Dear Colleague

This letter authorises the extended use of the following guidance until December 2022:

**Maintaining Clozapine Treatment During The Covid-19 Outbreak, Version 1**

This guidance remains clinically accurate and relevant.

If you have any queries regarding this please do not hesitate to contact the Pharmacy and Medicines Directorate.

Yours sincerely

Lesley Coyle
Chair of Medicines Guidelines and Policies Group
Maintaining Clozapine Treatment During The Covid-19 Outbreak

Co-ordinators: Principal Pharmacist, Cornhill
Consultation Group: Mental Health Operational Medicines Management Group
Approver: Director of Pharmacy

Signature: 

Identifier: NHSG/COVID19_MH/Clozapine/GADTC1080
Review Date: April 2021
Date Approved: April 2020

Uncontrolled when printed
Version 1

Executive Sign-Off
This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: ___________________
Responsibilities for implementation:

Organisational: Operational Management Team and Chief Executive
Sector: General Managers, Medical Leads and Nursing Leads
Departmental: Clinical Leads
Area: Line Manager

Review frequency and date of next review: This policy will be reviewed in one year or sooner if current treatment recommendations change.

Responsibilities for review of this document:

Lead Author/Co-ordinator: Principal Pharmacist, Cornhill

Revision History:

<table>
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<tr>
<th>Revision Date</th>
<th>Previous Revision Date</th>
<th>Summary of Changes (Descriptive summary of the changes made)</th>
<th>Changes Marked* (Identify page numbers and section heading)</th>
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* Changes marked should detail the section(s) of the document that have been amended, i.e. page number and section heading.
Maintaining Clozapine Treatment During The Covid-19 Outbreak

There are over 3500 patients in Scotland prescribed the second generation antipsychotic, clozapine. Continuing an unbroken supply of clozapine is essential to maintaining their mental health and wellbeing and preventing relapse. Clozapine supplies are linked to mandatory full blood count monitoring at weekly, fortnightly, or four weekly intervals. The Covid-19 outbreak presents a unique challenge to the continuous and safe maintenance of clozapine treatment. This document provides a potential approach to the management of clozapine patients during this national emergency.

There are three main issues to consider:

1. Maintaining routine full blood counts
2. Maintaining prescription supplies
3. Providing appropriate patient advice

1. Maintaining Routine Full Blood Counts

Covid-19 may result in patients self-isolating and being unable to attend for their full blood counts or being reluctant to travel to clinics for sampling. Similarly, there may be staffing issues that mean it becomes very difficult to maintain normal clinic approaches. In both instances a pragmatic approach is required that supports patient safety with regards to clozapine monitoring but also reflects the realities of the Covid-19 outbreak.

- **For patients who can’t or won’t travel to their usual blood sampling location:**
  - Strongly urge patients to attend as normal, if not symptomatic or self-isolating
  - Use the maximum validity possible between blood samples
  - Consider undertaking blood sampling in patients’ homes.

- **For patients self-isolating WITHOUT symptoms of COVID-19:** Use the maximum validity possible between blood samples i.e.:
  - Weekly patients 14 days. Mylan (our current supplier in Scotland) apply a 10 day validity to samples, unlike the other brands which have 14 days validity. In Scotland, we have 10 years’ experience of applying 14 days whilst using the other brands so the increased risk is acceptable. Note: Treatment from day 10 – 14 with Clozaril would be unlicensed.
  - Fortnightly patients 21 days
  - 4 weekly patients 42 days.

Given the current isolation advice this should support on-going dispensing in most instances.
If getting an FBC is deemed clinically necessary during the time a patient is self-isolating at home due to length of isolation then arrangements would be made for this to be done in their home by a member of the Mental Health Services Team, following current infection control guidance on use of PPE. Contact Pharmacy Department, Royal Cornhill Hospital (01224 557489) or Dr Grays Hospital (01343 567349) to arrange.

- **For patients self-isolating WITH symptoms of COVID-19:**
  - Patients presenting with **flu-like symptoms**
    - Take an **URGENT FBC** (suspect neutropenia).

  **Note:** Flu-like symptoms and a high temperature may suggest neutropenia so it is important to undertake a full blood count (FBC) as soon as possible.

  Patients presenting with **flu-like symptoms, chest pain and shortness of breath:**
  - **WITHOLD** clozapine (suspect myocarditis and investigate accordingly)
  - **NB:** if withheld for >48 hours dose re-titration is necessary

If getting an FBC is deemed clinically necessary during the time a patient is self-isolating at home due to symptoms consistent with neutropenia arrangements would be made for this to be done in their home by a member of the Mental Health Services Team, following current infection control guidance on use of PPE. Contact Pharmacy Department, Royal Cornhill Hospital (01224 557489) or Dr Grays Hospital (01343 567349) to arrange.

- **Services unable to undertake normal routine FBC blood sampling processes:**
  - If it proves impossible for services to undertake normal routine blood sampling processes consider dispensing off license without blood testing. This will require support from Clozapine Patient Monitoring Service (CPMS) and Board level governance approval. **This should be a last resort and would be unlicensed.** The patient’s responsible consultant and the specialist pharmacist should be contacted for advice as to patient suitability and a risk assessment completed by the consultant. See **Appendix 1.** This should be retained in the case notes and a copy sent to pharmacy.

  **NB:** This would **NOT** be appropriate for a symptomatic patient presenting with flu-like symptoms where an urgent FBC must be taken to rule out neutropenia.

- **Please record any actions taken and inform Pharmacy Department, Royal Cornhill Hospital (01224 557489) or Dr Grays Hospital (01343 567349) of any delays in blood testing.**
2. Maintaining Clozapine Supplies

Clozapine supplies to patients must be maintained to prevent unnecessary treatment breaks and potential relapse. The following actions are recommended:

- **Dispense to the maximum blood validity where necessary**: Most patients should continue to receive their normal supplies however it may be necessary and appropriate to dispense to the full blood count validity to support self-isolation or blood sampling difficulties.

- **Continue to dispense without a valid blood**: Depending on individual circumstances or service issues (but excluding COVID-19 symptomatic patients with flu-like symptoms) it may be necessary to dispense prescriptions without any valid bloods being available. **This should be a last resort and would be unlicensed**. This will require support from CPMS and Board level governance approval. The patient’s responsible consultant and the specialist pharmacist should be contacted for advice as to patient suitability and a risk assessment completed by the consultant. See Appendix 1. This should be retained in the case notes and a copy sent to pharmacy. Full blood counts should be obtained as soon as practicable.

- **Prescription collection and delivery**: Normal prescription collection or delivery processes may be disrupted. Patients should be advised to contact their local mental health services or pharmacy for advice if they are unable to collect their medicines themselves.

3. Providing Appropriate Patient Advice

Patients will be understandably anxious at this time providing appropriate reassurance may be necessary. Patients should be advised to follow national guidance about self-isolation and other measures but also to contact mental health services for advice about blood testing.

4. Dose Management

There is no clear evidence regarding the impact of Covid-19 on clozapine plasma levels. A pragmatic approach is advised.

- **For patients with mild respiratory symptoms** maintain the current dose and monitor for increased clozapine side-effects, making any adjustments to dose if clinically indicated
- **For patient with severe respiratory symptoms** suspend clozapine treatment until the symptoms resolve. If a treatment break of more than 48 hours occurs dose re-titration will be necessary. This should be done in consultation with the patient’s consultant psychiatrist and specialist pharmacist.
- **For smokers who are unable to continue smoking** due to illness consider a dose reduction, if clinically appropriate.
Other issues to consider

Amber and red alert protocols

Twice weekly blood tests for amber results should be attempted but may be impractical and therefore consideration should be given to maintaining standard routine blood tests for amber results. Consideration of individual patient circumstances, i.e. previous blood results history will be necessary. Complete Appendix 1 in consultation with the specialist pharmacist. This should be retained in the case notes and a copy sent to pharmacy.

Daily blood tests following a red result may also be impractical for community based patients. Consideration should be given to admitting all red alert patients to hospital to support the necessary blood testing.

Clozapine plasma levels

Clozapine plasma levels should be temporarily suspended. Undertaking additional plasma levels may be impractical and therefore clinical management of patients with pragmatic dose reductions is recommended.

Clozapine new starts and red re-challenges

Consideration should be given on a case by case basis to the benefits and risks of new starts and especially red re-challenges. Patients may be unwilling to come into hospital to start treatment and there may be pressure to use beds for higher priorities. Given the uncertain effects of Covid-19 on white blood cells it may be prudent to avoid exposing previously neutropenic patients to clozapine at this time.
Appendix 1

Extension of clozapine blood test validity

Centralised monitoring of leucocyte and neutrophil counts for patients taking clozapine is mandatory. The frequency of blood testing, and therefore duration for which a blood test is considered 'valid', is based on the risk of clozapine-induced neutropenia and agranulocytosis. Dispensing or administering clozapine outside these durations (i.e. without a valid FBC) is unlicensed. The risk of clozapine-induced neutropenia or agranulocytosis is highest in the first 18 weeks of treatment and reduces significantly from then on. Agranulocytosis can lead to fatal sepsis. In exceptional circumstances the decision to supply clozapine outside the licensed duration of a valid blood test may be taken to meet the needs of a specific patient. A risk assessment needs to be undertaken in consultation with the specialist pharmacist and the reasons for doing so should be fully explained to the patient and documented in the patient notes.

Please complete as fully as possible

Patient name: ……………………………
Date of birth: ……………………………
NHS number: …………………………….
Ethnicity: ………………………………
Diagnosis: ………………………………

Current medication (please list all, with doses, frequencies and formulation):

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<th>Dose</th>
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Current clozapine treatment

Start date on clozapine: ……………………………
Due date of next blood test: ………………………
Frequency of monitoring: …………………………

Expected treatment gap

Reason for expected treatment gap (i.e. explain why testing cannot be performed at the right time): ……………………………………………………………………………………………………..

Anticipated duration of treatment gap (i.e. when can a blood test reasonably be expected to be collected): …………………………………………………………………………………………….
Expected clinical consequence of a treatment gap: ..................................................

**Prior clozapine treatment**

Please provide details of abnormal FBC results for this patient in any prior episodes of clozapine treatment: .................................................................

**Comorbidities**

Comorbid medical history: .................................................................

Benign Ethnic Neutropenia Y/N

Completed by: (consultant psychiatrist): .................................................................

Date: ..................................................