

Quick reference: Clozapine

- Can be effective when other antipsychotics have failed
- Can have serious side effects
- High risk that mental health symptoms will return if treatment interrupted
- Risk of agranulocytosis
- Patients with signs/symptoms of infection need an immediate full blood count
- Other important side effects can include:
 - Constipation
 - Hypersalivation
 - Metabolic disturbances
 - Myocarditis and cardiomyopathy
 - Epileptic seizures
 - Nocturnal urinary incontinence
- Avoid drugs with potential for bone marrow suppression or constipation
- Some drugs and substances can increase or reduce clozapine serum levels, especially liver enzyme inhibitors or inducers
- Can interact adversely with cigarettes and caffeine

Blood collection, collation and dissemination of results is coordinated by a system involving pharmacies, all the pathology laboratories and mental health teams, and is backed up by a monitored database called ClopineConnect run by Douglas Pharmaceuticals. You can freephone the 24-hour ClopineConnect number should you have queries about the database or results for one of your patients.

CLOPINECONNECT: 0800 435 812

Agranulocytosis

KEY ACTION: Regular full blood counts. Test white blood cell (WBC) count weekly for the first 18 weeks and every four weeks thereafter. Request that copy of results be sent to the dispensing pharmacy and ClopineConnect (0800 435 812).

Immediately withdraw clozapine and contact Mental Health Services if:

- A WBC count falls below $3.5 (10^9/L)$ in the first 18 weeks of treatment; or
- A neutrophil count falls below $1.5 (10^9/L)$; or
- A WBC count falls below $3.0 (10^9/L)$, or there is a neutrophil count below 1.0, after week 18; or
- There is a single WBC drop of $\geq 3 (10^9/L)$; or
- There is a cumulative drop of $\geq 3 (10^9/L)$ within three weeks.

Because clozapine may need to be stopped.

Interruption of treatment

KEY ACTION: Resume at correct dose unless more than two days of doses have been missed. If two or more days of doses missed, consult the clozapine data sheet, *Re-starting Therapy* and let the Mental Health Team know.

Constipation

KEY ACTION: Immediate and active management such as regular osmotic laxatives and short-term stimulant laxative use. Avoid prescribing medication that causes constipation.

Hypersalivation

KEY ACTION: Treatment often successful. Prescribing terazosin (1-2mg at night) may be effective. Benzotropine (1-2mg) at night may also be effective but must be used cautiously because of constipation side effects.

Metabolic disturbances

KEY ACTION: Monitor for weight gain, lipid abnormalities and diabetes at baseline, three-monthly after starting, then annually (or more frequently if indicated). Primary care to take the lead with any indicated treatment.

Myocarditis and cardiomyopathy

KEY ACTION: Urgently investigate signs/symptoms of any adverse cardiac effects including unexplained fatigue, fever, chest pain, palpitations, and shortness of breath (e.g. ECG, FBC, troponin, CRP, chest x-ray and possible cardiology referral). If myocarditis is suspected immediately withdraw clozapine and contact the Mental Health Team.

Epileptic seizures

These are uncommon and clozapine does not necessarily need to be stopped as addition of sodium valproate will usually be effective. If seizures occur, contact the Mental Health Team.

Nocturnal urinary incontinence

KEY ACTION: Treatment often successful (desmopressin, oxybutynin and ephedrine may be effective). Please let the Mental Health Team know if this is a problem.

Drug interactions

KEY ACTION: Avoid drugs with the potential for bone-marrow suppression. The commonest examples are cotrimoxazole and carbamazepine. Some drugs and substances increase or reduce serum levels of clozapine - especially liver enzyme inducers and inhibitors. Care needs to be taken if co-prescribing.

Chemicals in cigarette smoke (not nicotine) can lower clozapine serum levels so sudden smoking cessation can cause a large rise in serum levels with associated toxicity. **Caffeine** can raise clozapine serum levels so sudden cessation of regular caffeine can cause a decrease in clozapine levels and possible return of mental health symptoms.

Our core values | Customer Focus 'eye' | Integrity 'sunrise' | Compassion 'bird' | Respect 'koru' | Openness 'flower'

