Clozapine Survey 2023

Medsafe, the Medicines and Medical Devices Regulatory Authority of Aotearoa New Zealand, welcomes participants to take part in this survey about clozapine.

The aim of this survey is to gain important insights into experiences of:

- people who take clozapine (whānau, family and/or caregivers may answer on their behalf if required)
- healthcare professionals who support people who take clozapine.

The survey is open to people living in New Zealand.

Additional background information

Early use of clozapine

Clozapine was first introduced for treatment of schizophrenia in Europe in 1971.[1]

During the 1970s and 1980s, cases of neutropenia and agranulocytosis (low neutrophil blood cell count) associated with clozapine were increasingly reported, and some people died. A cluster of cases reported in Finland in 1975 led to the withdrawal of clozapine from numerous countries.[1–3]

Clozapine-induced agranulocytosis is a life-threatening adverse drug reaction defined when the neutrophil count is less than 0.5 $x10^9$/L. Low levels of neutrophils increase the risk of severe infection.[1]

Review of early cases of clozapine-induced agranulocytosis found that introduction of a patient surveillance system for monitoring of blood cell counts could help limit the number and severity of cases.[3,4] It was also found that agranulocytosis was more likely to occur during the first 18 weeks of clozapine treatment.[3]

Clozapine was reintroduced in Europe in 1989 with patient surveillance systems. Because some patients with schizophrenic do not response to other medicines, it was important to have clozapine available as an alternative treatment for them.[1,4]

New Zealand information

Pharmaceutical companies supplying clozapine in New Zealand must have a blood monitoring and patient record database in place.

In 2021, there were at least 4,175 individuals treated with clozapine.[5] Clozapine is also dispensed from hospital pharmacies.

It is important that everyone involved in the care of people taking clozapine knows about clozapine side effects and monitoring requirements. Close monitoring of clozapine is necessary to reduce the occurrence of serious, sometimes fatal, adverse reactions.

People taking clozapine should be regularly reminded about how to take the medicine safely, the side effects to watch out for, and what to do if these occur.

Between 1 Jan 2000 and 4 July 2023, the Centre for Adverse Reactions Monitoring (CARM) New Zealand received 2,097 reports of suspected side effects to clozapine, with 4,512 reactions. Neutropenia (low neutrophil count) (243) was the most frequently reported reaction. Other frequently reported suspected adverse reactions included neutrophilia (high neutrophil count) (155), salivary hypersecretion (excessive saliva) (148), myocarditis (inflammation of heart muscle) (145), pneumonia (lung infection) (133), leucocytosis (high white blood cells) (131) and constipation (99). There were 33 reports of agranulocytosis. Serious gastrointestinal side effects reported included intestinal obstruction (47) and megacolon (enlarged intestine) (11).[6]

Medsafe has previously communicated safety information about clozapine[7,8], and most recently sought advice from the Medicines Adverse Reaction Committee (MARC) regarding haematological monitoring of clozapine.[9,10]

Medsafe asked the MARC to advise whether there is sufficient evidence that a change to the frequency and/or duration of haematological monitoring for patients taking clozapine would continue to mitigate the risks to patients, and if so, what change is supported by the evidence.

The Committee did not consider there was enough evidence for a change in monitoring, but recommended that a cross-organisational group be set up to holistically review:

- the benefits and risks of clozapine
- barriers to treatment
- haematological testing requirements.

Medsafe is first conducting this survey to gather information about clozapine use in New Zealand.

Medsafe, August 2023

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