Medication

CLOZAPINE INVESTIGATION REVIEW

MR-75D

General instructions for completing clozapine protocol forms

- This form is designed for medical officers to document the results of tests required for the monitoring of participants prescribed clozapine.
- All staff involved in monitoring clozapine must be registered with the monitoring provider (refer to your local Clozapine Coordinator or SA Health Pharmacist for more information).
- The full completion of this form is the minimum requirement for all participants prescribed clozapine under the TGA endorsed clozapine management protocols. Further monitoring may be required by individual health networks.
- All entries must be completed with a date, signature, name, designation and time.
- Incomplete entries are not valid, all boxes in each section must be completed and each section signed off.
- Plans for dealing with abnormal results should be documented in the medical record.
- Please use the comments section (below) to indicate blood tests out of the normal range e.g. WCC range, amber/red range.

WCC and NC	Range	Action
WCC >3.5 x 10^9/L and NC >2.0 x 10^9/L	GREEN	Clozapine therapy can continue or be titrated upwards as required
WCC 3.0-3.5 x 10^9/L and/or NC 1.5-2.0 x 10^9/L	AMBER	Requires increasing frequency of monitoring, to twice weekly
WCC <3.0 x 10^9/L and/or NC <1.5 x 10^9/L	RED	STOP clozapine immediately and repeat blood test within 24 hours. Contact Consultant Psychiatrist and arrange urgent medical review

Specific instructions for completing clozapine participant protocol - amber

If the participants blood results fall within the amber range (as indicated in the table above) please follow these instructions

- Participants on a weekly/monthly protocol should continue to have their clinical review observations documented on their current form (either *Clozapine Commencement Form, Clozapine Participant Protocol - 4 Weekly* or *Clozapine Participant Protocol - Recommencement as required)*
- Continue **twice weekly** white cell (WCC) and neutrophil (NC) counts until either:
  - WCC > 3.5 x 10^9/L **and** NC > 2.0 x 10^9L - Resume pre-amber monitoring protocol
  - **and/or** NC > 1.5 x 10^9L - Cease clozapine and commence red range monitoring protocol immediately

Specific instructions for completing clozapine participant protocol - red

If the participants blood results fall within the red range (as indicated in the table above) please follow these instructions

- Contact participant and advise to stop clozapine and repeat CBE blood test
- Contact consultant psychiatrist
- Cease clozapine immediately
- **Repeat and review** white cell (WCC) and neutrophil (NC) counts **within 24 hours**
- Notify consultant haematologist - refer to the clozapine manufacturer's protocol
- Continue **daily** white cell (WCC) and neutrophil (NC) counts until either:
  1. WCC > 3.0 x 10^9/L **and** NC > 1.5 x 10^9L - proceed with **twice weekly** blood monitoring until
  2. WCC > 3.5 x 10^9/L **and** NC > 2.0 x 10^9L - proceed with **weekly** blood monitoring for four (4) weeks
- Clozapine must not be restarted unless authorised by the clozapine manufacturer's consultant haematologist

Clozapine cessation date:	___ ___ / ___ ___ / 2 0 ___ ___
White cell count:	___ . ___ x 10^9/L
Neutrophil count	___ . ___ x 10^9/L
Last clozapine dose:	____ ____ ____ mg
Blood group:	O+ ☐ O- ☐ A+ ☐ A- ☐ B+ ☐ B- ☐ AB+ ☐ AB- ☐

Comments/contributing factors: ....

....

....

....

Full Name *(Please Print)*	Designation *(Please Print)*	
Signature	Date __ __/__ __/20 __ __	Time am __ __:__ __ pm

Monitoring requirement for participants prescribed clozapine

In order to comply with the TGA endorsed clozapine protocols, it is imperative that:

- the Medical Officer reviews the current white cell (WCC) and neutrophil counts before writing a clozapine prescription
- the participant is clinically assessed for signs and symptoms of infection before being given a clozapine prescription.

White cell counts are monitored weekly for the first 18 weeks and then every 28 days thereafter providing results remain in the green range (WCC> 3.5x10^9/L and neutrophil count > 2.0x10^9/L).

The decision to move a participant with amber results on weekly monitoring to 4 weekly monitoring should be guided by the clozapine manufacturers Consultant Haematologist.

The following must be completed within a 48 hour period commencing on the morning of the due date of the blood sample:

- Blood sample taken
- Haematology examination performed by the laboratory
- Clinical assessment of the participant by a suitably qualified health professional for signs and symptoms of infection
- Review of blood results by the clozapine registered Medical Officer and new prescription written if results are not in the red range
- Results entered into the relevant clozapine manufacturer's database by centre personnel or onto a paper Blood Count Form which is forwarded to pharmacy
- Medication dispensed by pharmacist after they review the blood results and prescription
- If applicable, a completed paper Blood Count Form should be faxed to the clozapine manufacturer's consumer monitoring database provider.

If a blood count is not received by the clozapine manufacturer's database provider within 48 hours after the blood due date, an alert will be generated by the clozapine database provider and an appropriate letter faxed & emailed to the Centre Co-ordinator, the Medical Officer and the Pharmacist who signed the most recent Blood Count Form.

If the participant has discontinued clozapine for any reason or there has been any therapy interruption greater than 72 hours, written notification should be faxed to the clozapine manufactures database provider.

<u>Recommencing clozapine after a period of interruption:</u>

Clozapine must be re-titrated from 12.5mg if the participant has missed the medication for more than 48 hours to reduce the risk of serious side effects. There are also additional monitoring requirements depending on the period of interruption. See table below:

Period of Interruption (time since last dose was taken)	Dosage / Monitoring Requirements
≤ 48 hours	No change to dosage or monitoring
> 48 hours & ≤ 72 hours	Start on 12.5mg and titrate up No additional monitoring requirements
> 72 hours & ≤ 28 days	Start on 12.5mg and titrate up **For 4 Weekly participants:** Weekly monitoring for 6 weeks. If no abnormality, resume 4 weekly monitoring **For Weekly participants:** Weekly monitoring for 6 weeks or as long as needed to reach 18 weeks (whichever is the greatest).
> 28 days	New participant registration form New pre-treatment result and monitoring same as new participant (18 weeks); no 6 hour vital signs monitoring required Start on 12.5mg and titrate up.

Cardiac Monitoring Guidelines

At all times	Educate participants and carers to report flu-like symptoms, GI upsets, dizziness or chest pain.
Pre-Commencement, within 6 months, then annually	Echocardiogram.
First 28 Days	Measure body temperature at the same time each day.
Baseline, day 7, 14, 21, 28, week 12 then annually	Troponin T or I, CRP, ECG (except day 21), Pulse, Blood Pressure, Respiratory rate.
If at any time • Temperature > 38°C or flu-like symptoms	Immediate CRP, Troponin and CBE.
• Troponin > 2 ULN and CRP elevated	Urgent transfer to Emergency department. Urgent cardiology consultation – query myocarditis. Urgent echocardiography.
• Troponin > 2 ULN and normal CRP	Urgent transfer to Emergency department. Urgent cardiology consultation – query acute coronary syndrome.
• Troponin 1 to ≤ 2 ULN and elevated CRP	Urgent cardiology consultation. Daily assess: troponin, CRP and symptoms until features normalise. Clozapine treatment can continue if not contraindicated by ongoing assessment.

Red 032 Pant Green Pant 129 Black MR75D Clozapine

Medication

CLOZAPINE INVESTIGATION REVIEW & PRESCRIPTION RECORD

(MR75D)

Facility: ....

Affix participant identification label in this box

UR No: ....

Surname: ....

Given Name: ....

Second Given Name: ....

D.O.B: .... Sex: ....

Community/Private Psychiatrist: .... **Participant CPN:** ....

Date bloods taken	Date bloods reviewed	Time bloods reviewed	Type of test	Results	Comments (*indicate WCC range if applicable*)	Prescription written	Number of days	Dose (mg)	Signature	Name (please print)	Designation
__ __/__ __/20 __ __	__ __/__ __/20 __ __	__ __:__ __ AM / PM				Y / N / NA					
__ __/__ __/20 __ __	__ __/__ __/20 __ __	__ __:__ __ AM / PM				Y / N / NA					
__ __/__ __/20 __ __	__ __/__ __/20 __ __	__ __:__ __ AM / PM				Y / N / NA					
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SA Health

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