East London
NHS Foundation Trust

IM Clozapine Protocol

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Approved by (Sponsor Group)	Medicines Management Committee
Ratified by:	Medicines Management Committee
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Services	Applicable
Trustwide	x
Mental Health and LD	
Community Health Services	

Version Control Summary

Version	Date	Author	Status	Comment
2.0	July 2020	Whitney Yeboah	Approved	Amendments to title changed to “IM Clozapine Protocol” Slight amendments to headings and structure of the protocol. Removed references in the protocol for DTC chair approval. All IM Clozapine initiations must be approved by Chief pharmacist or Deputy Chief pharmacist. This now matches the MDT assessment form in Appendix 2. Under Section 3 - Assessment and Decision changes to the paragraph “2. It can only be initiated by a Consultant …” Section 4 “Prescribing IM Clozapine” has been updated to incorporate changes to prescribing with EPMA-JAC.

Contents

Appendices

Clozapine is a dibenzodiazepine derivative and the prototype of the atypical antipsychotics. It has relatively weak dopamine receptor-blocking activity at D1, D2, D3, and D5 receptors but has a high affinity for the D4 receptor. Clozapine possesses alpha-adrenergic blocking, antimuscarinic, antihistaminic, antiserotonergic, and sedative properties.

Clozapine is used for the management of schizophrenia, however, because of the risk of agranulocytosis, it is reserved for patients who fail to respond to other antipsychotics, including other atypicals, or who have severe neurological effects with such drugs.

Clozapine use must be accompanied by strict procedures for the monitoring of white blood cell counts. To minimise the incidence of adverse effects, clozapine therapy should be introduced gradually, beginning with low doses and increasing according to response.

1.0. Introduction to IM Clozapine

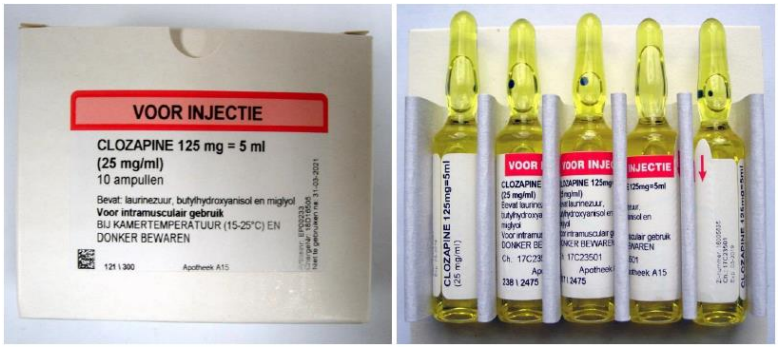
1.1 What is IM Clozapine?

Intramuscular clozapine is an unlicensed in UK. This 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 5millilitres (125mg). It is administered by deep intramuscular injection into the gluteal muscle.

The relaxing action of clozapine occurs within a few days. The period of action for one dose is from 12 to 24 hours.

Stability data available: to be stored below 25 degrees Celsius.



1.2 What is its licensing status?

Currently not licensed in UK, or in Netherlands.

1.3 What is the objective of using IM clozapine?

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

1.4 Does it work?

- **P. F.J. Schulte and al "Compulsory treatment with clozapine: A retrospective long-term cohort study", International Journal of Law and Psychiatry 30 (2007) 539-545** Clozapine is the gold standard in treatment-resistant psychotic patients. We know little about the effects of compulsory treatment in patients unwilling to accept

the necessary treatment. A cohort of 17 consecutive patients given compulsory treatment with clozapine was rated retrospectively by their treating psychiatrists on the basis of their case notes. CGI-S decreased significantly over time until last observation after a mean of more than 15 months. No patient deteriorated as measured u CGI-I. At last observation as many as 10 of the 11 patients still on clozapine were classified as “much to very much improved”. The degree of custodial restriction at last observation showed improvement in 11 patients and no change in six. No serious adverse events were observed. Conclusion: A trial of compulsory treatment with clozapine showed this treatment to be feasible, effective, safe and well tolerated.

- **R. Henri & R. Massey “*An evaluation of intramuscular clozapine in two forensic services*”. Southern Health NHS Foundation Trust & Mersey Care NHS Foundation Trust (2017)** The duality of the paucity of evidence supporting the use of IM clozapine and of the unlicensed status of this preparation, led to the development of two Trust Guidelines. Currently 4 patients out of 5 were stabilised on clozapine with a reduction in their symptoms, which would not have been possible without the option to give them IM clozapine.

- **P, Lokshin & Lerner, Vladimir & Miodownik, Chanoch & M, Dobrusin & Belmaker, Robert. (1999). “*Parenteral clozapine: five years of experience*”. Journal of Clinical Psychopharmacology. 19. 479-480.** Parenteral clozapine often resulted in quick sedation and improvement in behaviour and cooperativeness that permitted return to oral treatment. 27% of patients required only 3 days of parenteral clozapine. They became calmer and their behaviour became more organised, and they returned to oral medication. 71% of the patients received injections for 4 to 7 days before improvement enabled to return to oral medication. Only one patient required muscular administration of clozapine for 8 days.

2.0. Potential place in therapy

The injection can be considered only for selected inpatients within **PICU or Forensic services who** :

- Has treatment-refractory psychotic disorder
- No longer have the capacity to consent.
- Are refusing oral treatment after all approaches to administering oral clozapine have been taken.
- A liquid clozapine preparation can also be made, but the taste is not pleasant.
- The patient cannot swallow or does not want to swallow tablets nor accepting orodispersible treatment option.

The hope is that the prospect of the IM administration may encourage the patient to accept oral treatment instead.

3.0. Protocol for initiating a patient on IM Clozapine

3.1 Assessment and Decision

1. Clozapine injection can only be prescribed if approved by the MDT, a Second Opinion Appointed Doctor (SOAD) and local Clinical Director.
2. It can only be initiated by a Consultant and use of the product must be approved by the Clinical Director on an individual basis.
3. Clozapine injection must be specifically referenced by the SOAD on the T3 form as a named drug, stating the route of administration and dosing information.
4. 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.
5. The completed MDT Assessment Form (along with T3 form) must be emailed to the Chief Pharmacist or Deputy Chief Pharmacist together with the completed "Request and Risk Assessment for the use of Unlicensed Medicines" form found in the Medicines Policy
6. These two forms will form the basis upon which the Chief Pharmacist or deputy 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.
7. IM Clozapine may only be prescribed and administered once the MDT assessment form is complete.
8. IM Clozapine injection MUST be requested on an individual service user basis only.

The Consultant Psychiatrist initiating clozapine must document in the electronic patient record (RiO) the service user's ZTAS 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 RiO.

3.2 Registration of patients for IM Clozapine

- All patients and Consultants involved in the IM clozapine administration must be registered with the Zaponex Treatment Access System (ZTAS).
- Although the IM formulation is not manufactured by Zaponex, the monitoring service agreed to continue the supervision of side effects as IM administration is always intended for short term use possible.
- ZTAS also confirmed there is no need for "off licensed use" form to be completed. However, it should be noted that ZTAS does not hold any responsibility for the use of IM Clozapine; this rests with the service users' Consultant.
- The usual clozapine mandatory physical baseline and weekly blood monitoring, the necessary precautions for previous medical history, amber and red warnings apply.

3.3 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 and documented on RiO.
- According to Maudsley's Policy and Hertfordshire Partnership University Guidelines, generally the injection should be used for **no longer than two weeks at initiation stage**. In exceptional cases, the injection may be used for longer than two weeks if approved by the MDT, SOAD and Chief Pharmacist. Among the few studies

completed, a maximum of 8 days was necessary to either switch to oral administration or alternative treatment choice.

- *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*.

3.4 Treatment costs

- IM formulation comes from Netherlands 25mg/ml and comes as a box of 10x5ml.
- It currently costs **£759.33 + VAT (£911.20 including VAT)** per pack.
- Ampules cannot be re-used and any unused portion must be discarded. (According to Maudsley).
- Dose titration over 2 weeks costs around £2000 (based on the current pack cost). Clozapine injection costs around £100 per injection (or part thereof, as any unused portion must be discarded).
- 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.

4.0. Prescribing IM Clozapine

4.1 Prescribing considerations

- IM Clozapine should only be prescribed as part of an **IM/oral refusal plan**. Oral Clozapine must always be offered first for every administration.
- **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%. Any deviation from this consideration should be evaluated with the MDT before starting the IM administration of clozapine.
- Treatment should start on a Monday whenever possible, this will also fit better with clozapine monitoring e.g. blood sample.
- The responsible clinician must document a clear plan on RiO clearly stating that a patient can be offered IM Clozapine if refusing oral doses. All the relevant documents (i.e. MDT Assessment Form, ELFT Unlicensed Risk Assessment Form and T3 Form must be uploaded on RiO under Clinical Documents).

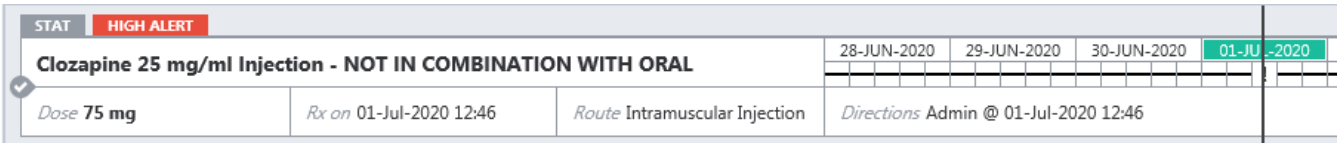
4.2 How to Prescribe IM Clozapine on JAC

IM Clozapine Titration (See Appendix 3 - Clozapine Injection Titration Chart)

- A specific “once daily oral titration” should be prescribed for patients deemed suitable for potential IM administration to avoid dosage confusion or to avoid IM administration where the patient has already received the morning oral dose of clozapine.
- Each dose on the titration chart must be signed and dated by the prescriber. Pharmacy validation must be obtained prior administration in order to access the medication.
- A dummy medicine should also be prescribed on JAC to indicate to the nurses on their administration round that a patient is on a Clozapine Injection Titration Chart (see screenshot below).

Clozapine Maintenance treatment: IM clozapine use only if refusal of oral treatment

- Maintenance doses should only be used in exceptional circumstances. The use of IM Clozapine beyond the two-week initiation phase requires further approval from the MDT, SOAD and Chief pharmacist or Deputy Chief pharmacist.
- Ensure the patient is on a 'once daily' dosing regimen for oral clozapine on JAC. This ensures the patient receives the correct IM clozapine dose for that 24-hour period.
- Always offer the oral dose first
- **If the patient refuses oral clozapine, the nurse must record the administration as a declined dose. This ensures that the oral dose cannot be administered again that day.**
- As per the plan stated on RiO, the duty/ward doctor (or non-medical prescriber) can prescribe the IM clozapine **STAT** dose only for that specific administration time.
- A doctor (or competent non-medical prescriber) must always be involved in the plan to administer IM Clozapine. Remember the **IM dose is HALF the ORAL dose.**
- Ensure you select the correct drug on JAC (see screenshot below).



4.3 Dosing & Administration

- The oral bioavailability of clozapine is about half that of the intramuscular injection. **The IM clozapine dose is half the oral clozapine dose**. For example, 50mg daily of the IM injection is roughly equivalent to 100mg daily of the tablets/oral solution.
- The usual dosage is 150 mg daily divided into several injections. Often the dosage is given individually on the basis of Therapeutic Drug Monitoring.
- The maximum dosage is up to 300 mg daily and it can be divided into several injections. Often the maximum dosage is given individually on the basis of Therapeutic Drug Monitoring.
- Clozapine solution for injection is exclusively for intramuscular administration. It is administered by deep intramuscular injection into the gluteal muscle.
- Amounts of injection fluid over 4 ml should be divided and administered at two injection sites. For injections above 4 millilitres it is better to spread out the injected fluid across two injection sites.
- 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.
- Please be aware that all the doses should be based on patient' response and tolerance (must be monitored daily)

4.4 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 (the last on a weekly basis for the first 4 weeks)
- Daily monitoring of blood pressure, pulse, respiratory rate and temperature after administration. These records may be difficult for many patients; every effort must be made to obtain these and patient refusal of observations must be documented on RiO.
- The NEWS 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.
- Importantly, patients should be observed for any signs of being unwell, such as pallor, cough, shortness of breath, sweating etc. and if observed these should be reported to the Consultant and recorded in the service user's notes.
- 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.
- If IM lorazepam is required leave at least ONE HOUR between administration of IM clozapine and IM lorazepam.

4.5 Side Effects

Below the side effects from EMC – Zaponex.
Oral and IM clozapine share the same side effect profile with the exception of pain at site of injection secondary to IM administration.

INFECTIONS AND INFESTATIONS	
Not known:	Sepsis
BLOOD AND LYMPHATIC SYSTEM DISORDERS	
Common:	Leukopenia/decreased WBC/neutropenia, eosinophilia, leukocytosis
Uncommon:	Agranulocytosis
Rare:	Anaemia
Very rare:	Thrombocytopenia, thrombocythaemia
IMMUNE SYSTEM DISORDERS	
Not known:	Angioedema, leukocytoclastic vasculitis
ENDOCRINE DISORDERS	
Not known:	Pseudophaeochromocytoma
METABOLISM AND NUTRITION DISORDERS	
Common:	Weight gain
Rare:	Impaired glucose tolerance, diabetes mellitus, obesity
Very rare:	Ketoacidosis, hyperosmolar coma, severe hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia
PSYCHIATRIC DISORDERS	

Common:	Dysarthria
Uncommon:	Dysphemia
Rare:	Restlessness, agitation
NERVOUS SYSTEM DISORDERS	
Very common:	Drowsiness/sedation, dizziness
Common:	Headache, tremor, rigidity, akathisia, extrapyramidal symptoms, seizures/convulsions/myoclonic jerks
Uncommon:	Neuroleptic malignant syndrome
Rare:	Confusion, delirium
Very rare:	Tardive dyskinesia, obsessive compulsive symptoms
Not known:	Cholinergic syndrome (after abrupt withdrawal), EEG changes, pleurothotonus, restless leg syndrome
EYE DISORDERS	
Common:	Blurred vision
CARDIAC DISORDERS	
Very common:	Tachycardia
Common:	ECG changes
Rare:	Circulatory collapse, arrhythmias, myocarditis, pericarditis/ pericardial effusion
Very rare:	Cardiomyopathy, cardiac arrest
Not known:	Myocardial infarction, sometimes fatal, myocarditis sometimes fatal, chest pain/angina pectoris, atrial fibrillation, palpitations, mitral valve incompetence associated with clozapine related cardiomyopathy.
VASCULAR DISORDERS	
Common:	Hypertension, postural hypotension, syncope
Rare:	Thromboembolism
Not known:	Hypotension, venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	
Rare:	Aspiration of ingested food, pneumonia and lower respiratory tract infection which may be fatal, sleep apnoea syndrome
Very rare:	Respiratory depression/arrest
Not known:	Pleural effusion, nasal congestion
GASTROINTESTINAL DISORDERS	
Very common:	Constipation, hypersalivation
Common:	Nausea, vomiting, anorexia, dry mouth
Rare:	Dysphagia
Very rare:	Parotid gland enlargement, intestinal obstruction/paralytic ileus/faecal impaction
Not known:	Megacolon, sometimes fatal intestinal infarction/ischaemia sometimes fatal, diarrhoea, abdominal

	discomfort/heartburn/dyspepsia, colitis
HEPATOBILIARY DISORDERS	
Common:	Elevated liver enzymes
Rare:	Hepatitis, cholestatic jaundice, pancreatitis
Very rare:	Fulminant hepatic necrosis
Not known:	Hepatic steatosis, hepatic necrosis, hepatotoxicity, hepatic fibrosis, hepatic cirrhosis, liver disorders including those hepatic events leading to life-threatening consequences such as liver injury (hepatic, cholestatic and mixed), liver failure which may be fatal and liver transplant.
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	
Very rare:	Skin reactions
Not known	Pigmentation disorder
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	
Not known:	Rhabdomyolysis, muscle weakness, muscle spasms, muscle pain, systemic lupus erythematosus
RENAL AND URINARY DISORDERS	
Common:	Urinary incontinence, urinary retention
Very rare:	Interstitial nephritis
Not known:	Renal failure Nocturnal enuresis
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	
Not known	Drug withdrawal syndrome neonatal
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	
Very rare:	Priapism
Not known	Retrograde ejaculation
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	
Common:	Fatigue, fever, benign hyperthermia, disturbances in sweating/temperature regulation
Very rare:	Sudden unexplained death
Not known	Polyserositis
INVESTIGATIONS	
Rare:	Increased CPK
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	
Uncommon:	Falls (associated with clozapine-induced seizures, somnolence, postural hypotension, motor and sensory instability)

References

1. NICE Clinical Guidelines CG 178 Psychosis and Schizophrenia in adult prevention and management, March 2014
2. Maudsley Prescribing Guidelines ED 13th
3. D.J. Stein, B. Lerer and S. M. Stahl “Essential Evidence Based Psychopharmacology”. 2nd Ed., Cambridge Univeristy Press, 2012
4. Apotheek A15 - Buys Ballotstraat 2 - 4207 HT Gorinchem - Tel. 0183-820800 - Fax 0183-820899 - www.apotheekA15.nl translated by Durbin PCL, “Clozapine injection 125 mg = 5 ml, ampoule 5 ml”, Last reviewed Aug 2017.
5. Tees, Esk and Wears Valley NHS Foundation Trust, Clozapine Intramuscular Injection: Application Process, September 2017.
6. Sussex Partnership NHS Foundation Trust – Protocol for the use of intramuscular (IM) clozapine injection, April 2017.
7. Southern Health NHS Foundation Trust – Clozapine intramuscular (IM) Guideline, inpatient only, June 2018.
8. Hertfordshire Partnership University NHS Trust –“Guidelines for the use of IM clozapine treatment for inpatients” Apr 2019
9. P, Lokshin & Lerner, Vladimir & Miodownik, Chanoch & M, Dobrusin & Belmaker, Robert. (1999). “Parenteral clozapine: five years of experience”. Journal of Clinical Psychopharmacology. 19. 479-480.
10. P. F.J. Schulte and al “Compulsory treatment with clozapine: A retrospective long-term cohort study”, International Journal of Law and Psychiatry 30 (2007) 539-545.
11. R. Henri & R. Massey “An evaluation of intramuscular clozapine in two forensic services”. Southern Health NHS Foundation Trust & Mersey Care NHS Foundation Trust
12. ZTAS monitoring service – MI log 5453
13. R. Henri, Southern Health “Guideline for the use of intramuscular (IM) clozapine treatment for inpatients” (2017)
14. Martindale – accessed form Medicines Complete at https://about.medicinescomplete.com/

Appendix 1 - Flowchart for IM Clozapine treatment

Identify suitable patients:
Inpatients, Forensic & PICU services
Treatment refractory and refusing oral treatment
(Previous clozapine treatment is not required)

Complete baseline observations
ECG, FBC, lipids, plasma glucose, U&Es, LFTs, CRP and troponin

Register with **ZTAS** or inform ZTAS of the
IM treatment plan

Complete MDT assessment form &
obtain approval
from MDT, CD, SOAD, and Chief Pharmacist/deputy chief pharmacist*

Complete Trust's for the use of **Unlicensed Medicines form &**
obtain approval

Specifically reference IM Clozapine on **T3 form**

Follow the correct prescribing process depending on which stage the patient is at with their IM Clozapine therapy (see section 4.0)

Always offer **oral clozapine first** and clearly
indicate the **route of administration** on the clozapine IM paper titration chart (where applicable)

Monitor the patient and using NEWS 2 chart / Rio
If not possible to do readings, document refusal and any physical observations for any signs of being unwell e.g. pallor, cough, shortness of breath, sweating
NB. If IM lorazepam is required leave at least ONE HOUR between administration of IM clozapine and IM lorazepam

Review regularly and document on clozapine IM chart (if applicable)
and RIO.

*or associates in their absence

Appendix 2: IM CLOZAPINE MDT ASSESSMENT FORM

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IM CLOZAPINE MDT ASSESSMENT FORM

Service User Name	
Ward	
RiO 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
Has the service user previously been prescribed clozapine?	YES/NO If yes, please state reason clozapine was stopped previously:
CRITERIA	
Date MDT discussion documented in service user record	
Name of Consultant	
Signature and date of Consultant	Signature: Date:
Name of Clinical Director or Associate Clinical Director approval	
Signature and date of Clinical Director or Associate Clinical Director approval	Signature: Date:
Date of SOAD recommendation	
Does the T3 form specify IM Clozapine? Please include T3 form with application	
Date completed application form sent to Chief Pharmacist or Deputy Chief Pharmacist	
Signatures Chief Pharmacist or Deputy Chief Pharmacist (or associates in their absence)	**Chief Pharmacist** Signature: Date: **Deputy Chief Pharmacist** Signature: Date:
Date service user registered with ZTAS	

Appendix 3: Clozapine Injection titration prescription chart.

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CLOZAPINE INJECTION TITRATION CHART
Equivalent doses

Name & Surname		**Consultant**	
DOB		**Ward**	
RIO number		**ZTAS number**	
Allergies		**CTT**	

CAUTION!

- **IM CLOZAPINE DOSE IS ONLY HALF THE ORAL DOSE**
- **IM CLOZAPINE IS ONCE DAILY DOSING**
- **IM CLOZAPINE IS ADMINISTERED INTO GLUTEAL MUSCLE**
- **ALWAYS OFFER ORAL CLOZAPINE FIRST and ADMINISTER IM CLOZAPINE IF ORAL DECLINED.**
- **DO NOT ADMINISTER PO AND IM TOGETHER.**
- **OFFER MONITOR PRE DOSE AND POST DOSE as per NEWS chart below**

DAY	DATE	ORAL dose Equivalent IM dose (25mg/ml)	Prescribed by	Pharmacy	Administered by Note: once daily Administration EITHER/OR
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)				

Appendix 4 : Monitoring Pre and Post Dose

Service user name:	Ward:	RiO number:	DOB:
Today's date:	Time monitoring initiated:	Time monitoring stopped:	

Instructions:

- If the service user consents to physical examination, **ALL** observations on this chart should be recorded. If observations are refused, then **respiratory rate** and level of **consciousness** should still be recorded.
- Observations in the **AMBER** range: refer to ward manager and a doctor; start continuous monitoring
- Observations in **RED** range: call ambulance and crash team

		Base line	15 mins	30 mins	45 mins	60 mins		75 mins	90 mins	105 mins	120 mins	135 mins	150 mins	165 mins	180 mins
Temperature	>38°C						If service user ambulatory and stable, doctor and nurse in-charge to review to consider discontinuing observations. Otherwise monitoring should continue until service user is ambulatory and stable								
	37.5-38°C														
	36-37.4°C														
	35-35.9°C														
	<35°C														
Respiratory rate	>25														
	20-25														
	5-19														
	<5														
Blood pressure ↔	>190														
	180														
	170														
	160														
	150														
	140														
	130														
	120														
	110														
	100														
	90														
	80														
	70														
	60														
	<50														
Heart rate	>190														
	160-189														
	50-159														
	<50														
O_2	90-100%														
	<90%														
Hydration	Well hydrated														
	Poorly hydrated														
Side effects	No side effects														
	Signs of side effects														
Consciousness	Asleep + unrousable														
	Asleep but rousable														
	Awake + calm														
	Awake + active														