Justice Health and
Forensic Mental Health Network

NSW GOVERNMENT

Justice Health NSW Procedure

Intramuscular (IM) Clozapine

Issue Date: September 2023

Together for
Healthier Tomorrows

Intramuscular (IM) Clozapine - Forensic Hospital

Procedure Number 6.101

Procedure Function Continuum of Care

Issue Date September 2023

Next Review Date September 2026

Risk Rating

Summary The procedure identifies the strict approval process and use of IM Clozapine for Forensic Hospital (FH) patients.

Responsible Officer Director of Nursing and Services, The Forensic Hospital

Applies to
☐ Administration Centres
☐ Community Sites and programs
☐ Health Centres - Adult Correctional Centres or Police Cells
☐ Health Centres - Youth Justice Centres
☐ Long Bay Hospital
☒ Forensic Hospital
Other:

CM Reference PROJH/6101

Change summary Update of linked associated policies/guidelines/procedures.

Authorised by The Forensic Hospital Policy and Procedure Committee and Justice Health NSW Drugs and Therapeutics Committee

Revision History

#	Issue Date	Number and Name	Change Summary
1	February 2022	DG3045/22	New Document
2	September 2023	DG37291/23	DG47613/23

Justice Health and Forensic Mental Health Network
PO BOX 150 Matraville NSW 2036
Tel (02) 9700 3000
http://www.justicehealth.nsw.gov.au

1. Table of Contents

2. Preface

Intramuscular (IM) clozapine is not listed under the Therapeutics Goods Administration (TGA) Australian Register of Therapeutic Goods (ARTG) formulary. The Justice Health and Forensic Mental Health Network (Justice Health NSW) Drugs and Therapeutics Committee has approved the use of IM clozapine, in exceptional circumstances, as a treatment of last resort for patients who qualify for IM clozapine under specific parameters:

a) patients detained at the Forensic Hospital,

b) aged between 18 years and 60 years of age,

c) have residual signs and symptoms of schizophrenia following a trial of two antipsychotic medications at therapeutic dosages for a minimum 6-weeks duration,

d) have a diagnosis of treatment resistant schizophrenia or treatment resistant schizoaffective disorder, and

e) has no known contraindications to oral clozapine

IM clozapine can only be obtained by following the steps outlined in this procedure. This procedure only considers treatment with IM clozapine as opposed to other routes of administration, such as the nasogastric route.

A patient can only be prescribed IM clozapine following review and assent by the Forensic Hospital IM Clozapine Review Committee. This is conducted on a case-by-case basis.

a) The Forensic Hospital IM Clozapine Review Committee is made up of the Clinical Director Forensic Hospital (CDFH), consultant psychiatrists, senior nursing staff and the clozapine co-ordinator.

Once a patient is deemed suitable for IM clozapine, application to the TGA must be made under the Special Access Scheme Category B. This is completed on a case-by-case basis.

Future versions of this procedure will consider prescription of IM clozapine as an authorised prescriber. This will allow importation of the IM formulation for a class of person as opposed to a case by case basis but will require Specialist College or Ethics approval in the first instance.

IM clozapine is not to be used as a substitute for patients established on oral clozapine who refuse their oral medication.

3. Procedure Content

3.1 What is IM clozapine

1. Clozapine is a unique antipsychotic medication with evidence for effectiveness in treatment resistant schizophrenia. IM clozapine is an unlicensed formulation of clozapine, which is produced in the Netherlands by Apotheek A15 and is exported to MedSurge health care who are a licenced sponsor in Australia. MedSurge are a Victorian based company who specialise in pharmaceutical and medical device supplies.
2. IM clozapine is a clear yellow solution for injection which can be stored at room temperature. The strength of the injection is 25mg/ml and each ampoule contains 5mls (125mg). IM clozapine is administered by deep intramuscular injection into the gluteal muscle. The injection is painful, with the maximal volume per ampoule for injection 4mls (100mg). It is recommended that injection sites be rotated as per usual IM practices.

3.2 What is the oral equivalent of IM clozapine

1. The bioavailability of IM clozapine is approximately double that of oral clozapine. For example, 50mg IM clozapine is roughly equivalent to 100mg oral clozapine. As such, when a patient transitions from IM clozapine to oral clozapine the dose should be appropriately adjusted. See the IM clozapine dose equivalent table at appendix 6.3.

3.3 What is the objective of using IM clozapine

1. IM clozapine is intended as a brief time-limited intervention. It is only available to those patients who qualify for *enforced treatment*. To qualify, patients must have an established diagnosis of treatment resistant schizophrenia or treatment resistant schizoaffective disorder.
2. IM clozapine is intended to help initiate patients on clozapine who qualify for but refuse the oral formulation. A secondary aim is to transition the patient to oral clozapine as soon as is practicable.
3. A patient *graduates* to IM clozapine once all other avenues for lessor restrictive treatment have failed. *IM clozapine is a treatment of last resort*.

3.4 Registration of patients on IM clozapine

1. Prior to starting IM clozapine, all patients must be registered with the external clozapine monitoring service, Clopine.
2. Where external monitoring for IM clozapine is not available with Clopine, the prospective patient's basic details and proposed transition time to oral clozapine are provided to Clopine. Once the patient transitions to oral clozapine, external monitoring from Clopine can commence.
3. At all times during the administration of IM clozapine, standard baseline and weekly blood monitoring will be undertaken identical to the Clopine Central Monitoring Protocol and the Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine, including review for amber and red alerts. The responsibility for oversight of IM clozapine blood monitoring lies with the prescribing consultant psychiatrist.

4. During the IM clozapine 2-week titration, the following information should be recorded in Justice Health Electronic Health System (JHeHS Progress notes) by the patient's treating psychiatrist each week. The Pharmacist dispensing the clozapine must also record this information in the JHeHS progress notes.
    a) Date
    b) Full Blood Count
    c) White Blood Cell Count
    d) Neutrophil Count
    e) Result = green / amber / red
    f) Dose

3.5 How long can IM clozapine treatment continue

1. IM clozapine should be used for the shortest duration possible. Prior to administration of IM clozapine the patient must be offered oral clozapine.
2. The need to continue IM clozapine should be discussed weekly at the MDT. In general, IM clozapine should be used for up to two weeks. In exceptional circumstances, the IM formulation may be used for longer than two weeks, if approved by the MDT and CDFH.

3.6 Justice Health NSW procurement of IM clozapine

1. IM clozapine is ordered from an international supplier under the TGA Special Access Scheme (SAS) on a case-by-case basis. Generally, a two-week supply of IM clozapine is ordered. The ordering and delivery process may take up to 8 weeks.

3.7 Process of initiating a patient on IM clozapine

1. The prospective patient is reviewed by the psychiatrist to determine if patient meets criteria to qualify for IM clozapine. All available collateral is reviewed to determine if clozapine has previously been trialled and if so, reasons for cessation.
2. The MDT discusses the suitability of patient for IM clozapine. This information is documented in JHeHS. A synopsis prepared by the patients' consultant psychiatrist covering the patients clinical condition and suitability for IM Clozapine is sent to the CDFH. The CDFH establishes a meeting of the IM Clozapine review committee to consider patients suitability.
3. If assent is given by the Review Committee and confirmed by the CDFH, the Justice Health NSW Chief Pharmacist and Clozapine Coordinator are informed of the patient's details for registration. For the full process see appendix 6.1 and appendix 6.2.
4. Work up of patient for clozapine bloods and ECHO as per Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine.
5. The TGA SAS form, category B is completed and sent off to the TGA for approval. An IPU form should be completed for review by the delegated CDFH. Note that IPU is only for a fortnight and if the patient continues IM treatment for longer than a fortnight a new IPU needs completion.
6. Notification of TGA approval should be sent to the Pharmacy Department via email. Thereafter, the order for IM clozapine is placed with the supplier.

7. Importation of IM clozapine is managed via regulatory processes overseen by Medsurge to the Justice Health NSW Pharmacy Department.
8. The patient is registered with the Clopine monitoring system prior to arrival of IM clozapine.
9. Psychoeducation is undertaken with the patient and the primary carer informed of the process of IM clozapine.
10. The patient is reviewed by their treating psychiatrist or registrar prior to each dose of IM clozapine. Oral clozapine is always offered prior to IM clozapine.
11. If clozapine is discontinued, the details of this must be documented in JHeHS. Clopine Central should be informed of the failed trial and medical management of potential cholinergic rebound should be considered.
12. If there is a medication related adverse event this should be reported to the patient's treating Consultant Psychiatrist and the Pharmacy Department. Adverse drug events are to be reported as per Section 12 of the Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine and an ims+ documented.
13. Any physical injury to patients or staff should be reported to the patient's treating Consultant, as well as documentation in the patient's JHeHS progress notes and ims+ documented.

3.8 Starting IM clozapine Responsibilities

1. **Registration**
   a) Clopine Central should be informed of the prospective patient prior to starting IM clozapine. This will allow for a more streamlined transition to oral medication monitoring.
2. **Pre-clozapine work up**
   a) Prior to starting IM clozapine a baseline work up must be completed as outlined in the Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine.
3. **Prescribing IM clozapine**
   a) IM clozapine should only be administered as a morning dose.
   b) Prior to each dose of IM clozapine the patient should be reviewed by the treating consultant or registrar. IM clozapine should be prescribed as a stat order on the patient's eMAR.
   c) If the patient elects to switch to oral clozapine this should be charted and given instead of IM clozapine. The dose equivalent of oral clozapine is double that of IM clozapine so the oral dose prescribed should be two times the dose of the IM clozapine for that day. Please refer to the IM clozapine dose table in appendix 6.3.
   d) Regarding weekends and public holidays; the consultant or registrar can pre-emptively chart IM clozapine for Saturday and Sunday and public holidays.
   e) If the patient chooses to accept oral clozapine on a weekend or public holiday the registrar on-call should contact the on-call psychiatrist for an oral dose equivalent order.
   f) When starting IM clozapine, consideration must be given to other antipsychotic medication, which are being given at the same time. The cumulative dose should not exceed 1000mg chlorpromazine.

4. **Dispensing**
   a) IM clozapine will be dispensed by the Justice Health NSW Pharmacy Department to individual patients. Supply is only to be used for the intended patient as labelled. All excess IM clozapine supply is to be returned to the Pharmacy Department.
   b) The patient should always be offered oral clozapine in the first instance, before IM clozapine is prepared. If the patient continues to refuse, IM clozapine can be administered.
5. **Administration**
   a) Following clinical review by the psychiatrist or registrar, IM clozapine is charted on a daily basis as a stat order on the patient's eMAR.
6. **Authorised Prescribers**
   a) All Staff Specialist Psychiatrists employed by Justice Health NSW are considered authorised prescribers of IM clozapine in the Forensic Hospital and registered with Clopine Central.

3.9 Monitoring of patient in IM clozapine treatment

1. After each IM clozapine injection, the patient should be monitored every 15 minutes for at least one hour. This includes monitoring of blood pressure, pulse, respiratory rate and temperature.
2. It is anticipated that for many patients such monitoring may be met with resistance. However, every effort should be made to obtain these measures.
3. If the patient refuses observations, this must be documented in JHeHS. When a patient is refusing vital sign monitoring other clinical indicators can be observed in the alternative. For instance, respiratory rate and level of consciousness should be recorded. In addition, other clinical indicators might include, signs of discomfort, shortness of breath, pallor, sweating and indicators of chest pain.
4. These clinical indicators should be recorded in the clinical record and a medical officer informed as soon as possible.
5. Weekly full blood count tests must be completed while on IM clozapine as per the Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine.
6. Weekly blood tests may represent a time of increased risk of aggression from patients toward staff. This may occur in the form of assault, injury during restraint or needle stick injury. Psychological injury should also be considered.
7. A safety huddle should be completed with the core intervention team prior to administration of IM clozapine or enforced bloods. The most appropriate setting for the intervention should be considered, as well as the use of VPM or need for mechanical restraint.
8. All relevant paraphernalia for venepuncture or IM medication administration should be prepared prior to room entry. Blood samples may be taken at the time of IM clozapine administration to reduce need for potential repeated VPM or use of mechanical restraint.

4. Definitions

Must

Indicates a mandatory action to be complied with.

Should

Indicates a recommended action to be complied with unless there are sound reasons for taking a different course of action.

5. Related documents

Legislations	
Justice Health NSW Policies, Guidelines and Procedures	Guideline 6.049 Medication Guidelines Guideline 6.051 Psychotropic Medications Guideline 6.053 Management of Patients on Clozapine Guideline 6.054 High Risk Medicines Management Framework
Justice Health NSW Forms	
NSW Health Policy Directives and Guidelines	
Other documents and resources	

6. Appendix

6.1 IM Clozapine pre assessment checklist

Patient Name	
Patient MRN	
Patient DOB	
Date Clopine informed of prospective titration and treatment plan?	
Has the patient previously trialled Clozpaine? Reason for cessation?	
Physical health concerns / contraindications?	
Review and approved by second Psychiatrist?	
Review and approved by the FH IMI clozapine review committee?	
Approved by the CDFH? Signed and dated?	
Chief Pharmacist informed of new registration?	
SAS category B form completed?	
TGA approval provided?	
Completed approval forms sent to sponsor and order placed?	

6.2 Approval of IM clozapine

Review Justice Health NSW Guideline 6.053 Guidelines for the Management of Patients on Clozapine		
Patient Name		
MRN		
DOB		
Actions to be undertaken once approval for IM clozapine given by IM clozapine review committee		
Task	**Date**	**Comments / issues arising**
History of previous bone marrow disorder, neutropenia, or previous complications on clozapine		
Complete physical examination		
Fasting BGL and HDL/LDL cholesterol, serum triglycerides, LFT, troponin I or T, CRP, blood group, ECG and ECHO		
Review of concomitant antipsychotics currently being administered		
Discussion with patient about IM clozapine and the common and rare side effects of clozapine		
MDT discussion of use of VPM, mechanical restraint at times of medication administration and taking bloods		
MDT discussion of challenges for specific patient with monitoring vital signs post IM injection		
Once medication in stock; IM clozapine is charted daily following patient review on STAT section of eMAR.		
NOK is informed of the trial of IM clozapine		

6.3 IM Clozapine Dose Equivalent Table

Oral clozapine is always offered prior to intramuscular dosing

Day	Oral dose *Always offer first*	IM clozapine dose (25mg/ml)
1	12.5mg	6.25mg (0.25ml)
2	25mg	12.5mg (0.5ml)
3	25mg	12.5mg (0.5ml)
4	50mg	25mg (1ml)
5	50mg	25mg (1ml)
6	75mg	37.5mg (1.5ml)
7	75mg	37.5mg (1.5ml)
8	100mg	50mg (2ml)
9	100mg	50mg (2ml)
10	125mg	62.5mg (2.5ml)
11	125mg	62.5mg (2.5ml)
12	150mg	75mg (3ml)
13	150mg	75mg (3ml)
14	175mg	87.5mg (3.5ml)