

Clozapine Intramuscular Injection: Application process

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What is IM clozapine?

Intramuscular clozapine is an unlicensed product made in the Netherlands by Brocacef and imported to the UK via Durbin PLC. It is a clear yellow solution for injection. The strength of the injection is 25mg/ml and each ampoule contains 5mls (125mg). It is administered by deep intramuscular injection into the gluteal muscle. The injection is painful and the maximum volume that can be injected into each site is 4ml (100mg). For doses greater than 100mg daily, the dose may be divided and administered into two sites.

Which patients can be prescribed IM clozapine?

The injection is indicated only for inpatients within Forensics services:

- With a treatment-refractory psychotic disorder
- Who no longer have the capacity to consent.
- Who are refusing oral treatment after all approaches to administering oral clozapine have been taken.

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Protocol Number	PHARM/0088/V2.0	Date of Review	01 April 2022 (extended)

It can be used for patients who have never been exposed to clozapine previously or patients previously treated with clozapine and known to have responded but relapsed owing to non-compliance.

The need for clozapine injection must:

- Be agreed by the MDT and fully documented in PARIS
- Discussed at a Forensic Consultant peer review meeting
- Approved by the SOAD (clozapine IM specifically referenced)
- The Responsible Clinician must also apply for approval for use using the Trust [single application form](#) ensuring the contents of [appendix 1](#) are included
 - The request will then be considered by an appropriate panel (which will include the Clinical Director, Chief Pharmacist and Head of Service or deputies, as a minimum).
 - Panel approval allows THREE titrations with IM clozapine to be attempted before further panel approval is required; however, CD approval is required for each titration.

What is the objective of using IM Clozapine?

The aim of using clozapine injection is a short-term intervention to initiate clozapine for patients who refuse medication, with a view to convert to oral clozapine as soon as possible.

Registration of patients for IM Clozapine

All patients for IM clozapine must only be registered with the appropriate clozapine patient monitoring service, Clozaril Patient Monitoring Service (CPMS) or Denzapine Monitoring Service (DMS), as the objective is to use the injection for the shortest possible time before switching to oral clozapine treatment. The usual clozapine mandatory baseline and weekly blood monitoring and the necessary precautions for amber and red warnings apply.

How long can the treatment continue for?

Clozapine injection should be used for the shortest duration possible. Before administering each injection, the patient should be offered clozapine orally. The need for ongoing IM treatment must be reviewed regularly by the MDT. In general, the injection should be used for no longer than two weeks; however, in exceptional cases, the injection may be used up to four weeks, with further CD approval. The original application form should be amended to include details of the patient's progress and the case for extending the duration.

What are the equivalent oral and IM doses?

The oral bioavailability of clozapine is about half that of the intramuscular injection. For example, 50mg daily of the IM injection is roughly equivalent to 100mg daily of the tablets.

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Starting clozapine IM injection

The patient must be registered with CPMS/DMS the week before commencing treatment. Treatment should start on a Monday whenever possible. Clozapine should be prescribed on the Prescription and Administration Record chart and annotated 'as per titration chart' – as an exception to Trust policy, the route may be stated as "PO/IM" to provide nurses with the options covered by the titration chart. The prescriber must complete the Clozapine IM Titration Chart ([Appendix 2](#)) and sign and date each dose. The patient should always be offered the oral clozapine first and if the patient continues to refuse, then the injection is administered. Courses lasting longer than 14 days will require an individualised titration chart which should be discussed with the Trust Pharmacy Team.

Contacting CPMS

CPMS/DMS are not responsible for monitoring FBC results when IM clozapine is used; it remains the responsibility of the Responsible Clinician. However, in order to be able to offer oral clozapine, the patient must be registered with CPMS/DMS and they must have up to date FBC blood results as per the patient's monitoring schedule. Otherwise, the frequency of contact with CPMS/DMS is to be determined on an individual patient basis.

Monitoring of patients on IM clozapine treatment

Baseline assessment before starting clozapine must include ECG, FBC, lipids, HbA1C, U&Es, LFT, CRP, troponin and prolactin. It is anticipated that daily monitoring of blood pressure, pulse, respiratory rate and temperature will be difficult for many patients; every effort must be made to obtain these and patient refusal of observations must be documented. Importantly, patients should be observed for any signs of being unwell, such as pallor, cough, shortness of breath, sweating etc. After each injection has been given the patient must be observed every 15 minutes for the first two hours to check for excess sedation. The usual weekly blood tests should be performed whilst on treatment; the sample could be taken at the same time as the administration of clozapine injection if needed.

N.B. If IM lorazepam is required leave at least ONE HOUR between administration of IM clozapine and IM lorazepam.

Monitoring Physical Observations

Monitoring physical observations should be carried out as per Clozapine Pathway and enter onto PARIS and EWS.

Cost of medication

Clozapine injection costs around £100 per ampoule (or part thereof, as any unused portion must be discarded). There would need to be a minimum order of 2 boxes of 10 ampoules which costs approx. £2,000.

Guideline written with acknowledgement and thanks to South London and Maudsley NHS Foundation Trust, Sussex Partnership NHS Foundation Trust, Southern Health Foundation Trust and Mersey Care NHS Foundation Trust.

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Appendix 1: Clozapine IM Injection Requirements Checklist

The following need to be in place before initiating IM Clozapine.

The contents of this table should be completed and copy and pasted into the [single application form](#).

Confirm that there are no significant physical health comorbidities that contra-indicate the use of clozapine?	
Has patient previously been prescribed clozapine? If yes, state reason clozapine was stopped previously	
MDT discussion documented in PARIS (state date)	
Peer Review Discussion (state date)	
SOAD approval (with clozapine IM specifically referenced)	
Staff involved in administration are familiar with Guidance	
Nursing Care Plans in place	

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Appendix 2: Clozapine IM Injection Titration Chart

Patients name		NHS number	
D.O.B.		CPMS Number	
Consultant		Ward/Clinical Team	

Monitor Physical Observations as per Clozapine Pathway and record on PARIS and EWS

CAUTION: IM CLOZAPINE IS ONLY HALF THE ORAL DOSE

Day	Date	Oral Dose	IM Clozapine (25mg/ml)	Prescriber's Signature	Specify route Given (PO or IM)	Given by (signature)
		ALWAYS OFFER FIRST BEFORE USING IM	ONLY USE IF ORAL DOSE REFUSED		If IM state side given (L) or (R) IM ROUTE – GLUTEAL ONLY	
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)			

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