

Affix patient identification label here

NIMC (clozapine titration)

Facility/service:

Ward/unit: Year: 20

Clozapine patient number (CPN):

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:

Clozapine monitoring (suggested guidelines only)*

Investigations	(✓) if required	Results										After 28 days
		Baseline		Date (day 7):		Date (day 14):		Date (day 21):		Date (day 28):		
		Date completed	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	Normal	
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"/>	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"/>	
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"/>	
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"/>	
Troponin	<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 at 3 months then annually
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"/>	
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"/>	Then continue consistent with local procedure for safe and quality use of clozapine
Liver function test (LFT)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>									
Urea and electrolytes (U&E)	<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 6 months then 12 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"/>									Then at 3 months then every 6 months
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 level	<input type="checkbox"/>											Then continue consistent with local procedure for safe and quality use of clozapine
Full physical exam	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>									
Height	<input type="checkbox"/>		m									Then continue monthly
Weight	<input type="checkbox"/>		kg	kg	kg	kg	kg	kg	kg	kg	kg	
Waist	<input type="checkbox"/>		cm									
BMI [weight (kg)/height (m ²)]	<input type="checkbox"/>											
Smoking – cigarettes per day	<input type="checkbox"/>											
	<input type="checkbox"/>											As required

These are suggested guidelines only, refer to the treating psychiatrist for individual monitoring requirements. Check Auslab / Auscare for normal and abnormal test parameters.

* Modified from: Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines. 10th ed. London(UK):Informa Healthcare UK Ltd; 2009.

Clozapine titration guide

Pre-commencement

- Assess current smoking status
- Review and document medical history
- Provide and explain clozapine brochure to consumer and family/carer
- Complete clozapine patient registration form and send to Clozapine Monitoring Centre
- Inform your local clozapine coordinator
- Provide pharmacist with blood test results and prescription
- Complete high cost eligibility form
- Complete clozapine monitoring see page 1

Blood test 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 procedure

Refer to hospital procedure. Where this is unavailable the following are suggested monitoring guidelines.

Initial dose:

1. Take temperature, pulse, respiration (TPR), and lying and standing blood pressure (BP) prior to administration of clozapine
2. Administer clozapine as prescribed
3. Repeat observations:
 - Half hourly for 2 hours
 - 1 hourly for 4 hours
4. If above observations are outside normal parameters, seek medical review

Subsequent dose:

1. Twice daily – TPR and lying and standing BP
2. Take observations pre-dose, and 4–6 hours post-dose

Smoking:

- If change in smoking status notify medical officer or prescriber

Management of side effects associated with clozapine therapy

Side 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	Potentially life threatening therefore effective treatment or prevention of constipation is essential. Recommend high-fibre diet. Use bulk forming laxatives and stimulants.
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.
Fever	First 3 weeks	Give antipyretic, perform urgent FBC and cardiac enzymes. Seek urgent medical review.
Seizures	May occur at any time	Consider prophylactic valproate if on high dose or with high plasma level.
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).
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.

* Modified from: Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines. 10th ed. London(UK):Informa Healthcare UK Ltd; 2009.

DO NOT WRITE IN THIS BINDING MARGIN

NIMC (clozapine titration)

fold line

DO NOT WRITE IN THIS BINDING MARGIN

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:
Not a valid prescription unless identifiers present

Address:

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 clozapine protocols 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

Date	Medicine Clozapine	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 day/month																												
Route Oral	Frequency Morning	Prescriber to enter individual doses																													Date day/month
Prescriber signature																															Dose
Prescriber name (please print)																															Dose
Contact details																															Dose
Pharmacy																															Prescriber initials
Comments																															0800hrs Administrator initials
Date	Medicine Clozapine	Dose																													Dose
Route Oral	Frequency Evening	Prescriber to enter individual doses																													Date day/month
Prescriber signature																															Dose
Prescriber name (please print)																															Dose
Contact details																															2000hrs Administrator initials
Pharmacy																															Pharmaceutical review
Comments																															Pharmaceutical 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.
Clozapine titration schedule and Clozapine blood results monitoring system (on page 3) are modified from Clozapine Titration Protocols.

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

- Obtain psychiatric review prior to recommending 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 test 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)