

CLOZAPINE - SAFE PRESCRIBING – WE ARE COUNTING ON YOU

- ▶ CLOZAPINE CAN CAUSE LIFE-THREATENING NEUTROPENIA/AGRANULOCYTOSIS
- ▶ RECOGNISING SIDE EFFECTS EARLY IN PRIMARY CARE MAY BE LIFE-SAVING
- ▶ PATIENTS REQUIRE RIGOROUS BLOOD MONITORING ON A REGULAR BASIS
- ▶ MYOCARDITIS/CARDIOMYOPATHY ARE RARE BUT POTENTIALLY SERIOUS REACTIONS
- ▶ SEVERE CONSTIPATION HAS CAUSED FATALITIES; MANAGE CONSTIPATION PROACTIVELY
- ▶ CLOZAPINE IS ASSOCIATED WITH MANY OTHER ADVERSE REACTIONS/INTERACTIONS

Clozapine (Clopine®, Clozaril®) has improved the lives of many patients with severe schizophrenia but it is considered a 'high-risk' medicine because it is associated with a significant risk of severe side effects, including neutropenia/agranulocytosis. Advise patients to be alert for symptoms of neutropenia (e.g. fever, sore throat). Anyone presenting with these needs an urgent full blood count, medical review, and their mental health team notified immediately.

Every patient taking clozapine undergoes rigorous blood monitoring on a regular basis, but despite this vigilance a death from agranulocytosis has occurred in NZ. Clozapine cannot 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 with clozapine [visit www.saferx.co.nz for further information].

Clozapine is associated with a small but significant risk of myocarditis/cardiomyopathy and fatalities have been reported in NZ. They may occur at any time; there is a greater risk of myocarditis within the first month of initiating clozapine. Symptoms are often non-specific and include (among others) flu-like illness, chest pain, dyspnoea, marked fluctuations in BP, and ECG changes. Patients presenting acutely should be referred urgently for a cardiology review.

Clozapine causes constipation in a significant number of patients and there have been deaths associated with bowel obstruction. The risk of severe constipation is

increased when clozapine is used with other medicines that are constipating, i.e. anticholinergics (e.g. tricyclic antidepressants), opiates, and calcium channel blockers. Proactive use of laxatives, monitoring bowel habit, and avoiding drug combinations that exacerbate constipation is recommended.

Clozapine shares many adverse effects that are common to other antipsychotic medicines, e.g. sedation and postural hypotension. 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, glucose and lipid parameters closely and encourage dietary/lifestyle modifications. If necessary, use risk-lowering medications when appropriate e.g. statins for elevated lipids.

Other problematic side effects that require ongoing monitoring and management include enuresis, hypersalivation, and tachycardia. In addition, clozapine can raise liver enzymes and monitoring is recommended. Clozapine also lowers the seizure threshold which can be troublesome at higher doses. Finally, clozapine interacts with a range of other medicines and its metabolism is affected by cigarette smoking [visit www.saferx.co.nz for further information].

KEY REFERENCES

1. Douglas Pharmaceuticals Ltd. Clopine tablets data sheet Dec 2008. www.medsafe.govt.nz/profs/Datasheet/c/Clopinetab.pdf [accessed on 06 Jul 10]
2. Novartis NZ Ltd. Clozaril tablets data sheet 03 Dec 2009. www.medsafe.govt.nz/profs/Datasheet/c/Clozariltab.pdf [accessed on 06 Jul 10]

[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