

Clozapine

Supporting guidance for primary care

Clozapine is an atypical antipsychotic used in Treatment Resistant Schizophrenia or psychosis in patients with Parkinson's disease. It is a **RED** drug and prescribed in secondary care services.

- Please ensure clozapine is added to and updated on the GP practice medical record in order to prevent missed drug interactions, side effects or omissions on admission to secondary care services ([see here for guidance](#)).
- Annotate with “dose determined by clozapine clinic”.
- Advise the patient to opt to make their “Summary Care Record” available for sharing with other healthcare providers.

It is a very effective medication, however, has a number of side effects, some of which can be serious and **potentially fatal**. Whilst all patients will attend clozapine clinics for routine monitoring, patients may present to primary care services with symptoms and it is therefore vital clinicians are aware of these and take appropriate action.

Drug-induced side effects

Action

Severe constipation

A common side effect related to the anticholinergic action of the medication. Exacerbated by other drugs with constipating effects. Can lead to a **fatal bowel obstruction** in some cases- see [MHRA Drug Safety Update](#).

- Inform the clozapine clinic/mental health team.
- Treat with laxatives as per local guidelines (where available) or [SPS guidance](#).
- Urgently refer to acute care if bowel obstruction/perforation suspected.

Neutropenia & agranulocytosis

A rare, but serious side effect which necessitates mandatory blood monitoring.

- If patient presents with symptoms of infection, urgently check FBC and contact clozapine clinic/mental health team if white cells are lowered or if any concerns.
- If WBC < 3 x 10⁹/L or Neutrophils < 1.5 x 10⁹/L, **withhold clozapine** and seek urgent advice.

Drug-induced side effects

Action

Pneumonia

Clozapine is associated with an increased risk of pneumonia. Infection itself also leads to a risk of clozapine toxicity.

- Inform the clozapine clinic/mental health team, who will check clozapine levels urgently.
- Treat infection or refer to acute care if symptoms are severe.

Cardiac side effects

Tachycardia is very common, particularly in early stages of treatment and is usually benign. However, **myocarditis** can present, usually in the first few weeks of treatment.

Cardiomyopathy can develop at any stage of treatment.

- Seek advice from cardiology if tachycardia occurs in the presence of chest pain, heart failure or signs of myocarditis. **Withhold clozapine** and contact clozapine clinic/mental health team urgently.
- If symptoms of heart failure develop, follow NICE guidance, test NT-proBNP levels and refer to cardiology if appropriate.

Myoclonic jerks/seizures

Can be a sign of clozapine toxicity but can occur within the therapeutic range.

- **Withhold clozapine** and inform the clozapine clinic/mental health team urgently.
- Do not initiate carbamazepine.

Hypersalivation

A common side effect, usually treated with off-label anticholinergic medication (e.g. hyoscine hydrobromide), prescribed by mental health team.

- May require GP to review other medications to reduce anticholinergic burden.

Lifestyle factors

Action

Weight gain

- Dietary counselling and lifestyle advice. If lifestyle interventions are unsuccessful, contact mental health team for advice as pharmacological management may be considered, e.g. metformin (off-label) or aripiprazole (adjunctive treatment).

Smoking

- Smoking cessation can lead to a substantial rise in clozapine plasma levels.
- If your patient wants to quit/cut down smoking, or there has been a change in smoking habit, inform the clozapine clinic/mental health team to facilitate baseline and ongoing plasma level monitoring and potential dose changes.

Miscellaneous

- **Alcohol** – enhance any drowsiness caused by clozapine; too much alcohol can be dangerous, inform the clozapine clinic/mental health team if alcohol intake has changed
- **Caffeine** - excessive use may increase clozapine levels; inform the clozapine clinic/mental health team if caffeine intake has changed (increased or decreased)

Missed Doses

- Any non-concordance (intended or unintended) MUST be flagged to the clozapine clinic/mental health team immediately.
- If the patient misses their clozapine dose for more than 48 hours, they will need to be seen by the clozapine clinic team and the dose re-titrated

Drug interactions: Primary care prescribing systems should flag potential interactions if clozapine is included on the system. Examples include erythromycin, clarithromycin, ciprofloxacin, omeprazole and oral contraceptives. Clozapine is contraindicated with medicines which suppress bone marrow function (e.g. carbamazepine).

Please refer to the [BNF](#) or [SmPC](#) for further advice or contact your local clozapine clinic or community mental health team as detailed on your patient's last clinic letter.

Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust Switchboard
Tel: **0191 246 6800**

Tees, Esk and Wear Valleys NHS Foundation Trust
Tel: **01325 552000**

References

1. Summary of Product Characteristics (SmPC) for Clozaril or Denzapine
<https://www.medicines.org.uk/emc>
2. Taylor, David, Barnes, Thomas E., Young, Allan. The Maudsley Prescribing Guidelines in Psychiatry. 13th Edition. 2018
Medicines and Healthcare products Regulatory Agency Drug Safety Update (26th October 2017). Clozapine: reminder of potentially fatal risk of intestinal obstruction, faecal impaction, and paralytic ileus.
<https://www.gov.uk/drug-safety-update/clozapine-reminder-of-potentially-fatal-risk-of-intestinal-obstruction-faecal-impaction-and-paralytic-ileus>
3. Medicines and Healthcare products Regulatory Agency Drug Safety Update (26th August 2020). Clozapine and other antipsychotics: monitoring blood concentrations for toxicity.
<https://www.gov.uk/drug-safety-update/clozapine-and-other-antipsychotics-monitoring-blood-concentrations-for-toxicity>
4. Specialist Pharmacy Service. Managing constipation in people taking clozapine (14 October 2022).
<https://www.sps.nhs.uk/articles/managing-constipation-in-people-taking-clozapine/>
5. Specialist Pharmacy Service. Managing constipation in people taking clozapine (14 October 2022).
<https://www.sps.nhs.uk/articles/managing-constipation-in-people-taking-clozapine/>

Version 3. Produced: 13/3/2024 Review date: 1/2/2026