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.

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 noncompliance.
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).

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 Clozaril Patient Monitoring Service (CPMS) as the objective is to use the injection for the shortest possible time before switching to oral Clozaril treatment. After treatment with clozapine injection has been agreed by the MDT and approved by the SOAD, CPMS will be informed of the treatment plan and the patient registered accordingly. 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.
In exceptional cases, the injection may be used for longer than two weeks, with further approval. The initial approval process should be repeated with the original application form 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.

Starting clozapine IM injection

The patient must be registered with CPMS 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 tablets first and if the patient continues to refuse, then the injection is administered.

Contacting CPMS

The frequency of contact with CPMS is to be determined on an individual patient basis. During the working week (Monday-Friday), pharmacy will contact CPMS to inform them if the clozapine dose for that day has been given via the oral or intramuscular route unless otherwise instructed. On Saturday and Sunday, ward nursing staff will contact CPMS on-call pharmacist on 01276 692504, to inform them if the clozapine dose for that day has been given via the oral or intramuscular route unless otherwise instructed.

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 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.

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	

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