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

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

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Quality Improvement and Change Management Unit in collaboration with North Metropolitan Mental Health Service

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Acknowledgements

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To obtain further information, contact the Quality Improvement and Change Management Unit, Department of Health, Western Australia.

Phone: (08) 9222 4008.

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 NIMC 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 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

URMN:
Family Name:
Given Name:
Address:
DOB: **Sex** ☐**M** ☐**F**

First prescriber to print patient name and check label correct:

……

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, UR 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

Ward/Unit …….. Consultant…….

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/Date	Sign
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 name
   - Reaction details (e.g. rash, diarrhoea)
   - Date of reaction (or approximate timeframe e.g. 20 years ago)
   - 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 diagnosis for the use of clozapine
- 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
- 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:

- Psychiatrist has completed and returned 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 viewed clozapine Patient Notification Form
- Patient/carer/family has been provided with the CMI and the treatment explained
- Patient has given informed consent or if applicable, second opinion obtained
- All Pre-Clozapine Baseline Tests have been performed **within 10 days** before commencing clozapine

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
- Respiratory Rate

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

Baseline (Prior to 1st dose)

Date:__/__/__ Time__:__ Temp: ____°C Pulse:____bpm BP:_____/____mmHg Respiratory Rate:_____breaths/minute

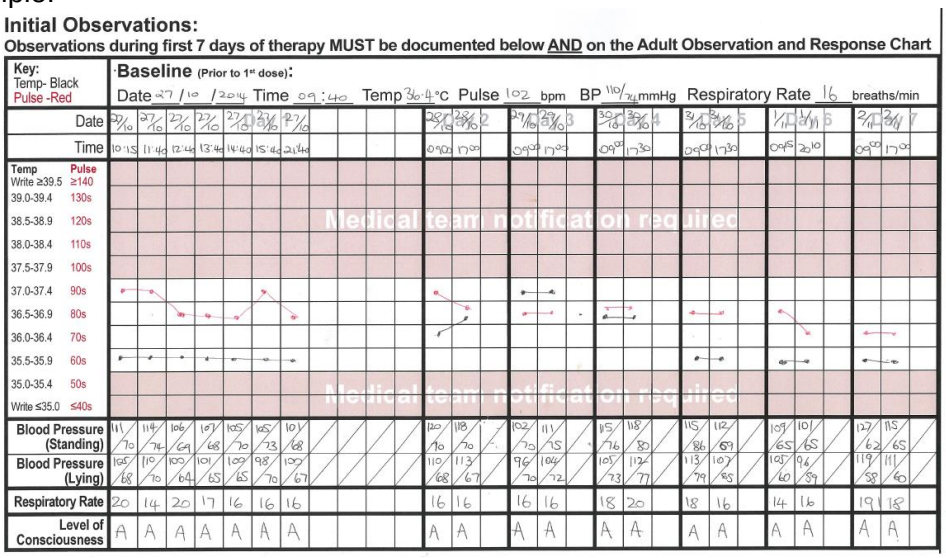
2.5.2 Observations for the first week of clozapine therapy

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

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

ESCALATION REQUIREMENTS:
Urgent medical team notification required if any of the following observed:
Temperature >38° C Pulse >100bpm Postural drop >30 mmHg Respiratory Rate <8 or >22 breaths/minute
Or patient is unresponsive
Maudsley Prescribing Guidelines 11th Edition 2012

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

A doctor (preferably 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 highlighted 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)**
Week 2 to 18:	Temperature, respiratory rate, pulse and BP daily **(mandatory)**
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. **Patient Clozapine 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 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 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 the pre-clozapine baseline tests. 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 avoids 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 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 nurse 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 Review'** 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 NIMC 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 NIMC 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 11th Edition is located on the chart.

Clozapine Dose Titration Schedule

This table serves as a guide only and dose titration should be individualised.
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

The following pre-clozapine baseline measurements **must** be completed **within 10 days** prior to commencing clozapine therapy:

- Blood group
- Full physical examination
- Full blood Count
- Troponin/ CK-MB
- Pregnancy test (if applicable)
- ECG (Echocardiogram)

The following pre-clozapine baseline measurements are also recommended:

- Smoking status
- Weight & Height
- Waist
- BMI
- Dietician review
- Liver Function Test
- Urea & Electrolyte
- Fasting plasma glucose
- Blood lipid

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. If this dose is tolerated, it may be feasible to titrate the dose to the therapeutic level more quickly than is recommended for initial treatment. • 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, 11th Edition. 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 2009

Side-effect	Signs and symptoms	Recommended Action
Neutropenia/ agranulocytosis	WBC < 3.0 x 109/L or Neutrophils < 1.5 x 109 /L. Flu-like symptoms such as sore throat & fever. (First 18 weeks – but may occur at any time)	Contact doctor. Stop clozapine. Contact haematologist at Clozapine Monitoring Centre.
Myocarditis/ cardiomyopathy	Fast or irregular heart beat at rest with rapid breathing, dyspnoea, hypotension, raised jugular venous pressure, fatigue, flu-like symptoms, chest pain or fever. (Cardiomyopathy may occur at any time. Myocarditis – within 6-8 weeks of starting)	Contact doctor and team. Withhold Clozapine. Repeat ECG and echocardiogram. Refer to cardiologist. If confirmed contact cardiologist at clozapine monitoring centre.
Fever	> 38º C (First 3 weeks)	Contact doctor. Reduce rate of dose titration of clozapine. Check FBC, WCC, Creatine Kinase, ECG and Echo. DO NOT give paracetamol until doctor notified and agranulocytosis / myocarditis excluded.
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.)	Contact doctor. Reduction in dose. Check with pharmacist for pharmacological options. Risk of seizures increases with higher plasma levels. Check plasma 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, decrease appetite or fatigue. (Usually persists)	Contact doctor. Recommend increased fluid intake and exercise. Treat like opioid-induced constipation, use osmotic laxatives and stimulants.
Nocturnal enuresis	Loss of bladder control, especially at night (bed-wetting). (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	Usually during the first years of treatment.	Dietary counselling before weight gain occurs is essential.
Nausea	First 6 weeks	May give antiemetic. Avoid prochlorperazine and metoclopramide if previously experienced Extra Pyramidal Side Effects (EPSE).

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. ClopineConnect ® CONTACT INFORMATION

ClopineConnect ®

Phone: 1800 656 403

Fax: 1800657454

Email: ClopineConnect@au.maynepharma.com

Hospira Pty Ltd Drug Safety Contact

Phone: 03 9868 0780

Fax: 03 9868 0787

Hospira Pty Ltd Medical Information

Phone: 1300 046 774

Fax: 03 9868 0111

Clopine Haematologist

Phone: 1800 656 403

Available 24 hours a day, 7 days a week

Clopine Consultant Cardiologist

Phone: 1800 656 403

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