

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 > 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.

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 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.

HOSPITAL NAME
CLOZAPINE INITIATION AND TITRATION CHART

Family Name: _____ 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 (complete Pre-commencement Screen) Recommencing after interruption of less than 28 days Continuing

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.

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	Pulse	Standing BP	Lying BP	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	
Write ≥39.5														
39.0-39.4														
38.5-38.9														
38.0-38.4														
37.5-37.9														
37.0-37.4														
36.5-36.9														
36.0-36.4														
35.5-35.9														
35.0-35.4														
Write ≤35.0														
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

DO NOT WRITE IN BINDING MARGIN

DO NOT WRITE IN BINDING MARGIN

BARCODE AREA

XXXXXX

XXXX

08/22

HOSPITAL NAME

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									
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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: Smoker 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)						Inpatients: minimum weekly Outpatients: check bowel habits at each review	
	Constipation monitoring	Daily checks for 4 weeks: Use bowel chart						
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		
	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	<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						
	LDL (fasting)	mmol/L						
	HDL (fasting)	mmol/L						
	Triglycerides (fasting)	mmol/L						
	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)							At 3 months, then 1, 2, 5yrs
Cardiac echocardiogram							When needed	
Beta HCG (female)								

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)