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Related Trust documents (to be read in conjunction with)

Formulary and Prescribing Guidelines, Section 2 – Treatment of Psychosis

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1 Introduction

- 1.1 Clozapine is an atypical antipsychotic which has a licence for the treatment of resistant schizophrenia. At Essex Partnership University NHS Foundation Trust (EPUT) clozapine has historically been prescribed in the hospital setting despite the European harmonisation of the product license in 2002 allowing the possibility of clozapine initiation in the community.
- 1.1 With increasing evidence that clozapine can be safely started in the community (Gonzalez et al, 2013), this protocol will allow patients in the Trust to access clozapine re-titrations without the need for hospital admission which should reduce the risk of relapse caused by delays in re-starting the medication whilst awaiting an inpatient admission.
- 1.2 This protocol should be read in conjunction with section 2 – Treatment of Psychosis, of the formulary and prescribing guidelines in mental health [Section 2 - Treatment of Psychosis](#) which provides information on the use of clozapine.
- 1.3 A summary flowchart for initiation of clozapine can be found in appendix 1.

2 Scope and purpose

- 2.1 This protocol is intended to be used to support nurses and support staff working in community settings carry out re-titrations of clozapine safely.
- 2.2 Patients will be usually managed by a Home First Team (HFT) to carry out the re-titration however in areas where virtual wards and/or remote physical health monitoring exists these may be utilised to carry out the physical health monitoring required to undertake clozapine re-titration. The Home First Team will retain overall clinical responsibility of the patient during titration. Once titration is complete clinical responsibility will be transferred back to the community mental health team

3 Referral to service

- 3.1 Patients will be referred to the appropriate HFT or virtual ward team for re-titration of clozapine
- 3.2 Patients may be supported during re-titration by the HFT or virtual ward alongside their usual community mental health team

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST**4 Responsibilities**

4.1 Referrer (CMHT)

- Ensure the referral meets the criteria and it is safe and appropriate for the patient to attempt a re-titration in the community. Ensure any baseline monitoring is undertaken and up to date ready to start the titration.

4.2 Prescriber

- Ensure that there is a legal prescription that is appropriate based on the patient's current clinical condition and legal status. Seek advice from pharmacy on appropriate schedules for re-titration on an individual patient basis.
- On-call consultants may be approached to provide support and advice to nursing staff carrying out clozapine titrations where there is a concern regarding the patient's physical or mental health.
- Where a patient is being supported by another team for monitoring such as a virtual ward, the medical responsibility for the patient remains with the prescriber in the mental health team.

4.3 Home First Team (HFT)

- Review referrals for community re-titrations and agree as appropriate. If a patient is not suitable, ensure this is properly and fully communicated to the referrer and any mitigating actions recorded in the patients' electronic record, to allow a future titration to be clearly set out. If not directly titrating the patient, support the team administering the medicines including accessing a supply of clozapine.

4.4 Administering nurse

- Ensure that patients' are monitored in line with this guidance and escalate patients in line with this guidance to the prescriber or to accident and emergency services when necessary. Ensure that the patient is aware and able to attend blood tests as necessary and communicate with pharmacy as needed to access further supplies of clozapine.
- The administering nurse will be expected to deal with any emergency situations that arise.
- Where the administering nurse is not a mental health nurse they should arrange with the HFT, prescriber or on-call consultant if any mental health concerns arise.

4.5 Pharmacy team

- Support the prescriber, HFT and administering team (if different) as needed to ensure clozapine titrations are carried out safely. Ensure supplies of clozapine are made appropriately and in time to reduce any delays in titration or missed doses.

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4.6 Patient and Carer

- Follow the advice of the prescriber and administering team. Ensure they are available at the appropriate time and place to allow for medicines to be administered. Contact the administering team if there are any problems with clozapine or any adverse effects.

5 Inclusion Criteria

5.1 Patients must have ALL of the following to be eligible for treatment:

- 5.1.1 18 years and over
- 5.1.2 Have capacity and consent to treatment with clozapine
- 5.1.3 Have had a treatment break of clozapine greater 48 hours
- 5.1.4 Be registered with the appropriate clozapine patient monitoring service
- 5.1.5 Be adherent to monitoring requirements including blood test monitoring, ECG and physical health monitoring required during titration.
- 5.1.6 Have a family member or carer present, or live in 24 hour supported accommodation, throughout the titration

5.2 A checklist for the requirements to be in place for the initiation of clozapine in the community can be found in appendix 2 which must be completed for each patient requiring community initiation of clozapine.

6 Exclusion criteria

- No consent given / unable to provide consent
- Under 18 years of age
- New or unstable physical health conditions
- Previously unable to titrate or difficulty titrating clozapine due to monitoring or physical health conditions
- Lives alone
- Red blood result at baseline or history of red blood results
- No prior treatment with clozapine
- Pregnant or breast-feeding
- Patients with active substance or alcohol use which may compromise safety of clozapine titration
- QT prolongation

6.1 The team can only accommodate one patient in their first week of clozapine titration at any one time. This is to ensure that the patient has the same care and monitoring, as they would do if they were initiated on clozapine in an inpatient setting.

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7 Cautions / further advice required

- Significant hypotension (systolic blood pressure <85mmHg)
- Symptomatic postural hypotension
- Persistent tachycardia
- On medications that prolong the QT interval
- Untreated constipation
- Previous bowel obstruction or bowel disease
- Uncontrolled epilepsy
- Severe liver disease
- Any other u physical health condition that may impact on the safe titration of clozapine
- Mental Capacity Act (MCA) - should the healthcare professional feel that the patient is unable to deliberate sufficiently with regard to the information they have been given, then the MCA should be followed.
- All concurrent medication should be checked for interactions with clozapine before administering (see appendix 1 of the British National Formulary (BNF) and the product's current Summary of Product Characteristics (SPC) for further information)

7.1 If there is a delay in starting the clozapine re-titration the pharmacy team must be contacted to ensure that the patient remain valid on the clozapine monitoring system.

8 Consent to treatment

8.1 Consent must be obtained and documented prior to administration.

8.2 Mental Capacity Act (MCA) - should the healthcare professional feel that the patient is unable to deliberate sufficiently with regard to the information they have been given, then the MCA should be followed.

8.3 The responsible clinician must ensure that any patients under a Community Treatment Order (CTO) has appropriate authorisation for administration of clozapine.

9 Actions to be taken if patient is excluded from treatment

9.1 Advise patient why they are being excluded and arrange for

9.2 Contact referrer to advise that the patient has not been able to start clozapine re-titration in the community. If patient condition dictates, arrange admission to hospital for assessment.

9.3 Complete all required documentation.

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10 Evaluation of treatment and follow-up

- 10.1 On completion of initial titration of clozapine the patient will be referred back to the community team
- 10.2 The patient will need to be referred back to the appropriate clozapine clinic, be informed of when they will need to attend their next appointment and be provided with sufficient supply of clozapine to last until then.

11 Advice to patient / carer

- 11.1 Ensure reason for intended treatment and method of administration is understood.
- 11.2 Ensure patient understands treatment time frame and on-going management plan.
- 11.3 Ensure patient understands the effect of the medication and the possible side effects.
- 11.4 Ensure patient knows who to contact and how should they have any concerns. In particular highlight the risks of
 - 11.4.1 Agranulocytosis and to contact their team if any unexplained fever, sore throat etc. develops
 - 11.4.2 Constipation and the need to maintain adequate diet and hydration
- 11.5 Provide manufacturer's Patient Information Leaflet and relevant Choice and Medication leaflets and explain mode of action, side effects, benefits.

12 Description of treatment

- 12.1 The individual titration will be prescribed using the community clozapine titration chart.
- 12.2 Titrations will usually start at 12.5mg daily but then can be increased by a maximum of 50mg daily
- 12.3 Titrations can be prescribed once daily or twice daily based on the patients' previous dose schedule.

13 Monitoring during treatment

- 13.1 Monitoring will be carried out in line with section 2 – Treatment of Psychosis, of the formulary and prescribing guidelines in mental health [Section 2 - Treatment of Psychosis](#).
- 13.2 Monitoring can be carried out remotely where the patient and carer agree. In this case once the pre-dose monitoring has been carried out a member of the team

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should contact the patient or carer to inform them to take the next dose. This should be recorded on the chart as self-administration.

13.3 A summary of monitoring requirements can be seen in appendix 1

14 Withholding treatment

- 14.1 If the patient appears to be heavily sedated, looks drowsy or experiencing any others side-effects i.e. flu like symptoms, the prescriber should be informed because the clozapine dose may need to be reduced. Out of hours the on-call consultant should be contacted for advice.
- 14.2 If any of the following observations are recorded then a doctor needs to be called immediately (out of hours this should be via the on-call consultant). Do not administer clozapine if any of the following pre-treatment observations are present:
- 14.1.1 Temperature of patient is $\geq 38^{\circ}\text{C}$
 - 14.1.2 Pulse rate is ≥ 100 beats per minute
 - 14.1.3 Lying and standing blood pressure shows a postural drop of >30 mmHg
 - 14.1.4 Systolic BP below 100mmHg and /or diastolic below 60 mmHg,
- 14.3 If the patient collapses, experiences breathing problems or has a seizure an ambulance should be called immediately.
- 14.4 If the patient appears to be showing signs of relapse, they are unable to keep themselves safe or there are concerns about safely managing them in the community then senior medical advice should be sought as it may no longer be appropriate to continue a community titration.
- 14.5 If the patient misses any doses the prescriber should be contacted for advice regarding next steps as in many cases a new prescription will be needed to alter the titration schedule.
- 14.6 If the patient misses 2 or more days of treatment re-titration starting again at 12.5mg daily will be required.

15 Adverse effects

| Side effect | How the patient may describe it | Advice to the patient / when to refer |
|--|---|---|
| VERY COMMON <i>(more than about 1 in 10 people might get these)</i> | | |
| Sleepiness | Feeling sleepy, drowsy or sluggish for a few hours after a dose | Don't drive or use machines. Sometimes splitting up your doses throughout the day with e.g. more in the evening, some throughout the day can help you feel less |

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| Side effect | How the patient may describe it | Advice to the patient / when to refer |
|--|--|--|
| | | sleepy at different times of the day so talk about this with your prescriber. |
| Hypersalivation | You dribble or drool, and your mouth gets full of saliva or spit. Your pillow is wet in the morning. | This is not dangerous, but can be upsetting. Your doctor may be able to give you a tablet (e.g. hyoscine) to help this. Propping up pillows at night helps some people a bit. There is an absorbent pillowcase available sometimes. There is also a handy fact sheet you can read on hypersalivation from clozapine . Click here for a handy fact sheet on dental health or here for a shorter leaflet . |
| Postural hypotension | A low blood pressure – this can make you feel dizzy. | Try not to stand up too quickly. If you feel dizzy, don't drive. |
| Weight gain | Eating more and putting on weight. | A diet full of vegetables and fibre may help prevent weight gain. Click here for a few tips on how to help you feel less hungry and lose weight. Click here for a handy fact sheet on weight gain with antipsychotics . |
| Constipation (see also "Rare but important" below) | When you want to poop but can't (the opposite of diarrhoea). You can't pass a motion. It is more likely if you take a higher dose, take an anticholinergic (e.g. procyclidine, benztropine) or take an opiate medicine (e.g. codeine, morphine) as these can cause constipation as well. | <p>This can usually be treated with laxatives. One type would be a softener (such as docusate, Laxido, Movicol or lactulose). These soften and lubricates naturally. Lactulose tastes sweet but isn't full of calories. The other would be a stimulant e.g. senna.</p> <p>Many people who are constipated don't realise they are, so taking a laxative every day to stop it happening is really important and recommended. Some people find taking lactulose every day helps them prevent problems. If you start to get constipated it's a good idea to carry on taking lactulose even if your bowels are OK, as this can help stop the problem. Make sure you also eat enough fibre, cereal or fruit and drink enough fluid. Get some exercise e.g. walking.</p> <p>If it goes on for more than 4-5 days see your doctor as this can be dangerous (see "rare but important" below). You really must ask</p> |

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| Side effect | How the patient may describe it | Advice to the patient / when to refer |
|---|---|--|
| | | about this <i>before</i> it gets really bad. Click here for a handy fact sheet on constipation with clozapine or a shorter highlights version on constipation with clozapine Watch a video here about constipation and clozapine . |
| COMMON (<i>fewer than about 1 in 10 people might get these</i>) | | |
| Parkinsonian (extra-pyramidal side effects or EPSEs) | Having shaky hands and feeling shaky. Your eyes and tongue may move on their own. You feel very restless. | It is not usually dangerous and is a well known side effect. If it is distressing or worries you, tell your doctor. He or she may be able to give you a medicine for it e.g. an anticholinergic drug. Click here for a handy fact sheet on EPSEs or here for a shorter leaflet . |
| Urinary incontinence, urinary retention, nocturnal enuresis | Not being able to have a wee, or passing urine when you don't want to e.g. during the night. | You should ask your doctor or nurse about this. It may be that a change in dose, or when you take your dose or doses might help. Sometimes taking an anticholinergic (e.g. procyclidine) or a low dose of a tricyclic (e.g. amitriptyline) can help. |
| Diabetes | You lose weight, pass lots of urine, and feel thirsty and hungry all the time. | Tell your doctor if you get these symptoms. You can then have some simple tests to see if you are getting diabetes. |
| Palpitations | A fast heart beat. | Let your doctor know, especially if this happens in the first few weeks. |
| RARE but important (<i>can be serious if not dealt with quickly</i>) | | |
| Agranulocytosis or neutropenia | Low numbers of white cells in the blood. You may get more infections. | This will be picked up from your blood tests. It happens in about 2 or 3 in 100 people. Always tell your doctor or carer if you get an unexpected fever, sore throat or illness. |
| Infections, fever or flu-like symptoms | A high temperature. | Make sure you check with your doctor or pharmacist to make sure you do not have a blood problem. If not, try paracetamol. Always tell your doctor or carer if you get an unexpected fever, sore throat or illness. If you get an infection this can have an effect on your blood levels (and, if you get dehydrated, making constipation worse) so be aware of any change in side effects. |

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| Side effect | How the patient may describe it | Advice to the patient / when to refer |
|--------------------------------------|---|--|
| | | Contact your prescriber if you have any concerns. |
| Constipation (severe) | If you have been constipated and it's getting bad you may get stomach pain and/or being sick (especially if smelly), high temperature, feel uncomfortable or bloated below your stomach or have horrible diarrhoea (this can be poo squeezing past a block) | Rarely clozapine can cause really bad constipation. If you get any of these symptoms listed it could be a sign your bowels or gut is getting blocked. You must see your doctor straight away who must take it seriously . You may need urgent treatment. Click here for handy fact sheets on constipation with clozapine Watch a video here about constipation and clozapine . |
| VTE – venous thromboembolism | Chest pain, worse if you breathe deeply or cough. Coughing up blood, dizziness or fainting. Rapid breathing, short of breath or odd heartbeat | See your Doctor straight away or call the emergency services (e.g. 999 in UK). The symptoms could be caused by a blood clot moving around the body. It mostly happens in older people |
| NMS (Neuroleptic Malignant Syndrome) | Fever or high temperature, sweating and confusion. Racing heart beat, muscle stiffness, difficulty moving | See your Doctor straight away if you have had a change in dose or taken other antipsychotics. Click here for a handy fact sheet on NMS or here for a shorter leaflet . |
| Seizures | Having a fit or convulsion. | Stop taking clozapine and contact your doctor straight away. |
| Cardiomyopathy | Where the heart muscles become inflamed. This leads to chest pain, and an odd heart rate. | If you get any of these symptoms, you must contact your doctor as soon as possible. You will almost certainly need to stop clozapine. It usually happens in the first 2-3 weeks after starting clozapine. |

Table 1 Taken from the Choice and Medication Clozapine monograph - [» Clozapine \(choiceandmedication.org\)](#)

For a complete list please see the Summary of Product characteristics (SPC) (<https://www.medicines.org.uk/emc>) and the BNF

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard continued monitoring of the benefit/risk balance of the medicinal product. Healthcare

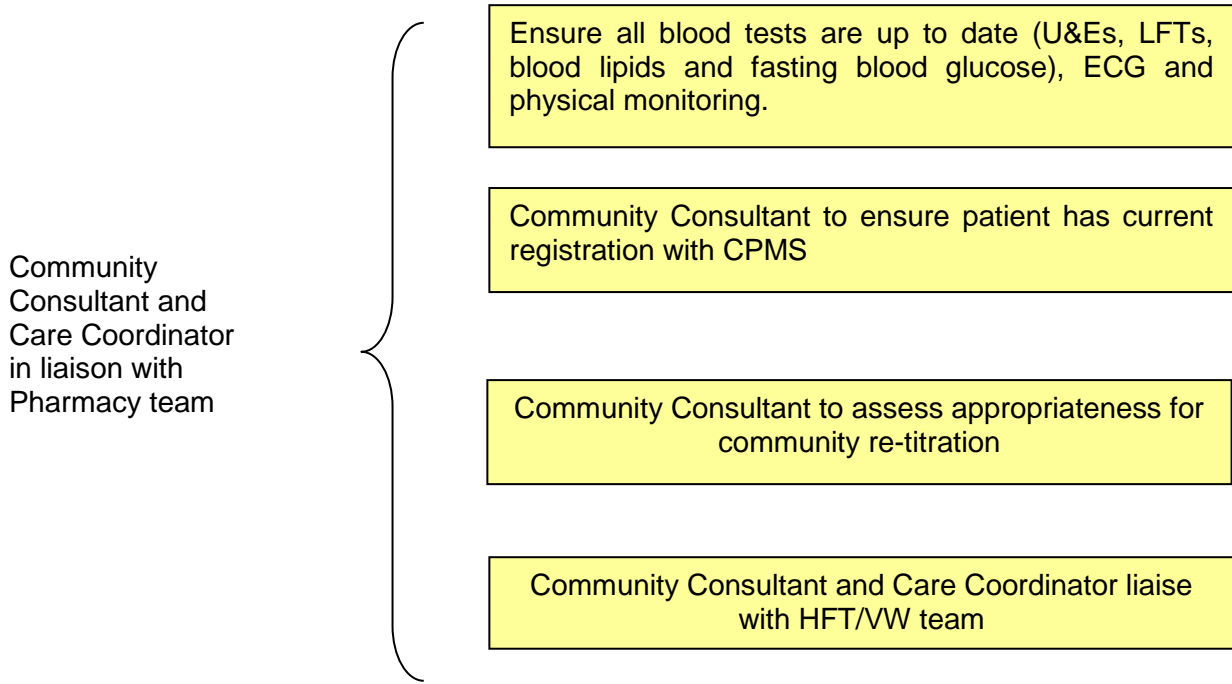
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Appendix 1: Flow chart for clozapine initiation in the community



CRHT from Day one until maintenance dose has been reached.

| Initiation Period | Blood Monitoring | Physical Health Monitoring | Action |
|--------------------------------|------------------|---|------------------------------------|
| Day 1 | ----- | Before 1 st dose and at 30 mins and 1 hours post dose(BP lying/standing, pulse, temperature) | HFT or VW |
| Day 2 – 7 | FBC | Before the dose and at 30 mins and 1 hours post dose(BP lying/standing, pulse, temperature) | HFT/ VW FBC at clozapine clinic |
| Day 8 until dose is stabilized | Weekly FBC | BP lying/standing, pulse and temperature four times a day | HFT/VW & Clozapine Clinic |

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Appendix 2: Checklist for clozapine initiation in the community

| | YES | NO | SIGNATURE | COMMENTS |
|---|-----|----|-----------|----------|
| Does the patient meet any exclusion criteria that prohibits clozapine initiation in the community? | | | | |
| Is the patient happy to be re-titrated in the community? | | | | |
| Will the patient be adherent to clozapine and the mandatory blood tests? | | | | |
| Do the multidisciplinary team and Home First team and virtual ward if applicable, agree to re-titration in the community | | | | |
| Is the patient's physical health stable for initiating clozapine in the community? | | | | |
| Has the patient ever had any issues with previous titrations or re-titrations that may make community re-titration unsuitable? | | | | |
| Have the following tests been completed in line with monitoring requirements? U&Es including eGFR, Blood lipids (ideally fasting), BMI (weight/height), fasting blood glucose, LFTs , Blood pressure and ECG | | | | |

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| Is the patient's mental health stable for initiating clozapine in the community? | | | | |
| Does the patient have family/ carer support? | | | | This is essential as someone must be able to stay overnight and at weekends with the Service User during the clozapine titration period. |
| Is the patient currently registered with the Clozaril Patient monitoring service (CPMS)? | | | | Patient's on a treatment break may have been de-registered Please record the CPMS number here..... |
| Has the patient and carer been provided with up to date information on clozapine and its side effects and with details of who to contact in case they need support or have any concerns with clozapine? | | | | » Printable leaflets (choiceandmedication.org) |
| Has the appropriate prescription chart been completed and clozapine ordered from pharmacy | | | | |
| Are any monitoring charts in place <ul style="list-style-type: none"> • Clozapine initiation monitoring record • Clozapine physical monitoring record • NEWS • Stool Chart (if required) • GASS-C | | | | |