

Guideline for the use of intramuscular (IM) clozapine treatment

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.

Who can have IM clozapine?

Clozapine injection may only be prescribed and administered on the direct written authority of the Director of Pharmacy (david.taylor@slam.nhs.uk). The injection is indicated only for patients with a treatment-refractory psychotic disorder who are refusing oral treatment. 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, approved by the SOAD and fully documented in EPJS using the assessment form (see appendix 1).

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 be registered with the Zaponex Treatment Access System (ZTAS) as the objective is to use the injection for the shortest possible time before switching to oral treatment. After treatment with clozapine injection has been agreed by the MDT and approved by the SOAD, ZTAS 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 if approved by the MDT, SOAD and Director of Pharmacy.

What is the oral equivalent of the IM?

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/oral solution.

Starting clozapine injection

The patient must be registered with ZTAS the week before commencing treatment. Treatment should start on a Monday whenever possible. Clozapine should be prescribed on the main drug chart and annotated 'see separate clozapine titration chart'. Each dose on the titration chart must be signed and dated by the prescriber. The chart (see appendix 2) must be attached to the main drug chart. The patient should always be offered the tablets/oral solution first and if the patient continues to refuse, then the injection is administered.

Nursing staff must clearly indicate the route of administration used on the titration sheet.

Monitoring of patients on IM clozapine treatment

Baseline assessment before starting clozapine must include ECG, FBC, lipids, plasma glucose, U&Es, LFT, CRP and troponin. 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.

Costs

Clozapine injection costs around £100 per injection (or part thereof, as any unused portion must be discarded).

Appendix 1: Clozapine Injection MDT Assessment Form

Name of Patient	
Date of birth	
Indication for clozapine	
Date patient registered with ZTAS	
Are there significant physical health co-morbidities that contra-indicate the use of clozapine?	
Previously on clozapine? If yes, state reason clozapine was stopped previously	
Date of Director of Pharmacy approval	
Date of SOAD approval	
Date MDT discussion documented in ePJS	

Appendix 2: Clozapine Injection Titration Chart

Week One

Name:

Date of birth:

ALWAYS OFFER ORAL CLOZAPINE FIRST

Day	Date	Oral dose	IM clozapine (25mg/ml) <i>ONLY if oral refused</i>	Prescriber's signature	Specify route given (PO or IM) <i>If IM state side given (L) or (R)</i>	Given by	Pre-dose				2 hours post dose			
							RR	Pulse	Temp	BP	RR	Pulse	Temp	BP
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)											

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Disclaimer: There is very limited clinical experience with intramuscular clozapine. The product is unlicensed in the UK and South London and Maudsley NHS Foundation Trust (SLAM) has not conducted any quality assurance testing on the product. There are no data to compare the pharmacokinetic profiles of the oral and the intramuscular routes, therefore the oral to IM equivalence is an estimation. The optimum duration of treatment has not been established. SLAM will not take any responsibility for the use of this product outside of SLAM.

Clozapine Injection Titration Chart (continued)

Week Two

Name:

Date of birth:

ALWAYS OFFER ORAL CLOZAPINE FIRST

Day	Date	Oral dose	IM clozapine (25mg/ml) <i>ONLY if oral refused</i>	Prescriber's signature	Specify route given (PO or IM) <i>If IM state side given (L) or (R)</i>	Given by	Pre-dose				2 hours post dose			
							RR	Pulse	Temp	BP	RR	Pulse	Temp	BP
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)											