AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

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NIMC (clozapine titration) User Guide

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This document is available on the Commission web site at www.safetyandquality.gov.au

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NIMC (clozapine titration) User Guide

Research shows that many adverse events reported in Australian hospitals are associated with medicines. It also shows that improvements to medication chart design can improve the safety of medication processes in hospitals.

The Australian Commission on Safety and Quality in Health Care surveyed psychiatric acute service users of the National Inpatient Medication Chart (NIMC) in late 2011. The survey found that many services had issues with ordering and recording titrating clozapine doses on the NIMC and that it presented a barrier to effective, standardised use of the NIMC in acute psychiatric services. The NIMC and Psychiatric Acute Services Survey Report[1] recommended that a national adult clozapine titration chart be made available to assist acute services manage recording clozapine titration.

The NIMC (clozapine titration)[2] was made available nationally in 2012. It is an ancillary NIMC and is designed to be used in conjunction with either the NIMC (acute) or NIMC (long-stay).

The NIMC (clozapine titration) is based on the Queensland Health Adult Clozapine Titration Chart which resulted from the significant work of Queensland Health Safe and Quality Use of Medicines, Medication Services Queensland, the Clozapine Working Party and representatives from Royal Brisbane and Women's, Logan, Mackay and Ipswich hospitals.

The NIMC (clozapine titration) is a version of the Queensland Health clozapine titration chart that has been modified for national use.

1. Purpose

- The NIMC (clozapine titration) is intended to be used as a record of the prescribing, monitoring and administration of clozapine titration for adult inpatients.
- The NIMC (clozapine titration) should be used for patients who are on a titrating clozapine regimen. Maintenance doses should be ordered on the NIMC.

2. General instructions

- Every clinician prescribing clozapine has a responsibility to ensure that the order is legible to ensure safe communication to other health professionals involved in dispensing, administering and reconciling the order and subsequent clinical decision making.
- The NIMC (clozapine titration) is a legal document and therefore must be written in a clear and unambiguous form. All orders are to be written in ink. No matter how accurate or complete an order is, it may be misinterpreted if it cannot be read. Water soluble ink (e.g. fountain pen) should not be used. Black ink is preferred.
- Every clinician administering clozapine has a responsibility to ensure they can clearly read and understand the order before administering any medicines. For all incomplete or unclear orders, the prescriber should be contacted for clarification. Never make any assumptions about the prescriber's intent.
- Every NIMC (clozapine titration) must have the patient's identification details completed.

- Every clozapine order must be complete and include:
    - date
    - route (Oral pre-printed)
    - generic drug name (Clozapine pre-printed)
    - dose ordered in metric units and Arabic numerals (mg pre-printed)
    - frequency (Morning and Evening pre-printed)
    - times (0800 and 2000 are pre-printed)
    - prescriber's signature
- A medicine order is valid only if the authorised prescriber enters all the required items.
- Dangerous abbreviations must be avoided. Only accepted abbreviations may be used (refer to the National Recommendations for Terminology, Abbreviations and Symbols to be used in the Prescribing and Administering of Medicines[3]).
- No erasers or "whiteout" can be used i.e. orders MUST be rewritten if any changes are made, especially changes to dose and/or frequency
- Doses must be written using metric and Arabic (1, 2, 3) systems. Never use Roman numerals (i, ii, iii, iv).
- Never use a trailing zero (.0) after a decimal point as it may be misread if the decimal point is missed (e.g. 1.0 misread as 10)
- "mg" has been pre-printed in the daily individual dose section of the NIMC (clozapine titration).

Consistent documentation allows accurate interpretation of orders

The NIMC (clozapine titration) is intended to reflect best practice and assist clinicians to safely prescribe, dispense, administer and reconcile clozapine orders, monitor patients commencing on a clozapine titration regimen and minimise the risk of adverse drug events.

National, state and territory legislation, regulation and policies apply to ensure this highly specialised, and high risk, medicine is prescribed, dispensed, administered and monitored safely. Current requirements include:

- registration with a clozapine patient monitoring service
- pre-treatment haematological and metabolic screening
- ongoing haematological and metabolic monitoring

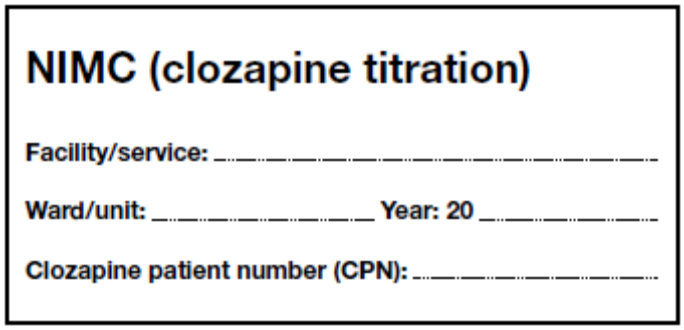
Implementation, education and evaluation resources

The Australian Commission on Safety and Quality in Health Care makes available a range of materials to support use of the NIMCs including NIMC (clozapine titration).

The resources are available from the Commission web site at www.safetyandquality.gov.au/our-work/medication-safety/medication-chart/support-material/

3. NIMC (clozapine titration) pages 1 and 2

3.1	Patient location
	Purpose To establish the patient's location and record the clozapine patient number


NIMC (clozapine titration)

Facility/service: _____

Ward/unit: _____ Year: 20 _____

Clozapine patient number (CPN): _____

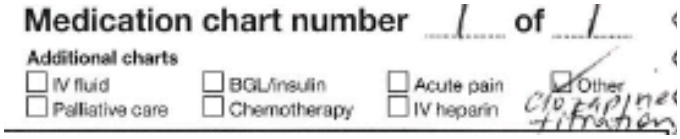
Figure 1 above shows the NIMC (clozapine titration) patient location and clozapine patient number details section

	Use • Record the facility name and ward or unit name • Fill in the pre-printed year space 20_____ • Record the clozapine patient number (CPN) which is issued by the Clozapine Monitoring Centre
	Risk addressed Patient location details are additional patient identification information. Requiring the CPN on the chart before ordering commences ensures that the appropriate registration process has occurred.

Figure 2 below shows the clozapine registration prompt


Do not prescribe clozapine until approved by Clozapine Monitoring Centre and clozapine patient number allocated

3.2	Cross-referencing the NIMC (clozapine titration) on the current NIMC
	Purpose To cross-reference the NIMC (clozapine titration) to the patient's main medication chart, the NIMC (acute) or NIMC (long-stay)


Medication chart number 1 of 1

Additional charts

☐ IV fluid ☐ BGL/insulin ☐ Acute pain ☑ Other Clozapine titration

☐ Palliative care ☐ Chemotherapy ☐ IV heparin

Figure 3 above shows the NIMC (acute) and NIMC (long-stay) additional charts section with use of the NIMC (clozapine titration) chart cross-referenced to it

	Use • Tick the Other box in the NIMC additional charts section • Write clozapine titration under or next to the ticked Other box
	Risk addressed Alerting other health professionals that a NIMC (clozapine titration) chart is in use reduces the chance of missed or duplicate doses.

3.3	Patient identification
	Purpose To establish the patient's identity before prescribing commences

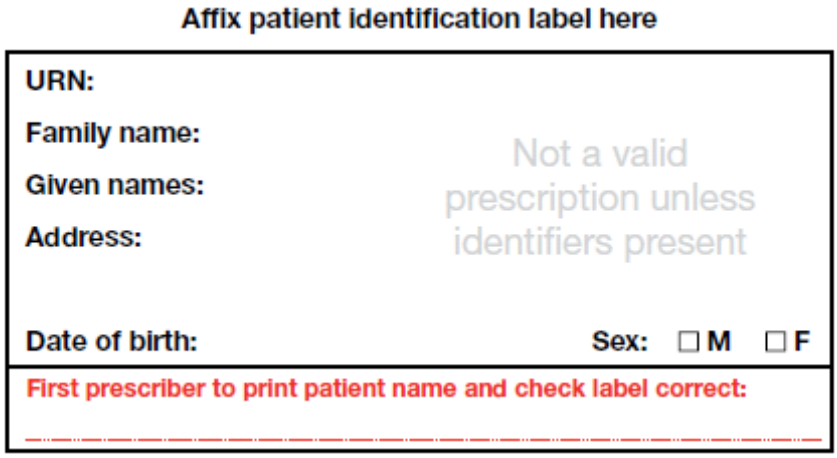


Figure 4 above shows the NIMC (clozapine titration) identification section

Use

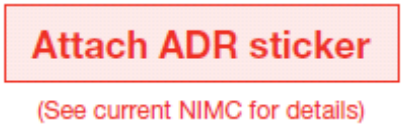
- Adhere a patient identification label in the space provided or hand write the **patient UR number**, **first and family name**, **date of birth** and **gender** in legible print on pages 2 and 4
- If a printed patient identification label is used, the first prescriber must check the patient's identity and print the patient's name under the labels to document confirmation that it is the correct patient
- Clozapine should not be administered if the prescriber does not document the patient identification
- An additional patient identification space is provided on the top of page 3 (see below)

Risk addressed

Not correctly identifying patients can result in missed or incorrect doses or patients being ordered or administered the wrong medicine.

Figure 5 below shows the additional patient identification space at the top of page 3.

Family name:	Given name(s):	URN:

3.4	Allergies and ADR alert
	Purpose To communicate the existence of previous allergies, adverse drug reactions and related information
 **Figure 6 above shows the NIMC (clozapine titration) ADR sticker section**	
	Use • Record previous ADRs and allergies and related details on the NIMC • Fix an ADR alerts sticker on the NIMC (clozapine titration) chart if patient has an ADR or allergy
	Risk addressed Failure to communicate previous ADRs and allergies can result in re-prescribing of offending medicines and avoidable patient harm.

4. NIMC (clozapine titration) pages 2 and 3

4.1	Prescribing titrating clozapine
	Purpose To document clozapine prescribing

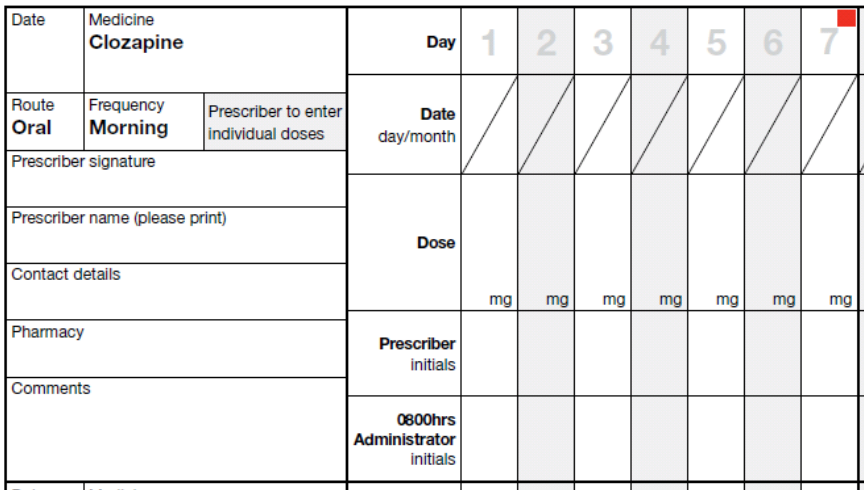


Figure 7 above shows the clozapine ordering section for morning doses

Use

- Record the date the medicine order is written
- Enter the date (day and month) for each day clozapine is prescribed along the horizontal date section
- Clozapine is pre-printed and there is space available for specifying a suspension or tablet if required
- If once daily doses only are prescribed, the prescriber must strike out the section which will not be used (see Figure 8 below).
- Strike doses which are not required (see Figure 9 below).
- Prescriber signs the order and prints name and contact details
- Daily orders should be entered and each one initialled

Risk addressed

Standardising medicines prescribing and administering, and presentation of related information, reduces the risks of error through slips and lapses.

Figure 8 below shows morning order and administration sections struck out

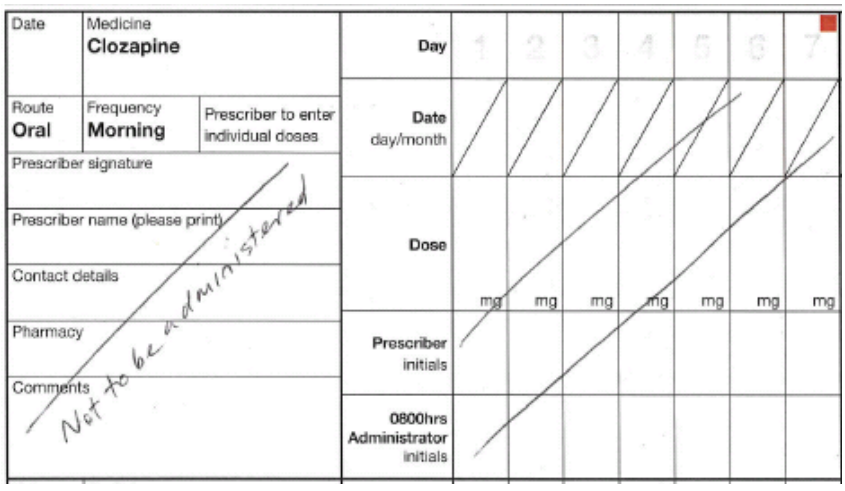
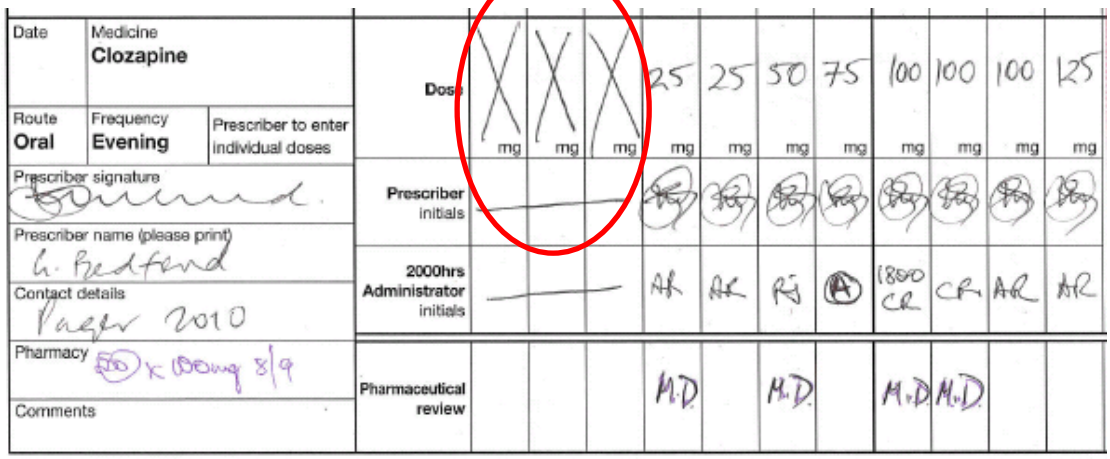


Figure 9 below shows the first three days of evening doses not required struck out to reduce the risk of inadvertent administration



Date	Medicine		
	Clozapine		
Route **Oral**	Frequency **Evening**	Prescriber to enter individual doses	
Prescriber signature			
Prescriber name (please print)			
Contact details			
Pharmacy			
Comments			

Dose	~~X~~ mg	~~X~~ mg	~~X~~ mg	25 mg	25 mg	50 mg	75 mg	100 mg	100 mg	100 mg	125 mg
Prescriber initials											
2000hrs Administrator initials				AR	AR	RJ	A	1800 CR	CR	AR	AR
Pharmaceutical review				M.D.		M.D.		M.D.	M.D.		

Clozapine titration schedule

Figure 10 below shows the suggested clozapine titration schedule

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				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.

Restarting clozapine titration

Figure 11 below shows the guidance provided on restarting clozapine titration after a break of greater than forty-eight hours

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 test monitoring section on page 4.

4.2	Ceasing titrating clozapine
	Purpose To document ceased medicines

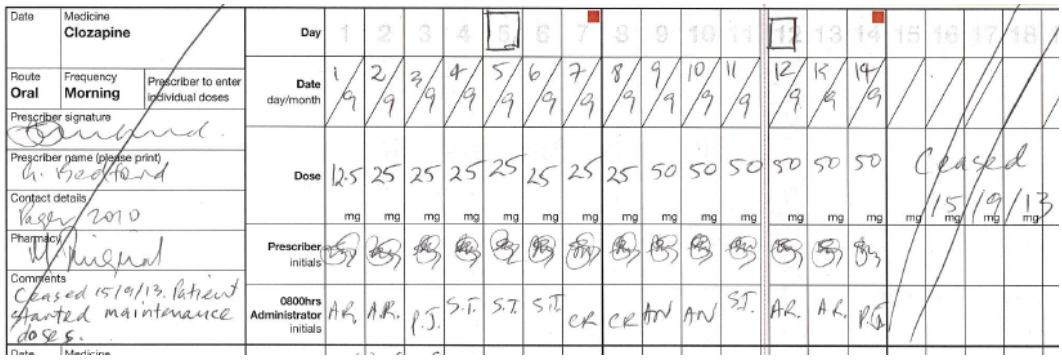


Figure 12 above shows ceased clozapine order

	Use • Strike out the order but leaving it legible • Write the reason for changing the order, the date and initial • A new order should be written if an order needs to be increased or decreased
	Risk addressed Clearly ceasing orders reduces the risk of inadvertent administration. Clearly communicating reasons for the change enables medication reconciliation at discharge.

4.3	Recording administration of titrating clozapine
	Purpose To document clozapine administration

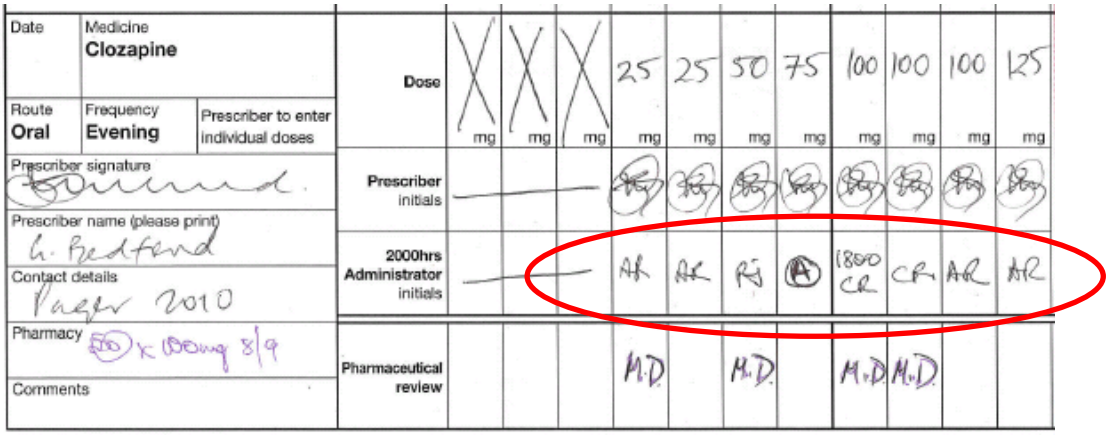


Figure 13 above shows the clozapine evening administration section

	Use • Check patient identity, check dose direction, administer medicine • Initial order • Write the time clozapine was administered above the initials if not administered at 0800 or 2000 (the pre-printed administration times) • Enter appropriate code if dose not administered and circle it. Notify prescriber if the dose is refused by the patient. • If the dose is withheld, document reason in the patient's medical notes.

	Risk addressed Standardising medicines prescribing and administering, and presentation of related information, reduces the risks of error through slips and lapses. Circling the reason for not administering code prevents confusion with initials.

Figure 14 below shows the reason for not administering code legend

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)

It is appropriate to withhold the medicine if:

- there is a known allergy or adverse drug reaction to clozapine
- the NIMC (clozapine titration) is full (i.e. there is no space to sign for administration) then the medicine order is not valid. A new NIMC (clozapine titration) must be written as soon as possible.

Generally medicines should not be withheld if the patient is pre-operative or nil by mouth / fasting unless specified by the prescriber.

4.4	**Pharmaceutical review**
	Purpose To document pharmaceutical review of medicines orders

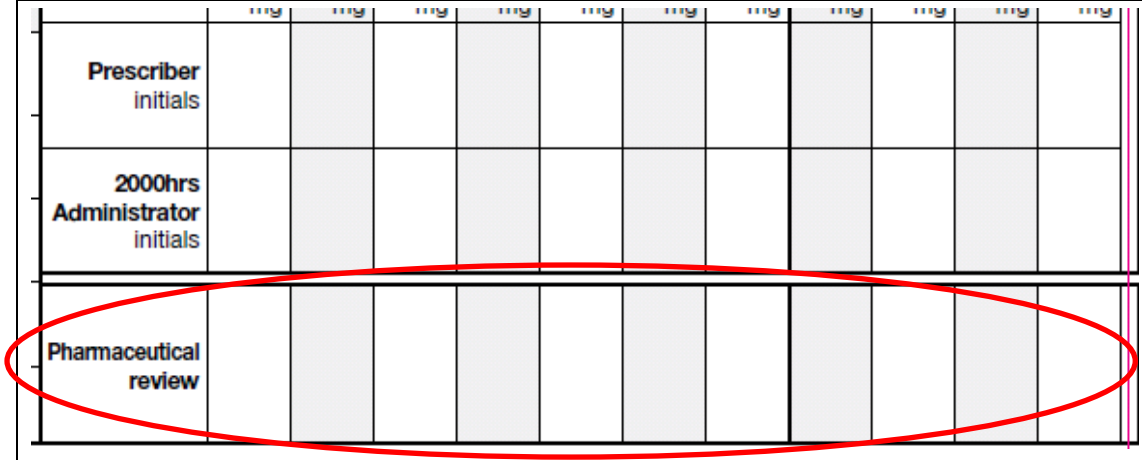


Figure 15 above shows the pharmaceutical review document space

	Use • Review orders • Initial in space provided
	Risk addressed Unclear, unsafe and inappropriate medicine orders can risk patient safety.

4.5	Monitoring clozapine titration
	Purpose To provide advice and prompts for patient monitoring during clozapine titration

Clozapine blood results monitoring system

Clozapine can cause a reduction in the number of white blood cells in patients and regular blood sampling is required to identify this. An alert system which gives guidance on whether therapy should be continued or ceased according to the patient's blood result is provided on page 3.

Figure 16 below shows the clozapine blood results monitoring table and decision support

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.

Weekly monitoring

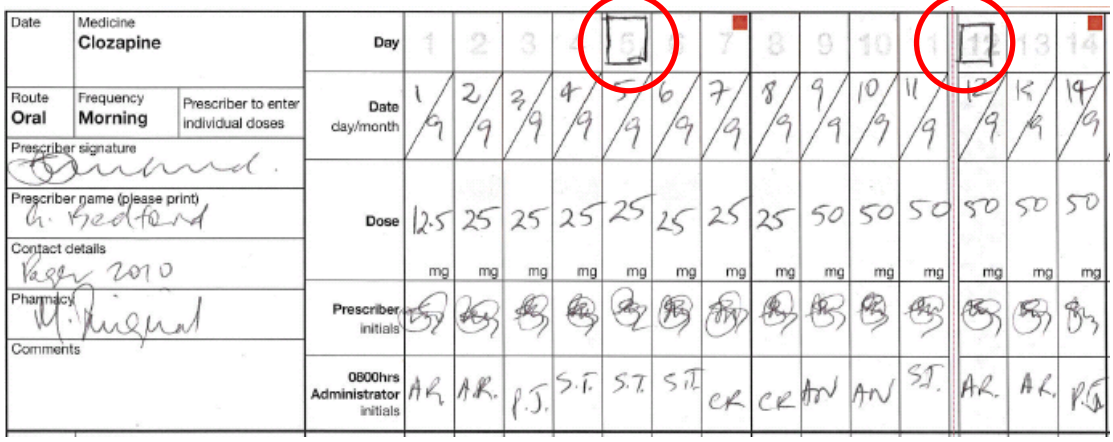
Figure 17 below shows the weekly monitoring prompt

A red coloured square is printed on days 7, 14, 21 and 28 as a reminder that patients require blood or metabolic monitoring on a weekly basis as indicated in the baseline measurements section of the clozapine monitoring table on page 1.

Figure 18 below shows the pre-printed weekly blood monitoring square

Additional tests may be indicated by the prescriber drawing a darkened line around the day box on the required day for testing (see Figure 19 below).

Figure 19 below shows additional weekly test reminders penciled in by the prescriber



5. NIMC (clozapine titration) page 4

5.1 Pre-commencement

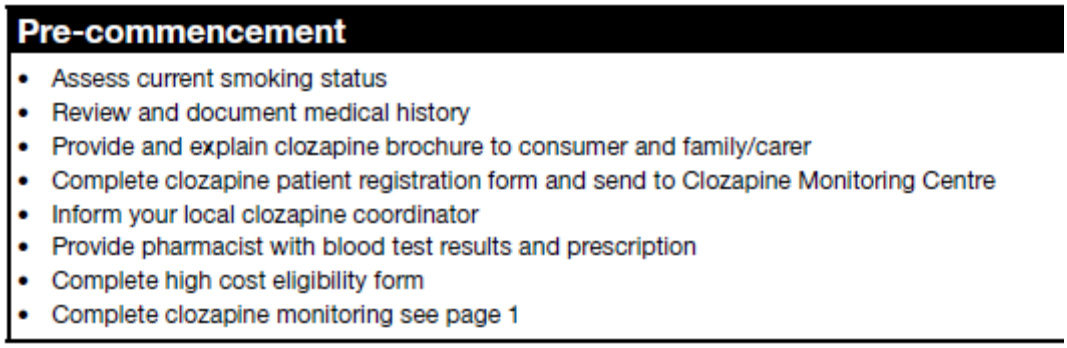
In order to minimise the effect of haematological adverse events, health professionals treating patients with clozapine are required to register their patients with the Clozapine Monitoring Service.

All patients, prescribers, dispensing pharmacists, clozapine coordinators and centres using clozapine must be registered with the Clozapine Monitoring Service.

Refer to local procedures or guidelines for pre-commencement tests and specific paperwork requirements needed to commence a patient on clozapine.

Disregard the instruction to complete high cost eligibility form if not applicable.

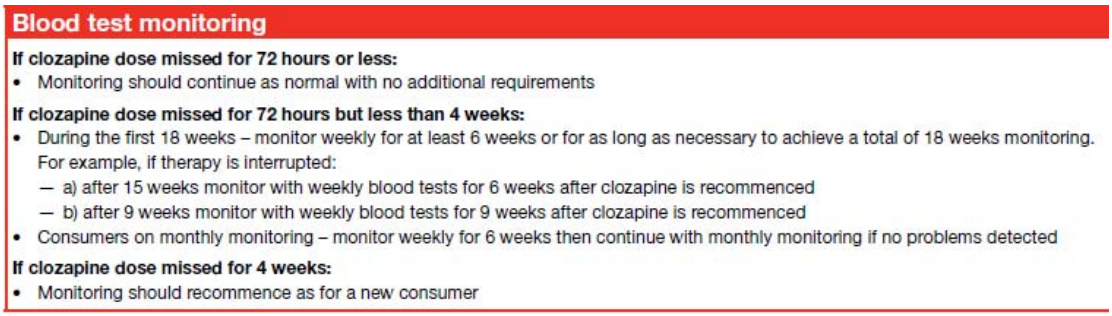
Figure 20 below shows suggested pre-commencement actions



5.2 Blood test monitoring

All patients recommencing clozapine following an interruption in treatment must have a pre-treatment blood test. This includes patients with therapy interruptions of less than a week.

Figure 21 below shows suggested actions for restarting clozapine titration



5.3 Reviewing the patient including observation procedure

The patient should have a regular medical and nursing review to identify adverse reactions and effectiveness of clozapine treatment.

For suggested nursing observations, refer to the observation procedure on the NIMC (clozapine titration) at page 4. Advice can be sought from the treating psychiatrist if a different titration regimen is required.

Figure 22 below shows the suggested observation procedure

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

Patients must be kept under close supervision and their vital signs monitored for six hours following the first dose of clozapine. Any adverse events associated with the initial and subsequent doses need to be referred to a doctor and recorded. Subsequent doses should have vital signs monitored twice daily.

Temperature

Transient elevations of temperature are most common in the first three weeks of treatment. Raised temperatures above 38˚C should be investigated to rule out the possibility of underlying infection, neutropaenia or neuroleptic malignancy syndrome.

Pulse

Clozapine is associated with an increased risk of myocarditis, especially in the first 2 months of treatment. Cases of cardiomyopathy have also been reported. Persistent tachycardia at rest, or tachycardia accompanied by palpitations, arrythmias, chest pain, shortness of breath or symptoms of heart failure should be urgently investigated for myocarditis or cardiomyopathy. If myocarditis or cardiomyopathy is diagnosed or suspected, stop clozapine and refer to a cardiologist.

Blood Pressure (lying and standing)

Hypotension and circulatory collapse may be profound and may be accompanied by cardiac and / or respiratory arrest. This occurs most commonly during the titration period. This risk is reduced by small, slow increases in dose. The patient should be closely supervised and lying and standing blood pressure monitored to record the presence of a postural drop.

Smoking Status

A change in smoking status can have an adverse effect on the patient's clozapine blood levels. Abrupt cessation of smoking may lead to clozapine intoxication. Patients that smoke should be informed that if they decide to stop smoking, they are encouraged to do so but must inform their nurse or doctor as a dose adjustment may be necessary.

5.4 Management of side effects

Clozapine treatment has well documented side effects, some of which are life threatening. All adverse drug reactions, whether expected or unexpected, should be reported immediately to the Therapeutic Goods Administration (and no later than three working days after the reaction) either online or using the 'blue card'. Copies of the 'blue card' (Report of Suspected Adverse Reaction to Drugs and Vaccines) are available at www.tga.gov.au/safety/problem-medicines-forms-bluecard.htm

A list of some side effects, as well as the time course and recommended action, has been included on page 4 of the NIMC (clozapine titration) (see Figure 23 below). The action section includes both medical and nursing responses that can be used if an event occurs.

Figure 23 below shows the suggested management of side effects associated with clozapine therapy

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.

6. Clozapine monitoring

Metabolic and haematological monitoring of patients is required as clozapine is associated with a number of serious adverse effects such as blood dyscrasias, myocarditis and cardiomyopathy.

The collection and recording of baseline, then periodic, measurements is recommended to ensure early detection of serious adverse effects. White blood cell count and neutrophil blood count are required to be registered with the Clozapine Monitoring Centre prior to dispensing clozapine.

Patients require a full medical examination prior to the planned initiation of clozapine. A check list of investigations for monitoring clozapine monitoring is provided in the table on page 1 of the NIMC (clozapine titration). The table is reproduced in Figure 24 below.

Baseline tests required should be indicated by the prescriber by ticking the 'if required' column. There is a section for baseline, day 7, 14, 21 and 28 test results to be documented. The shaded sections indicate that these tests are not necessary at this time but they can be instigated at the request of the treating psychiatrist. The last column of the chart indicates the recommended frequency of each test after the initial titration period.

If any of these results are outside normal parameters, or if results reveal particular physical health concerns, these should be raised with the treating team who must make a decision on whether or not to proceed with the prescribed course of treatment.

These are suggested guidelines only and the treating psychiatrist may request further tests according to the clinical results or hospital policy. A tick box "if required" column is available to indicate if specific tests are required e.g. instead of ordering a full blood count (FBC), a neutrophils test may be ordered.

It is expected that the patient results will be checked and recorded primarily by medical officers using the check list on the NIMC (clozapine titration) with references for normal and abnormal test parameters available from the pathology system and documented in the clinical notes.

The suggested clozapine monitoring investigations in the NIMC (clozapine titration) have been modified from the Maudsley Prescribing Guidelines[4].

Figure 24 below shows the suggested clozapine monitoring investigations

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	Abnormal	
Full blood count (FBC)	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Then continue weekly first 18 weeks then monthly
White blood cell (WBC)	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Neutrophils	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Eosinophils	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Troponin	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Then at 3 months then annually
C-reactive protein (CRP)	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	
Electrocardiograph (ECG)	☐		☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	Then continue consistent with local procedure for safe and quality use of clozapine
Liver function test (LFT)	☐		☐	☐									
Urea and electrolytes (U&E)	☐		☐	☐									
Blood group	☐												
Plasma glucose – fasting	☐		☐	☐									Then at 6 months then 12 months
Total cholesterol – fasting	☐		☐	☐									Then at 3 months then every 6 months
Low density lipoprotein (LDL) – fasting	☐		☐	☐									
High density lipoprotein (HDL) – fasting	☐		☐	☐									
Triglycerides - fasting	☐		☐	☐									
Beta human chorionic gonadotropin (Beta HCG) – female	☐		☐+	☐-									As required
Cardiac ECHO	☐		☐	☐									Then continue consistent with local procedure for safe and quality use of clozapine
Clozapine level	☐												
Full physical exam	☐		☐	☐									
Height	☐		m										
Weight	☐		kg		kg		kg		kg		kg		Then continue monthly
Waist	☐		cm								cm		
BMI [weight (kg)/height (m²)]	☐												
Smoking – cigarettes per day	☐												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.

Full blood count (FBC)	
	A pre-treatment full blood count is a requirement for registering a patient with the Clozapine Monitoring Centre. The test is to be repeated weekly for 18 weeks and then monthly. The results are recorded and sent to the Clozapine Monitoring Centre prior to prescribing. The NIMC (clozapine titration) has an area for recording this result for four weeks and the subsequent results are then recorded in the clinical file.

White blood count (WBC)	
	Clozapine can only be commenced if a white blood cell count (WBC) is greater than 3.5 x 10^9/L. If the WBC is 3.0–3.5 X 10^9/L, the blood test should be repeated in one week. If the blood results remain in this range clozapine treatment can commence under medical supervision. The results are sent to the Clozapine Monitoring Centre for recording prior to writing the order. This blood test is to be done weekly for 18 weeks and then monthly.
Neutrophils	
	A neutrophil count of greater than 2.0 x 10^9/L is required to commence clozapine treatment. The results are sent to the Clozapine Monitoring Centre for recording prior to writing the prescription. This blood test is to be done weekly for 18 weeks and then monthly.
Eosinophils	
	Unexplained eosinophilia may occur, especially in the initial weeks of treatment with clozapine. Discontinuation of therapy is recommended if the eosinophil count rises above 3.0 x 10^9/L. Therapy should restart only after the eosinophil count has fallen below 1.0 x 10^9/L and at the discretion of the treating psychiatrist. This blood test is to be done weekly for 18 weeks and then monthly.
Troponin	
	Tthe presence of non-specific cardiac symptoms and family history of heart failure should be noted. Testing to measure the baseline markers of myocardial damage include using a troponin I or T assay and serum creatinine. Alternatively, where a troponin test is not available, creatine kinase monobasic isoenzyme (CK-MB) could be used. This blood test is to be done weekly for 18 weeks and then 3 monthly then annually.
C-reactive protein (CRP)	
	CRP is a non-specific marker of inflammation and may provide an early warning of the development of myocarditis caused by clozapine. This blood test is to be done weekly for 18 weeks and then 3 monthly then annually.
Electrocardiograph (ECG)	
	A baseline ECG is required. It is recommended to be repeated at 3 months and then every 6 months.
Liver function test (LFT)	
	A baseline liver function tests are required. If results are outside normal parameters, commencement of clozapine is at the discretion of the treating psychiatrist. It is recommended that liver functions be tested annually.
Urea and electrolytes (U&E)	
	A baseline U&E test is required. It is recommended that U&E be tested annually.
Blood group	
	This is required for registration and identification purposes by the CPMS.
Plasma glucose - fasting	
	It is a requirement of CPMS registration that the fasting plasma glucose level of the patient is measured.
Total cholesterol - fasting	
	Increases in cholesterol levels have been observed in patients taking clozapine; a baseline level should be taken prior to commencing.

Low density lipoprotein (LDL) - fasting	
	A baseline LDL level is required. It is recommended to be tested at 3 months and then every 6 months.
High-density lipoprotein (HDL) - fasting	
	A baseline HDL level is required. It is recommended to be tested at 3 months and then every 6 months.
Triglycerides - fasting	
	A baseline triglyceride level is required. It is recommended to be tested at 3 months and then every 6 months.
Beta human chorionic gonadotropin (Beta HCG) - famale	
	A beta HCG test should be done to confirm if the patient is pregnant. The adverse pharmacological and toxicological effects of clozapine in adults may also occur in the foetus. Therefore, clozapine should not be used in pregnancy or in women likely to become pregnant, unless the expected benefit of treatment is considered to outweigh the potential risk to the foetus.
Cardiac ECHO	
	It is advised that patients undergo echocardiography to test for the development of adverse cardiac events and to provide a baseline reading against which any future events may be measured. Then follow local procedures/ guidelines.
Clozapine level	
	When a patient has ceased clozapine and is being considered for re-titration or recommencement, a serum clozapine level needs to be measured prior to initiation. The frequency of this test is at the discretion of the treating psychiatrist.
Full physical exam	
	A full medical examination is required prior to commencement of clozapine
Height	
	Height is recorded in metres to assist with body mass index calculation.
Weight	
	An area has been provided for a base line and weekly recording of a patient's weight in kilograms (and in which "kg" is pre-printed).
Waist	
	A baseline waist measurement is required and recorded in centimetres with "cm" pre-printed on the NIMC (clozapine titration). Weekly recording of waist measurement is recommended as an increase in waist measurement is a sign of weight gain.
BMI	
	The body mass index is required as a measure of metabolic changes that may occur with clozapine treatment. (BMI = weight (kg) / height (m)).
Smoking – cigarettes per day	
	Baseline smoking habits, followed by weekly recordings, should be documented. Abrupt cessation of smoking may lead to clozapine toxicity. Patients who smoke need to inform their prescriber if they stop smoking as dose adjustment may be necessary.

Related resources

1. National Safety and Quality Health Service Standards 2011
   www.safetyandquality.gov.au/our-work/accreditation/nsqhss/
2. National Standards for Mental Health Services 2010
   www.health.gov.au/internet/main/publishing.nsf/Content/mental-pubs-n-servst10

References

1.Australian Commission on Safety and Quality in Health Care. National Inpatient Medication Chart and Psychiatric Acute Services Survey January 2012. 2012:1-37.

2.Australian Commission on Safety and Quality in Health Care. NIMC (clozapine titration). 2012:4.

3.National terminology, abbreviations and symbols to be used in the prescribing and administering of medicines in Australian hospitals. 2008. (Accessed 8 April, 2009, at http://www.safetyandquality.gov.au/internet/safety/publishing.nsf/Content/D0DABD9912D44A14CA257516000FDABB/$File/18202.pdf)

4.D. Taylor CP, S. Kapur,. Maudsley Prescribing Guidelines. 10th Edition. 2009.