

Clozapine (Zaponex within RDaSH)

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 omission 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 Constipation 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 applicable) or [ZTAS Guidance](#)
- Urgently refer to acute care if bowel obstruction/perforation suspected.

Neutropenia

Mainly in the early stages of treatment
 And will normally be picked up by routine monitoring

- Neutropenia may occur with clozapine, monitor for signs of infection
- Refer to clinic if signs if identified

Infection /Inflammation (pneumonia especially)

May occur naturally, this can lead to increased levels
 Monitor for any signs of toxicity
 Excessive sedation, altered levels of consciousness
 Unsteadiness.

- Contact the clinic urgently who may request urgent levels and temporarily reduce the dose

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. **Without 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.
Follow local seizure pathway and inform clinic urgently.

- **Refer to Clinic, for possible dose adjustment** and inform the clozapine clinic/mental health team
- **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). And sign posting

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.

RDaSH Clozapine Teams:-

Rotherham: Ferham Clinic, Ferham Road, Rotherham (Tel: 03000215777).

Doncaster: Bungalow 4, St Catherine's Close, Tickhill Road Site, Doncaster (Tel: 03000212401).

North Lincolnshire: Elizabeth Quarter, Scunthorpe (Tel: 03000216300).

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 (14th October 2022)
<https://www.sps.nhs.uk/articles/managing-constipation-in-people-taking-clozapine/>