St Patrick's Mental Health Services

Medication Safety Newsletter

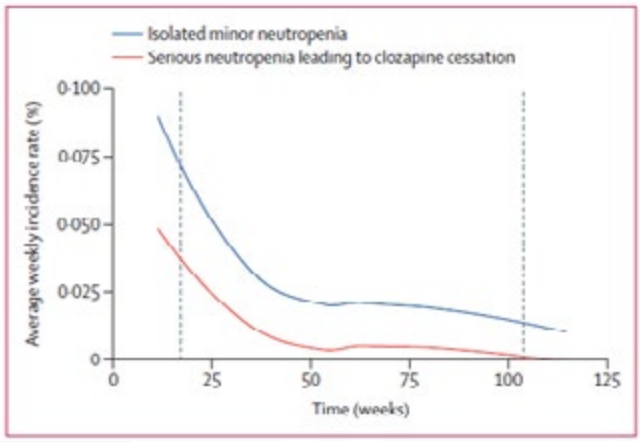
Issue 17 | 2025 | Clozapine blood monitoring regulations

Upcoming changes in clozapine blood monitoring regulations

Clozapine remains the gold standard of antipsychotic treatment in managing treatment-resistant schizophrenia (TRS). The most widely accepted definition of TRS includes:

1. Persistent positive symptoms of at least moderate severity on a standardized rating scale, with at least moderate functional impairment lasting ≥ 3 months.
2. Insufficient response to treatment with ≥ 2 different antipsychotics, each requiring ≥ 6 weeks of adherence to a dosage equivalent to ≥ 600 mg chlorpromazine/ day.

Clozapine and agranulocytosis: Clozapine treatment has been associated with a range of blood dyscrasias, the most serious of which is agranulocytosis. Agranulocytosis is a life-threatening condition defined by a reduction in the absolute neutrophil count (ANC) to very low levels, typically below 0.5x10^9/L. Agranulocytosis is an uncommon, dose-independent side effect of clozapine, with current cumulative risk estimates between 0.4-1.4% of people prescribed clozapine. Risk associated with non-clozapine antipsychotics is approximately 0.13%. Agranulocytosis can occur at any time. However, most cases occur within the first 12 months, and 70% within the first 18 weeks of treatment.



Risks associated with clozapine-induced agranulocytosis have been managed in most countries through mandatory haematological monitoring and precautionary ANC thresholds for clozapine discontinuation to identify those at imminent risk of agranulocytosis.

New observational research has demonstrated a very low absolute risk of agranulocytosis following two years of clozapine treatment without previous episodes of neutropenia. A 2024 study of 26,630 of people taking clozapine found at two years treatment the average weekly rolling incidence of serious neutropenia was 0.001%. Risk remains above rates with non-clozapine antipsychotics. Cases of neutropenia (but not agranulocytosis), particularly later in clozapine treatment, are often coincidental to the use of clozapine.

Revised changes to blood count monitoring (BCM) associated with clozapine

In July 2025, the European Medicines Agency recommended less frequent haematological monitoring following 12 months of uneventful, continuous clozapine treatment. Changes are summarised below. **Note these changes are not yet implemented as of the date of this newsletter.**

Duration of treatment	Current BCM	Changes to BCM
First 18 weeks	Weekly	**No change**
19 – 52 weeks	Fortnightly	**No change**
1 – 2 Years	Four weekly	**Once every 12 weeks ***
>2 years	Four Weekly	**Once a year***

- Monitoring now recommended solely on the basis of ANC only. No monitoring of total white cell count will be required.
- The colour code **GREEN (ANC>2.0x10^9/L)**, **AMBER (ANC 1.5-2 x10^9/L)**, **RED (ANC<1.5 x10^9/L)** threshold system on which a pause or discontinuation of clozapine is recommended will remain the same.

* in patients without prior neutropenia.

Written by Niamh Curley, Ita Fitzgerald and Margaret Brooks, Pharmacy Department, SPMHS. References available upon request.