

CLOZAPINE – SAFE PRESCRIBING – WE ARE COUNTING ON YOU

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- ▶ REGULARLY CHECK FOR SYMPTOMS OF NEUTROPENIA AND AGRANULOCYTOSIS
- ▶ ASSESS FOR MYOCARDITIS AND CARDIOMYOPATHY
- ▶ MANAGE CONSTIPATION PROACTIVELY
- ▶ BE AWARE OF OTHER ADVERSE REACTIONS AND INTERACTIONS WITH CLOZAPINE

Clozapine has drastically improved the lives of patients with resistant schizophrenia, but it can cause many serious side effects that may present first in primary care. Clozapine is associated with a significant risk of neutropenia, which may progress to a potentially fatal agranulocytosis.

REGULARLY CHECK FOR SYMPTOMS OF NEUTROPENIA AND AGRANULOCYTOSIS

Please advise patients to be alert for symptoms of neutropenia (eg fever, sore throat or flu-like symptoms). Anyone taking clozapine and presenting with these symptoms needs an urgent full blood count, medical review, and their mental health team notified immediately.

Everyone taking clozapine must undergo rigorous blood monitoring on a regular basis. However, despite this vigilance, deaths from agranulocytosis have occurred in New Zealand. Clozapine must not be prescribed for patients with bone marrow suppression or those with a history of clozapine-induced blood dyscrasias.

Be aware there are many medicines that may increase the risk of neutropenia when used concurrently with clozapine, such as some antibiotics (eg co-trimoxazole and erythromycin), carbamazepine, and antineoplastics that are associated with bone marrow suppression.

ASSESS FOR MYOCARDITIS AND CARDIOMYOPATHY

Clozapine is associated with a small but significant risk of myocarditis and cardiomyopathy; fatalities have been reported in New Zealand. There is a greater risk of myocarditis within the first 2 months of initiating clozapine, whereas cardiomyopathy usually has a latent onset at approximately 9 months after starting clozapine.

Symptoms are often non-specific and include (but are not limited to) flu-like illnesses, unexplained fatigue, chest pain, dyspnoea or marked fluctuations in blood pressure. Patients presenting with these symptoms should be referred urgently for a cardiology review.

MANAGE CONSTIPATION PROACTIVELY

Clozapine causes constipation in 14 to 60% of patients. There have been several deaths reported in New Zealand caused by complications of severe constipation associated with clozapine.

The risk of severe constipation is increased when clozapine is used concurrently with other medicines that are also constipating, such as anticholinergics (eg tricyclic antidepressants), opioids, and calcium channel blockers.

Proactive use of laxatives, dietary advice, monitoring bowel habit, and avoiding drug combinations that exacerbate constipation is recommended.

BE AWARE OF OTHER ADVERSE REACTIONS AND INTERACTIONS WITH CLOZAPINE

Clozapine shares many adverse effects that are common to other antipsychotic medicines, eg sedation and postural hypotension, although the risk of these can be reduced with slow dose titration.

Weight gain and glucose intolerance (leading to type 2 diabetes) may occur. Monitor weight, HbA1c and lipid parameters closely and encourage dietary and lifestyle modifications. If necessary, use risk-lowering medications eg statins for elevated lipids.

Other problematic side effects that require ongoing monitoring and management include enuresis, hypersalivation, and tachycardia. Clozapine lowers the seizure threshold, which can be troublesome at higher doses; uncontrolled epilepsy is a contraindication to clozapine use.

Finally, clozapine interacts with a range of medicines and its metabolism is also affected by cigarette smoking. Please visit the full bulletin on www.saferx.co.nz for further information.

➔ continued

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KEY REFERENCES

1. Douglas Pharmaceuticals Ltd. Clopine tablets data sheet 19 November 2012. www.medsafe.govt.nz/profs/datasheet/c/clopinetaboralsuspen.pdf (Accessed 10-12-12).
2. Novartis NZ Ltd. Clozaril tablets data sheet 26 June 2012. www.medsafe.govt.nz/profs/datasheet/c/clozariltab.pdf (Accessed 10-12-12).
3. Clozapine impacts on the colon. Prescriber Update 2011;32(2):14-15 www.medsafe.govt.nz/profs/particles/clozapinejune2011.htm (Accessed 11-02-13).

[CLICK HERE FOR FURTHER INFORMATION ON CLOZAPINE AND A FULL REFERENCE LIST](#)

For further information on other high-risk medicines visit our website at: www.saferx.co.nz

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DISCLAIMER: This information is provided to assist primary care health professionals with the use of prescribed medicines. Users of this information must always consider current best practice and use their clinical judgement with each patient. This information is not a substitute for individual clinical decision making. Issued by the Quality Use of Medicines Team at Waitemata District Health Board, email: feedback@saferx.co.nz