

## Advice on Clozapine Monitoring during COVID-19

8<sup>th</sup> April 2020

This document provides advice to doctors, nurses and pharmacists on how to maintain the safe and appropriate prescription and supply of clozapine during the COVID-19 crisis.

- **Potential Impact COVID-19 on clozapine levels**

Serious infections are sometimes associated with an increase in clozapine levels. This may occur due to metabolic effects and/or abrupt cessation of smoking which slows hepatic clearance of clozapine. Clinical signs are likely to identify rising clozapine levels before the results of plasma clozapine blood tests are available.

Action: Patients with suspected or confirmed COVID-19 should be monitored for clinical signs of increasing clozapine plasma levels e.g. increased sedation, hypersalivation, constipation.

- **Impact of COVID-19 on blood tests**

The purpose of monitoring white cell count (WCC) and absolute neutrophil counts (ANC) is to protect patients from neutropenia and agranulocytosis. Over 80% of cases of agranulocytosis occurs in the first 18 weeks of treatment. By the end of the first year of treatment, the risk of agranulocytosis is comparable to that of other antipsychotics.

Coronavirus infection may reduce lymphocyte count but may not reduce neutrophils.

Current data suggests that COVID-19 infection results in 9-45% of patients having a WCC of less than  $4.0 \times 10^9/L$ .<sup>1-5</sup> Lymphocytopenia (lymphocytes  $<1.5 \times 10^9/L$ ) has been reported in 33–83% of patients with COVID-19 infection.<sup>1-6</sup> As the monitoring parameters for clozapine include total WCC, a reduction in WCC may occur where, under normal circumstances, clozapine treatment would be interrupted. Notably, multiple studies have found neutrophil counts to remain in the normal range (median  $3.0 - 5.0 \times 10^9/L$ ) or be raised during COVID-19 infection.<sup>1,2,6</sup>

WCC and absolute neutrophil count (ANC), are important monitoring parameters used by clozapine monitoring systems.

Action: If a patient with a confirmed/suspected COVID-19 infection presents returning a WCC below the “green” range ( $3.5 \times 10^9/L$  or less) as per the clozapine monitoring protocols, it is important to consider the absolute neutrophil count (ANC) before deciding on any changes to treatment.

- **Management of patients with suspected/confirmed COVID-19 infection**

Generally, continuation of clozapine is imperative unless ANC/plasma clozapine levels dictate treatment cessation. Always consider the risks associated with discontinuing effective antipsychotic therapy.

All patients experiencing symptoms of COVID-19 infection must have a blood sample taken immediately to assess any effect on the patient’s WCC, ANC and plasma clozapine levels. Based on these results, clinical judgement must be exercised to decide how treatment is to

proceed. Communication between prescribers and pharmacists and adequate documentation is imperative in maintaining patient safety and accountability in these scenarios.

- **Obtaining blood samples**

Pathwest has developed a home-visit service for patients in isolation due to suspected/confirmed COVID-19 infection. The required tests can be ordered using standard Pathwest pathology forms. Call 6457 3281 for further advice.

There are circumstances where it may not be possible for a blood sample to be taken, e.g. patient's home is deemed unsafe by PathWest. In these scenarios, clinical judgement must be exercised to decide how treatment is to proceed in the absence of recent blood test monitoring.

- **Notifying the Clozapine Monitoring System**

It is important to contact

ClopineCentral™ (Telephone: 1800 656 403; email: [clopinecentral@pfizer.com](mailto:clopinecentral@pfizer.com))

or

CPMS™ (Telephone: 1800 501 768; Email: [cpms@cpharm.com.au](mailto:cpms@cpharm.com.au))

for advice, with a view to request dispensation if appropriate. If a clinical decision has been made to continue therapy outside of the recommendations of the protocol (i.e. ANC is within the required range) this also needs to be registered when prescribing or dispensing clozapine for a patient.

- **What to tell your patient**

If your patient is concerned that they may have contracted COVID-19, you can direct them to the following resources:

- Coronavirus Health Information Line: 1800 020 080
- WA Health Department resources: [www.health.gov.au/covid19-resources](http://www.health.gov.au/covid19-resources)

A fact sheet on COVID-19 and clozapine is also available from Choice and Medication™:

<https://www.choiceandmedication.org/wadoh/generate/handyfactsheetclozapinecovid19au.pdf>

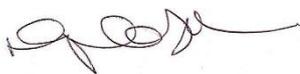
This document has been endorsed by the Office of the Chief Psychiatrist.

- **Further Information**

Statewide Psychotropic Drug Information Centre

Phone: 9347 6400 (8:30 am to 4:30 pm)

Email: [druginformation.graylands@health.wa.gov.au](mailto:druginformation.graylands@health.wa.gov.au)



Nathan Gibson  
Chief Psychiatrist



Sue Bascombe  
A/ Chairperson WAPDC



Christopher Etherton-Beer  
WATAG Chairperson

## References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;
2. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020;
3. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*. 2020;
4. Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England journal of medicine*. 2020;
5. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2020;
6. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA - Journal of the American Medical Association*. 2020;
7. Taylor DM, Young AH, Barnes TRE. *The Maudsley Prescribing Guidelines in Psychiatry 13th Edition*. Vol. 13, Wiley Blackwell. 2018. 1–854.