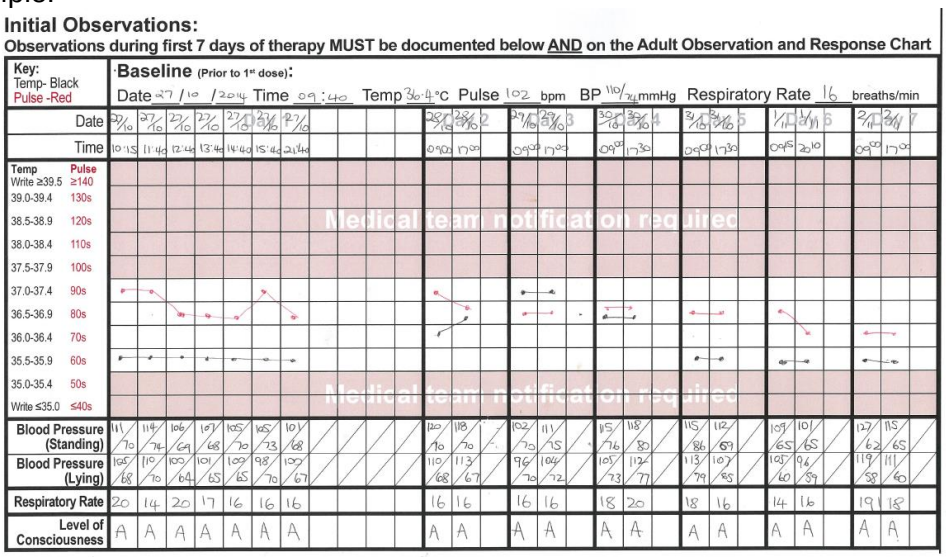
2.5.2 Observations for the first 7 days of clozapine therapy

Observations for the first week of clozapine therapy must be recorded on the WA Clozapine Initiation and Titration Chart AND on the Adult Observation and Response Chart.

The following observations **must** be conducted and documented in the corresponding spaces of the observation chart:

- Temperature (To be plotted using a black ink pen)
- Pulse (To be plotted using a red ink pen)
- BP (To be written legibly)
- Respiratory Rate (To be written legibly)
- Level of consciousness (To be written legibly)

For example:



The person conducting the observations must record the date and time of that specific observation in the spaces provided.

2.5.3 Prompts when to notify doctor with a concerning observation

All nursing staff should be familiar with the prompts for when to notify a doctor with a concerning observation.

A doctor (preferably in the patient's clinical care team) **must** be informed of any results showing cause for concern or if a patient refuses observations.

The area of the observation chart that is shaded in red also prompts the need when to notify a doctor.

2.5.4 Recommended guidelines for frequency of clozapine observations

All nursing staff should be familiar and adhere to the recommended guidelines for frequency of clozapine observations.

Recommended guidelines:

Day 1:	Temperature, respiratory rate, pulse and BP hourly for the first six hours **(mandatory),** then every six hours for the first 24 hours (observations after the first six hours is only recommended if patient is still awake). Additional columns are available to allow increase monitoring if deemed necessary
Day 2 to 7:	Temperature, respiratory rate, pulse and BP twice daily **(mandatory)** or more frequently if clinically required
Week 2 to 18:	Temperature, respiratory rate, pulse and BP daily **(mandatory)** or more frequently if clinically required
After 7 days, observations **must** be continued based on the above guidelines on the Adult Observation and Response Chart.	

3. MIDDLE PAGES OF CLOZAPINE INITIATION CHART

3.1 Clozapine Only Medication Orders

The chart has been formatted to facilitate the escalating dose of clozapine.

The following information should be documented by the prescriber:

a. **Formulation**
   Considering clozapine comes in either tablets or suspension, it is advisable to document the type of formulation
b. **Clozapine Patient Number**
   This number is only allocated once the patient is registered with the clozapine monitoring service
c. Indication
   This allows the order to be reviewed in the context of why clozapine was prescribed

The **'Pharmacy use'** section is for the use by the clinical pharmacist to give recommendations or instructions on safe administration of clozapine.

The '**Weekly monitoring until'** is used to record the date until when clozapine weekly monitoring should be continued.

A clozapine order is valid only if the prescriber enters:

a. **Date prescribed**
   The date of the clozapine order **must** be the date the drug is to be administered and **must** be written **within 10 days** of when FBC, CRP and troponin are taken. The clozapine order **must** only be prescribed when the patient receives a valid patient clozapine number.
   To allow proper monitoring, commence clozapine in the morning and avoid weekends (preferable to start early in the week).
b. **Blood test due**
   Tick the appropriate day when the next blood test is due.
c. **Doctor (Prescriber) Signature and PRINT Name**
   The signature of the prescriber must be written to complete each day of clozapine order. Each medication order must also have the printed name of the prescriber.
d. **Dose**
   Doses must be written using **metric** and **Arabic** (1, 2, 3…) systems. Never use Roman numerals (i, ii, iii…).

Two nurses are to '**double sign'** each dose indicating dose checked and administered.

The **'Drug level'** section should be used to document clozapine drug level.

The clinical pharmacist will sign the **'Pharmacy'** section as a record that they have reviewed the clozapine initiation chart on that day.

Reason for not administering

When it is not possible to administer the prescribed medicine, the reason for not administering must be recorded by entering the appropriate code as per the WA HMC medication charts (refer across) and circling this code.

Reason For Not Administering (codes must be circled)							
Absent	(A)	On Leave	(L)	Refused-notify doctor	(R)	Vomiting – notify doctor	(V)
Fasting	(F)	Not Available - obtain supply and/or notify doctor, consider incident report	(N)	Withheld-enter reason in clinical record	(W)	Self- Administering – observed or claimed	(S)

- If a patient refuses clozapine, the **treating team must be notified**.
- If clozapine is withheld, the reason must be documented in the patient's medical notes.
- If clozapine is not available on the ward, it is the nurse's responsibility to notify the pharmacy and/or obtain supply or to contact the treating team to advise that the medicine is not available.

Ceased Order

Once clozapine dose has stabilised, clozapine can be ceased on the WA Clozapine Initiation and Titration Chart and prescribed on the WA HMC chart.

When ceasing an order, the original order must not be obliterated. The doctor must:

- Draw a clear line through the order
- Write the reason for changing the order (cease, increased dose etc.)
- Initial and date the cessation of the order

3.2 Clozapine Titration Schedule

Clozapine should be commenced at a low dose and increased gradually in order to minimise side-effects. A suggested dosage escalation based on the Maudsley Prescribing Guidelines is located on the chart.

Clozapine Dose Titration Schedule

This table serves as a guide only and dose titration should be individualised – refer to treating psychiatrist.
Patients > 65 years of age may require a slower dose increase titration regimen.
Titration beyond 200mg/day: If well tolerated, the daily dose may be increased slowly in increments of 25-50mg (maximum 100mg/week).

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Morning	12.5mg	25mg	25mg	25mg	25mg	25mg	25mg	25mg	50mg	50mg	50mg	50mg	50mg	50mg
Evening				25mg	25mg	50mg	75mg	100mg	100mg	100mg	125mg	125mg	125mg	150mg

Dosage escalation should be titrated to each individual and the Pharmacy Department can be contacted if there are any concerns.

3.3 Monitoring and Blood Testing

The Monitoring checklist contains a suggestive list of measurements that are recommended for patients on clozapine. These are suggested guidelines only and do not replace the need for clinical discretion. Refer to the treating psychiatrist for individual monitoring requirements.

The following pre-clozapine baseline measurements **must** be completed prior to commencing clozapine therapy:

- Blood group
- Full physical examination
- Full blood count (FBC)* including:
  - White cell count (WBC)
  - Neutrophils (NC)
  - Eosinophils
- Troponin/ CK-MB*
- C-Reactive Protein (CRP)*
- Beta HCG (if applicable for females)
- Echocardiogram (ECG)
  - QT interval

*These are to be completed within **10 days** before clozapine commencement.

The following pre-clozapine baseline measurements are also recommended:

- Smoking status
- Weight & Height
- Waist circumference
- Body Mass Index (BMI)
- Dietician review
- Liver Function Test
- Urea & Electrolytes
- Fasting plasma glucose
- Fasting lipid profile

The person conducting the monitoring **must** record and date the measurements in the space provided. Should it be required, there are spaces to record weekly measurements up to 28 days. The full blood count **must** be recorded every week in the spaces provided.

The chart also provides a suggestive guideline for the frequency of monitoring.

Blood samples generally taken on the same day of the week (usually taken on Tuesdays).

4. BACK PAGE OF CLOZAPINE INITIATION CHART

4.1 Clozapine Blood Results Monitoring System

Clozapine can cause agranulocytosis, which is a potentially fatal adverse effect. Therefore, as part of the monitoring process, all patients on clozapine **must** have regular full blood counts.

The chart provides a traffic light system with the classification of each colour and the recommended action.

Clozapine Blood Results Monitoring System		Recommended Action
Green Range	WBC greater than 3.5 x 10^9/L AND Neutrophils greater than 2.0 x 10^9/L	Continue clozapine therapy
Amber Range	WBC 3.0 - 3.5 x 10^9/L AND/OR Neutrophils 1.5 - 2.0 x 10^9/L	Continue clozapine therapy with twice-weekly blood tests until return to "green" range
Red Range	WBC less than 3.0 x 10^9/L AND/OR Neutrophils less than 1.5 x 10^9/L	Stop clozapine therapy immediately. Contact haematologist and Clozapine Monitoring Centre

It is the responsibility of the clinical team to ensure results are safe.

4.2 Recommencing Therapy After Interruption

This section provides the recommended guidelines when recommencing clozapine in the event of a missed dose **over 48 hours ago**.

Recommencing Therapy after Interruption
Dosing recommendations if clozapine dose is missed for > 48 hours • Obtain psychiatric review prior to recommencing clozapine • Recommence at 12.5mg once or twice daily on the first day. Refer to what side effects the patient had previously when starting clozapine. The rate of re-titration can be adjusted to take into account emergent side effects and period of interruption • This is a guide only – for further dosing options refer to treating psychiatrist.

If the last prescribed dose was taken **within 48 hours**, then the dose should be given at the normal time. Staff should not attempt to make up for the missed dose by giving more.

4.3 Blood Test Monitoring After Interruption of Therapy

This section provides the recommended guidelines for blood test monitoring in the event of missing a dose **less than 72 hour**; **more than 72 hours but less than 4 weeks** and **more than 4 weeks.**

Blood Test Monitoring after Interruption of Therapy			
Monitoring frequency	**Clozapine missed for < 72 hours**	**Clozapine missed > 72 hours but less than 4 weeks**	**Clozapine missed > 4 weeks**
Weekly	No change in monitoring	Monitor weekly for at least 6 weeks or for as long as necessary to achieve a total of 18 weeks of weekly monitoring	Recommence as for a new patient
Monthly		Monitor weekly for 6 weeks then continue with monthly monitoring if no problems detected	

The treating team **must** adhere to these guidelines when doses are missed.

4.4 Side Effects Associated with Clozapine Therapy

This list of side effects is adapted from the Maudsley Prescribing Guidelines. It provides a list of the more common side effects that are related to clozapine and their signs and symptoms.

Staff should carefully monitor patients for side-effects and respond to the recommended action. For a list of pharmacological options and actions, the treating team should contact the clinical pharmacist.

Side effects Associated with Clozapine Therapy Modified from Maudsley Prescribing Guidelines 13th ed 2018		
Side effect	**Signs and symptoms / Onset**	**Recommended Action**
Neutropenia / agranulocytosis	WBC < 3.0 x 10^9/L or Neutrophils < 1.5 x 10^9/L. Flu-like symptoms such as sore throat & fever. (First 18 weeks – but may occur at any time)	Contact doctor. Withhold clozapine. Contact haematologist at Clozapine Monitoring Centre.
Myocarditis / cardiomyopathy	Fast or irregular heartbeat at rest with rapid breathing, dyspnoea, hypotension, raised jugular venous pressure, fatigue, infective symptoms (including gastrointestinal, urinary, and/or respiratory), chest pain or fever. Cardiomyopathy may occur at any time. Myocarditis – within 6 weeks of starting)	Withhold Clozapine. Repeat ECG and echocardiogram. Check C-Reactive Protein (CRP) and troponin. Refer to cardiologist. If confirmed contact cardiologist at clozapine monitoring centre.
Fever	> 38° C (First 3 weeks)	Contact doctor. Reduce rate of dose titration of clozapine. Check FBC, WBC, neutrophils, troponin and CRP. Physical examination for signs of infection. Consider ECG, Echocardiogram. Give paracetamol and notify doctor to exclude agranulocytosis / myocarditis.
Seizures	Increases with high doses, rapid dose titration, concurrent use of drugs that lower seizure threshold and preexisting seizure disorders and concurrent illness. (May occur at any time)	Medical emergency, manage seizure and withhold clozapine for one day. Consider prophylactic antiepileptic. Dose may need to be reduced. Risk of seizures increases with higher serum levels. Check serum levels.
Hypersalivation	Excessive drooling – Very troublesome at night. (First few months)	Contact doctor. Check with pharmacist for pharmacological options.
Constipation	Less frequent bowel motions, hard stools, abdominal bloating, cramping or pain, decreased appetite or fatigue. (Usually persists) Severe Clozapine Induced Gastrointestinal Hypomotility (CIGH) can be fatal.	Contact doctor. Recommend increased fluid intake and exercise. Consider pre-emptive laxatives for all patients. Review contributing medicines and consider dose reduction. Treat CIGH aggressively with laxatives and consider cessation of clozapine if treatment fails. Avoid bulk forming laxatives.
Nocturnal enuresis	Loss of bladder control, especially at night. (May occur at any time)	Contact doctor. Avoid fluids after 7pm. Check males for other causes. Continence referral. Check with pharmacist for pharmacological options.
Weight gain	This may occur early in treatment and can be significant	Dietary and lifestyle counselling before weight gain occurs. Ongoing monitoring and support.
This is not an exhaustive list of side effects. Please see product information for further advice. It is recommended that concurrent use of antipsychotic therapy be avoided where possible as this increases the patient's risk of side effects.		

5. Contact Information

CLOPINE™ (Pfizer)

Medical Information https://www.pfizermedicalinformation.com.au/en-au/clopine or phone 1 800 675 229 (9AM to 5PM AEST) Monday to Friday

ClopineCentral™ is a registry service designed to provide patient haematological monitoring. https://www.clopine.com.au/ClopineCentral/

Please visit www.clopine.com.au or phone 1800 656 403.

Clopine Hub contains information for health care professionals to optimise patient care and supplement the support from ClopineCentral™. Access protocol information, patient support materials and other useful resources. www.clopinehub.com.au

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