

Clozapine information for GPs

Clozapine should only be prescribed by psychiatrists, is monitored by the Community Mental Health Clozapine Clinic and supplied by the hospital pharmacy department. **Familiarity with clozapine will protect patients treated with clozapine from adverse events associated with its use.**

The brand currently approved for use in HPFT is Denzapine, produced by Britannia Pharmaceuticals Ltd, which is also responsible for providing the Denzapine Monitoring Service (DMS).

Indication

- Clozapine is the antipsychotic of choice in Treatment Resistant Schizophrenia. It can also be used in patients with psychosis in Parkinson's disease when other treatment strategies have failed.

Mandatory blood tests

- Blood monitoring is required because of the risk of agranulocytosis/neutropenia
- Patients are required to have regular FBCs taken every 1-4 weeks (interval determined by how long they have been taking clozapine). This is done in HPFT clozapine clinics.
- The monitoring service monitors the FBCs and assigns the result: Green (ok), Amber (warning, needs additional monitoring), red (stop clozapine and follow Red Alert Advice)
- If the patient doesn't have an up to date FBC clozapine cannot be continued. The dispensing pharmacy is only allowed to supply as many days' worth of clozapine as the blood test allows.
- Patients who present with any signs or symptoms of infection must have an immediate WBC check to rule out agranulocytosis. Results should be communicated to DMS.

Constipation

- Constipation is common with clozapine and affects up to 60% of patients. Constipation with clozapine needs to be treated promptly as it can lead to paralytic ileus, faecal impaction and bowel obstruction. It can be fatal.
- Patients on clozapine do not always self-report even life threatening constipation.
- If a patient presents to you with constipation, please ensure immediate and active management such as regular osmotic and stimulant laxative use.
- If a patient presents with abdominal pain and/or absent or high pitched bowel sounds, abdominal dilation, temperature/fever, blood or mucus in stools, weight loss, overflow diarrhoea or vomiting please **transfer them to the local A&E for immediate treatment.**
- Avoid prescribing medication that causes constipation (e.g. anticholinergics, opioids)

Hypersalivation

- Hypersalivation is common, unpleasant for the patient and occurs more often at night.
- Management advice includes using two pillows at night, and putting a towel over the pillow.
- Medication options include hyoscine hydrobromide (Kwells), sucked or chewed up to three times a day (off-label use).

Myocarditis/cardiomyopathy

- Cardiomyopathy and fatal myocarditis have been associated with clozapine (risk of myocarditis is highest during the first 2 months of treatment).
- Suspect cardiac complications if a patient experiences persistent tachycardia at rest, palpitations, arrhythmias, chest pain or heart failure develops. In these cases clozapine should be promptly stopped and the patient referred to a cardiologist.

Diabetes

- Clozapine may induce hyperglycaemia, impaired glucose tolerance and diabetic ketoacidosis. As many as a third of patients may develop diabetes after 5 years of treatment, the majority of these within the first 6 months.



Other side effects

- Include drowsiness and sedation, dizziness, tachycardia (can be transient or may be a sign of something more sinister), weight gain, risk of seizures (doses >600mg/day).
- For a full list of side effects please see BNF/SPC and suggested references.

Drug interactions

- Clozapine interacts with many other medications for a variety of reasons. If any medicines are to be started or stopped during clozapine treatment, appropriate information sources should be consulted to check potential interactions.
- Drugs with substantial potential to cause agranulocytosis should not be used with clozapine (e.g. carbamazepine, co-trimoxazole, trimethoprim, chloramphenicol). It is advisable to perform an extra FBC at the end of a course of antibiotics.
- Some drugs increase or reduce serum levels of clozapine especially liver enzyme inducers and inhibitors. Erythromycin and ciprofloxacin may increase clozapine levels.

Smoking

- Smoking can reduce clozapine levels by up to 50%. This is due to the hydrocarbons in the smoke inducing liver enzymes.
- If your patient is usually a smoker and has reduced or stopped smoking (even if they are on NRT or vaping) their clozapine levels could rise to potentially toxic levels. It is essential that the HPFT team are informed so they can consider a dose reduction.

Caffeine

- The plasma concentration of clozapine is increased by caffeine intake and decreased by nearly 50% following a 5-day caffeine-free period. Dosage changes of clozapine may be necessary when there is a significant change in caffeine-drinking habit.

48 hour rule

- If a patient misses 48 hours or more of clozapine doses the clozapine must be discontinued and slowly re-titrated by HPFT. **Please inform HPFT if you suspect non-compliance.**
- This is because tolerance to common side effects such as postural hypotension and tachycardia are lost very quickly. Restarting at their usual dose could be potentially very dangerous.

Recording clozapine on GP records

- An audit (June 2019) showed that only 54% of clozapine patients had clozapine recorded on GP records, and only 51% had clozapine show up on Summary Care Records.
- In order to improve patient safety and safe prescribing please add clozapine to the patient's medication record using the information below: "Guidance document on recording non practice medication"
https://www.enhertscg.nhs.uk/sites/default/files/content_files/Prescribing/Primary_Care_Resources/Guidance%20on%20recording%20non%20practice%20medication.pdf

Useful sources of information

- The specialist mental health team managing the patient
- Summary of Product Characteristics for Denzapine (SPC) is available from www.medicines.org.uk
- Denzapine Monitoring Service (DMS) can be accessed via www.denzapine.co.uk. Alternatively, telephone on 0333 200 4141.
- Yukselen T, Seal J, Varma S, et al. Role of primary care in supporting patients who are taking clozapine. Drug and Therapeutics Bulletin 2019;57:42-47

Document taken from Appendix 14, HPFT Clozapine Policy v6.3, expiry date 16/09/2022

<https://hertfordshirenhs.interactgo.com/Interact/Pages/Content/Document.aspx?id=4564&Searchd=0>

Document will be reviewed in line with HPFT Clozapine Policy review date.