

## Guidelines for the use of Intramuscular (IM) Clozapine treatment for inpatients

Guidelines for the use of intramuscular clozapine treatment for inpatients and the monitoring required.

### HPFT Guideline

Version	1.0
Executive Lead	Executive Director of Quality and Medical Leadership
Lead Author	Deputy Chief Pharmacist
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Target Audience	Practitioners in the inpatients setting involved in using IM clozapine where the oral route is refused

<b>Title of document</b>	Guidelines for the use of Intramuscular (IM) Clozapine treatment for inpatients ONLY		
<b>Document Type</b>	Guidelines		
<b>Ratifying Committee</b>	Drugs and Therapeutics Committee		
<b>Version</b>	<b>Issue Date</b>	<b>Review Date</b>	<b>Lead Author</b>
1.0	16/04/2019	16/04/2022	Georgia Michael Deputy Chief Pharmacist
<b>Staff need to know about this guideline because (complete in 50 words)</b>	<ul style="list-style-type: none"> <li>• Clozapine injection is not licensed for use in the UK.</li> <li>• The Trust has approved its use, in exceptional circumstances during the two weeks at the initiation stage.</li> <li>• Clozapine injection can only be prescribed if approved by MDT, SOAD, Clinical Director and DTC.</li> <li>• It can only be prescribed by a Consultant.</li> </ul>		
<b>Staff are encouraged to read the whole guideline but I (the Author) have chosen three key messages from the document to share:</b>	<ol style="list-style-type: none"> <li>1. IM Clozapine is an unlicensed product and the bioavailability differs to that of the oral form. 50mg of IM injection is roughly equivalent to 100mg of the tablets</li> <li>2. It should only be used if the oral dose is refused during the first two weeks during the initiation period</li> <li>3. After administration of each dose of IM Clozapine, the patient must be observed every 15 minutes for the first two hours to monitor for excessive sedation.</li> </ol>		
<b>Summary of significant changes from previous version are:</b>	New guidelines		

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## 1. Key Points

- Clozapine injection is not licensed for use in the UK.
- The Trust has approved its use, in exceptional circumstances, for service users that are inpatients.
- Clozapine injection should only be used as a last resort and is limited to two weeks at the initiation stage.
- Clozapine injection can only be obtained by following these guidelines.
- Clozapine injection can only be prescribed if approved by a Second Opinion Appointed Doctor (SOAD).
- It can only be prescribed by a Consultant and use of the product must be approved by the Clinical Director on an individual basis.
- The oral bioavailability of clozapine is about half that of the intramuscular injection.
- Clozapine injection is expensive. Dose titration over 2 weeks costs £2000.

## 2. 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.
- The clozapine titration should follow once daily doses as per Appendix 1.
- Injection sites should be rotated as per usual IM practice. See Trust Injection Procedure policy  
<http://trustspace/InformationCentre/TrustPolicies/Lists/Policies/Attachments/315/Injection%20Procedure.pdf>
- The product packaging is shown below.



- A Patient Information Leaflet is available which has been translated from Dutch to English by Durbin PLC.

### 3. Which service users can be prescribed IM Clozapine?

- IM Clozapine is indicated ONLY for inpatients with a treatment-refractory psychotic disorder that are refusing oral treatment.
- IM Clozapine may need to be administered under restraint if the service user declines IM administration. To be administered in line with the Trust's RESPECT training.
- It can be prescribed for service users who have never previously received clozapine or for service users who have previously been treated with clozapine and are known to have responded to it but who have subsequently relapsed owing to non-adherence.
- The initial need for clozapine injection MUST be:
  - Agreed by the multidisciplinary team (MDT)
  - Approved by the Clinical Director (CD) and SOAD
- Clozapine injection must specifically referenced by the SOAD on the T3 form as a named drug, stating the route of administration and dosing information.
- These recommendations, from three independent parties (MDT, CD and SOAD) MUST be fully documented on the IM Clozapine MDT Assessment Form (Appendix 2) and must be signed by the Consultant and recorded in the service user's electronic notes.
- The completed MDT Assessment Form (along with T3 form) must be emailed to the Chair of the Drugs and Therapeutics Committee (DTC) and to the Chief Pharmacist together with the completed "Request and Risk Assessment for the use of Unlicensed Medicines" form found in the Medicines Policy - <http://trustspace/InformationCentre/TrustPolicies/Pages/Medicines.asp>
- These two forms will form the basis upon which the DTC Chair and Chief Pharmacist will formulate their decision to either grant their approval for use of IM Clozapine for a particular service user, or to refuse such approval.
- IM Clozapine may only be prescribed and administered following the written approval of the DTC Chair.
- IM Clozapine injection MUST be requested on an individual service user basis only.

### 4. What is the objective of using IM Clozapine?

- IM Clozapine is a **short-term intervention** to initiate clozapine in service users with treatment-resistant schizophrenia who refuse oral clozapine, with a view to convert to oral clozapine as soon as possible.
- It should only be used when all other approaches have failed and only in those who are predicted to respond to clozapine treatment.
- Treatment with IM Clozapine should be limited to two weeks at the initiation stage.
- The use of IM Clozapine cannot be used as a tool to discourage oral non-compliance post two week initiation period.

### 5. Registration of service users for IM Clozapine

- After IM Clozapine has been approved by the DTC Chair, the service user must be registered with the Denzapine Monitoring Service (DMS) as the aim is to use IM Clozapine only for the shortest possible time before switching to oral clozapine.
- DMS should be informed of the treatment plan and the usual clozapine mandatory baseline and weekly blood monitoring should take place.
- The DMS precautions for amber and red warnings apply to the use of the clozapine injection.
- However, it should be noted that DMS does not hold any responsibility for the use of IM Clozapine; this rests with the service users' Consultant.

## 6. How long can the treatment continue for?

- IM Clozapine should be used for the shortest duration possible. Before administering each injection, the service user must be offered oral clozapine. Oral clozapine during titration is on a once a day regime (see Appendix 1).
- In general, the injection should be used for no longer than two weeks at initiation stage.
- The need for on-going IM treatment must be reviewed regularly by the MDT.
- In exceptional cases, the injection may be used for longer than two weeks if approved by the MDT, SOAD, CD and the DTC Chair.
- If the service user accepts oral doses initially and then after a few weeks starts to refuse it, the service user should be allowed to refuse oral clozapine. Once 48 hours or more have elapsed, clozapine should be re-titrated using IM Clozapine, if necessary.

## 7. 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.

## 8. Starting IM Clozapine

- The service user **MUST** be registered with the DMS the week before commencing treatment as per the Trust's Clozapine Policy.
- The initiation of clozapine in HPFT is restricted to Consultant Psychiatrists registered with the DMS.
- The Consultant Psychiatrist initiating clozapine must document in the electronic patient record (EPR) the service user's DMS number and details of the individual(s) to be contacted, should a query/problem arise. An alert informing other healthcare professionals that clozapine is prescribed, must also be placed on the EPR.
- IM Clozapine should not be prescribed with other antipsychotic medications (oral or IM). However, if this is necessary in exceptional cases, then the other antipsychotics doses should be reduced so that the total BNF cumulative dose does not exceed 100%.
- Treatment should start on a Monday whenever possible, this will also fit better with clozapine monitoring e.g. blood sample.
- Service user's team must make a decision regarding IM Clozapine administration during titration at the weekends and this must be clearly documented in the notes.
- Any changes in the service user's presentation during the weekend should be discussed with the on call Consultant.
- Clozapine must be prescribed on the main drug chart and this must be cross-referenced to the separate Clozapine Injection Titration Prescription Chart (Appendix 1) which **MUST** be attached to the service user's main drug chart.
- Each dose on the clozapine injection titration chart must be signed and dated by the prescriber.
- The service user must always be offered oral clozapine first and if the service user refuses, then IM Clozapine should be administered.
- The administration of clozapine IM must be when there are appropriate number of staff with the right competencies on the unit to carry out the necessary monitoring and the use of restraint if required.
- Nursing staff **must clearly indicate the route of administration** used on the clozapine injection titration chart, which has both oral and IM doses specified on it.

## 9. Monitoring of service users prescribed IM Clozapine

- Baseline Assessments before starting clozapine must include:
  - ECG
  - Full Blood Count
  - Fasting lipids
  - Fasting Plasma Glucose / HbA1C
  - U&Es
  - LFT
  - CRP
  - Troponin
- It is anticipated that daily monitoring of blood pressure, pulse, respiratory rate and temperature will be difficult to achieve for many service users. However, every effort must be made to obtain these and the service user's refusal of observations must be documented in the service user's notes.
- Importantly, service users should be observed for any signs of being unwell, such as pallor, cough, shortness of breath, sweating, drowsiness, dizziness etc. and if observed these should be reported to the Consultant and recorded in the service user's notes.
- **After each dose of IM Clozapine, the service user MUST be observed every 15 minutes for the first two hours to monitor for excessive sedation.**
- The NEWS 2 observation chart should be completed every 15 minutes after each dose for the first two hours as this will cover blood pressure, pulse, respiratory rate, temperature and consciousness.
- The recommended initiation monitoring schedule for in-patients found within the Trust's Clozapine Policy (Appendix 3) should also be followed - <http://trustspace/InformationCentre/TrustPolicies/Lists/Policies/Attachments/146/Clozapine%20Policy%20Version%205.1.pdf>.
- The usual weekly blood tests should be performed whilst on treatment; the sample can be taken at the same time as the administration of clozapine injection.
- The usual precautions for amber and red warnings relating to treatment with clozapine apply (refer to the Trust's Clozapine Policy for further details).
- **N.B. If IM lorazepam is required leave at least ONE HOUR between administration of IM clozapine and IM lorazepam.**

## 10. How is IM Clozapine obtained?

- Clozapine injection will not be held as stock on any Trust wards/units. It may ONLY be obtained on a named-patient basis, with a special order, and will usually take two weeks to arrive in the pharmacy department from the time of its ordering.

## 11. Costs

- Clozapine injection costs around £100 per injection (or part thereof, as any unused portion must be discarded).
- Clozapine injection is available for order by pharmacy in boxes of 10 ampoules, total cost £1,156 (including VAT).

## 12. Further information

- Please refer to:
  - The current Trust Clozapine Policy.
  - The current Trust Injection Procedure.

## 13. Summary

- Before IM Clozapine can be prescribed the following must take place:
  - Use to be approved by MDT
  - Use to be approved by Clinical Director and SOAD
  - T3 form updated
  - IM Clozapine MDT Assessment Form completed
  - Unlicensed request form completed
  - Use to be approved by DTC Chair and Chief Pharmacist
- The administration of IM Clozapine must be a whole MDT process and an MDT meeting must take place before each administration.
- IM Clozapine will only be used as the last resort and the administration will be stopped as soon as the service user agrees to oral clozapine treatment.
- The MDT will discuss the need for further IM Clozapine treatment and the discussion will be documented clearly in the service user's notes.
- The MDT should comprise where possible of the team's Consultant, nursing staff and staff involved in restraining.
- Service user's team must make a decision regarding IM Clozapine administration at the weekends during titration and this should be clearly documented in the notes.
- Any changes in the service user's presentation during the weekend should be discussed with the on call Consultant.
- IM Clozapine use should be limited to two weeks at the initiation stage.
- Where IM Clozapine is prescribed for longer than 2 weeks, this needs to be approved by the MDT, SOAD, CD and the DTC Chair. This should only occur in exceptional circumstances.

## 14. References / Acknowledgements

- Durbin PLC - [www.durbin.co.uk](http://www.durbin.co.uk)
- Sussex Partnership NHS Foundation Trust – Protocol for the use of intramuscular (IM) clozapine injection, April 2017.
- Southern Health NHS Foundation Trust – Clozapine intramuscular (IM) Guideline, inpatient only, June 2018.
- Barnet, Enfield and Haringey Mental Health NHS Trust, Guidelines for the use of intramuscular (IM) clozapine treatment for inpatients, February 2018.
- Tees, Esk and Wears Valley NHS Foundation Trust, Clozapine Intramuscular Injection: Application Process, September 2017.

## 15. Version Control

- Version control for the Procedural Document Management System

Version	Date of Issue	Author	Status	Comment
V1	16/04/2019	Georgia Michael	Deputy Chief Pharmacist	New Guidelines Recommendations from DTC 18/3/19: <ul style="list-style-type: none"> <li>Remove restrictions of PICU and Forensic patients only.</li> <li>Drug of last resort and use is limited to two weeks at initiation stage only</li> <li>Cannot be used as a tool to threaten oral non-compliance post two week initiation period</li> </ul>
V1.1	13/08/2019	Georgia Michael	Deputy Chief Pharmacist	Comments from Heads of Nursing <ul style="list-style-type: none"> <li>Section 3 to include RESPECT training reference</li> <li>Section 4 – change the word “threaten”</li> <li>Section 8 – the use of the word “MUST” instead of should.</li> <li>Section 8 – include “appropriate number of staff with the right competencies”</li> </ul>

## 16. Consultation

- In the case of the Procedural Document Management System, the following have been consulted so far.

Job Title of person consulted
Clinical Director - West Strategic Business Unit
Clinical Director – Learning Disabilities and Forensics Strategic Business Unit
Clinical Director – East and North Strategic Business Unit
Drugs and Therapeutics Committee members
Heads of Nursing
Deputy Director of Nursing & Quality
Senior Professional Lead: PMAV

## Part 2 - Appendices

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## CLOZAPINE INJECTION TITRATION PRESCRIPTION CHART

(Must be attached to the service user's main prescription chart and cross referenced within the main chart)

<b>SU's Name:</b>		<b>Consultant name</b>	
<b>Date of birth</b>		<b>Ward</b>	
<b>NHS number</b>		<b>DMS number</b>	

Please refer to allergies and Mental Health Act Sections on the main prescription chart.

- **CAUTION: IM CLOZAPINE DOSE IS HALF THE ORAL DOSE (e.g 50mg oral = 25mg IM)**
- **CAUTION: IM CLOZAPINE IS ONCE DAILY DOSING**
- **CAUTION: DURING CLOZAPINE TITRATION INVOLVING IM CLOZAPINE THE ORAL DOSE IS ADMINISTERED ONCE A DAY**
- **CAUTION: IM CLOZAPINE IS ADMINISTERED INTO GLUTEAL MUSCLE**
- **CAUTION: ALWAYS OFFER ORAL CLOZAPINE FIRST**

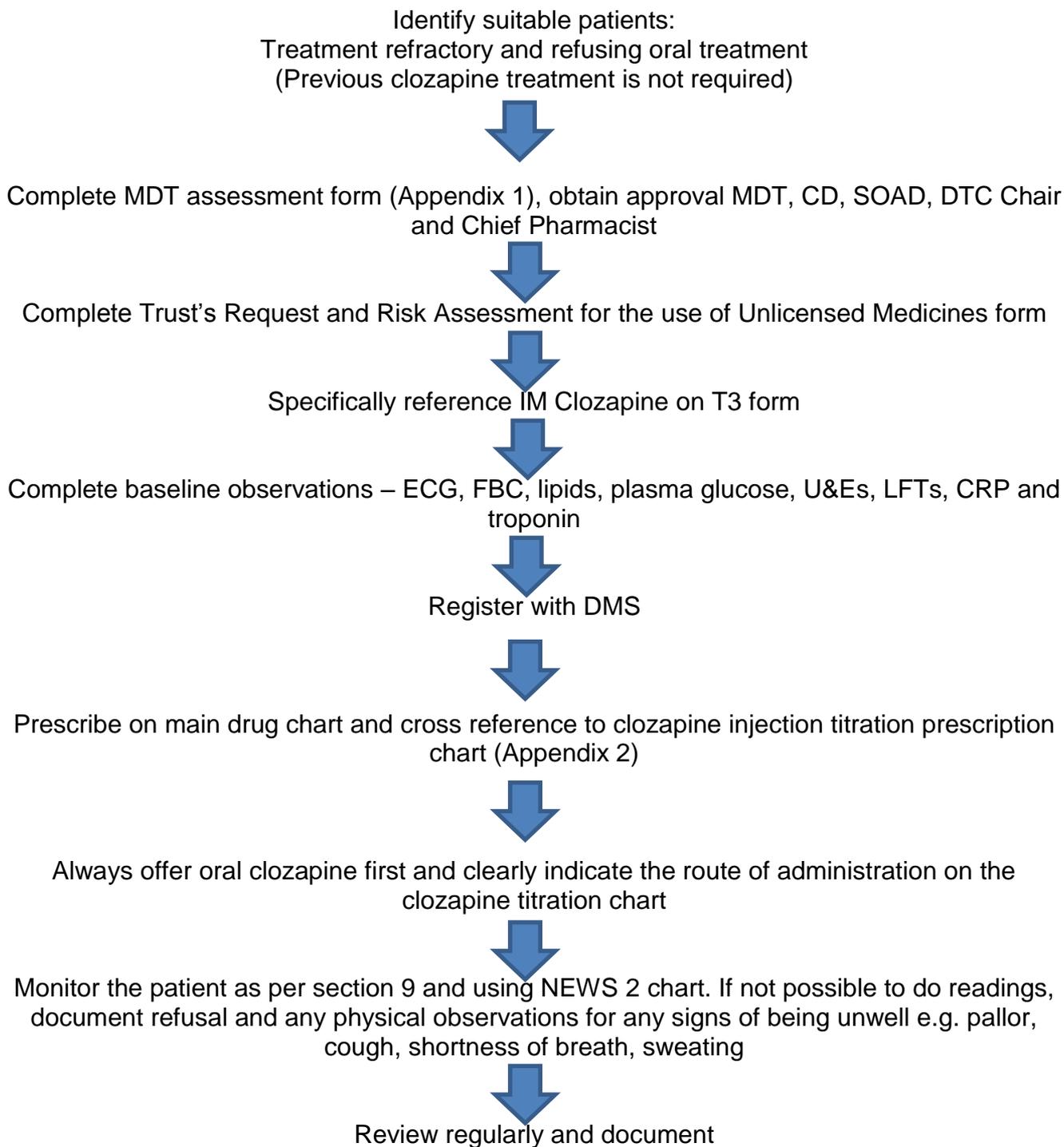
Day	Date	Clozapine oral dose – once a day dose	IM Clozapine dose (25mg/ml) ONLY if oral refused	Prescriber's signature and date	Specify route given (PO or IM) If IM state side given (L) or (R)	Please tick if restraint was used if IM given	Administrator signature and date and time given	Pharm Screen
1		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)					

## IM CLOZAPINE MDT ASSESSMENT FORM

Service User Name	
Ward	
Date of Birth	
NHS number	
Consultant	
Indication for IM Clozapine	
Does the service user have any physical health co-morbidities that lead to the contraindication of clozapine?	Yes / No (delete one)
Has the service user previously been prescribed clozapine?	Yes / No (delete one) If yes, please state reason clozapine was stopped previously:

Criteria	
Date MDT discussion documented in service user record	
Date of Clinical Director approval	
Date of SOAD recommendation	
Does the T3 form specify IM Clozapine? Please include T3 form with application	
Name of Clinical Director	
Signature and date of Clinical Director	Signature: Date:
Name of Consultant	
Signature and date of Consultant	Signature: Date:
Date completed application form sent to DTC Chair and Chief Pharmacist	
Date of DTC Chair and Chief Pharmacist approval	
Signatures and date of Chair of DTC and Chief Pharmacist	<b>Chair of DTC</b> Signature: Date:  <b>Chief Pharmacist</b> Signature: Date:
Date service user registered with DMS	

### Flowchart for IM Clozapine treatment



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

	<i>we are...</i>	<i>you feel...</i>
<b>Our Values</b>	<b>Welcoming</b>	✔ Valued as an individual
	<b>Kind</b>	✔ Cared for
	<b>Positive</b>	✔ Supported and included
	<b>Respectful</b>	✔ Listened to and heard
	<b>Professional</b>	✔ Safe and confident

**Our**  **values**  
 Welcoming Kind Positive Respectful Professional