

Office of the Chief Psychiatrist

COVID-19 Positive Clozapine Management Guideline

24 September 2024

This revised guideline has been prepared to be used in response to people prescribed clozapine who have a positive COVID-19 test either by PCR or Rapid Antigen Test (RAT).

During the pandemic much information and evidence was gathered relating to how people prescribed clozapine were affected by COVID-19. We know that clozapine is associated with increased risk of pneumonia¹. There is evidence that clozapine may lead to secondary antibody deficiency, which may lead to people on clozapine being more susceptible to viral respiratory infections such as influenza and COVID-19.² It is also well documented that infection can substantially increase clozapine levels. Clozapine toxicity, pneumonia and delirium are the main COVID-19 complications that have been seen in people prescribed clozapine.³

The purpose of this guideline is to provide a consistent management approach across the state to ensure that the risk of infection, toxicity due to increased clozapine levels and other adverse events due to their COVID-19 diagnosis are minimised for this group of people, whilst continuing to ensure that they receive appropriate clozapine care.

This information is supplementary to the SA Health [Clozapine Management Clinical Guideline](#) (CMCG). Information contained in this guideline will be incorporated into the CMCG at the next review.

This guideline applies to the clozapine clinics currently held within SA Health clozapine centres and to people prescribed clozapine in GP shared care.

The COVID-19 positive clozapine management guideline has taken into consideration the current information we have available regarding COVID-19 positive people taking clozapine.

International case series have shown that COVID-19 infection is associated with a drop in neutrophils⁴. There are also reports of elevated clozapine levels associated with COVID-19 infection^{5,6}. Surveillance across SA has been consistent with these observations. Whilst most people do not experience problems with clozapine during COVID-19 infection, there have been a significant number of clozapine consumers who have experienced a significant drop in white cell count going into the AMBER range and/or RED range necessitating clozapine cessation. Other people have had a dramatic increase in their clozapine level more than 1100ug/L. It is important to also be aware that COVID-19 vaccination can be associated with raised clozapine levels⁷ and that there is a need to monitor symptomatically, with blood tests if indicated.

As there are seemingly different responses to the COVID-19 infection it is important to maintain a consistent approach to management of COVID-19 positive people. Clozapine should not be ceased just due to a positive COVID-19 test.

The current accepted course of action is to implement the following additional haematological/ cardiac monitoring, noting that this management guideline is to be used in conjunction with existing CPMS and SA Health AMBER/RED protocols and SA Health Cardiac Guidelines:

- For a person in shared care, where the GP is willing, and in regional areas where the GP service is the only option, the GP remains the lead care provider with additional care coordination and specialist advice from the MHS. If the GP is unable to provide the required additional support, then the person is to be managed by the CMHS until

COVID-19 negative and all parameters are back to normal.

- Weekly blood testing including:
 - **CBE** to monitor WCC and NC
 - **Troponin** for cardiac assessment of potential myocarditis
 - **CRP** for cardiac assessment, acknowledging that this may be raised due to the infection.
 - **Clozapine level** – to monitor for clozapine toxicity and assess the need for dosage adjustment.
- Twice weekly telephone contact to monitor for side effects, potential signs of clozapine toxicity and mental wellbeing and to closely monitor for physical health complications including pneumonia or cardiac issues.
- Review of the person's current supply and liaison with community pharmacy may be needed including delivery or collection arrangements. Often, the person will already have clozapine on hand, however if they are due for a new prescription, it is recommended that only one week supply of medication is provided to ensure review and allow for potential dosage change if required.
- Blood test monitoring to continue at the weekly rate until the person is COVID-19 negative and symptom free and any elevated clozapine levels or abnormal blood results have returned to baseline. Mental health services may supply RAT tests for weekly monitoring as required. Of course, should the person record an AMBER or RED result or a raised Troponin then usual management protocols of increased blood monitoring are to be enacted, incorporating the additional blood testing.
- [Current SA Health COVID-19 recommendations](#) are that the person should stay at home until acute symptoms have cleared, usually 5-7 days.
- Where the COVID-19 infection has resulted in an increased clozapine level, consideration is to be given to the risk of clozapine toxicity. If the person become symptomatic with fever and flu-like symptoms, the emergence of signs and symptoms of clozapine toxicity may require clinicians to reduce the dose of clozapine by as much as half. Continue the lower dose until 3 days after the fever has subsided, then increase clozapine in a stepwise manner to the pre-fever dose.⁸
- In considering a dose reduction, close monitoring of the individual persons clinical context is required to ensure that the risk of relapse with a lower dose is weighed against the clinical risk of toxicity, sedation, myoclonus and seizure, constipation, and potential aspiration resulting in pneumonia.
- An extra clozapine level is to be taken one week following the absence of symptoms to ensure levels are returning to normal for the person and monitor any dosage adjustment requirements. If the clozapine level remains elevated, weekly clozapine levels are to continue until the person's levels have returned to their clinical range.
- Antiviral treatments should be considered for people prescribed clozapine, with either IV remdesivir or oral Lagevrio® recommended. **Under no circumstances should a person prescribed clozapine take Paxlovid as this can cause significant elevation of clozapine levels.** [See Antiviral treatments for mild COVID-19 disease](#)
- Following resolution of COVID-19 ensure person has sufficient clozapine supply to align with next due blood monitoring and clozapine appointment.

Most people on clozapine who are COVID-19 positive can be managed at home but the situation may dramatically change if the person goes into the RED or becomes clozapine toxic. Careful monitoring and oversight assist most people to safely stay on clozapine while unwell with COVID-19.

While hospital admission is not usually required, admission to an appropriate medical unit, or psychiatric unit if mentally unwell may be warranted.

- **It is recommended that anyone who is COVID-19 positive and returns a RED blood result should be managed as a medical admission** with CL input until they are stabilised. Cessation of clozapine will be required, potentially triggering rebound psychosis.

SA Pathology provides an in-home phlebotomy service for any person unable to access a collection centre. SA Pathology domiciliary service can be contacted on 82223000

In Regional areas where an in-home service may not exist it is recommended to liaise and collaborate with the local community nursing team.

An SLS and eCPMS notification is required to be made for all people on clozapine who are COVID-19 positive.

The eCPMS notification will assist in a timely rechallenge if a person is required to cease clozapine due to a RED result whilst COVID-19 positive.

The SLS notification will assist in tracking people on clozapine who are COVID-19 positive to better inform updates to the management guideline.

More consumer information on COVID-19 and clozapine can be found [here](#).

References:

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3. Selene R T Veerman, Jan P A M Bogers, Dan Cohen, Peter F J Schulte. COVID-19: Risks, Complications, and Monitoring in Patients on Clozapine Pharmacopsychiatry 2022 Jan;55(1):48-56. doi: 10.1055/a-1562-2521
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7. Thompson D et al Elevated clozapine levels and toxic effects after SARS-CoV-2 vaccination. Psychopharmacology for the Clinician J Psychiatry Neurosci 2021;46(2)
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