MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Clozapine: Proposed changes to blood monitoring and prescribing requirements – consultation questions for healthcare professionals

Consultation outcome

August 2026

Contents

About the consultation

From August to October 2025, Medsafe sought feedback on proposed changes to the blood monitoring and prescribing requirements for clozapine. We conducted this consultation on behalf of the companies that distribute clozapine-containing medicines in New Zealand.

Clozapine is an antipsychotic medicine indicated for treatment-resistant schizophrenia. To increase the safety of people taking clozapine, there are restrictions on use of the medicine in New Zealand. In some people, clozapine can cause neutropenia (a reduction in neutrophils, a type of white blood cell), increasing the risk of severe infections. Currently, patients taking clozapine must have regular blood tests throughout treatment to check for neutropenia.

Medsafe has reviewed the clozapine blood monitoring requirements, and we have identified several opportunities to optimise them. With the expanded roles of some healthcare professions, we also sought feedback on who should initiate clozapine treatment, and which prescribers can continue clozapine treatment.

We proposed four major changes to the clozapine blood monitoring requirements.

1. Duration of blood monitoring
2. Monitoring thresholds
3. Management of low blood count results ('red' results)
4. Who can prescribe clozapine.

We also sought feedback about Point-of-Care testing and educational needs for healthcare professionals.

Consultation results

Thank you to everyone who responded to the survey. We have analysed and summarised the responses. The results are divided into the following sections.

- Overview of respondents
- Duration of blood monitoring
- Monitoring thresholds
- Management of low ANC results ('red' results)
- Who can prescribe clozapine
- Point-of-Care testing
- Educational needs

Each question shows the number of participants who agreed or disagreed with proposed changes (where relevant). We have summarised the comments into common themes. Refer to each section for the consultation outcome and finalised changes to clozapine blood monitoring requirements.

We have also created four flow diagrams of blood monitoring requirements to help with understanding the changes. These are attached at Appendix 1.

Overview of respondents

Option	No.	Percent
Medical doctor	55	45.1%
Pharmacist	30	24.6%
Nurse	33	27.0%
Other healthcare professional	4	3.3%
Not Answered	0	0.0%
Total	**122**	**100.0%**

We received 122 responses to the consultation. Of the 55 medical doctor respondents, 44 self-identified as working in psychiatry and 11 self-identified as working in general practice. Nurse practitioners who selected 'other HCP' were reassigned to the nurse category. Of the 33 nurse respondents, 11 self-identified as nurse practitioners, 1 as a nurse prescriber and 19 as mental health nurses. Of the 30 pharmacist respondents, 5 self-identified as pharmacist prescribers.

There were 4 other healthcare professional respondents: 1 clinical psychologist, 1 pharmacy technician and two professional organisations. A further 2 professional body organisations selected the pharmacist and medical doctor categories.

You can view the submissions that we have the permission to publish.

Duration of blood monitoring

Proposals for change

Medsafe proposes that blood monitoring can be stopped after a defined period of time (we propose 1, 2 or 3 years) if the patient meets the following criteria:

- has been taking clozapine consistently for [1, 2 or 3] years
- has a history of ANC ≥1.0x109/L (or ≥0.5x109/L in benign ethnic neutropenia [BEN]) while taking clozapine
- has had no previous confirmed clozapine-induced severe neutropenia/agranulocytosis
- is adherent to treatment
- is independent and able to self-manage their medical care
- is able to identify signs and symptoms of infection. If they occur, is able to notify a healthcare professional to obtain a blood test and be medically assessed.

We expect that most people who take clozapine will meet the above criteria.

After stopping regular blood monitoring, agranulocytosis monitoring should continue. The patient would self-monitor for signs and symptoms such as fever, fatigue, sore throat, mouth ulcers and other symptoms of infection. If these signs and symptoms occur, the patient would need to have a blood test to check their ANC. Therefore, the patient must be able to recognise and report signs/symptoms of possible infection to their healthcare professional.

The clozapine blood monitoring database will have a new status to indicate that the patient is eligible for clozapine treatment, but they do not need regular blood tests.

Question 5: Do you agree that ongoing blood monitoring can be stopped after a period of time?

Option	No.	Percent
Yes	92	75.4%
No	29	23.8%
Not Answered	1	0.8%

Question 6: When should blood monitoring be stopped?

Option	No.	Percent
After 1 year of continuous clozapine treatment	22	18.0%
After 2 years of continuous clozapine treatment	46	37.7%
After 3 years of continuous clozapine treatment	20	16.4%
Other. Please suggest an alternative below.	28	23.0%
Not Answered	6	4.9%

Comments from respondents

Most respondents agreed that mandatory blood monitoring can be stopped after a period of time. The preferred option was that ongoing blood monitoring may be stopped after a period of 2 years of continuous treatment for patients meeting the eligibility criteria.

Some respondents said that the minimum monitoring period should be consistent with the greatest period of risk of severe neutropenia after clozapine initiation and pointed to evidence that the risk of neutropenia decreases substantially after the early treatment period and is minimal after 2 years of treatment.

Other respondents did not support stopping monitoring entirely but were open to reducing its frequency after a period of stability. Another suggestion was for staged reductions in monitoring frequency at the prescriber's discretion. These respondents commonly suggested shifting to 3-monthly or annual testing after one to 3 years, aligning with routine clinical reviews or metabolic monitoring.

Some respondents, particularly GPs, nurses and some pharmacists, opposed stopping monitoring at any point. They considered that agranulocytosis can occur unpredictably, even after many years, and expressed concern that many patients taking clozapine lack the ability to self-identify and act on symptoms of concern. Some patients may become non-adherent to treatment, have worsening of their mental health or become unable to self-monitor for signs of infection, even after a long stable period. Respondents described examples of long-term stable patients whose neutropenia was detected only through routine testing.

One respondent considered that no mandatory blood monitoring is necessary, as the risk of neutropenia is similar to that of other antipsychotics.

There was also concern that the option to stop blood monitoring could be applied too widely, leading to patients who are not appropriate candidates stopping their regular blood monitoring. There were comments that stopping blood monitoring could lead to patients disengaging from treatment and support. Prescribers should have the discretion to continue monitoring and decide blood test frequency on a case-by-case basis.

Medsafe's response

The rates of severe neutropenia in people initiating clozapine are higher than for other medicines and not all patients are able to recognise and respond to signs of infection, therefore supporting the need for mandatory blood monitoring. For example, a study estimated rates of neutropenia-associated hospitalisation of 2.2 (95% confidence interval [CI]: 1.3–3.9) per 1,000 person-years for people taking clozapine and 0.2 (95% CI: 0.003–1.3) per 1,000 person-years for people taking olanzapine.[1] An analysis of the Viatris Australian and New Zealand clozapine monitoring database found that the cumulative incidence of serious neutropenia leading to cessation was 0.9% at 18 weeks and 1.4% at 2 years.[2]

As noted in the evidence review, the risk of severe neutropenia is highest during the first months of treatment and is low after 2 years of treatment. The consultation feedback supports the shift to non-mandatory blood monitoring after 2 years of treatment based on clinical judgement.

There were concerns that patients taking clozapine are generally not able to self-identify symptoms of infection and obtain a blood test, that the eligibility criteria would be applied too widely, or that patients may disengage from treatment after stopping blood monitoring. Patients who are not independent, not able to self-manage their medical care, and not able to identify signs and symptoms of infection would not be eligible to stop blood monitoring according to the eligibility criteria (see question 7 below). Patients will still have monthly contact with a pharmacist when they collect their clozapine.

[1] Sarpatwari A, Mahesri M, Lii J, et al. 2026. Risk of neutropenia-related hospitalisation among clozapine initiators. *BMJ Mental Health* 29(1): e302122. DOI: 10.1136/bmjment-2025-302122 (accessed 17 July 2026).

[2] Northwood K, Myles N, Clark SR, et al. 2024. Evaluating the epidemiology of clozapine-associated neutropenia among people on clozapine across Australia and Aotearoa New Zealand: a retrospective cohort study. *Lancet Psychiatry* 11(1): 27–35. DOI: 10.1016/s2215-0366(23)00343-7 (accessed 17 July 2026).

Medsafe will provide an annual consent form which can be used by prescribers that confirms the patient continues to meet the eligibility criteria and is able to self-monitor for symptoms.

Healthcare professionals and their patients can choose to continue monitoring beyond a period of 2 years if appropriate, at a frequency that is tailored to the patient's needs and circumstances. Patients who have stopped mandatory monthly monitoring can still be monitored as needed, but this would not be a requirement for clozapine dispensing. Monitoring of other adverse reactions is outside the scope of this consultation. However, we agree that this is very important and encourage organisations providing education to healthcare professionals to include comprehensive guidance on monitoring patients for other adverse reactions.

There were comments that after a specified time period, the monitoring frequency should decrease from monthly to 3-monthly or annually. However, as clozapine-induced severe neutropenia has an acute onset, there would be a low likelihood of identifying it with less frequent blood monitoring. Instead, following 2 years of continuous treatment, prescribers can use their clinical judgement to determine blood monitoring frequency in patients meeting the criteria for self-monitoring.

Outcome

Patients may stop mandatory monthly blood monitoring after a period of 2 years of continuous treatment, if they meet the eligibility criteria.

Question 7: Please select the criteria that will identify the patients who can stop ongoing blood monitoring (you can choose more than one option).

Option	No.	Percent
Have been taking clozapine consistently for [1, 2 or 3] years	95	77.9%
Have a history of ANC ≥1.0x10^9/L (≥0.5x10^9/L in BEN) while on clozapine	74	60.7%
Have had no previous confirmed clozapine-induced severe neutropenia/agranulocytosis	93	76.2%
Are adherent to treatment	92	75.4%
Are independent and self-manage their medical care	71	58.2%
Are able to identify signs and symptoms of infection, notify a healthcare professional accordingly and obtain a blood test	84	68.9%
Other. Please comment below.	35	28.7%
Not Answered	6	4.9%

Comments from respondents

Most respondents supported the proposed eligibility criteria.

There were many comments that patients in supported accommodation, rest homes, long-term inpatient care, forensic settings or palliative care should be eligible to stop ongoing blood monitoring as these patients are supported by carers and/or healthcare teams who can monitor for signs and symptoms of infection. There was concern that many patients taking clozapine would be ineligible to stop mandatory monitoring due to the eligibility criteria to be independent, self-managing medical care and able to identify symptoms of an infection and obtain a blood test.

Suggested amendments to the criterion 'are able to identify signs and symptoms of infection' included adding 'OR have a carer who can' or 'OR are under the close supervision of a person or facility who can do this on their behalf'. Respondents noted that consequently, patients discharged from these facilities would

need to be reviewed for whether they meet the criteria to continue clozapine treatment without ongoing blood monitoring.

Other suggested criteria included the following.

- No concomitant medicines or comorbid medical conditions that may cause neutropenia.
- No history of non-adherence to treatment as an outpatient.

A respondent considered that the criterion for 'ANC $\geq 1.0 \times 10^9$/L ($\geq 0.5 \times 10^9$/L in BEN)' is not needed because there are many reasons for a drop in neutrophils that are not related to clozapine. The criterion for 'no previous confirmed clozapine-induced severe neutropenia' was considered adequate.

Respondents emphasised that mandatory monitoring should continue for patients with cognitive impairment or limited insight, and routine monitoring should not be discontinued unless agreed by a multidisciplinary team. Additionally, capacity and insight of patients may change with age and time. Some people may continue to lose their cognitive abilities and no longer be able to monitor for infection symptoms or seek medical attention.

The safety of stopping ongoing blood monitoring depends on availability of adequate time and resources for good patient education, and timely access to blood tests, results and clinical follow-up.

Medsafe's response

For patients in supported accommodation and inpatient settings, Medsafe has concerns around placing responsibility on non-healthcare professionals to recognise and act urgently on signs and symptoms of infections that are potentially fatal in severe neutropenia. We consider this responsibility to be outside their role.

We acknowledge that the capacity and insight of patients may change with age and time, impacting their ability to manage their medical care and identify symptoms of infection. As described above, there will be an annual consent form that confirms the patient continues to meet the eligibility criteria for no mandatory ongoing monitoring.

Medsafe agrees with the addition of a criterion that the patients must have no concomitant medicines or comorbid medical conditions that may cause neutropenia, unless they have a history of stable ANC during the course of the treatment or condition, or use of the medicine.

We agree that the criterion to have no history of confirmed clozapine-induced severe neutropenia is sufficient, and that the criterion for no history of 'red' results (ie, unrelated to clozapine) is not needed.

In line with the comments received, we have amended the criterion 'are adherent to treatment' to 'have a history of good adherence to treatment as an outpatient'.

Outcome

The revised criteria to identify patients who can stop ongoing blood monitoring are the following.

- Have been taking clozapine consistently for 2 years.
- Have had no previous confirmed clozapine-induced severe neutropenia/agranulocytosis.
- Have a history of good adherence to treatment as an outpatient.
- Are independent and self-manage their medical care.
- Are able to identify signs and symptoms of infection, notify a healthcare professional accordingly and obtain a blood test.
- Patients taking concomitant medicines or with other medical conditions that may cause neutropenia are eligible if they have a history of stable ANC.

Question 8: Do you agree that after stopping ongoing blood monitoring, monitoring of clozapine-induced agranulocytosis should be via signs and symptoms of infection, and if these occur, the patient should have a blood test to check ANC?

Option	No.	Percent
Yes	92	75.4%
No. Please suggest an alternative below.	27	22.1%
Not Answered	3	2.5%

Comments from respondents

The majority of respondents (75%) agreed that after stopping ongoing blood monitoring, monitoring of clozapine-induced agranulocytosis should be via signs and symptoms of infection, and if these occur, the patient should have a blood test to check ANC. Some respondents (22%), including many GP respondents, did not agree that ongoing blood monitoring should stop.

There were comments that the symptoms that trigger a blood test should be specified. For example, a mild URTI (rhinorrhoea) in winter should not trigger a blood test, but fever, chills, weakness, sore throat, bleeding gums, bone pain, hypotension, tachycardia and shortness of breath could all be red flags.

There were concerns around making patients responsible for reporting symptoms of infection. People with treatment-resistant schizophrenia often have negative symptoms including apathy or amotivation that may prevent them from being proactive in seeking medical advice. Other factors such as cognitive impairment, learning difficulties or financial difficulties may impact patients' ability to seek medical care. Difficulties around accessing timely blood tests and clinical follow-up were highlighted. Clinicians should have the discretion to continue regular monitoring in patients with barriers to self-management or accessing care.

Some respondents considered that monitoring should include a wellness check at the time of dispensing as an additional safety net, and that pharmacists should be able to record this in the clozapine blood monitoring database.

There were comments around the limited utility of the current requirement for monthly testing, as clozapine-induced severe neutropenia usually develops rapidly.

There were comments that after 2 years, blood monitoring should continue at a reduced frequency, such 6-monthly or annually, or be stepped down over time. Respondents emphasised the importance of ongoing 3-monthly comprehensive monitoring for other adverse reactions, including metabolic syndrome, constipation, gastro-oesophageal reflux, sialorrhea, nocturnal enuresis, tachycardia, sleep apnoea and sedation. Some respondents commented that ANC should still be checked as part of these reviews.

Medsafe's response

Medsafe agrees that the data sheet should specify the symptoms that trigger a blood test. The data sheet will be updated to state that patient should receive a blood test if flu-like symptoms occur, such as fever or sore throat, or there is other evidence of infection. Other red flags include chills, weakness, bleeding gums, mouth ulcers, unusual sweating, bone pain, hypotension, tachycardia, shortness of breath, dysuria/urinary frequency and diarrhoea. Medsafe will also produce a patient leaflet that includes this information.

We acknowledge concerns around placing the onus on patients to report symptoms of infection. Patients will only be eligible to stop ongoing blood monitoring if they are able to report symptoms and self-manage medical care and want to do this. Patients with cognitive or learning difficulties or significant negative symptoms impacting their ability to manage their care would not be eligible. Stopping ongoing mandatory blood monitoring is not compulsory.

Respondents suggested that pharmacists should check that the patient is well at the time of dispensing. Medsafe acknowledges that this pharmacist check can be recorded in the pharmacy's records as an additional safety net, but is not compulsory.

Healthcare professionals may continue to check ANC/FBC at their discretion, for example, as part of regular clinical reviews. However, this will not be a requirement for clozapine to be dispensed in patients who meet the criteria and have consented to stop ongoing mandatory monthly monitoring. Clozapine-induced neutropenia has an acute onset. Infrequent blood monitoring is unlikely to identify early reductions in neutrophils.

The blood monitoring requirements covered by this consultation relate to mandatory testing (ie, what must be recorded in the clozapine blood monitoring database to allow dispensing of clozapine). Monitoring of other adverse reactions is very important but is outside the scope of this consultation. We encourage organisations providing education to healthcare professionals to include comprehensive guidance on monitoring patients for other adverse reactions.

Outcome

After stopping ongoing mandatory blood monitoring, monitoring of clozapine-induced severe neutropenia should be via signs and symptoms of infection, and if these occur, the patient should have a blood test to check ANC. The data sheet will be updated with this information, and Medsafe will also create a patient leaflet. Healthcare professionals may continue to carry out blood monitoring based on clinical judgement.

Question 9: How long should blood tests be valid for?

Option	No.	Percent
48 hours (ie, a reduction)	2	1.6%
No need to change, keep it at 72 hours	63	51.6%
96 hours (ie, an increase)	39	32.0%
Other. Please suggest an alternative below.	13	10.7%
Not Answered	5	4.1%

Question 10: Please provide the rationale for your answer to question 9 (ie, how long blood tests should be valid for).

Comments from respondents

The majority of respondents agreed that blood test results should remain valid for 72 hours for the purpose of clozapine dispensing.

Comments in support of a 72-hour period of validity included the following.

- The lifespan of neutrophils is 3-4 days, meaning that neutrophil levels could change within this time frame.
- Transient changes in ANC, unrelated to clozapine, are likely to revert to normal/near normal levels within this timeframe.
- If there were more than 3 missed doses, re-titration would be needed.
- The current timeframe works well.

We have summarised other comments below.

Some respondents said the period of validity should correspond to the mandatory testing frequency and length of time the patient has been taking clozapine. For example, during the first 18 weeks of treatment and weekly blood tests, the blood test results should be valid for 72 hours (ie, clozapine must be dispensed within 72 hours of the test). When testing is reduced to monthly, the blood test result should be valid for a longer period, such as 96 hours to 7 days.

Other respondents said the blood test results should be valid for a longer period to increase flexibility for patients, especially when pharmacies are closed, clinicians are unavailable, or for people in rural areas. Changes in neutrophil counts are slow and having a validity period of 96 hours would have minimal additional risk to patients. The risk of rebound psychosis resulting from interrupted clozapine supply also warrants a longer period of validity. Retesting patients who are late to collect their medicine may result in more testing than necessary.

Extending the period of validity could result in dispensing against outdated results and weaken safeguards designed to ensure timely monitoring.

There are local variations in practice and there should be clear national requirements to avoid confusion for patients, pharmacies and prescribers. The national dispensing protocol has been updated and states that a weekly blood test is now valid for 10 days and a 4-weekly blood test is valid for 6 weeks.

Medsafe's response

The period of validity refers to the window following a 'green' blood test result during which clozapine can be dispensed. Most respondents agreed that a validity period of 72 hours ensures that the result reflects the patient's current haematological status, which can change rapidly, but also allows flexibility for the patient. Dispensing within this timeframe also prevents extended periods without monitoring.

Outcome

Blood tests will continue to be valid for 72 hours for patients having weekly blood tests. Monthly test results will be valid for 7 days to allow more flexibility.

Monitoring thresholds

Current requirements

A 'traffic light' system illustrates the thresholds for actions to take with clozapine following a blood test result, as shown in Table 1.

Table 1: Monitoring thresholds and patient management for clozapine blood counts

Thresholds			Patient Management
Colour	Blood cell count (x10^9/L)		
	WBC	ANC	
Green	≥3.5	≥2.0	Continue clozapine
Amber	≥3.0 – <3.5	≥1.5 – <2.0	Continue clozapine Increase blood test monitoring to twice weekly until blood counts stabilise or increase
Red	<3.0	<1.5	Stop clozapine Daily blood tests until blood counts recover Monitor for infection If a subsequent blood test confirms the red result, clozapine must not be restarted

Key: WBC = white blood cells; ANC = absolute neutrophil count.

Source: Viatris. 2024. *Clozaril New Zealand Data Sheet* 25 July 2024 URL: www.medsafe.govt.nz/profs/Datasheet/c/Clozariltab.pdf (accessed 5 March 2025).

Proposed changes

Medsafe proposes measuring ANC only, changing the ANC thresholds for each colour and introducing different thresholds for benign ethnic neutropenia (BEN), as outlined in Table 2.

Table 2: Proposed changes to blood counts, monitoring thresholds and patient management

Thresholds				Proposed Patient Management
Colour	Current (x10^9/L)	Proposed (x10^9/L)		
	ANC	ANC (standard)	ANC (BEN)	
Green	≥2.0	≥1.5	≥1.0	Continue clozapine
Amber	≥1.5 – <2.0	1.0 – <1.5	0.5 – <1.0	Continue clozapine Increase monitoring to twice weekly until ANC stabilises or increases
Red	<1.5	<1.0	<0.5	Refer to Figure 1 and Table 3 in the next section

Key: ANC = absolute neutrophil count; BEN = benign ethnic neutropenia

Sources:

Novartis Pharmaceuticals Corporation. 2023. *Clozaril United States Label* May 2023. URL: www.accessdata.fda.gov/drugsatfda_docs/label/2023/019758s103lbl.pdf (accessed 5 March 2025).

Verdoux H, et al. 2025. The time has come for revising the rules of clozapine blood monitoring in Europe. A joint expert statement from the European Clozapine Task Force. *Eur Psychiatry* 68(1): e17. DOI: 10.1192/j.eurpsy.2024.1816 (accessed 5 March 2025).

Note we are not proposing any changes to the special monitoring arrangements (eg, patients undergoing chemotherapy) where the thresholds for monitoring may be adapted under the guidance of a consultant haematologist and the pharmaceutical company.

Question 11: Do you agree that blood monitoring should measure ANC only (ie, remove the requirement for WBC)?

Option	No.	Percent
Yes	94	77.1%
No. Please state your reasons below.	23	18.8%
Not Answered	5	4.1%

Comments from respondents

Most respondents (77%) agreed that that blood monitoring should measure ANC only (ie, remove the requirement for WBC).

Comments in support of removing the requirement for WBC included the following.

- ANC is the most clinically relevant parameter.
- WBC tends to be more labile for reasons unrelated to clozapine (eg, viral infection) and is unlikely to be clinically relevant.
- Aligns with European treatment guidelines.

Comments against removing the requirement for WBC included the following.

- WBC adds context to ANC and having both provides a clearer clinical picture.
- When ordering blood tests, there is no option to order ANC only.
- Viral causes of infection could potentially be overlooked if WBC is not monitored.
- Monitoring WBC provide a longitudinal view of worsening levels.

Medsafe's response

Medsafe acknowledges that WBC and trends over time may be a useful parameter for evaluating the patient's overall clinical picture. The proposed changes are only to the mandatory monitoring requirements for the detection and management of neutropenia, and not infections in the absence of neutropenia. Clozapine-induced neutropenia develops rapidly, meaning that gradual decreases over time are unlikely to be relevant.

Clinicians can still monitor WBC at their discretion, but monitoring of WBC will not be compulsory and dispensing of clozapine will not be contingent on normal WBC results. 'Amber' and 'red' results will be defined by absolute ANC levels and not a relative drop.

Outcome

Mandatory blood monitoring will consider ANC only.

Question 12: For standard monitoring (ie, patients who do not have BEN), do you agree with the 'green' ANC threshold change to ≥1.5 x10^9/L?

Option	No.	Percent
Yes	103	84.4%
No. Please suggest an alternative below.	13	10.7%
Not Answered	6	4.9%

Question 13: For standard monitoring, do you agree with the 'amber' ANC threshold range change to 1.0 – <1.5 x10^9/L?

Option	No.	Percent
Yes	103	84.4%
No. Please suggest an alternative below.	11	9.0%
Not Answered	8	6.6%

Question 14: For standard monitoring, do you agree with the 'red' ANC threshold change to <1.0 x10^9/L?

Option	No.	Percent
Yes	104	85.3%
No. Please suggest an alternative below.	11	9.0%
Not Answered	7	5.7%

Comments from respondents

Most respondents agreed with the proposed changes to the 'green', 'amber' and 'red' ANC thresholds. Lowering the thresholds may reduce unnecessary retesting and treatment interruptions, while still providing an appropriate safety net.

Some respondents considered the current threshold to be clinically appropriate, for example to catch reductions early. Baseline ANC could help to inform thresholds, and the relative drop could also be considered.

Medsafe's response

Although the thresholds are changing, the clinician will still be aware of early decreases in ANC and changes relative to baseline that don't meet the thresholds for action and can use their clinical judgement to investigate and put appropriate safety nets in place.

Outcome

We will be adopting the new ANC thresholds.

Question 15: For people with BEN, do you agree with the introduction of ANC thresholds for 'green', 'amber' and 'red'?

Option	No.	Percent
Yes	101	82.8%
No. Please suggest an alternative below.	11	9.0%
Not Answered	10	8.2%

Comments from respondents

Most respondents agreed with the proposed ANC thresholds for BEN. The thresholds will reduce unnecessary treatment interruptions and support equitable access to clozapine.

Other comments included the following.

- The term 'Duffy antigen receptor for chemokines' (DARC) is preferred to BEN.
- The understanding of BEN in the New Zealand demographic is vague, particularly the incidence in Māori and Pacific Island populations, and it is better to remain cautious in this population.
- Having two sets of thresholds may cause confusion.
- There needs to be a process for identifying patients with BEN.

Medsafe's response

We will use the term Duffy antigen receptor for chemokines (DARC) in addition to BEN. The diagnosis of DARC/BEN in the New Zealand population should continue according to the current process. The clozapine blood monitoring databases already include special monitoring capability which can accommodate the DARC/BEN thresholds. The data sheet will be updated to reflect this information.

Outcome

We will adopt the new ANC thresholds for DARC/BEN.

Question 16: Do you have any other comments or feedback about Medsafe's proposals for changes to blood counts and monitoring thresholds for clozapine?

Comments from respondents

The feedback reflects a strong view that current clozapine monitoring requirements should be updated to align with current evidence and reduce burdens on patients and services. Many respondents believe the proposed changes will reduce excessive testing for stable patients, minimise anxiety and disruption, and remove barriers that deter people from starting a highly effective treatment. Several respondents emphasised that the changes could support wider and quicker access to clozapine, which in turn may improve outcomes and save lives for people with schizophrenia. Others noted that the proposals align with international guidance and evidence, and expressed confidence that the new thresholds will prompt clinical attention only when it is clinically needed.

Some respondents highlighted the importance of maintaining strong oversight and ensuring vulnerable groups are not neglected. They cautioned that reducing blood test frequency may reduce touchpoints with healthcare providers, which can be valuable for monitoring broader physical health concerns such as cardiovascular risk and diabetes. There were also concerns regarding clozapine's other known risks, particularly bowel obstruction, with calls for greater focus on bowel health and compulsory prescriber education. Additional suggestions included testing clozapine levels alongside full blood counts to support

monitoring of metabolism and adherence, and continuing mandatory monitoring in older adults, who may require closer oversight.

A number of respondents identified specific clinical and operational requirements needed to support safe implementation of changes to clozapine blood monitoring. These included rapid access to haematologist advice, and clear national guidance covering eligibility, benign ethnic neutropenia, and pathways for restarting treatment. They stressed the need for coordinated systems across prescribers, pharmacies, and the clozapine blood monitoring databases to ensure timely communication, avoid dispensing barriers and protect continuity of care.

Structured patient education was seen as critical so patients can recognise symptoms of infection, seek prompt assessment and access timely blood tests.

Respondents emphasised that the clozapine blood monitoring database must be updated at the time the changes are implemented.

Medsafe's response

Annual eligibility checks, via a consent form, will manage issues around blood monitoring in aging or vulnerable patients. It is not compulsory to stop mandatory monthly blood monitoring after 2 years of treatment.

The development of national guidance and treatment algorithms falls outside of Medsafe's remit and is part of wider health system responsibilities.

The comments about other monitoring (eg, clozapine levels, constipation, C-reactive protein, troponin) are outside of the scope of this consultation. However, we agree that this is very important and encourage education providers within the health system to include comprehensive guidance on monitoring to healthcare professionals.

Medsafe will produce a patient leaflet to help support patient education that healthcare professionals can give to patients.

Management of low ANC results ('red' results)

Current requirements

Currently, people who experience a 'red' result with clozapine must stop treatment. If the 'red' result is confirmed by a subsequent blood test, clozapine must not be restarted. However, stopping clozapine suddenly can lead to a rapid deterioration in the patient's mental state and cause symptoms related to cholinergic rebound.

Proposed changes

The risk that a 'red' result represents clozapine-induced severe neutropenia may depend on many factors, such as time to onset, neutrophil patterns (quick recovery versus progressive sustained drop), and use of other medicines. Medsafe proposes that management of 'red' blood test results for people taking clozapine changes from an immediate stop of clozapine to an immediate clinical review to determine the cause. The patient will require daily blood monitoring during this investigation while maintaining their clozapine treatment (see Figure 1, next page).

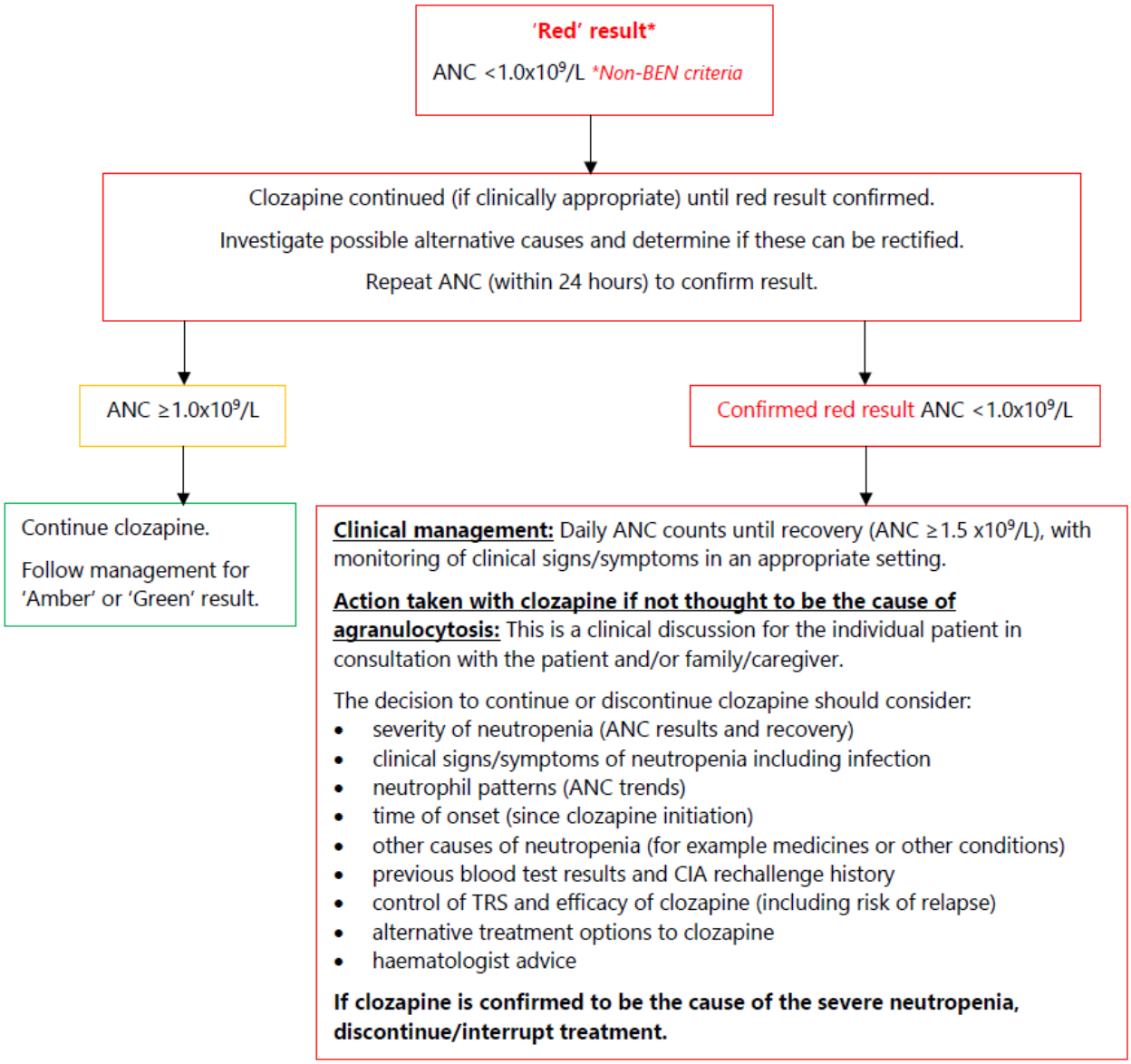
If a patient has stopped clozapine treatment due to a red result, we propose that treatment can be restarted under the conditions outlined in Table 3.

Table 3: Proposed actions to take with clozapine after treatment interruption

Reason for interruption	Action to take with clozapine
Interruption due to a red result, but **NOT** related to clozapine	Restart clozapine when ANC has recovered to green and when the patient is physically well. Blood monitoring can return to the patient's usual frequency (including if the patient had no monitoring) unless additional monitoring is clinically indicated.
Red result **CAUSED** by clozapine during the regular blood monitoring period *OR* after monitoring period has ended	Restarting clozapine is generally not recommended – unless the benefits outweigh the risks in an individual patient. **Only** restart clozapine when ANC has recovered to green and when the patient is physically well. Restart blood monitoring as if they are a 'new' patient (ie, weekly ANC for 18 weeks, then 4-weekly ANC). Consider using a slower titration of clozapine. Clearly document the decision to restart in the patient's clinical notes and CPMS.
Interruption **NOT** due to a red result after blood monitoring period has ended	Restart clozapine. There is no need to restart blood monitoring, irrespective of the duration of interruption.

Key: ANC = absolute neutrophil count; CPMS = clozapine patient monitoring system.

Figure 1: Proposed management of a 'red' ANC result



Key: ANC = absolute neutrophil count; BEN = benign ethnic neutropenia; CIA = clozapine-induced agranulocytosis; TRS = treatment-resistant schizophrenia

Question 17: Do you agree that the action taken with clozapine following a confirmed 'red' blood test result should first involve an investigation of the cause and a discussion with the individual rather than immediately stopping clozapine?

Option	No.	Percent
Yes	104	85.3%
No. Please suggest an alternative below.	12	9.8%
Not Answered	6	4.9%

Comments from respondents

The majority of respondents agreed that following a confirmed 'red' blood test result there should first be an investigation of the cause and a discussion with the individual rather than immediately stopping clozapine.

Abrupt cessation of clozapine can have severe psychiatric consequences, including rebound psychosis and destabilisation. The risks of stopping clozapine need to be balanced against the risks of continuing treatment. International practice and consensus guidelines support investigation of 'red' results and individualised decision making, rather than an automatic stop. Investigation of the cause must take place immediately and without delay.

Some respondents considered that clozapine should always be stopped if ANC is extremely low (eg, $<0.5 \times 10^9$/L). Some proposed continuing clozapine during the investigation only if the patient is clinically stable and under close supervision, with documentation of the decision and rationale, and that stopping should remain the default option. Haematologist consultation was repeatedly identified as essential before deciding to continue treatment after a red result.

A minority of respondents opposed continuing clozapine during investigation of 'red' results, arguing that it is safer to always immediately stop clozapine. Others expressed practical concerns about the feasibility of rapid investigation and haematology input, particularly in resource-limited or rural settings. There were warnings that shifting the decision to individual clinicians could lead to inconsistent practice from inexpert clinicians.

Respondents stressed the importance of involving patients, caregivers and family in decision-making.

Medsafe's response

Medsafe agrees that red results should be discussed with a haematologist, as proposed in the consultation (Figure 1 above). We note that the clozapine sponsors (companies) have haematologists available to provide advice.

Some respondents stated that clozapine should always be stopped immediately if the ANC result is very low ($<0.5 \times 10^9$/L). Other respondents said that clozapine treatment should continue during the investigation only if the patient is clinically stable and under close supervision, with documentation of the decision and rationale. Medsafe considers that this should be a clinical decision, allowing flexibility for treatment decisions to be based on individual circumstances. Prescribers can still elect to stop clozapine immediately, but this will not be compulsory. As outlined in the proposal, all treatment decisions should be made in consultation with the patient, carers and family.

Outcome

The data sheet will be updated to enable individual treatment decisions when investigating and managing 'red' results. Refer to flow diagrams in Appendix 1.

Question 18: Please select the relevant factors to consider when deciding whether to continue clozapine treatment. Select all those that apply.

Option	No.	Percent
Severity of neutropenia (ANC results and recovery)	107	87.7%
Clinical signs/symptoms of neutropenia including infection	103	84.4%
Neutrophil patterns (ANC trends)	94	77.1%
Time of onset (since clozapine initiation)	101	82.8%
Other causes of neutropenia (for example medicines or other conditions)	108	88.5%
Previous blood test results and clozapine-induced agranulocytosis (CIA) rechallenge history	101	82.8%
Control of treatment-resistant schizophrenia and efficacy of clozapine (including risk of relapse)	97	79.5%
Alternative treatment options to clozapine	87	71.3%
Haematologist advice	101	82.8%
Patient and/or caregiver input	96	78.7%
Other. Please comment below.	8	6.6%
Not Answered	5	4.1%

Comments from respondents

The majority of the respondents agreed with the proposed relevant factors to consider when deciding when to continue clozapine treatment.

Suggested other factors to consider included the following.

- Smoking status.
- Patient's ability to self-monitor for clinical signs and symptoms of neutropenia and other 'safety nets' that may support safe ongoing treatment.
- Longitudinal blood results including CBC.
- Patient and caregiver input.

Other comments included that agranulocytosis is a potentially fatal condition and must take precedence over considerations of clozapine's effectiveness. Determining whether neutropenia is caused by clozapine or other factors can be challenging, and in cases where the cause is unclear, detailed investigations (eg, for viral infections such as EBV) may be necessary to enable clozapine rechallenge.

Medsafe's response

Medsafe agrees that smoking status, patient insight and safety nets, longitudinal blood results and investigations to exclude viral infections are important factors for clinicians to consider on a case-by-case basis. The listed factors were not intended to preclude consideration of other factors or limit decision-making. As outlined in the proposal, all treatment decisions should be made in consultation with the patient, carers and family.

Outcome

The data sheet will be updated to include the factors to consider when deciding whether to continue clozapine treatment.

Question 19: Do you agree that if clozapine caused the severe neutropenia, then clozapine should be discontinued?

Option	No.	Percent
Yes – temporarily	91	74.6%
Yes – permanently	22	18.0%
No. Please suggest an alternative below.	4	3.3%
Not Answered	5	4.1%

Comments from respondents

The majority of respondents (75%) selected the option to temporarily discontinue clozapine if it caused the severe neutropenia. Fewer respondents (18%) selected the option to permanently discontinue clozapine if it caused the severe neutropenia.

Temporary cessation was seen as appropriate while a clinical review is undertaken, with any decision to restart clozapine made only once neutropenia has fully resolved and the clinical appropriateness of recommencing treatment has been carefully assessed in consultation with the patient and haematology. In some instances, the benefits of restarting treatment after temporary interruption will outweigh the risks (eg, intractable psychotic relapse). One respondent suggested that if severe neutropenia recurs on rechallenge, clozapine should be considered the definitive cause and rechallenge should not be attempted in future.

The decision to discontinue and rechallenge clozapine should involve the patient and their family/caregiver, and every effort should be made to continue clozapine where appropriate. For many people, the risks of clozapine are outweighed by their improved quality of life.

There were comments that colony-stimulating factors (eg, pegfilgrastim) can be used to treat neutropenia and should be funded for clozapine patients.

Some respondents supported permanent discontinuation if clozapine is confirmed as the cause of severe neutropenia. Rechallenge in this situation carries a high risk of recurrence, which can be life-threatening.

Medsafe's response

There was support for the option for temporary discontinuation of clozapine where clozapine was determined to have caused severe neutropenia, with the option to rechallenge in future.

As outlined in the evidence review, an analysis of the UK Central Non-Rechallenge Database (CNRD) found that of the 519 out of 3,731 patients who were rechallenged on clozapine after CNRD registration, 100 (19%) had recurrence of neutropenia and 419 (81%) were successfully rechallenged. This included 46 patients with ANC $<1.0x10^9$/L, of whom 36 (78%) were rechallenged successfully.[3] An analysis of Finnish data identified 231 people who developed severe neutropenia whilst taking clozapine and found that of the 76 people (33%) who were rechallenged, 11 (14%) had another severe neutropenia event. These findings support the option for rechallenge of clozapine after a 'red' result.[4]

[3] Oloyede E, Whiskey E, Casetta C, et al. 2022. Relaxation of the criteria for entry to the UK Clozapine Central Non-Rechallenge Database: a modelling study. *Lancet Psychiatry* 9(8): 636–44. DOI: 10.1016/s22150366(22)00188-2 (accessed 17 July 2026).

[4] Rubio JM, Kane JM, Tanskanen A, et al. 2024. Long-term persistence of the risk of agranulocytosis with clozapine compared with other antipsychotics: a nationwide cohort and case-control study in Finland. *Lancet Psychiatry* 11(6): 443–50. DOI: 10.1016/s2215-0366(24)00097-x (accessed 17 July 2026).

Therefore, Medsafe agrees that the data sheet should include the option to rechallenge with clozapine following suspected clozapine-induced severe neutropenia in exceptional cases. The benefits and risks of rechallenge must be carefully balanced for the individual in consultation with a haematologist. If clozapine-induced severe neutropenia recurs upon rechallenge, clozapine must then be stopped, and the patient should never be rechallenged again.

Outcome

A confirmed 'red' result that is considered to be related to clozapine should result in discontinuation of clozapine, but future rechallenge may be an option in exceptional cases, providing all the caveats discussed above are considered. People with unsuccessful rechallenge (ie, a further episode of clozapine-induced severe neutropenia) should not be rechallenged again. This will be reflected in the data sheet.

Question 20: If clozapine-induced severe neutropenia is suspected, should there be an option to reduce the dose of clozapine as opposed to immediate discontinuation?

Option	No.	Percent
Yes	75	61.5%
No. Please suggest an alternative below.	39	32.0%
Not Answered	8	6.5%

Comments from respondents

Many respondents (61%) supported having the option to reduce the dose of clozapine as opposed to immediate discontinuation, if clozapine-induced severe neutropenia is suspected. Approximately one third of respondents (32%) did not support dose reduction as a management strategy.

Clozapine-induced neutropenia is not dose dependent, so changing the dose would not reverse the neutropenia. Clozapine should be prescribed at the lowest effective dose. While gradual tapering is appropriate when discontinuation is elective (ie, not due to severe neutropenia), this is not a safe strategy in suspected clozapine-induced severe neutropenia. Ways of managing anticholinergic rebound and the risk of relapse (alternative antipsychotic) must be considered when stopping clozapine.

Medsafe's response

Medsafe agrees that reducing or tapering the dose of clozapine in suspected clozapine-induced severe neutropenia to mitigate rebound psychosis is not appropriate due to the life-threatening nature of severe neutropenia, which is not dose-dependent.

Outcome

Reducing or tapering the clozapine dose will not be an option in the management of severe neutropenia suspected to be caused by clozapine.

Question 21: Do you agree that clozapine rechallenge following suspected clozapine-induced agranulocytosis can be considered, if the benefits outweigh the risks for the individual?

Option	Total	Percent
Yes	108	88.5%
No. Please suggest an alternative below.	8	6.6%
Not Answered	6	4.9%

Comments from respondents

The majority of respondents agreed that clozapine rechallenge following suspected clozapine-induced severe neutropenia/agranulocytosis can be considered, if the benefits outweigh the risks for the individual. There were comments that the decision to rechallenge should be made with psychiatrist and haematologist input, with enhanced blood monitoring.

Other respondents disagreed that rechallenge could be considered, as they perceived risk of recurrence of severe neutropenia to be high.

Medsafe's response

Patients with previous severe neutropenia/agranulocytosis caused by clozapine may be at risk of recurrence on rechallenge. However, there may be situations where the clinical benefits of clozapine in managing intractable psychotic relapse outweigh the risks of recurrence of neutropenia. Additionally, there is not always a definitive cause identified for neutropenia. Therefore, Medsafe agrees that clozapine rechallenge following suspected clozapine-induced severe neutropenia/agranulocytosis should be an option in exceptional cases. Rechallenge may be considered in selected cases after carefully balancing the benefits and risks for the individual in consultation with a haematologist.

Outcome

The data sheet will be updated.

Question 22: Do you agree that if clozapine is rechallenged following suspected clozapine-induced severe neutropenia/agranulocytosis, the monitoring frequency and duration should start as for a 'new' patient (ie, weekly blood tests for the first 18 weeks, then every 4 weeks)? Select all those that apply.

Option	No.	Percent
Yes – if the patient has been taking clozapine for less than a year	25	20.5%
Yes – no matter how long the patient has been taking clozapine	84	68.9%
No – if the patient has been taking clozapine for less than a year, they should go back to the previous frequency	2	1.6%
No – if the patient has been taking clozapine for long enough not to require blood monitoring	4	3.3%
I have an alternative suggestion. Please describe below.	7	5.7%
Not Answered	8	6.6%

Comments from respondents

The majority of respondents (69%) agreed that that if clozapine is rechallenged following suspected clozapine-induced severe neutropenia/agranulocytosis, the monitoring frequency and duration should restart as for a 'new' patient, no matter how long the patient has been taking clozapine. Fewer respondents (20%) agreed that monitoring should restart as for a 'new' patient if the patient has been taking clozapine for less than a year.

There were comments that the risk of recurrence of severe neutropenia is high, and monitoring should therefore be weekly for the first 18 weeks, then monthly thereafter. A respondent highlighted a case of severe neutropenia in a patient successfully treated with clozapine for many years, with recurrence upon rechallenge that was detected by routine monitoring.

Other comments said the frequency and duration of monitoring should be decided on a case-by-case basis, with haematologist input. Another respondent considered that ANC monitoring should be daily following clozapine rechallenge.

Medsafe's response

Patients with previous clozapine-induced severe neutropenia/agranulocytosis may be at high risk of recurrence on rechallenge. Medsafe considers that that if clozapine is rechallenged following suspected clozapine-induced severe neutropenia, the monitoring frequency and duration should restart as for a 'new' patient, no matter how long the patient has been taking clozapine.

Outcome

If clozapine is rechallenged following suspected clozapine-induced severe neutropenia/agranulocytosis, the monitoring frequency and duration will restart as for a 'new' patient, no matter how long the patient has been taking clozapine.

Question 23: Do you agree that if a patient experiences severe neutropenia that is not caused by clozapine and restarts treatment, the frequency of monitoring can return to the patient's usual monitoring frequency (which could be no monitoring)?

Option	No.	Percent
Yes	68	55.7%
No. Please suggest an alternative below.	45	36.9%
Not Answered	9	7.4%

Comments from respondents

There wasn't a strong consensus among respondents as to whether or not a patient who experiences severe neutropenia that is not caused by clozapine and restarts treatment should return to their usual monitoring frequency (which could be no monitoring).

Some respondents considered that the monitoring regimen could return to the usual frequency if there was clear clinical information indicating that the neutropenia was not related to clozapine.

Some respondents considered that the cause of neutropenia is often unclear, and clozapine may be a contributing factor. Patients should therefore restart monitoring as for a 'new' patient.

Other respondents commented that there should be some monitoring after restarting clozapine following neutropenia considered unrelated to clozapine, but that this monitoring could be less frequent and/or

shorter in duration than for a new patient. Some respondents said that the decision to restart ANC monitoring, including monitoring frequency, should be a case-by-case clinical decision.

Medsafe's response

The evidence review did not identify evidence that previous neutropenia unrelated to clozapine increases the risk of clozapine-induced severe neutropenia. In a retrospective cohort study of people enrolled in the Viatris clozapine blood monitoring database across Australia and NZ, competing risks regression for events according to previous clozapine exposure showed that for patients re-trialling clozapine who had not previously had a serious neutropenic event, the incidence of any neutropenic event was much lower than in patients with no previous clozapine exposure. This suggests that it is not essential for patients rechallenging clozapine after treatment interruption to restart haematological monitoring if there has been a cumulative 2 years of unremarkable monitoring.[5]

Therefore, Medsafe considers that the frequency of monitoring can return to the patient's usual monitoring frequency if neutropenia was not caused by clozapine. Clinicians can elect to monitor ANC when re-titrating clozapine based on their clinical judgement, but this will not be compulsory.

Outcome

If a patient experiences severe neutropenia that is not caused by clozapine and restarts treatment, the frequency of monitoring can return to the patient's usual monitoring frequency (which could be no mandatory monitoring).

Question 24: Do you agree that patients who have stopped ongoing monitoring and who have interrupted treatment for any duration for reasons not related to neutropenia can continue with no haematological monitoring when clozapine is restarted?

Option	No.	Percent
Yes	56	45.9%
No. Please suggest an alternative below.	54	44.3%
Not Answered	12	9.8%

Comments from respondents

There was no consensus from respondents as to whether patients who have stopped ongoing monitoring and who have interrupted treatment for any duration for reasons not related to neutropenia can continue with no haematological monitoring when clozapine is restarted.

Some respondents said that monitoring should be restarted as for a new patient if they have discontinued clozapine (eg, for more than 72 hours). There was a comment that the risk of neutropenia on restarting appears to be similar to that after first initiation.

Other respondents considered that there should be some monitoring, but less than for a new patient. For example, at least one ANC measurement taken, or a shorter period of weekly then monthly testing. Some respondents considered that the monitoring regimen should be individualised and consider how long the patient has been off clozapine.

[5] Northwood K, Myles N, Clark SR, et al. 2024. Evaluating the epidemiology of clozapine-associated neutropenia among people on clozapine across Australia and Aotearoa New Zealand: a retrospective cohort study. *Lancet Psychiatry* 11(1): 27–35. DOI: 10.1016/s2215-0366(23)00343-7 (accessed 17 July 2026).

Medsafe's response

Medsafe agrees that patients who have stopped ongoing monitoring and who have interrupted treatment for any duration for reasons not related to neutropenia can continue with no haematological monitoring when clozapine is restarted, based on the clinician's clinical judgement – particularly if the period of interruption is longer than 4 weeks. Clinicians can use their clinical judgement whether or not to monitor ANC when re-titrating clozapine in these patients, but monitoring will not be compulsory.

Outcome

Patients who have stopped ongoing monitoring and who have interrupted treatment for any duration for reasons not related to neutropenia can continue with no haematological monitoring when clozapine is restarted.

Question 25: Do you have any other considerations or comments relating to Medsafe's proposals for changes to management of 'red' blood test results?

Comments from respondents

Clozapine should not be automatically discontinued when another clear cause for the neutropenia has been identified. Decisions should be made collaboratively between the clinician and the patient. There was a comment that if a person's low ANC is associated with a viral illness, there should be no requirement for them to be fully 'physically well' before restarting clozapine.

Several submissions stressed the need for safe and consistent practice when restarting treatment. There needs to be national guidance and standardised clinical algorithms to ensure consistent management across regions and mental health services. Additionally, there should be explicit guidance on the need to re-titrate clozapine after treatment interruption, along with reminders for prescribers to monitor for other serious adverse reactions during re-titration.

There were concerns about potential unintended impacts of stopping ongoing blood monitoring. For example, stopping routine blood tests, combined with prescribing rules that allow 'stable' patients to see their GP only once per year, may result in inadequate follow-up. This could lead to metabolic and gastrointestinal monitoring being deprioritised. There was a comment that long-term clozapine use may also increase the risk of other haematological conditions, and regular blood counts may still be needed to detect or manage disorders such as myelodysplastic syndrome.

Finally, respondents noted that pharmacists must have real-time access to haematology results to safely dispense clozapine.

Medsafe's response

The proposed changes are intended to allow more flexibility for clinicians to use their clinical judgement around managing the risk of neutropenia with clozapine. Clinicians can choose to continue monitoring based on clinical judgement.

The changes to monitoring requirements will be reflected in the data sheet and the clozapine blood monitoring database. The data sheet already includes information on restarting clozapine after treatment interruption. Prescribers should refer to local guidelines for further information on re-titration.

Who can prescribe clozapine

Current requirements

Under the current restrictions, only the following healthcare professionals may prescribe clozapine.

- Registered medical practitioners as defined in the Health Practitioners Competence Assurance Act 2003 who are certified by the Medical Council of New Zealand as competent in the scope of practice of psychiatry (ie, psychiatrists).
- Medical practitioners or nurse practitioners, who are under the supervision of the persons referred to above.
- Medical officers who are in the employment of Te Whatu Ora, and are under the supervision of persons who are registered medical practitioners as defined in the Health Practitioners Competence Assurance Act 2003 who are certified by the Medical Council of New Zealand as competent in the scope of practice of psychiatry.
- Registered medical practitioners as defined in the Health Practitioners Competence Assurance Act 2003 who are registered with the Medical Council of New Zealand within the vocational scope of practice of general practice. The general practitioner must be continuing the prescribing of clozapine for a specific patient whose illness is well-controlled in collaboration, or following consultation, with a Community Mental Health Team.

Proposed changes to clozapine prescribing restrictions

Following a 2024 petition to the House of Representatives to remove the clozapine prescribing restrictions for nurse practitioners, Medsafe proposes amending the restrictions to those shown in Table 4.

Table 4: Proposed prescribing restrictions for clozapine

Prescriber type	Initiate prescribing (new patients and patients restarting treatment)	Continue prescribing
Psychiatrist[a]	Yes	Yes
Medical practitioner[b] under the supervision or in consultation with a psychiatrist	Yes	Yes
Medical practitioner[b] working in a community mental health team	No	Yes
Nurse practitioner[c] under the supervision or in consultation with a psychiatrist	No	Yes
Nurse practitioner[c] working in a community mental health team	No	Yes
Nurse prescriber[d] under the supervision of a psychiatrist	No	Yes
Pharmacist prescriber[e] under the supervision of a psychiatrist	No	Yes

Notes

a. Psychiatrist: Registered medical practitioners as defined in the Health Practitioners Competence Assurance Act 2003 who are certified by the Medical Council of New Zealand as competent in the scope of practice of psychiatry.
b. Medical practitioners: Registered medical practitioners as defined in the Health Practitioners Competence Assurance Act 2003 who are registered with the Medical Council of New Zealand within a vocational scope of practice or general scope of practice. This definition includes vocationally trained hospital consultants, GPs and RMOs practicing in a general scope.
c. Nurse practitioner: Registered nurse as defined in the Health Practitioners Competence Assurance Act 2003 and certified by the Nursing Council of New Zealand in the scope of nurse practitioner.
d. Nurse prescriber: Registered nurse designated to prescribe from a schedule of medicines.
e. Pharmacist prescriber: Pharmacists who have completed an accredited postgraduate programme and have the prescriber scope of practice.

Question 26: Do you agree with the proposal for who can initiate clozapine treatment?

Option	No.	Percent
Yes	73	59.8%
No. Please suggest an alternative below.	46	37.7%
Not Answered	3	2.5%

Comments from respondents

The majority of respondents (59.8%) agreed with the proposed prescribing restrictions. Comments from respondents regarding initiation of clozapine treatment varied widely. Some opposed the proposal because they wanted a broader range of health professionals to be able to initiate clozapine prescribing. Others disagreed on the grounds that prescribing should remain the responsibility of psychiatrists, or that primary care – particularly general practitioners – should be excluded from initiating treatment. The table below summarises the key themes raised by respondents.

Theme	No.
Initiation of prescribing should be broader, and include:	**42**
Medical practitioners working in a community mental health team	8
Nurse practitioners under psychiatrist supervision/consultation	13
Nurse practitioners working in a community mental health team	11
Nurse prescribers under the supervision of a psychiatrist	1
Pharmacist prescribers	5
Any prescriber under psychiatrist supervision	2
Other medical specialists (neurology and geriatrics)	2
Initiation of prescribing should stay the same OR be *more* restrictive	**19**
Initiation should be by psychiatrists or medical practitioners under supervision only	10
Initiation should not be done by general practitioners/primary care	9

Note: Some respondents raised topics relating to multiple themes, so the total number of responses in the table is greater than the number of respondents who provided feedback to this question.

Among those who suggested alternative prescribers, many recommended that nurse practitioners – either working under psychiatrist supervision or as part of a community mental health team – should be able to initiate clozapine. Medical practitioners working within community mental health teams were also frequently identified as appropriate initiators. In contrast, several respondents argued that initiation should remain restricted to psychiatrists, or medical practitioners working under psychiatric supervision. Others expressed strong concerns about transferring initiation responsibilities to primary care, emphasising that general practitioners should not undertake this role.

Medsafe's response

Medsafe agrees with enabling medical practitioners working in community mental health teams to initiate prescribing of clozapine. The prescribing restrictions will be amended accordingly.

Please note that for prescribers other than psychiatrists (eg, general practitioners, nurse practitioners and pharmacist prescribers), prescribing of clozapine would need to fall within their specific scope of practice. All prescribers of clozapine are expected to provide care that includes all aspects of monitoring, beyond blood monitoring (eg, metabolic monitoring, constipation monitoring, response to treatment).

The proposed changes to prescribing restrictions are intended to enable prescribing by different healthcare professional types and reduce barriers to patient access to clozapine. The changes do not create an expectation that these healthcare professional types must prescribe clozapine or take on duties outside their scope of practice.

Question 27: Do you agree with the proposal for who can continue clozapine treatment?

Option	No.	Percent
Yes	93	76.2%
No. Please suggest an alternative below.	24	19.7%
Not Answered	5	4.1%

Comments from respondents

The majority of respondents (76.23%) agreed with the proposal for who can continue clozapine treatment.

Of the 24 respondents who did not agree, 23 provided comments. Most of these comments opposed the proposal because they believed certain health professionals should be excluded from being able to continue prescribing clozapine. Several respondents also expressed concerns about continuation of clozapine treatment shifting away from secondary care. Some respondents supported the proposal overall, but disagreed with specific elements. The table below summaries the key themes raised by respondents.

Theme	No.
Continuation should be by secondary care only	6
Disapproval of continuation by nurse practitioners	3
Disapproval of continuation by general practitioners	2
Disapproval of continuation by nurse prescribers	6
Disapproval of continuation by pharmacist prescribers	5
Approval of continuation by nurse practitioners	5
Approval of continuation by general practitioners	1
Approval of continuation by nurse prescribers	2
Approval of continuation by pharmacist prescribers	3

Note: Some respondents raised topics relating to multiple themes, so the total number of responses in the table is greater than the number of people who provided feedback to this question.

Among those who disagreed with the proposal, many suggested that nurse prescribers and pharmacist prescribers should not be able to continue clozapine treatment. Some also recommended that general practitioners and nurse practitioners be excluded from continuation responsibilities. In contrast, many respondents supported the inclusion of nurse practitioners, and to a lesser extent nurse prescribers and pharmacist prescribers.

Medsafe's response

As stated above, prescribing of clozapine must fall within an individual healthcare professional's scope of practice. The proposed changes to prescribing restrictions are intended to enable prescribing by different healthcare professional types and reduce barriers to patient access to clozapine. The changes do not create an expectation that these healthcare professional types must prescribe clozapine or take on duties outside their scope of practice.

Question 28: Do you have any comments or feedback relating to Medsafe's proposed prescribing restrictions for clozapine?

Comments from respondents

There were 35 respondents who offered substantive feedback. These comments included expressions of support for the proposal, concerns about specific elements, overall disagreement, and questions or suggestions for improvement. The table below summarises the key themes identified in the responses.

Theme	No.
Overall support for the proposal	9
Support for prescribing rights for nurse practitioners	6
Existing monitoring databases are not fit for purpose	3
Concerns regarding general practitioner prescribing	6
Psychiatrist supervision is necessary for prescribing	4
Query the expertise of nurse and pharmacist prescribers	2
More clarity around certain aspects of the proposal needed	5
General lack of support for the proposal	1
Other suggestions/questions	5

Note: Some respondents raised topics relating to multiple themes, so the total number of responses in the table is greater than the number of people who provided feedback to this question.

Many respondents expressed general support for the proposal, with several endorsing clozapine prescriber rights for nurse practitioners. However, others argued that clozapine prescribing should remain under psychiatrist supervision only, or that any involvement of other health professionals should occur strictly under psychiatric oversight.

A number of respondents raised concerns about general practitioner involvement in clozapine prescribing, citing issues related to clinical expertise, workload pressures, and appropriate funding. There were also concerns about the adequacy of current monitoring databases, and whether nurse and pharmacist prescribers possess the necessary qualifications to continue supply of clozapine.

Several respondents requested greater clarity regarding certain aspects of the proposal, including the definition of "specialist supervision", the delineation of clinical responsibility for patient care and monitoring, and which medical specialties would be authorised to initiate and continue clozapine prescriptions.

Medsafe's response

The proposed changes to prescribing restrictions are intended to enable prescribing by different healthcare professional types and reduce barriers to patient access to clozapine. The changes do not create an expectation that these healthcare professional types must prescribe clozapine or take on duties outside their scope of practice.

We expect that only stable patients who are well-established on clozapine and living in the community would be placed under the care of GPs with their agreement. We consider GPs well-placed to manage these types of patients where it falls within their scope of practice. The broad expertise of GPs means that they are better able to provide comprehensive care for patients living and working in the community.

Outcome

We will amend the clozapine prescribing restrictions to state that medical practitioners working in a community mental health team may initiate clozapine. All other proposed restrictions will be adopted.

We expect all prescribers to ensure that they fully understand the safety profile of clozapine and risk management measures that are needed to ensure patients remain as safe as possible while taking clozapine.

Point-of-Care testing

Current requirements

Point-of-Care (POC) tests for neutrophil counts are not currently an option.

Proposed changes

We would like to enable use of POC tests of appropriate quality and accuracy after the first 18 weeks of clozapine treatment. Point-of-Care test devices are not regulated in New Zealand. However, some brands have been accepted in other countries.

POC testing could be particularly useful in New Zealand where many people have barriers to accessing blood tests. For example, the pharmacist could do the POC test before dispensing the patient's next prescription.

We propose enabling the clozapine blood monitoring database to allow a POC test result to be entered as an alternative to a laboratory blood test result.

However, the health system would need to make POC tests of appropriate quality and accuracy available and fund them.

Question 29: Do you agree that Point-of-Care tests of appropriate quality and accuracy should be an alternative to laboratory blood tests after 18 weeks of treatment with clozapine?

Option	No.	Percent
Yes. Please state your reasoning below.	107	87.7%
No. Please state your reasoning below.	8	6.6%
Not Answered	7	5.7%

Question 30: Do you have any other comments or feedback relating to Point-of-Care testing for clozapine?

Comments from respondents

Most respondents agreed that Point-of-Care (POC) tests of appropriate quality and accuracy should be an alternative to laboratory blood tests after 18 weeks of treatment with clozapine.

Respondents commented that availability of POC testing has the potential to reduce barriers to clozapine initiation, reduce the burden on patients, support adherence to treatment and reduce treatment interruptions. It could reduce barriers for people living rurally, and those with an aversion to needles or venous access issues. POC testing would also provide an opportunity for other clinical checks. One respondent considered that POC testing should be available at any time during treatment.

Some respondents emphasised the need for POC tests of appropriate quality and accuracy (ie, to avoid false-positive or false-negative results). Others commented that POC tests are unregulated and should not be used.

The clozapine blood monitoring database must allow pharmacists to record and share Point-of-Care test results with clinicians. Respondents also highlighted the importance of access to specialist advice when interpreting results, warning that without this support, patient safety could be compromised.

There were comments that POC testing would need to be funded. Respondents also noted challenges around availability of resources to provide this service in a pharmacy setting. For example, pharmacies would need adequate funding, training and accreditation, and a private consultation space.

POC testing could be a useful option in primary care settings. Patients will still need to attend labs for other tests such as metabolic screening. There was concern that introducing POC testing might unintentionally reduce the frequency of metabolic monitoring.

Others commented that POC testing should not be used by patients at home and patients should ideally attend the same pharmacy each time to maintain continuity and oversight. Some suggested that POC testing may be most appropriate for patients who are well established and stable on clozapine with an established relationship with their prescriber (eg, for at least 3 years). Another respondent considered that to support adherence, blood tests should be done by experienced nurses who can minimise venous damage.

Medsafe's response

The majority of respondents supported POC testing.

The companies have confirmed that results from POC testing can be entered into the clozapine blood monitoring database. The health system can now choose whether to implement the use of POC tests to reduce burden on healthcare professionals and patients.

Outcome

The clozapine blood monitoring databases allow for manual entry of test results and therefore POC test results can be entered

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Educational needs

Question 31: What are your educational needs for clozapine prescribing and safety monitoring (both now and following any changes)?

Comments from respondents

Respondents emphasised the need for comprehensive education for healthcare professionals on all aspects of clozapine prescribing and monitoring. They recommended compulsory training for prescribers and anyone interpreting blood test results, supported by regular refresher sessions. Suggestions included the development of clear treatment algorithms and guidelines, accessible points of contact for advice, and opportunities for supervision or case review with psychiatrists.

Suggested resources included updated Community Health Pathways guidance, written communications, and education from community mental health services. Respondents also proposed multiple formats for education delivery, including BPAC articles, webinars through the Goodfellow Unit, e-learning modules, and updates to data sheets, NZF, Healthify, and professional body communications. If introduced, there needs be education on Point-of-Care testing.

For patients, respondents recommended providing patient information leaflets in different languages. A smartphone application to help individuals track neutrophil results, monitor upcoming blood tests, and recognise symptoms requiring urgent attention was suggested.

Medsafe's response

Medsafe will produce a patient leaflet and communicate changes to relevant stakeholders involved in healthcare professional education.

The companies supplying clozapine can also provide database support and access to a consultant haematologist who can provide expert haematological advice.

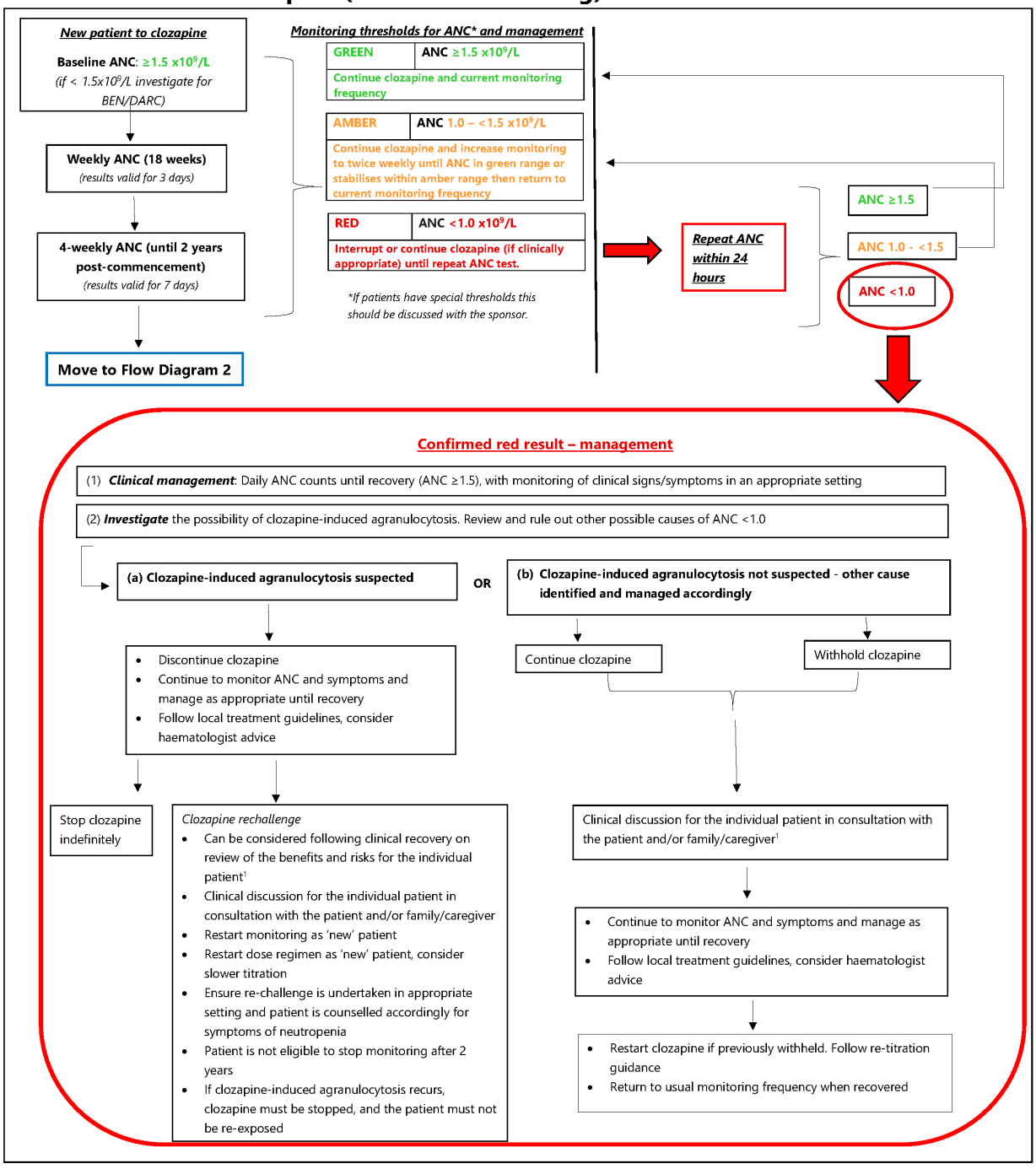
We encourage other groups who create guidelines and advice to note these changes to clozapine blood monitoring requirements, so they can update their guidance accordingly.

Appendix 1 – Flow diagrams

The flow diagrams are:

- Flow diagram 1: Clozapine Blood Monitoring Requirements: 0 – 2 years from commencement of clozapine (standard monitoring)
- Flow diagram 2: Clozapine Blood Monitoring Requirements: >2 years from commencement of clozapine (standard monitoring)
- Flow diagram 3: Clozapine Blood Monitoring Requirements: interruption or discontinue of clozapine for non-haematological reasons
- Flow diagram 4: Clozapine Patient Monitoring

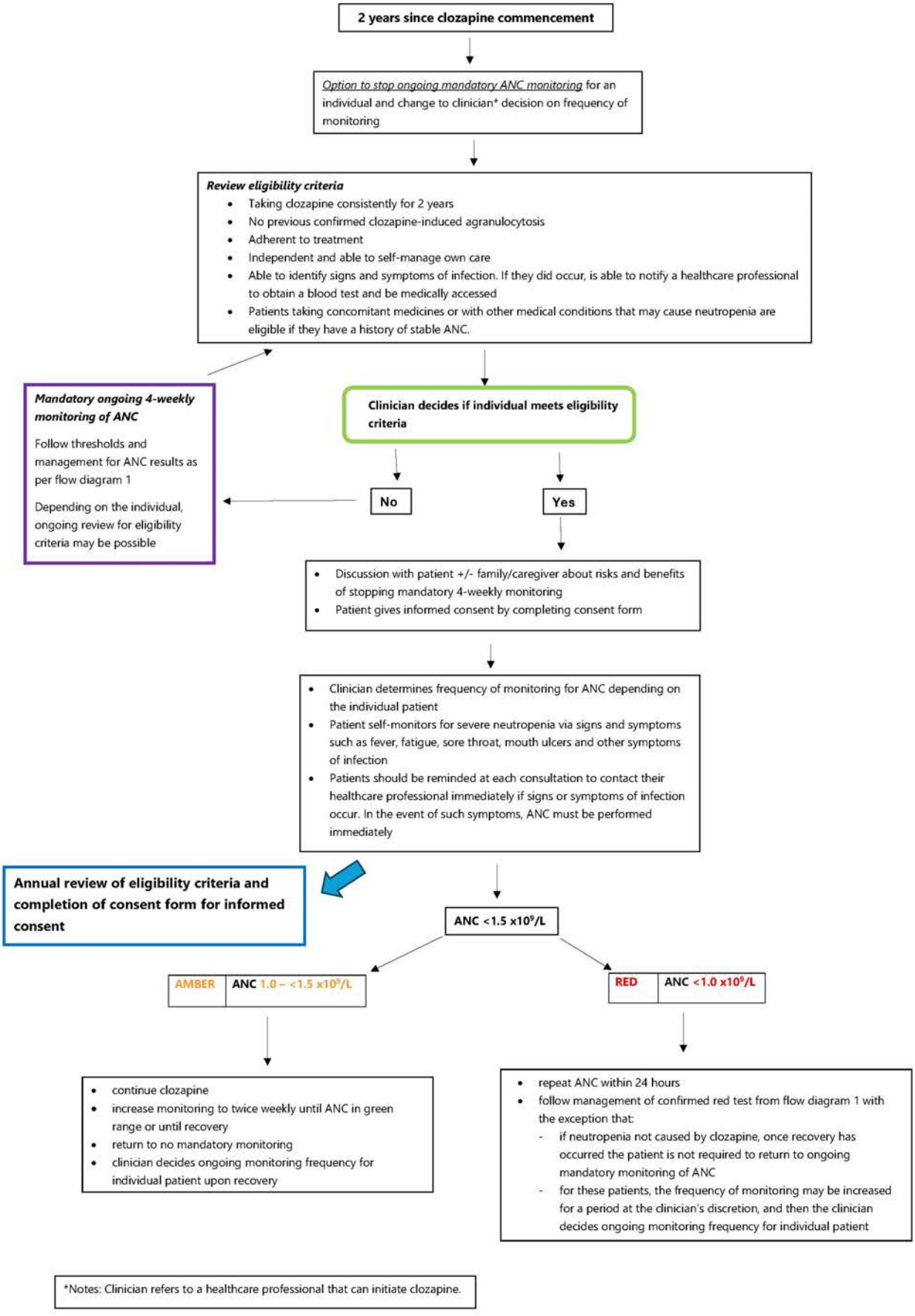
Flow diagram 1: Clozapine Blood Monitoring Requirements: 0 – 2 years from commencement of clozapine (standard monitoring)



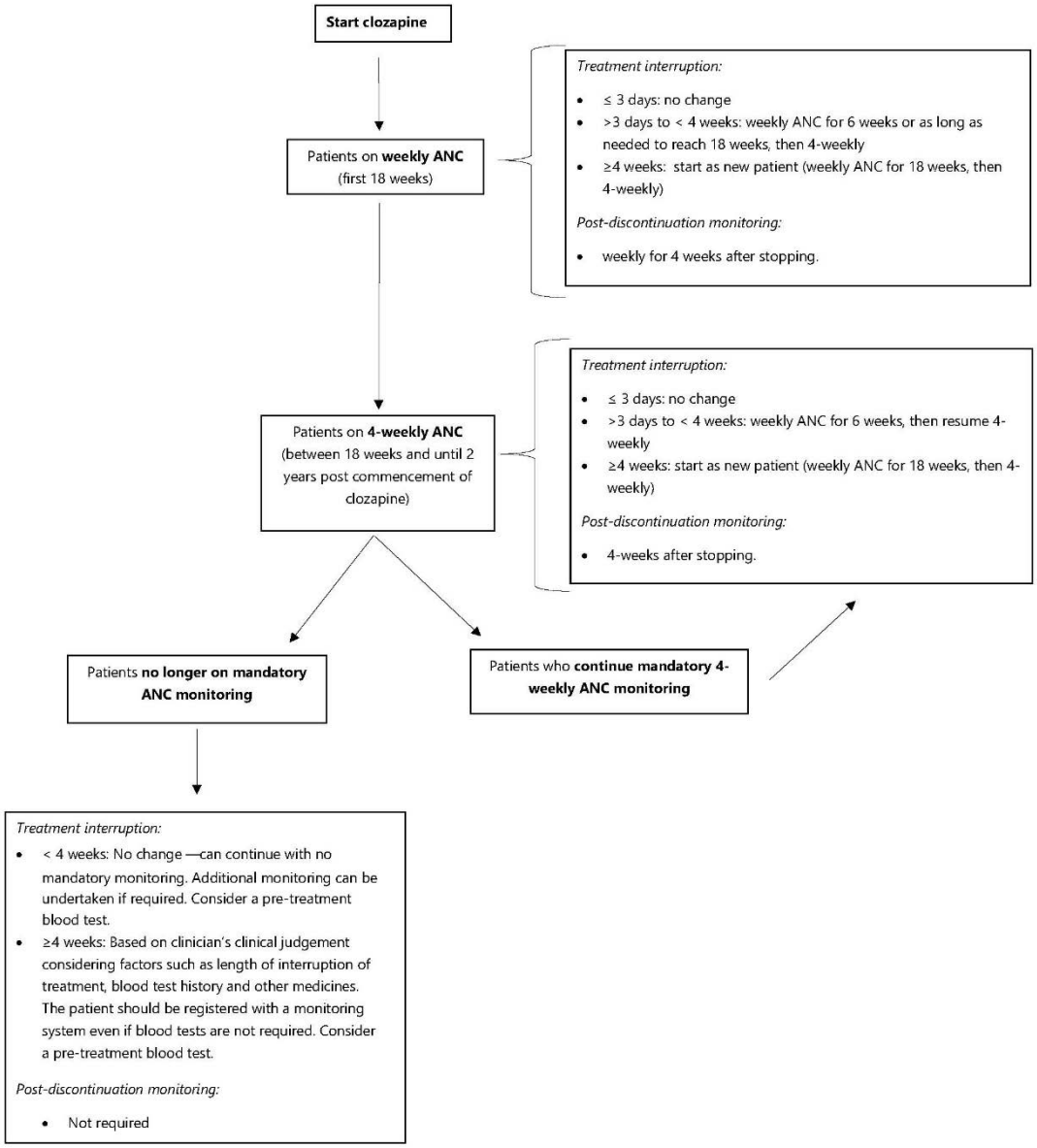
Notes:

- [1]Factors to consider when deciding whether clozapine is to be continued or withheld following a red ANC that is determined not to be related to clozapine:
  - Severity of neutropenia (ANC results and recovery), clinical signs/symptoms of neutropenia including infection, neutrophil patterns (ANC trends), time of onset (since clozapine initiation)
  - Other causes of neutropenia (for example medicines or other medical conditions)
  - Previous blood test results, clozapine-induced agranulocytosis history (including rechallenge history)
  - Control of treatment-resistant schizophrenia and efficacy of clozapine (including risk of relapse), alternative treatment options to clozapine
  - Haematologist advice
  - Patient and/or family/caregiver input
- [1]The factors above should also be considered on discussions relating to clozapine rechallenge.

Flow diagram 2: Clozapine Blood Monitoring Requirements: >2 years from commencement of clozapine (standard monitoring)



Flow diagram 3: Clozapine Blood Monitoring Requirements: interruption or discontinuation of clozapine for non-haematological reasons



Flow diagram 4: Clozapine Patient Monitoring