

Affix patient identification label here

NIMC (clozapine titration)

Facility/service:

Ward/unit: Year: 20

Clozapine patient number (CPN):

URN:
 Family name:
 Given names:
 Address:
 Date of birth: Sex: M F
First prescriber to print patient name and check label correct:

Not a valid prescription unless identifiers present

Clozapine monitoring (suggested guidelines only)*

Investigations	Date completed	Results												After 28 days
		Baseline		Date (day 7):		Date (day 14):		Date (day 21):		Date (day 28):		After 28 days		
		Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal			
Full blood count (FBC)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Then continue weekly first 18 weeks then monthly	
White blood cell (WBC)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Neutrophils	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Eosinophils	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Troponin – high sensitivity I or T	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Then weekly for the next two weeks, then 6-monthly thereafter unless clinically indicated per local protocol	
C-reactive protein (CRP)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Electrocardiograph (ECG)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Then continue as per local protocol	
Liver function test (LFT)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Urea and electrolytes (U&E)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		
Blood group	<input type="checkbox"/>													
Plasma glucose – fasting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>										Then at 3 months then every 6 months	
Total cholesterol – fasting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
Low density lipoprotein (LDL) – fasting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
High density lipoprotein (HDL) – fasting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
Triglycerides – fasting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
Beta human chorionic gonadotropin (Beta HCG) – female	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>										As required	
Cardiac ECHO	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
Clozapine plasma level	<input type="checkbox"/>	The clozapine plasma level (trough level or 12 hours post-dose) may help guide the therapeutic dose per local protocol.											Then continue as per local protocol	
Full physical exam	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>											
Height	<input type="checkbox"/>		m											
Weight	<input type="checkbox"/>		kg		kg		kg		kg		kg		kg	
Waist	<input type="checkbox"/>		cm										cm	
BMI [weight (kg)/height (m ²)]	<input type="checkbox"/>													
Constipation	<input type="checkbox"/>	Check bowel habits daily for 4 weeks											Continue weekly	
Smoking – cigarettes per day	<input type="checkbox"/>												As required	

These are suggested guidelines only, refer to the treating psychiatrist for individual monitoring requirements. Check pathology system for test parameters.

* Adapted from: Taylor D, Barnes T, Young A. The Maudsley Prescribing Guidelines in Psychiatry, 14th Edition Wiley Blackwell 2021.

Clozapine titration guide

Pre-commencement

- Assess current smoking status
- Review and document medical history, cardio-metabolic risk factors and drug interactions
- Assess bowel habits, including presence of any unnecessary anticholinergic or other constipating agents
- Provide and explain clozapine brochure to consumer and family/carer
- Complete clozapine patient registration form and send to Clozapine Monitoring Centre. To be approved before prescribing
- Inform your local clozapine coordinator
- Provide pharmacist with blood test results and prescription
- Complete high cost eligibility form
- Complete clozapine baseline monitoring (see page 1)

Blood monitoring

If clozapine dose missed for 72 hours or less:

- Monitoring should continue as normal with no additional requirements

If clozapine dose missed for 72 hours but less than 4 weeks:

- During the first 18 weeks – monitor weekly for at least 6 weeks or for as long as necessary to achieve a total of 18 weeks monitoring. For example, if therapy is interrupted:
 - a) after 15 weeks, monitor with weekly blood tests for 6 weeks after clozapine is recommenced
 - b) after 9 weeks, monitor with weekly blood tests for 9 weeks after clozapine is recommenced
- Consumers on monthly monitoring – monitor weekly for 6 weeks then continue with monthly monitoring if no problems detected

If clozapine dose missed for 4 weeks:

- Monitoring should recommence as for a new consumer

Observation protocol

Refer to local protocol. Where unavailable, Medical Officer to select applicable observation protocol below.

- First ever clozapine dose**
 - Prior to clozapine dose take baseline temperature, pulse, respiration (TPR) and lying and standing blood pressure (BP)
 - Administer clozapine as prescribed
 - Repeat observations:
 - every half an hour for 2 hours
 - every hour for 4 hours
 - If above observations are outside normal parameters, seek medical review
- Re-titration after treatment break (over 48 hours since last dose)**
 - Prior to clozapine dose take baseline temperature, pulse, respiration (TPR) and lying and standing blood pressure (BP)
 - Administer clozapine as prescribed
 - Repeat observations:
 - 30 minutes after dose then TWICE daily (default, unless alternate option completed below by Medical Officer)
 - minutes after dose then daily
 - If above observations are outside normal parameters, seek medical review

Subsequent titration doses: Observations (TPR and lying and standing BP) should be recorded at least once daily, half an hour after a dose is administered. In inpatient settings more frequent observations are appropriate (per local protocol). Where possible, observations should continue for 28 days unless a Medical Officer provides alternative directions on the required frequency and duration of physical observations.

Smoking: If change in smoking status notify a Medical Officer

Management of common adverse effects with clozapine therapy (suggested guidelines only)*

Adverse effect	Time course for onset	Recommended actions
Neutropenia / Agranulocytosis	First 18 weeks (but may occur at any time)	Refer to Clozapine blood results monitoring system table on page 3. Admit to hospital if agranulocytosis is confirmed. Symptoms may include a sore throat or fever.
Myocarditis / Cardiomyopathy	Myocarditis – within 6–8 weeks of starting Cardiomyopathy – may occur at any time	Cease clozapine. Admit to hospital if myocarditis or cardiomyopathy is confirmed. May present with flu-like symptoms.
Constipation	Usually persists and requires continuous monitoring/treatment – Clozapine Induced Gastrointestinal Hypomotility (CIGH)	Severe CIGH can be fatal and should be treated promptly and aggressively. Advise patients of risks before commencing and importance of monitoring bowel function. Recommend high-fibre diet, fluids, exercise and laxatives (such as docusate with senna or macrogol).
Sedation	First few months May persist, but usually wears off	Give smaller dose in the morning. Reduce dose if necessary – check plasma level.
Hypersalivation	First few months Very troublesome at night	Manage according to severity of symptoms. See literature for pharmacological options.
Hypotension	First 4 weeks	Reduce dose or slow down rate of increase. Advise consumer to slowly stand up from a lying or sitting position.
Hypertension	First 4 weeks, but sometimes longer	Increase dose slowly. Hypotensive therapy may be necessary.
Tachycardia	First 4 weeks, but sometimes persists	Common in early stages. If persistent at rest and associated with fever, hypotension or chest pain may indicate myocarditis. Refer to cardiologist.
Weight gain	Usually during the first year of treatment	Ensure dietary counselling before weight gain occurs. Consider metformin therapy per local protocol or evidence-based guidelines.
Fever	First 4 weeks	Give antipyretic, perform urgent FBC and cardiac enzymes. Seek urgent medical review.
Seizures	May occur at any time	If seizures develop, check clozapine levels, seek neurology consult, order EEG and consider starting anti-seizure medicine. Withhold clozapine for one day, and restart at half the previous dose, or per local protocol.
Nausea	First 6 weeks	May give anti-emetic. Avoid prochlorperazine and metoclopramide if caused previous Extra Pyramidal Side Effects. Consider Gastro Oesophageal Reflux Disease (GORD) and appropriate management per local protocol or evidence-based guidelines.
Nocturnal enuresis	May occur at any time	Review dose schedule. Avoid fluids before bedtime. Seek medical review.

This is not an exhaustive list of side effects. Please see product information for further advice.

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NIMC (clozapine titration)

DO NOT WRITE IN THIS BINDING MARGIN

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NIMC (clozapine titration)

Facility/service:

Ward/unit: Year: 20

Clozapine patient number (CPN):

Attach ADR sticker
(See current NIMC for details)

Affix patient identification label here

URN:

Family name: Given names: Address:
Not a valid prescription unless identifiers present

Date of birth: Sex: M F

First prescriber to print patient name and check label correct:

.....

Family name: Given name(s): URN:

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 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 or Neutrophils less than 1.5 x 10 ⁹ /L	Stop clozapine therapy immediately. Refer to local clozapine protocol for management guidelines.

Do not prescribe clozapine until approved by Clozapine Monitoring Centre and Clozapine Patient Number allocated

Conduct weekly blood monitoring as indicated in Clozapine monitoring on page 1

		Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Day		
		Date	/ /																												Date		
Date	Medicine	Dose	mg																												Dose		
Route	Frequency	Prescriber to enter individual doses	Prescriber initials																													Prescriber initials	
Prescriber signature																															0800hrs Administrator 1 initials		
Prescriber name (please print)																															2000hrs Administrator 1 initials		
Contact details																															Administrator 2 initials (if required by local procedures)		
Pharmacy																															Administrator 2 initials (if required by local procedures)		
Comments																															Pharmacist review		
Date	Medicine	Dose	mg																												Dose		
Route	Frequency	Prescriber to enter individual doses	Prescriber initials																													Prescriber initials	
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Prescriber name (please print)																															2000hrs Administrator 1 initials		
Contact details																															Administrator 2 initials (if required by local procedures)		
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Contact details																															Administrator 2 initials (if required by local procedures)		
Pharmacy																															Administrator 2 initials (if required by local procedures)		
Comments																															Pharmacist review		

Clozapine titration schedule (this table is a guide only)

If rapid or slower titration required refer to the treating psychiatrist.
In an attempt to minimise side effects the following dosing schedule is suggested:

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	X	X	X	25mg	25mg	50mg	75mg	100mg	100mg	100mg	125mg	125mg	125mg	150mg

Titration beyond 200mg/day: If well tolerated, the daily dose may be increased slowly in increments of 25–50mg.

Dosing recommendations if clozapine dose is missed for greater than 48 hours

- Obtain psychiatric review prior to recommencing clozapine.
- Recommence at 12.5mg once or twice daily on the first day. If well tolerated, the dose may be increased slowly as suggested in the Clozapine titration schedule (on page 2 opposite).

This is a guide only – for further dosing options refer to treating psychiatrist.
For frequency of blood testing required, refer to Blood monitoring section (on page 4).

Reason for not administering
Codes MUST be circled

Absent	(A)	On leave	(L)
Fasting	(F)	Not available – obtain supply or contact prescriber	(N)
Refused – notify prescriber	(R)	Withheld – enter reason in clinical record	(W)
Vomiting	(V)	Self administered	(S)