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

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.

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	

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.

WA Health acknowledges contributions from Queensland Health Medication Management Services in the development of this chart.

DO NOT WRITE IN BINDING MARGIN

This chart must be used under the supervision of a psychiatrist.

Please use ID label or block print

HOSPITAL NAME

WA CLOZAPINE INITIATION AND TITRATION CHART

Family Name: NOT A VALID PRESCRIPTION UNLESS IDENTIFIERS PRESENT	UMRN	SEX
Given Name(s)	D.O.B.:	

Address:

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 .....

First prescriber to print patient name and check label correct:

Ward/Unit _____ **Consultant** _____

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:

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.
Week 2 to 18 Temperature, respirations, pulse and blood pressure taken daily or more frequently if 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 1st 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	
Date																				
Time																				
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																				

Medical team notification required

Medical team notification required

(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 > 100 bpm Postural drop > 30 mmHg Respiratory Rate < 8 or > 22 breaths/minute
Or patient is unresponsive

xxx
01/24

HCHxxxxxxxx

WA CLOZAPINE INITIATION AND TITRATION CHART

MRXXX

HOSPITAL NAME

WA CLOZAPINE INITIATION AND TITRATION CHART

Year 20 ___ ___

Please use ID label or block print

Family Name: NOT A VALID PRESCRIPTION UNLESS IDENTIFIERS PRESENT	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	Prescriber 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									
	2									
	3									
	4									
	5									
	6									
	7									
	8									
	9									
	10									
	11									
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DO NOT WRITE IN BINDING MARGIN

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 200 mg/day: If well tolerated, the daily dose may be increased slowly in increments of 25-50 mg (maximum 100 mg/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

Monitoring Checklist – Baseline Measurements When Commencing Clozapine

Blood group _____ Height _____m Smoking status: ☐ Smoker ☐ Non Smoker

	Intervals	Pre-clozapine baseline Date	Pre-clozapine baseline Results	Day 7 Date:	Day 14 Date:	Day 21 Date:	Day 28 Date:	Minimum ongoing monitoring
To be completed by doctor / nurse / dietician	Dietician review		☐ 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		☐ Performed					Annually
	Full Blood Count		☐ Performed	☐ Performed	☐ Performed	☐ Performed	☐ 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	
	Neutrophils Absolute		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	
	Liver function test		☐ Performed					6 monthly
	Urea & Electrolytes		☐ Performed					6 monthly
	Fasting plasma glucose		mmol/L					At 3 months, 6 months, then 6 monthly
	Total cholesterol (fasting)		mmol/L					
	LDL (fasting)		mmol/L					
	HDL (fasting)		mmol/L					
	Triglycerides (fasting)		mmol/L					
	Troponin		nanograms/L	nanograms/L	nanograms/L	nanograms/L	nanograms/L	As clinically indicated thereafter
	C-Reactive Protein (CRP)		mg/L	mg/L	mg/L	mg/L	mg/L	
	ECG (QT interval)							Weekly for first 4 weeks, then as clinically indicated
	Cardiac echocardiogram							At 3 months, then 1, 2, 5 yrs
	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)