Clozapine intramuscular injection: Guidance and governance process

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What is clozapine intramuscular injection?

Clozapine IM injection is **NOT a depot / long-acting formulation**. It is NOT a substitute for stable oral therapy in patients who are poorly compliant.

Clozapine IM injection is an unlicensed product made in the Netherlands by Apotheek A15 and imported to the UK via Mawdsleys. It is a clear yellow solution for injection and is short-acting. The strength of the injection is 25 mg/ml and each ampoule contains 5 ml (125 mg). 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 4 ml (100 mg). For doses greater than 100 mg daily, the dose may be divided and administered into two sites.

Cost of medication

Clozapine injection costs around £100 per ampoule (or part thereof, as any unused portion must be discarded). The cost of a minimum supply of 10 ampoules (the pack size) would therefore be approx. £1,000.

What is the objective of using clozapine injection?

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

Which patients can be prescribed clozapine injection?

The injection is indicated only for inpatients:

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

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

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 not be used for longer than two weeks; however, in exceptional cases, the injection may be used for up to four weeks. The application form (see below) should indicate if use for longer than two weeks is anticipated.

Registration of patients for clozapine injection

All patients being considered for clozapine injection must be registered with the patient monitoring service [Clozaril Patient Monitoring Service (CPMS) or Denzapine Monitoring Service (DMS)] relevant to the intended oral therapy, as the objective is to use the injection for the shortest possible time before switching to oral clozapine. It is advised that the potential use of clozapine injection is not referenced on the registration form. The usual mandatory baseline and weekly blood monitoring for clozapine, and the necessary precautions for amber and red warnings, apply.

What are the equivalent oral and IM doses?

The bioavailability of clozapine via intramuscular injection is about double that via oral administration. Therefore, a 50 mg dose of the IM injection is roughly equivalent to a 100 mg dose of the tablets.

Starting clozapine injection

The patient must be registered with CPMS/DMS the week before commencing treatment. Treatment should start on a Monday whenever possible.
For titrations where clozapine injection has been approved as a back up to oral dosing, **once daily dosing** should be employed to minimise episodes of restraint and to minimise waste/cost. Single daily doses of clozapine injection will be limited by the volume that can be administered per injection site (max. 4 ml = 100 mg IM = 200 mg ORAL). Once the patient is reliably accepting oral doses, the dose can be split into two divided doses if necessary.

The planned titration with oral clozapine should be prescribed on EPMA in the usual way. The local pharmacy team should be consulted on how to prescribe the equivalent IM dose on EPMA. The patient should always be offered oral clozapine first and if the patient continues to refuse, then the injection is administered .

Contacting CPMS

CPMS/DMS are not responsible for monitoring FBC results when clozapine injection 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 clozapine injection

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.

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 processes and entered onto Cito.

What is the application / approval process?

The need for clozapine injection must:

- Be agreed by the MDT and the agreement fully documented in Cito
- Be discussed at an appropriate Consultant peer review meeting for the relevant specialty.

The Responsible Clinician must then apply for approval for use using the Trust single application form ensuring the following information and requirements are covered in the supporting information

- 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 and agreement documented in Cito (state date)
- Peer review discussion and support documented in Cito (state date)
- Staff involved in administration of clozapine are familiar with this guidance
- Nursing Care Plans are in place

The application will then be considered by an appropriate panel which will include the relevant AMD/lead psychiatrist, Chief Pharmacist and relevant General Manager or deputies, as a minimum.

If approved, relevant MHA documentation (T2/T3/S62) must be updated to cover both oral and IM routes of administration and be authorised as necessary.

Approval allows up to THREE titrations with clozapine injection to be attempted before a further application and approval is required; however, AMD/lead psychiatrist approval is required for each titration to commence.

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