Essex Partnership University
NHS Foundation Trust

Document title:	**PROTOCOL FOR CLOZAPINE CLINIC OPERATION**		
Document reference number:	N/A (Supplement to Formulary & Prescribing Guidelines Section 2 – Treatment of Psychosis)	**Version number:**	1.0
Document type: (Policy/ Guideline/ SOP)	SOP	**To be followed by:** (Target Staff)	Community Mental Health Teams
Author:	Advanced Community Mental Health Pharmacist, CMHTs		
Approval group/ committee(s):	Medicines Management Group		07 March 2024
Professionally approved by: (Director)	Director of Pharmacy		
Executive Director:	Executive Nurse		
Approval group/ committee(s):	Medicines Management Group		07 March 2024
Ratification group(s):	Not Applicable		
Key word(s) to search for document on Intranet / TAGs:	Clozapine; Assay; PocHI	**Distribution method:**	☐Intranet

Initial issue date:	07 March 2024	**Last Review date:**	07 March 2024	**Next Review date:**	07 March 2025	**Expiry Date:**	Date

What we do together matters

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

Related Trust documents (to be read in conjunction with)
(Refer to the main body of the text) Formulary and Prescribing Guidelines – Section 2 – Treatment of Psychosis Formulary and Prescribing Guidelines – Section 2 supplement – Protocol for Community Re-titration of Clozapine

Document review history:			
Version No:	**Authored/Reviewer:**	**Summary of amendments/ record documents superseded by:**	**Issue date:**
1.0	Faarooq Patel, Advanced Community Mental Health Pharmacist, CMHTs	New document (supplement to F&PG Section 2)	13 March 2024
			Date
			Date
			Date
			Date
			Date
			Date
			Date
			Date
			Date
			Date
			Date

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

Contents

1 Introduction 4

2 Principles 4

3 Scope 4

4 Definitions / Glossary 5

5 Responsibilities 5

6 Ordering and supply of Clozapine 6

7 Clozapine Clinic Appointment 7

8 Clozapine Assay 9

9 Transfer of Patients 10

10 Monitoring and audit 12

11 Approval and implementation 12

12 Preliminary equality analysis 13

13 References 13

Appendix 1: Clozapine Clinic supply record 14

Appendix 2: Clozapine Physical health monitoring record 16

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

1 Introduction

1.1 Clozapine is the only drug with established efficacy in reducing symptoms and the risk of relapse for adults with treatment-resistant schizophrenia. Treatment resistance is defined as a lack of satisfactory clinical improvement despite the use of adequate doses of at least two different antipsychotic agents, including an atypical antipsychotic agent, prescribed for adequate duration. It is also licensed for the treatment of psychosis in Parkinson's disease.

1.2 Although clozapine is a highly effective medication it is associated with potentially serious side effects including agranulocytosis and therefore is subject to strict regulatory requirements. For this reason, this Standard Operating Procedure (SOP) has been developed to support clozapine clinic staff within Community Mental Health Teams (CMHTs) to provide a safe and effective service to support patients and associated users.

1.3 In combination with the mandatory Clozapine Patient Monitoring Service (CPMS), the SOP aims to support patients who are attending clozapine clinics within the community including housebound patients.

2 Principles

2.1 The aim of this SOP is to provide guidance to support staff involved with clozapine provision to patients served by EPUT community clozapine clinics

2.2 The guidance will identify clear roles and responsibilities for Medical, Nursing, Pharmacy and non-registered staff.

2.3 The SOP will detail the monitoring required at each clinic appointment and advise what further steps are to be followed if amber or red results are produced.

2.4 Procedures for patient transfers between clozapine clinics and inpatient services are outlined within the SOP.

3 Scope

3.1 The SOP will apply to all medical, nursing and pharmacy staff involved with prescribing, administration, monitoring and supply of clozapine (within community clozapine clinics provided by Essex Partnership University trust.

3.2 Patients who are prescribed Clozaril® should have their blood samples managed using the PocHI machine unless the PocHI system is either unavailable in the clinic or they are housebound (see sections 5.2, 5.3 and 6.1).

3.3 Patients who are prescribed alternative brands of clozapine such as Zaponex® or Denzapine® or those who are unable to attend the clinic, will have their blood samples

managed by an alternative route (not PocHI) and supplies of clozapine to these patients will be released by pharmacy in the traditional manner following a valid blood result (see sections 5.2, 5.3 and 6.1). They will not be pre-dispensed clozapine in advance.

3.4 All staff involved are responsible and accountable for ensuring they have read, understood and follow the guidance within this document.

4 Definitions / Glossary

Term	Definition / Meaning
BMI	Body Mass Index
CPMS	Clozaril® Patient Monitoring System
PocHI	Point of Contact Haematology Investigation machine
SOP	Standard Operating Procedure
GASS	Glasgow Antipsychotic Side-effect Scale

5 Responsibilities

5.1 Consultant Psychiatrist

- Initiate clozapine for any patient
- Named supervising specialist on CPMS for patients under their care.
- Takes overall clinical responsibility for patient on clozapine.
- Responsible for
    - Reviewing the medication as stated in the care plan.
    - reviewing any alerts received from CPMS including liaison with CPMS regarding patient specific queries when required.
    - Ensuring any additional monitoring is undertaken and followed up as and when required
    - overseeing the prescribing of clozapine to community patients.
    - Ensuring periodic review of the patient as per the care plan and Trust guidelines, including assessing adherence, response to the treatment and side effects monitoring
-
    - informing the clozapine clinic, clozapine monitoring service and pharmacy team of
        - any changes to the dose or discontinuation of clozapine .
        - any changes to the responsible consultant either in the community or transfer to an inpatient setting.

  - any circumstances change that may alter the requirements of clozapine (E.g. an interacting medication)
  - Any break in treatment over 48 hours
- Responsible for informing the patients' GP that the patient is taking clozapine and highlighting the requirement to inform the CMHT of any regular medication changes

5.2 **Clozapine Clinic Nurse**

- Ensure competency in the use of PocHI machines and registration with Sysmex
- Ensure the PocHI machine is maintained and calibrated in line with the manufacturer's guidance
- Obtain blood sample and process using PocHI machine or send to the appropriate laboratory for testing.
- Ensure safe handling of medication remains in line with this SOP at all times.
- For PocHI patients release quarantined clozapine to patient upon valid blood result (green or amber).
- Inform consultant, patient's care coordinator and pharmacy team if there is non-attendance/non-adherence in excess of 48 hours. See Treatment break Section 2- Treatment of Psychosis.
- Provide pharmacy with complete list of patients due to be seen in clozapine clinic at least 2 weeks before the clinic is due. (Appendix 1).
- Assess, record and where necessary, liaise with medical team relating to any side effects experienced by patient.
- Action the requests from pharmacy relating to clozapine prescriptions/clinic lists.
- Responsible for informing pharmacy of any dose changes, changes in testing frequency, admissions or discontinuations.
- Responsible for informing pharmacy of any patients taking a brand other than Clozaril®® or for any patients whose blood samples are not analysed using a PocHI machine.
- Responsible for uploading results for non-PocHI patient to CPMS or other clozapine monitoring systems

5.3 **Pharmacy Team**

- Inform clinic when patients' prescriptions will need reissuing.
- Supply medication to clozapine clinic according to list provided by clinic staff.
- Clozapine pharmacist or nominated deputy to review alerts sent by CPMS and inform relevant clozapine clinic staff to action.
- Respond to blood results where appropriate. Ensure that this is recorded in the patient's case notes. Inform the care coordinator and the consultant as soon as possible.
- Responsible for releasing supplies of non-Clozaril® brands of clozapine following confirmation of a valid blood result.

- Responsible for releasing supplies of clozapine for patients whose blood samples are not analysed using a PocHI machine following confirmation of a valid blood result either on the CPMS system or systems used by non-Clozaril® brands.

6 Ordering and Supply of Clozapine

- Clozapine must be prescribed by a suitably trained and appropriately qualified healthcare professional. This can be either the consultant or a suitably trained competent medical or non-medical prescriber. The named supervising specialist registered with CPMS should be in agreement if anyone other than themselves takes on the responsibility for prescribing and monitoring the patient.

- New clozapine prescription pads can be ordered from CLP SOP5 Appendix 1-Order & Receipt Form for FP10s . Completed prescriptions plus any correspondence relating to clozapine supply to the clinics should be emailed to: epunft.pharmacyhomecare@nhs.net.

- Prescriptions are repeatable for a maximum of 6 times at which point a new prescription must be written and sent to the pharmacy. If there are any amendments to the clozapine dose or monitoring requirements e.g. a change from weekly to every 2 weeks, a new prescription will need to be provided. Pharmacy staff will inform clozapine clinic staff when a new prescription is required although clinic staff should be proactive and maintain their own record of when a patient's prescription will need to be reissued. Any changes to the clozapine prescription outside of the normal review process must be promptly communicated to the pharmacy team to prevent the incorrect dose being dispensed.

- Clozapine clinic staff must provide pharmacy with a completed list of patients to be seen at the clozapine clinic (see Appendix 1) at least **TWO WEEKS** before the clinic date to ensure sufficient time for dispensing activities, follow up on queries and delivery of medication. clozapine will be dispensed and delivered by EPUT Pharmacy to the clozapine clinics.

- Upon receipt of medication the clinic staff must check the medication received and sign for receipt (see Appendix 1). Medication must be quarantined until the patient for whom it is intended has a valid blood result (green or amber). The pharmacy team should be alerted immediately if there are any discrepancies. Medication should then be stored securely as outlined in **CLP13 Policy for the Safe and Secure Handling of Medicines**

- When the patient attends for their appointment and a valid blood result has been obtained, medication should be supplied to the patient after being cross checked against the valid prescription.

- **Under no circumstances must pre-dispensed clozapine be amended within the clinic or provided to a patient for whom it was not intended.** If clinic staff require medication changes they must liaise with Pharmacy.

6.1 Patients who have their blood analysed by non-PocHI methods e.g. housebound patients, patients where access to a PocHI machine is unavailable, patients on non Clozaril® brands such as Zaponex® or Denzapine®

- The clinic is responsible for informing pharmacy of such patients and for uploading valid blood results to the relevant monitoring system (see section 5.2).

- Pharmacy will release supplies for non PocHI patients following confirmation via the relevant monitoring system of a valid blood result (see section 5.3).

7 Clozapine Clinic Appointment

The following should be carried out at every clozapine clinic appointment

- Full Blood Count (see **7.1**) and any other mandatory blood tests required
- Side effect monitoring (see **7.2**) including bowel habit changes
- Review of smoking status (see **7.3**)
- Blood pressure, pulse, temperature
- Weight, height and BMI
- Review of patients' mental state and adherence/confirmation of last dose taken
- Offer patient the opportunity to address any concerns relating to treatment and ensure this is recorded in the patients' medical record/ care plan
- Supply of medication once a satisfactory full blood count result shows on the relevant monitoring database. Next appointment given to patient.
- Supply patient information leaflets (PILs) or any other information leaflets or resources relating to clozapine
- Documentation of discussion including any actions to be followed up in the electronic patient record

In addition, the following tests should be carried out on an annual basis:

- Fasting lipid profile
- Blood glucose
- Liver Function test
- Urea and Electrolytes

7.1 Full Blood Count (FBC)

All patients receiving clozapine should have a **FULL BLOOD COUNT (FBC) either Weekly, Fortnightly or Four Weekly** according to manufacturer's instructions

Blood samples will usually be analysed via the clinic room PocHi machine by suitably trained staff who are registered with Sysmex. Clinics without access to a PocHi machine or housebound patients/those unable to attend the clinic may have agreements in place with pathology providers who take/analyse patients' blood samples. In such instances it is advisable to ensure blood samples are taken on a Monday/Tuesday to allow time for processing. Clozapine may only be supplied to the patient after entering results onto CPMS and a green/amber result obtained. Extra care should be taken around public holidays to ensure results can be followed up accordingly.

Blood test validity is graded by a traffic light system as per the table below:

Monitoring Service Blood Alert level	Action required
Green	Continue clozapine treatment
Amber	Re-spin then re-analyse blood sample in PocHi machine to confirm amber result. If result is still amber, issue appointment for follow-up blood sample as per CPMS protocol (twice-weekly bloods until green result produced). Issue full supply of medication and document arrangements for the follow up blood tests on patients' medical record.
Red Management of a red result is under the clinical leadership of the service user's consultant psychiatrist. The consultant psychiatrist must liaise with CPMS.	Re-spin then re-analyse sample in PocHI machine to confirm second red result. **THE PATIENT MUST STOP TAKING CLOZAPINE IMMEDIATELY IF A SECOND RED RESULT IS CONFIRMED AFTER RE-SPINNING AND SUPPLY MUST BE WITHHELD**. Question the patient on how they feel physically. Counsel patient on symptoms to look out for (sore throat, temperature, flu like symptoms) and what to do if they experience any of them (access medical attention) Liaise with CPMS, record result in patients' medical record. Inform consultant/care coordinator/carer and give appointment for follow-up blood sampling. Sample blood daily until haematological abnormality is resolved and monitor for

	infection. Refer to CPMS guidelines and Section 2 of the Trust Formulary and Prescribing Guidelines for the management of red results

Clinic staff should cross check Clozapine supply with patient's clozapine prescription prior to supply (upon satisfactory monitoring and valid blood results)

7.2 Side-effect monitoring

Side-effects associated with Clozapine should be monitored using **Appendix 2**

Constipation is a very common but potentially serious adverse effect which can lead to paralytic ileus and death. **Patients should be asked specifically regarding any changes in bowel habits (constipation /diarrhoea) at every appointment**. See Section2: Treatment of Psychosis of the Formulary and Prescribing Guidelines for full information.

If patients report any side effects, clozapine clinic staff must document in the patients' medical record and communicate the information to the Consultant/Medical team for follow up review which should include GASS clozapine.

If patient is showing signs of serious side effects this may require urgent medical attention.

7.3 Smoking Status

Smoking can reduce clozapine plasma levels by up to 70%. If someone taking clozapine stops smoking, it is expected that their plasma clozapine level will increase rapidly resulting in toxicity. Patients smoking status should be reviewed at **every** appointment and also upon hospital discharge/admission. If any change in smoking status is reported it may be necessary to arrange a clozapine assay (**see section 8.0 Clozapine assay).** See Section2: Treatment of Psychosis of the Formulary and Prescribing Guidelines for full information. Patients who wish to stop smoking should be encouraged to discuss this with clinic staff in the first instance to avoid sudden cessation and a possible subsequent rise in clozapine blood levels.

7.4 Non Attendance

In the event of patient non-attendance at the clozapine clinic, every effort must be made to contact the patient. If the patient is unable to be reached, the patient's consultant, care coordinator and pharmacy should be informed and this must be documented in the patients' medical record. **A treatment break of greater than 48 hours is clinically significant as the patient is at risk of profound hypotension. The clozapine dose will therefore need to be re-titrated and monitoring frequency may change**. The clozapine monitoring service should also be notified. Treatment break guidance should be followed (Section2: Treatment of Psychosis).

7.5 Patients intending to travel away from their clozapine clinic

Patients planning a trip away from their usual residence should be provided with advice on obtaining supplies and the requirement for blood tests at the appropriate interval should be emphasised.

If a patient is going to be away from the UK for a period that would mean that a supply could not be made for the duration of their trip a non-formulary application can be made to request for an extension in supply outside of the normal monitoring frequency. This would be assessed on an individual basis and must be agreed in advance of travel and would constitute off-label use of clozapine.

8 Clozapine Assay

8.1 Clozapine assays (additional cost involved) may be requested by the patient's Consultant/Senior prescriber only. Please see Section2: Treatment of Psychosis of the Formulary and Prescribing Guidelines for full information on when to review a patient according to clozapine blood levels.

9 Transfer of Patient

9.1 Transfer of patient to another clozapine clinic/ward within EPUT Trust

The referring clozapine clinic staff should liaise with the patient and the receiving clozapine clinic to arrange for a suitable appointment date for the patient. Pharmacy must be informed via email (epunft.pharmacyhomecare@nhs.net) to ensure update of information on the CPMS portal and to prevent transfer of medication to the clinic if the patient is to be admitted to an inpatient bed. Referring clinic staff must ensure patient has sufficient medications till next appointment according to monitoring frequency and current blood test results.

The receiving clozapine clinic will be responsible for ensuring CPMS details are updated accordingly using relevant "Patient change details form".

9.2 Accepting patients from EPUT inpatient wards to clozapine clinic

The receiving clinic must liaise with the inpatient ward to ensure the patient will be discharged with sufficient medication to last until the next clozapine clinic appointment (according to monitoring frequency and blood test results). Staff must ensure CPMS details (location, supervising specialist) are updated accordingly using relevant "Patient change details form".

9.3 Accepting patients from another Trust

Receiving clozapine clinic staff to gather detailed information regarding patients monitoring frequency, last blood result, brand of clozapine prescribed and clinic progress notes. Clinic staff to update CPMS to amend patient records if the patient was previously taking Clozaril® and registered with CPMS. If the patient was prescribed

another brand of clozapine other than Clozaril® a new patient registration form must be completed accordingly. Upon successful registration with CPMS, the patient can be booked for a clinic appointment following procedures regarding ordering and supply of clozapine outlined above in Section 6. The responsibility for the patient remains with referring clinic until the patient is accepted and attends the clinic appointment.

10 Monitoring and audit

Effectiveness of this clinical guideline will be monitored through the Trust Clinical Governance department.

The Trust Clinical Governance Department will co-ordinate an annual audit of this topic, which will include as a minimum the audit of prescribing and monitoring of patients prescribed valproate. The results will be presented to Clinical Advisory Group (CAG) for review and identification of any actions required.

Training requirements will be monitored by the Workforce, Development and Training Department.

11 Approval and implementation

11.1 This clinical guideline will be made available across the organisation via the Trust intranet.

11.2 All Medicines Clinical Guidelines will be approved by the Clinical Governance & Quality Sub-Committee, which is the specialist group with the authority to approve Medicines documents. These will then be forwarded to the Policy team for processing and upload to the Trust intranet and storage in the Trust Policy Library system.

11.3 It is the author's responsibility to inform the Clinical Governance & Quality Sub-Committee of the approved documents when they are uploaded to the Trust's Intranet.

12 Preliminary equality analysis

12.1 The Trust is committed to the provision of a service that is fair, accessible and meets the needs of all individuals.

13 References

Clozaril® SmPC
Clozaril® 25 mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

NICE Quality statement 4: Treatment with clozapine | Psychosis and schizophrenia in adults | Quality standards | NICE

Rosenheck R, Cramer J, Xu W, Thomas J, Henderson W, Frisman L, et al for the Department of Veterans Affairs Cooperative Study Group on Clozapine in Refractory Schizophrenia. A comparison of clozapine and haloperidol in hospitalized patients with refractory schizophrenia. *N Engl J Med* 1997; **337**: 809-15.]

Wahlbeck K, Cheine M, Essali A, Adams C. Evidence of clozapine's effectiveness in schizophrenia: a systematic review and meta-analysis of randomized trials. *Am J Psychiatry* 1999; **156**: 990-9

Formulary and prescribing guidelines. Section 2 - Treatment of Psychosis

Clozapine Clinic Standard Operating Procedure-East London NHS Foundation Trust

Sysmex Diagnostics. Poch-100i Basic User Guide. System Instructions for use.

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

Appendix 1: CLOZAPINE CLINIC SUPPLY RECORD

The clozapine clinic nurse will supply EPUT Pharmacy with a list of patients to be seen at the next clinic, at **least TWO weeks** in advance using this form, **email to** epunft.pharmacyhomecare@nhs.net. Patient will only be supplied with the dispensed medication when a valid green blood result is confirmed at the clinic.

Any uncollected medicines must be kept in a locked clinic cupboard and **pharmacy notified**. Pharmacy will keep clinic lists as a record of supply to the clinic for Three Months. The clozapine clinic must keep this form as a record of supply to the patient for 8 weeks.

Any Additional Clinic Information

Address of Clinic: Contact phone number:						Date of Clinic: - W/C	
Name of Patient	*CPMS/ ZTAS Number*	*No. of Weeks*	*Meds Given Out*	*Qty Given to patient*	*Checked on arrival by (inc date)*	*Blood results Checked by:*	*Handed to patient by - Comments*
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

Address of Clinic: Contact phone number:						Date of Clinic: - W/C	
Name of Patient	*CPMS/ ZTAS Number*	*No. of Weeks*	*Meds Given Out*	*Qty Given to patient*	*Checked on arrival by (inc date)*	*Blood results Checked by:*	*Handed to patient by - Comments*
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25mg				
			Clozapine 100mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				
			Clozapine 25 mg				
			Clozapine 100 mg				
			Other (see script)				

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

If Appendix 2: CLOZAPINE PHYSICAL HEALTH MONITORING RECORD

Name	DOB	NHS number	CPMS

Date:												
Blood glucose												
BP												
Pulse												
Weight kg												
Temperature												
Height												
Smoking status												
ECG (annually)												

Side Effect monitoring

Dry mouth												
Restlessness												
Blurred Vision												
Confusion												
Diarrhoea												
Constipation												
Excessive sweating												
Excessing salivation												
Muscle Spasms												
Nausea or Vomiting												
Sedation												
Tremor												
Other												
Signed by												

KEY: 0= none 1= minor 2= moderate 3=severe

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST

ESSEX PARTNERSHIP UNIVERSITY NHS FOUNDATION TRUST