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

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

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

Version 5, 2024

Contents

Acknowledgements

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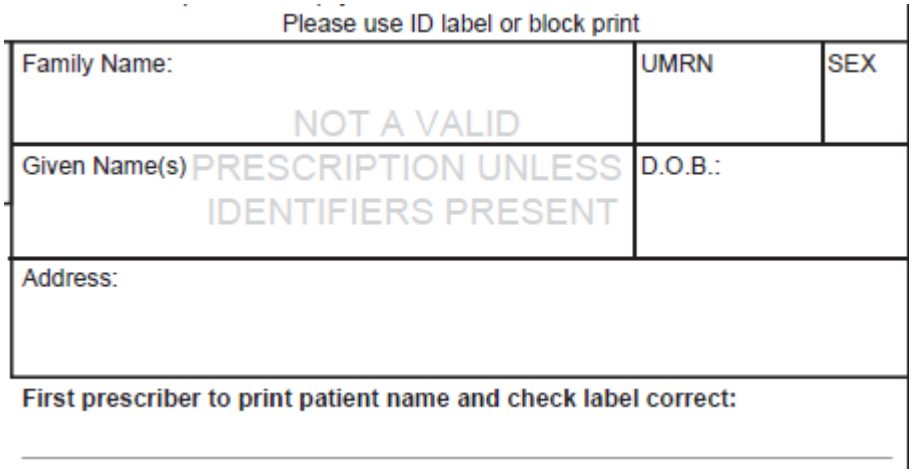
1. General instructions

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 WA Clozapine Initiation and Titration Chart should be completed for all inpatients initiated and re-titrated on clozapine.
- The WA Hospital Medication Chart (HMC) medication chart must be annotated clearly to identify when a WA Clozapine Initiation and Titration Chart is in use.
- The WA Clozapine Initiation and Titration 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 completes all required sections of the WA Clozapine Initiation and Titration Chart.
- Only use acceptable abbreviations.
- No erasers or whiteout can be used.
- The *Guidelines for the Safe and Quality Use of Clozapine in the WA health system* provide further clinical guidance regarding the initiation and titration of clozapine.

2. Front page

2.1 Identification of the patient

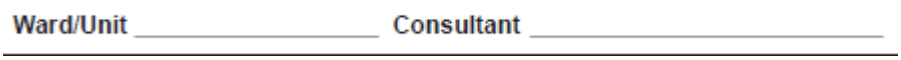


A watermark has been placed on the "Patient Identification Section" as a reminder that a prescription is not valid unless the patient's identifiers are present on pages 1 and 2 of the chart; that is:

- 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 ADRs, the "Nil Known" box should be ticked and the person documenting the information must date and sign the entry.
- If a patient's ADR history 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, the ADR needs to be completely documented according to the WA Clinical Alert (MedAlert) Policy MP 0053/17.

2.4 Preparation Prior to Clozapine Initiation

2.4.1 Pre-commencement screen

Prior to commencing/charting clozapine the following section of the chart should be reviewed. This section will guide the clinician which section of the chart needs to be completed.

Tick the applicable box:
☐ Initiating / Recommencing after interruption of 3 months or more (complete pre-commencement screen)
☐ Recommencing after interruption of more than 48 hours up to 3 months (refer to dose and monitoring requirements on page 4)
☐ Continuing titration

Pre-commencement Screen

Pre-commencement Screen is required to be completed: ☐ Yes ☐ No
All sections below must be completed prior to clozapine initiation or when clozapine has been discontinued for 3 months or more.

Medical History:

Patient has chronic medical conditions ☐ No ☐ Yes Details_____
Patient has a personal or family history of cardiovascular disease ☐ No ☐ Yes Details _____
Patient has a history of epileptic seizures ☐ No ☐ Yes Details _____

Clozapine checklist:

☐ Patient has been adequately trialled on 2 or more other antipsychotics ☐ No ☐ Yes Details_____
☐ Clozapine registration form for new patients has been submitted
☐ 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), CRP and troponin to be performed within 10 days before clozapine commencement.

Consultant Name: Signature: Date:

Tick the applicable box:
☐ Initiating / Recommencing after interruption of 3 months or more (complete pre-commencement screen)
☐ Recommencing after interruption of more than 48 hours up to 3 months (refer to dose and monitoring requirements on page 4)
☐ Continuing titration

The clinician is to tick the most appropriate box for their patient, per the following circumstances:

Initiating / Recommencing after interruption of 3 months or more *(complete pre-commencement screen)*

- A new patient is commencing clozapine for the first time (where dose titration is needed, the pre-commencement screen must be completed, weekly monitoring for 18 weeks needs to be commenced and the patient needs to be registered with a clozapine monitoring service)
- A patient that was discontinued on clozapine for a period of 3 months or more and is now recommencing clozapine (where dose titration is needed, the pre-commencement screen must be completed, weekly monitoring for 18 weeks needs to be commenced and the patient needs to be re-registered with a clozapine monitoring service).

Recommencing after interruption of more than 48 hours up to 3 months *(refer to dose and monitoring requirements on page 4)*

- A patient who has missed more than 48 hours but not more than 72 hours of clozapine therapy (where dose re-titration is needed but additional monitoring is not required)
- A patient who has missed more than 72 hours but not more than 28 days of clozapine therapy (where dose re-titration is needed, and weekly monitoring needs to be recommenced for 6 weeks or as long as necessary to achieve 18 weeks of weekly monitoring if already on weekly monitoring)
- A patient who has missed more than 28 days but not more than 3 months of clozapine therapy (where dose re-titration is needed, and weekly monitoring for 18 weeks needs to be recommenced).

Continuing titration

- A patient who is continuing clozapine dose titration (if dose has not yet stabilised at completion of the previous WA Clozapine Initiation and Titration Chart).

The initiation of clozapine treatment can **only** be authorised by a Consultant Psychiatrist.

The treating team **must** document:

- 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.

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

Clozapine checklist:

- ☐ Patient has been adequately trialled on 2 or more other antipsychotics ☐ No ☐ Yes Details_____
- ☐ Clozapine registration form for new patients has been submitted
- ☐ 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), CRP and troponin to be performed within 10 days before clozapine commencement.

Consultant Name: Signature: Date:

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
- Blood pressure (BP) (standing and lying)
- Respiratory Rate

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

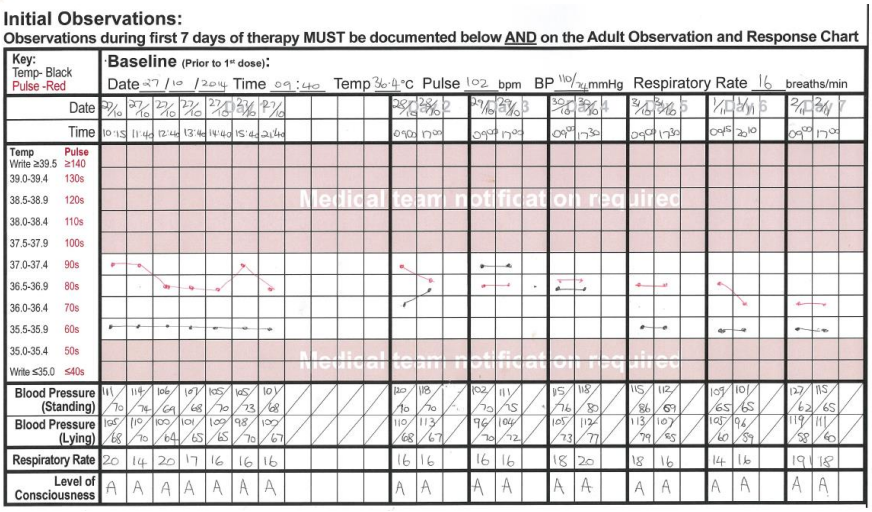
The person conducting the baseline observations must record the date, time and observations in the provided space.

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)



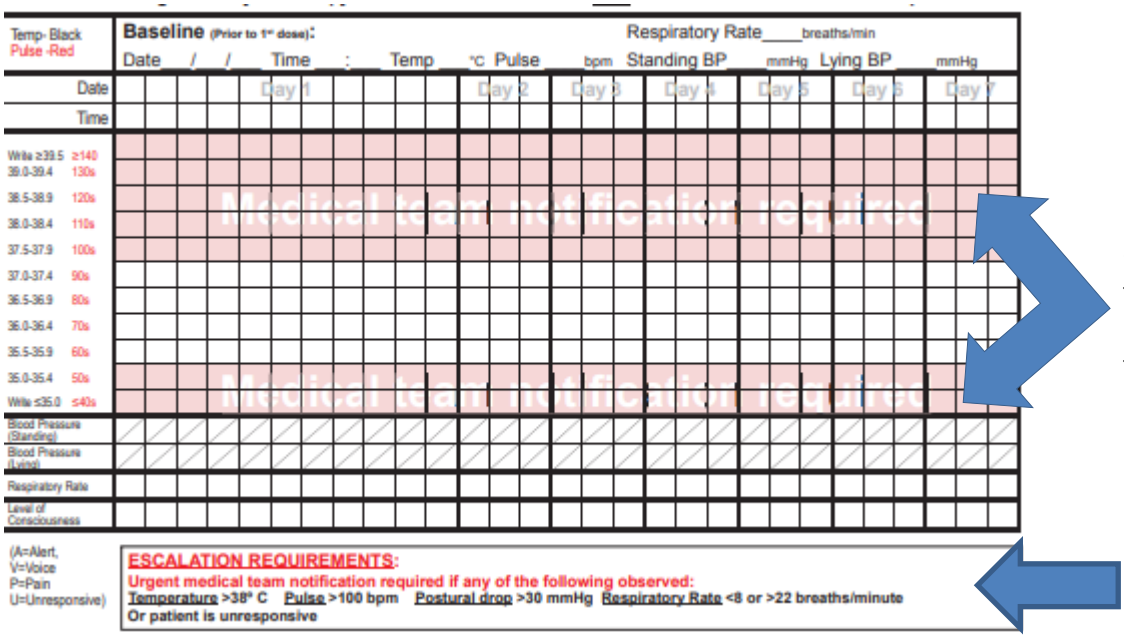
The person conducting the observations must record the date and time of that specific observation in the spaces provided.

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 observations showing cause for concern or if a patient refuses observations.

The chart provides escalation parameters if met by a patient that require urgent medical notification. In addition, the shaded areas on the observation chart section of the clozapine chart also act as prompts to notify a doctor.



Observations in the shaded area require medical team notification.

These observations require *urgent* medical team notification.

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

3.1 Clozapine Only Medication Orders

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

Clozapine Dose Orders

⚠ *DO NOT prescribe clozapine until approved by Clozapine Monitoring Centre and Clozapine Patient Number allocated. Commence clozapine preferably in the morning to allow hourly monitoring for the first six hours.*

Medication **Clozapine** Formulation: Clozapine Patient Number:

Route: **oral** Indication:

Pharmacy use: Weekly monitoring until : / /

Date	Day	Blood test due (✓)	Prescriber		Morning dose 08:00hr	Nurse initials Nurse 1/ Nurse 2	Night dose 20:00hr	Nurse initials Nurse 1 / Nurse 2	Drug level	Pharmacy
			Signature	Name (PRINT)						
	1									
	2									
	3									
	4									
	5									
	6									

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 baseline 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. **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 to the bottom of page 3 of the chart) 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.

Transitioning to the WA Hospital Medication Chart

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 transitioning the prescription,

- Do not obliterate the prescription and administration section (page 2) of the WA Clozapine Initiation and Titration Chart.
- Instead, the doctor must draw a clear line through the section, annotate to indicate the prescription has been continued on the WA HMC, initial and date.
- If required, continue to document essential monitoring of the WA Clozapine Initiation and Titration Chart.

Ceasing the WA Clozapine Initiation and Titration Chart

The WA Clozapine Initiation and Titration Chart has space to document the prescription and administration of 28 days of clozapine therapy and 28 days of monitoring. If the chart is completed or if clozapine therapy is ceased, the full chart should be ceased.

When ceasing the WA Clozapine Initiation and Titration Chart, the doctor must:

- Not obliterate the chart.
- Draw a clear line through the each of the 4 pages of the chart.
- Initial and date the cessation of the chart.
- It is important to document the reason for ceasing, especially if it is due to an adverse effect.

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	12.5 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	25 mg	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Evening				25 mg	25 mg	50 mg	75 mg	100 mg	100 mg	100 mg	125 mg	125 mg	125 mg	150 mg

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 provides a list of measurements to be completed at baseline and during clozapine therapy. These are the recommended minimum monitoring requirements and do not replace the need for clinical discretion. Refer to 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*
- C-Reactive Protein (CRP)*
- Beta HCG (if applicable for females)
- Electrocardiogram (ECG)
  - QT interval
- Echocardiogram

*These are to be completed within **10 days** before clozapine commencement. PathWest now uses the Abbott high sensitivity Troponin I test, which is reported in nanogram/L.

The following pre-clozapine baseline measurements are also recommended:

- Smoking status
- Dietician review
- Weight & Height
- Waist circumference
- Body Mass Index (BMI)
- 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 FBC **must** be recorded every week in the spaces provided.

The chart also provides minimum recommendations for the frequency of ongoing monitoring. Blood samples generally taken on the same day of the week.

After 28 days, measurements may continue to be documented on the Clozapine Monitoring Form – Parts A and B

4. Back page

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 FBCs.

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 more than 48 hours • Obtain psychiatric review prior to recommencing clozapine • Recommence at 12.5 mg 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 therapy being interrupted for **72 hours or less**; **more than 72 hours but less than 28 days** and **more than 28 days.**

Blood Test Monitoring after Interruption of Therapy			
Monitoring frequency	**Clozapine missed for 72 hours or less**	**Clozapine missed for more than 72 hours up to 28 days**	**Clozapine missed for more than 28 days**
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 the Maudsley Prescribing Guidelines 14th ed 2021
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 4 weeks of starting)	Withhold Clozapine. Repeat ECG and echocardiogram. Check C-Reactive Protein (CRP) and troponin. Refer to cardiologist.
Fever	> 38° C (First 4 weeks)	Contact doctor. Reduce rate of dose titration of clozapine. Check 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. Withhold clozapine for one day and restart at half the dose. Consider prophylactic antiepileptic. Risk of seizures increases with higher serum clozapine levels; check serum clozapine 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 1800 675 229 (9AM to 5PM AEST) Monday to Friday

ClopineCENTRAL™ is a registry service designed to provide patient haematological monitoring. 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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