




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

WA Clozapine Initiation and Titration Chart

Version 08/22 of Chart

Introduction

- Clozapine is a high risk medication
 - It was released in early 1970s and withdrawn from market due to incidents of neutropenia, myocarditis and sudden death.
 - Re-introduced for use in Australia with stringent monitoring and guidance for use in conjunction with the Clozapine Monitoring System (ClopineCentral™)
 - Specialised chart developed for WA Health to co-ordinate management of clozapine.
 - This presentation will provide education on features, prompts and alerts in the chart.
- 


General Requirements

- Chart to be completed for all in-patients initiated and re-titrated on clozapine
- The National Inpatient Medication Chart **MUST** be annotated clearly to identify when a clozapine chart is in use

Medication chart number of

Additional charts

<input type="checkbox"/> IV fluid	<input type="checkbox"/> Variable dose	<input type="checkbox"/> Acute pain	<input checked="" type="checkbox"/> Other
<input type="checkbox"/> Palliative care	<input type="checkbox"/> BGL/insulin	<input type="checkbox"/> Anticoagulation	Clozapine Chart
<input type="checkbox"/> Chemotherapy			



Additional Charts – Tick if in use

<input type="checkbox"/> Blood Glucose Level (BGL) monitoring	<input type="checkbox"/> Subcutaneous Insulin or	<input type="checkbox"/> Intravenous Insulin Infusion)
<input checked="" type="checkbox"/> Clozapine	<input type="checkbox"/> Intravenous (IV) Fluid	<input type="checkbox"/> Chemotherapy
<input type="checkbox"/> Agitation & arousal	<input type="checkbox"/> Palliative care	<input type="checkbox"/> Acute Pain
<input type="checkbox"/> Long acting injection	<input type="checkbox"/> Variable dose	<input type="checkbox"/> Other




Chart Layout

This chart must be used under the supervision of a psychiatrist.
Please use ID label or block print

HOSPITAL NAME CLOZAPINE INITIATION AND TITRATION CHART		Family Name: NOT A VALID	UMRN	SEX																																																																																																																																																																																																																																									
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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																																																																																																																																																																																																																																													

Front Page:

- Patient Identification
- Allergies and Adverse Drug Reactions
- Pre-commencement documentation and checklist
- Observations
 - Temperature
 - Pulse
 - Blood pressure
 - Respiratory rate
 - Level of consciousness

MRXX CLOZAPINE INITIATION AND TITRATION CHART

DO NOT WRITE IN BINDING MARGIN

BARCODE AREA
XXXXXX

xxx
08/22

HCHXXXXXXXX

Chart Layout

HOSPITAL NAME

CLOZAPINE INITIATION AND TITRATION CHART

Year 20 ____

Please use ID label or block print.

Family Name:	UMRN	SEX
Given Name(s):	D.O.B.:	
Address:		

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 Signature	Name (PRINT)	Morning dose 08:00hr Nurse initials Nurse 1 / Nurse 2	Night dose 20:00hr Nurse initials Nurse 1 / Nurse 2	Drug level	Pharmacy
1								
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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

Monitoring Checklist – Baseline Measurements When Commencing Clozapine

Blood group		Height		m		Smoking status:		<input type="checkbox"/> Smoker	<input type="checkbox"/> Non Smoker
Intervals	Pre-clozapine baseline		Day 7	Day 14	Day 21	Day 28	After 28 days		
	Date	Results	Date:	Date:	Date:	Date:			
Dietician review		<input type="checkbox"/> Performed							Annually
Weight		kg							Weekly first 18 weeks - then every 28 days
Waist circumference		cm							Weekly first 18 weeks - then every 28 days
BMI (weight (kg) / height (m) ²)									Weekly first 18 weeks - then every 28 days
Constipation monitoring	Daily checks for 4 weeks: Use bowel chart								
Full physical exam		<input type="checkbox"/> Performed							Annually
Full Blood Count		<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed			Weekly first 18 weeks - then every 28 days
White Blood Count		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L			Weekly first 18 weeks - then every 28 days
Neutrophils Absolute		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L			Weekly first 18 weeks - then every 28 days
Eosinophils Absolute		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L			Weekly first 18 weeks - then every 28 days
Liver function test		<input type="checkbox"/> Performed							6 monthly
Urea & Electrolytes		<input type="checkbox"/> Performed							6 monthly
Fasting plasma glucose		mmol/L							At 3 months, 6 months, then 6 monthly
Total cholesterol (fasting)		mmol/L							At 3 months, 6 months, then 6 monthly
LDL (fasting)		mmol/L							At 3 months, 6 months, then 6 monthly
HDL (fasting)		mmol/L							At 3 months, 6 months, then 6 monthly
Triglycerides (fasting)		mmol/L							At 3 months, 6 months, then 6 monthly
Troponin		micrograms/L	micrograms/L	micrograms/L	micrograms/L	micrograms/L			Weekly first 4 weeks, at 3 and 6 months, then every 6 months
C-Reactive Protein (CRP)		mg/L	mg/L	mg/L	mg/L	mg/L			Weekly first 4 weeks and as clinically indicated thereafter
ECG (QT interval)									At 3 months, then 1, 2, 5yrs
Cardiac echocardiogram									When needed
Beta HCG (female)									When needed

These are suggested guidelines only and do not replace the need for clinical discretion. Refer to the treating psychiatrist for individual monitoring requirements

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)

Inside Page: (Opens into A3)

- Dose Orders
- Suggested Dosing Regimen
- Monitoring

Chart Layout

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

Recommencing Therapy after Interruption

<p>Dosing recommendations if clozapine dose is missed for > 48 hours</p> <ul style="list-style-type: none"> 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.
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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	

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 $< 3.0 \times 10^9/L$ or Neutrophils $< 1.5 \times 10^9/L$. 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	$> 38^\circ C$ (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.

Back Page:

- Clozapine blood results monitoring system
- Guidelines for recommencing therapy after interruption
- Guidelines for blood test monitoring after interruption of therapy
- Alerts on side-effects associated with therapy

Patient Identification

Family Name:	UMRN	SEX
Given Name(s)	D.O.B.:	
Address:		

NOT A VALID PRESCRIPTION UNLESS IDENTIFIERS PRESENT

First prescriber to print patient name and check label correct:

- ✓ Affix patient ID label or write information on pages 1 and 2 of chart
- ✓ If using labels: First prescriber **MUST HANDWRITE (PRINT)** patient name and **CHECK LABELS** are correct

Allergies & Adverse Reactions (ADR)

Accurate information prevents harm from known ADRs

Adverse Drug Reaction

Attach ADR Sticker

ALLERGIES & ADVERSE REACTIONS (ADR)		
<input type="checkbox"/> Nil Known <input type="checkbox"/> Unknown (tick appropriate box or complete details below)		
Drug (or other)	Reaction/Type/Date	Initials

Sign..... Print Date

TICK BOX if patient has 'Nil

- ✓ Known' or 'Unknown' allergies or ADRs
- ✓ If ADR exists, then **affix ADR sticker** to page 1 and document:
 - Drug name
 - Reaction details
 - Date of reaction
 - Sign entry

Pre-commencement Screen



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: _____

Pre-commencement Screen

- A tick box to indicate if pre-commencement screen is required to be completed
- A section to ensure a medical history is obtained from the patient
- A checklist to ensure all pre-commencement clozapine requirements have been completed

Pre-commencement Screen

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: _____

✓ Complete "Clozapine checklist".

Prompts to:

- return completed 'Clozapine Referral Form' to a pharmacist
- check PBS eligibility
- consider continuation of supply
- provide 'Clozapine Notification Form'; CMI and explain treatment
- obtain consent/second opinion
- obtain all Pre-Clozapine Baseline Tests within 10 days

Preparation Prior to Initiation

Pre-commencement Screen		
Pre-commencement Screen is required to be completed: <input type="checkbox"/> Yes <input type="checkbox"/> 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	<input type="checkbox"/> No <input type="checkbox"/> Yes	Details _____
Patient has a personal or family history of cardiovascular disease	<input type="checkbox"/> No <input type="checkbox"/> Yes	Details _____
Patient has a history of epileptic seizures	<input type="checkbox"/> No <input type="checkbox"/> Yes	Details _____
Clozapine checklist:		
<input type="checkbox"/>	Patient has been adequately trialed on 2 or more other antipsychotics	<input type="checkbox"/> No <input type="checkbox"/> Yes Details _____
<input type="checkbox"/>	Clozapine registration form for new patients has been submitted	
<input type="checkbox"/>	PBS eligibility	
<input type="checkbox"/>	Continuation of supply at a registered clozapine centre has been considered	
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<input type="checkbox"/>	Patient/guardian has given informed consent or second opinion obtained (<i>if applicable</i>)	
<input type="checkbox"/>	All Pre-Clozapine Baseline Tests have been performed before clozapine commencement	
<input type="checkbox"/>	Full blood picture (FBP), CRP and troponin to be performed within 10 days before clozapine commencement.	
Consultant Name:	Signature:	Date:

✓ All sections **MUST BE** completed and consultant to print name, sign and date

Initial Observations

Careful observations to identify adverse events and respond appropriately

Monitoring: Refer to hospital procedure. Where this is unavailable the following are recommended monitoring guidelines.
 Day 1 Temperature, respirations, pulse and blood pressure hourly for the first six hours, then every six hours for the first 24 hours
 Day 2 to 7 Temperature, respirations, pulse and blood pressure taken twice daily or more frequently if clinically required.

Initial Observations:
 Observations during first 7 days of therapy **MUST** be documented below **AND** on the Adult Observation and Response Chart

Temp- Black Pulse -Red	Baseline (Prior to 1 st dose):		Respiratory Rate _____ breaths/min										
	Date / /	Time : :	Temp ____°C	Pulse ____bpm	Standing BP ____mmHg	Lying BP ____mmHg	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Write ≥39.5	≥140												
39.0-39.4	130s												
38.5-38.9	120s												
38.0-38.4	110s												
37.5-37.9	100s												
37.0-37.4	90s												
36.5-36.9	80s												
36.0-36.4	70s												
35.5-35.9	60s												
35.0-35.4	50s												
Write ≤35.0	≤40s												
Blood Pressure (Standing)													
Blood Pressure (Lying)													
Respiratory Rate													
Level of Consciousness													

(A=Alert,
 V=Voice
 P=Pain
 U=Unresponsive)

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

← **Record Baseline (Prior to 1st dose)**

- Date
- Time
- Pulse
- Blood pressure
- Respiratory Rate

← **Record the first 7 days of observations**

- Temperature – Black
- Pulse- Red
- Blood Pressure (standing and lying)
- Respiratory Rate
- Level of Consciousness

After 7 days, continue observations with TPR & BP Chart

Initial Observations

Monitoring: Refer to hospital procedure. Where this is unavailable the following are recommended monitoring guidelines.
 Day 1 Temperature, respirations, pulse and blood pressure hourly for the first six hours, then every six hours for the first 24 hours
 Day 2 to 7 Temperature, respirations, pulse and blood pressure taken twice daily or more frequently if clinically required.

Initial Observations:
 Observations during first 7 days of therapy **MUST** be documented below **AND** on the Adult Observation and Response Chart

Temp- Black Pulse-Red	Baseline (Prior to 1 st dose):		Respiratory Rate ___ breaths/min										
	Date ___/___/___	Time :___:___	Temp ___°C	Pulse ___bpm	Standing BP ___mmHg	Lying BP ___mmHg	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Write ≥39.5	≥140												
39.0-39.4	130s												
38.5-38.9	120s	Medical team notification required											
38.0-38.4	110s												
37.5-37.9	100s												
37.0-37.4	90s												
36.5-36.9	80s												
36.0-36.4	70s												
35.5-35.9	60s												
35.0-35.4	50s	Medical team notification required											
Write ≤35.0	≤40s												
Blood Pressure (Standing)													
Blood Pressure (Lying)													
Respiratory Rate													
Level of Consciousness													



Prompts for frequency of monitoring



Prompts to identify when to notify a doctor who will be able to advise on whether to continue treatment





(A=Alert, V=Voice, P=Pain, U=Unresponsive)
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

Dose orders

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									

Document:

- ✓ Formulation (suspension / tablets)
- ✓ Clozapine Patient Number
- ✓ Indication
- ✓ Weekly monitoring until : / /

Dose orders



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									



Doses **ONLY** to be prescribed when approved by clozapine monitoring centre and clozapine patient number allocated

Clearly document:

- ✓ Date when medication started (Chart can accommodate 28 days)
- ✓ Prescriber PRINT name and sign
- ✓ Dose - morning (8:00) and/or night (20:00). Commence clozapine in the morning and avoid weekends
- ✓ Nurse to double-sign each individual dose indicating dose checked and administered
- ✓ Drug level
- ✓ Pharmacy- To identify medication chart has been reviewed by pharmacist

Clozapine – Dosing Regimen

Cautious titration and a divided dosage are necessary to minimise adverse events (e.g. hypotension, seizures, sedation...)

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

Quick reference for the suggested starting regimen for clozapine
(Maudsley Prescribing Guidelines)

This is **ONLY** a guide and dose titration should be individualised

Monitoring Checklist

Complete all baseline measurements not more than 10 days of commencing clozapine. Date and document or tick the corresponding boxes

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

- Blood group
- Full physical examination
- Pregnancy test Beta HCG (if applicable for females)
- Troponin/ CK-MB
- Echocardiogram (ECG)
- Full Blood Count
- C-Reactive Protein (CRP)

The following pre-clozapine baseline measurements are also recommended:

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

Monitoring Checklist – Baseline Measurements When Commencing Clozapine								
Blood group		Height		Smoking status: <input type="checkbox"/> Smoker <input type="checkbox"/> Non Smoker				
Intervals	Pre-clozapine baseline		Day 7	Day 14	Day 21	Day 28	After 28 days	
	Date	Results	Date:	Date:	Date:	Date:		
To be completed by doctor / nurse / dietician								
Dietician review		<input type="checkbox"/> Performed						Annually
Weight		kg						Weekly first 18 weeks – then every 28 days
Waist circumference		cm						
BMI weight (kg) / height (m ²)								
Constipation monitoring	Daily checks for 4 weeks: Use bowel chart							Inpatients: minimum weekly Outpatients: check bowel habits at each review
To be completed by doctor:								
Full physical exam		<input type="checkbox"/> Performed						Annually
Full Blood Count		<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed		Weekly first 18 weeks - then every 28 days
White Blood Count		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	
Neutrophils Absolute		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	
Eosinophils Absolute		x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	
Liver function test		<input type="checkbox"/> Performed						6 monthly
Urea & Electrolytes		<input type="checkbox"/> Performed						6 monthly
Fasting plasma glucose		mmol/L						
Total cholesterol (fasting)		mmol/L						At 3 months, 6 months, then 6 monthly
LDL (fasting)		mmol/L						
HDL (fasting)		mmol/L						
Triglycerides (fasting)		mmol/L						
Troponin		micrograms/L	micrograms/L	micrograms/L	micrograms/L	micrograms/L		Weekly first 4 weeks, at 3 and 6 months, then every 6 months
C-Reactive Protein (CRP)		mg/L	mg/L	mg/L	mg/L	mg/L		
ECG (QT interval)								Weekly for first 4 weeks and as clinically indicated thereafter
Cardiac echocardiogram								At 3 months, then 1, 2, 5yrs
Beta HCG (female)								When needed
These are suggested guidelines only and do not replace the need for clinical discretion. Refer to the treating psychiatrist for individual monitoring requirements								

Monitoring Checklist

Monitoring Checklist – Baseline Measurements When Commencing Clozapine								
Blood group _____		Height _____ m		Smoking status: <input type="checkbox"/> Smoker <input type="checkbox"/> Non Smoker				
Intervals	Pre-clozapine baseline		Day 7	Day 14	Day 21	Day 28	After 28 days	
	Date	Results	Date:	Date:	Date:	Date:		
To be completed by doctor / nurse / dietician	Dietician review	<input type="checkbox"/> Performed						Annually
	Weight	kg						Weekly first 18 weeks – then every 28 days
	Waist circumference	cm						Weekly first 18 weeks – then every 28 days
	BMI weight (kg) / height (m ²)							Weekly first 18 weeks – then every 28 days
Constipation monitoring	Daily checks for 4 weeks: Use bowel chart							Inpatients: minimum weekly Outpatients: check bowel habits at each review
To be completed by doctor	Full physical exam	<input type="checkbox"/> Performed						Annually
	Full Blood Count	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	<input type="checkbox"/> Performed	Weekly first 18 weeks - then every 28 days
	White Blood Count	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	Weekly first 18 weeks - then every 28 days
	Neutrophils Absolute	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	Weekly first 18 weeks - then every 28 days
	Eosinophils Absolute	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	x10 ⁹ /L	Weekly first 18 weeks - then every 28 days
	Liver function test	<input type="checkbox"/> Performed						6 monthly
	Urea & Electrolytes	<input type="checkbox"/> Performed						6 monthly
	Fasting plasma glucose	mmol/L						At 3 months, 6 months, then 6 monthly
	Total cholesterol (fasting)	mmol/L						At 3 months, 6 months, then 6 monthly
	LDL (fasting)	mmol/L						At 3 months, 6 months, then 6 monthly
	HDL (fasting)	mmol/L						At 3 months, 6 months, then 6 monthly
	Triglycerides (fasting)	mmol/L						At 3 months, 6 months, then 6 monthly
	Troponin	micrograms/L	micrograms/L	micrograms/L	micrograms/L	micrograms/L	micrograms/L	Weekly first 4 weeks, at 3 and 6 months, then every 6 months
	C-Reactive Protein (CRP)	mg/L	mg/L	mg/L	mg/L	mg/L	mg/L	Weekly for first 4 weeks and as clinically indicated thereafter
ECG (QT interval)							Weekly for first 4 weeks and as clinically indicated thereafter	
Cardiac echocardiogram							At 3 months, then 1, 2, 5yrs	
Beta HCG (female)							When needed	



Space to document measurements for 28 days if required




Prompts for frequency of monitoring beyond first month of therapy.

These are suggested guidelines only and do not replace the need for clinical discretion. Refer to the treating psychiatrist for individual monitoring requirements

Haematological Monitoring

- Regular full blood counts are required as clozapine can cause agranulocytosis
- WBC and Neutrophil counts must be performed :
 - At least weekly for the first 18 weeks of therapy
 - At least every four weeks (28 days) after the first 18 weeks of therapy
- Blood results are classified as **green**, **amber** or **red**



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

Classification of each colour and the recommended action

Haematological Monitoring


POST-THERAPY BLOOD TESTING:

WEEKLY monitoring

Patients on weekly monitoring at the time of discontinuation **MUST** continue to have 4 weeks of weekly monitoring

MONTHLY monitoring

Patients on monthly monitoring at the time of discontinuation **MUST** have one further test one month after discontinuation



Recommendations for recommencing therapy after interruption

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.

Suggested Action:

If clozapine is missed for > 48 hours, 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. For further dose options refer to the patient's treating psychiatrist.

Recommendations for Missed Doses



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	

Different monitoring frequency is required when clozapine is missed for:


- < 72 hours
- > 72 hours but less than 4 weeks
- > 4 weeks

Side-effects


Side effects Associated with Clozapine Therapy <small>Modified from Maudsley Prescribing Guidelines 13th ed 2018</small>		
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.		

- This is **NOT** a complete list of clozapine related side effects
- Signs and symptoms of side effects
- To increase awareness of possible side effects
- Prompts for nurses to contact doctor if any of the side effects are present

Forms required for patient registration before initiation

- Before initiating clozapine, contact clinical pharmacist
 - Forms that are still required to be completed:
 - » **Clozapine Registration for New Patients Referral Form**
(For registration of patient: Contact clinical pharmacist)
 - » **Clozapine Notification Form /Consent Form**
(Patient information)
- 

Summary

- Baseline monitoring **MUST** be performed no more than 10 days before commencing treatment
 - Clozapine **MUST** only be prescribed when patient is allocated a clozapine number
 - Current Clozapine Initiation Chart to be kept with other medication charts
 - Commence clozapine in the morning – avoid weekends (preferable to start early in the week)
- 

Summary

- Printed resources available from pharmacy:
 - » Clozapine Registration for New Patients Referral Form
 - » Clozapine Counselling Points
 - » Clozapine Consumer Medication Information
 - Please forward any comments or queries on the Clozapine Initiation and Titration Chart to your clinical pharmacist or DoH.MedicinesandTechnologyUnit@health.wa.gov.au
- 