ALGORITHM FOR MONITORING & SUPPLY OF CLOZAPINE DURING THE COVID-19 PANDEMIC

Tees, Esk and Wear Valleys NHS
NHS Foundation Trust

Patient well, not "at risk" and not self-isolating

Attend clinic or GP surgery for blood test as normal

Patient self-isolating

Personal symptoms (**see note 1**)

Household symptoms (patient well)

MILD/MODERATE symptoms of COVID-19
- should not attend healthcare setting for blood test
- can blood sample be taken at home on day it is due?

Yes

Advise patient to not take morning dose of clozapine on day of test (so that trough serum levels can be checked for possible impact of symptoms and/or change in frequency/intensity of smoking)

Home visit for blood sampling (**see note 2**)

(See note 3)
GREEN - issue new supply of clozapine; arrange next blood test in line with monitoring frequency
AMBER – issue new supply; arrange repeat blood test every 2-3 days until GREEN
RED – do not issue new supply; take sample to confirm

No

SEVERE respiratory infection (COVID-19):
- WITHOLD clozapine until symptoms resolve; re-titrate if withheld >48 hours since last dose (**see general note B**)

WEEKLY monitoring
Arrange blood test **within 3 days of due date** (within 10 days of last test)

2-WEEKLY monitoring
Arrange blood test **within 7 days of due date** (within 21 days of last test)

4- WEEKLY monitoring
Arrange blood test **within 14 days of due date** (within 42 days of last test)

Does the patient have enough tablets until date of re-arranged test?

Yes

No action required

No

Contact supplying Trust dispensary to request additional supply up to validity of last blood test

Patient shielding due to physical health condition (see general note A)

Can blood sample be taken at home without risk to the patient?

Yes

Can blood sample be taken at home on the day it is due?

Yes

Home visit for blood sampling (see note 2 – check of serum levels only required if change in smoking status or habit)

No

No

⚠ If blood test cannot be completed within these extended deadlines, further supply of clozapine is unlicensed – this should only be considered in exceptional circumstances (**see note 4**)

This algorithm may not cover all possible scenarios; seek advice from the pharmacy team on any specific cases not resolved by it, or any that require difficult decisions to be made

1. Assessing symptoms - COVID-19 vs Myocarditis vs Neutropenic sepsis:

Symptoms similar to COVID-19 can arise from incidental (non-COVID) infections associated with neutropenia. For patients with symptoms of infection, including fever, sore throat & flu-like symptoms, an **urgent neutrophil count** is recommended

Consider – when did symptoms start? Is there a cough? How's the FBC?

- Myocarditis – most likely in first month of treatment; may cause fever, ↑respiratory rate & chest pain, but not cough; signs =↑pulse rate, ↑CRP, ↑troponin; if suspected, STOP clozapine (notify CPMS - 08457 698269; cpms@mylan.co.uk)
- Neutropenic sepsis – most likely in first year of treatment (reducing risk as time goes on); likely to present as fever, sore throat & chills (not cough); signs = **↓ neutrophils;** if suspected, STOP clozapine (notify CPMS - 08457 698269; cpms@mylan.co.uk)
- COVID-19 – fever and/or cough; signs = ↑lymphocytes, **neutrophils stable or ↑** (i.e. no neutropenia); clozapine can be continued in mild-moderate disease, WITHOLD if severe respiratory disease (hospitalisation)

Bottom line (as a general guide, not definitive) - if no cough, unlikely to be COVID-19; if outside first few months of treatment, unlikely to be myocarditis or neutropenic sepsis

2. Home visit for blood sampling:

- Use PPE and hygiene measures as per IPC advice
- Collect sufficient samples for FBC (at path lab or on Pochi at Trust base) & serum levels (Viapath) – only one sample is needed if FBC is checked on Pochi as this sample can also be sent to Viapath for levels; otherwise two samples are required. *N.B. in patients without symptoms, a check of serum levels is only required if there has been a change in smoking status or habit*
- Check smoking status and, if smoker, any change in frequency/intensity – if changed, be prepared to reduce dose
- Check physical health status – BP/pulse, weight, assess for constipation
- Re-assure patient that it is safe to continue taking clozapine

3. Assessment of Full Blood Count (impact of COVID-19):

Coronavirus infection may depress lymphocyte count, but does not seem to reduce neutrophils. It's likely that patients with COVID-19 will have a low white cell count (WCC), due to reduced lymphocytes. As the monitoring parameters include WCC, a reduction of lymphocytes may lead to blood results that, under normal circumstances, require increased monitoring (AMBER) or interruption of treatment (RED) to protect the patient from neutropenia or agranulocytosis. Where a low WCC occurs in the presence of a normal or non-dangerous neutrophil count in the context of COVD-19 infection, refer to this guidance to assess if clozapine can be safely continued – discuss with CPMS if necessary (08457 698269)

4. Clozapine supply in the absence of a valid FBC:

In all cases, this would be outside the terms of the product licence, and must be approved by the CD/ACD*; CPMS must also be notified***.

HIGH RISK - for patients on WEEKLY monitoring (up to 18 weeks' treatment), the risk of neutropenia or agranulocytosis remains significant - the interval between FBCs should not exceed 10 days if possible. Supplies beyond the 10 days permitted within the product licence will not be issued by pharmacy without confirmation of approval from the CD/ACD**, and will be a maximum of 4 days' supply;

MEDIUM RISK – patients on 2-WEEKLY monitoring (19-52 weeks' treatment) & patients on 4-WEEKLY monitoring who do not meet the criteria below should be assessed on an individual basis, taking into account any history of low WCC on clozapine. Supplies beyond the 21/42 days permitted within the product licence will not be issued by pharmacy without confirmation of approval from the CD/ACD**, and will be a maximum of 7/14 days' supply respectively;

LOW RISK - for patients on 4-WEEKLY MONITORING, if….

- they have been on continuous treatment >12 months, **and**
- they have no historical neutrophil count <2000 (<1500 if history of BEN), **and**
- there is no safe or practical option for a blood test

…..clozapine can be supplied for up to 12 weeks from the most recent **GREEN** result, with the approval of the CD/ACD**, supplied in 28-day instalments

**RC to seek approval via email, cc'd to tewv.pharmacyadmin@nhs.net, using this form to provide details (or as a prompt to doing so)*

***CD/ACD to notify RC of approval by email, cc'd to tewv.pharmacyadmin@nhs.net*

****RC responsibility, after CD/ACD approval; CPMS – 08457 698269; cpms@mylan.co.uk*

General notes:

A. Patients on clozapine are only required to shield if they have existing severe respiratory disease, or are at high risk of immunosuppression due to treatment with immunosuppressant drugs, or have been advised to do so for another specific reason unrelated to clozapine therapy.

B. "Severe" generally means hospital admission / unconscious, ventilated & unable to take medication orally. If clozapine is withheld >96 hours since last dose, this normally requires re-registration & weekly FBC monitoring for 6 weeks – contact CPMS to discuss (08457 698269)

C. For CPMS – read DMS / ZTAS for patients on Denzapine or Zaponex respectively

Protocol number:	PHARM-0140-v1
Approved by:	Clinical Advisory Committee
Date of Approval:	28th April 2020
Date of Review:	1st April 2021