Clozapine Policy
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1.0 Introduction

1.1 Clozapine is an atypical antipsychotic that is commonly used in ELFT. Its ability to rarely cause neutropenia and agranulocytosis has led to the MHRA stipulating that this drug may only be used in combination with a strict blood test monitoring regime.

1.2 These together with other aspects of clozapine’s adverse effect profile have led to it being a hospital prescribed drug within many trusts including ELFT. Consequently its initiation and maintenance spans both inpatient and outpatient services. Treatment often involves many members of the ELFT MDT in addition to other healthcare providers including the service user’s GP.

1.3 The Clozapine Clinic exists to ensure that the many statutory and clinical requirements for treatment with this drug are coordinated and undertaken whilst providing advice, support and consultancy to service users, their carers and all healthcare professionals involved in their care. For information on the operational elements of this clinic, please refer to the Clozapine Clinic Standard Operating Procedure.

2.0 Aim of this Policy

2.1 To set out the requirements for the initiation, maintenance and monitoring of clozapine in inpatient and outpatient settings throughout ELFT.

3.0 Inclusion and exclusion criteria for treatment with clozapine

3.1 Inclusion Criteria

3.11 Service users with a confirmed diagnosis of schizophrenia who:

- Have not responded to two antipsychotics of which one is an atypical antipsychotic medication.
- Experience unacceptable side effects/intolerance to typical or atypical antipsychotics
- Experience tardive dyskinesia.

3.12 Service users who have severe, untreatable neurological adverse reactions to other antipsychotics including atypical psychotic disorders occurring during the course of Parkinson’s disease in cases where standard treatment has failed.

3.13 Service users with other diagnoses (for example bipolar disorder) may be considered for treatment with clozapine. Clinicians should refer to the ELFT Unlicensed Medicine Policy for further information.
3.2 Exclusion Criteria

3.21 Hypersensitivity to the active substance or to any of the excipients.

3.22 Service users unable to undergo regular blood tests.

3.23 Service users unable to attend the Clozapine Clinic (the Clozapine Clinic cannot undertake home visits).

3.24 Impaired bone marrow function, history of toxic or idiosyncratic granulocytopenia/agranulocytosis (with the exception of from previous chemotherapy), or history of clozapine induced agranulocytosis.

3.25 Uncontrolled epilepsy.

3.26 Alcoholic and other toxic psychoses, drug intoxication, comatose conditions.

3.27 Circulatory collapse and/or CNS depression of any cause.

3.28 Severe renal or cardiac disorders (e.g. myocarditis). Active liver disease associated with nausea, anorexia or jaundice; progressive liver disease, hepatic failure.

3.29 Paralytic ileus.

3.30 Clozapine must not be started concurrently with substances known to have a substantial potential for causing agranulocytosis; Depot antipsychotics, carbamazepine, chloramphenicol (excluding eye or ear drops) and sulphonamides should be avoided. Any concurrent treatment with any of these substances will require authorisation via appendix 3 of the ELFT Unlicensed Medicines Policy.

In those service users established on clozapine who then require chemotherapy it may be possible to continue both concurrently. However, this will require pre-treatment authorisation by a consultant oncologist, haematologist and psychiatrist. An unlicensed use of Zaponex form is also required to be faxed to ZTAS and appendix 3 of the ELFT Unlicensed Medicines Policy must also be completed. Before treatment starts there must be a clear plan in place regarding monitoring of the WBC and responsibilities for action if it drops. Clinicians should contact the Clozapine Clinic for further information.

3.31 For a full and up to date list of the indications, cautions, contraindications and any other information regarding clozapine the clinician should refer to the Zaponex SPC.
Adverse Effects of Clozapine Requiring Mandatory Monitoring in ELFT

4.1 Agranulocytosis/Neutropenia

4.11 The cumulative risk of agranulocytosis is approximately 0.8%, although 70% of all cases occur within the first 18 weeks of treatment. The incidence of neutropenia is approximately 3%. The clinical signs and symptoms of agranulocytosis/neutropenia may include flu like symptoms, sore throat and raised temperature and all clinical staff should be aware of these. Routine blood monitoring is mandatory and will identify sub-clinical cases.

4.12 Benign Ethnic Neutropenia (BEN)

Approximately 25% to 50% of persons of African descent and other Middle Eastern groups have BEN resulting in low leukocyte and neutrophil counts. This may have been identified during the referral/registration process for starting clozapine. If a diagnosis of BEN is suspected it is essential that a haematologist reviews the service user before starting treatment. A successful diagnosis of BEN will result in lowered white blood cell level requirements preventing blood test management problems and false amber and red results in the future. ZTAS can provide a haematologist if required.

4.13 Required Monitoring:

The service user will require regular full blood count (FBC) and differentials for as long as they are treated with clozapine. This is mandatory in the UK and clozapine cannot be supplied without this. The frequency will be as follows:

- Weekly for the first 18 weeks of treatment.
- Fortnightly during weeks 18-52
- Four weekly thereafter for as long as the service user remains on clozapine treatment. In some cases it may be deemed clinically necessary to undertake a FBC more frequently, e.g. in those service users who continue to produce multiple red then amber/green results (see below).

Blood tests will be categorised as follows:

<table>
<thead>
<tr>
<th>Category</th>
<th>White Blood Cell Count</th>
<th>Absolute Neutrophil Count</th>
<th>Platelet Count</th>
</tr>
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<tbody>
<tr>
<td>GREEN</td>
<td>Normal pt</td>
<td>Normal pt</td>
<td>Normal pt</td>
</tr>
<tr>
<td></td>
<td>≥ 3500 (3.5x10^9)</td>
<td>≥ 2000 (2.0x10^9)</td>
<td>≥50 000/mm³ (50x10⁹/L)</td>
</tr>
<tr>
<td></td>
<td>BEN pt</td>
<td>BEN pt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 3000 (3.0x10^9)</td>
<td>≥ 1500 (1.5x10^9)</td>
<td></td>
</tr>
<tr>
<td>AMBER</td>
<td>Normal pt</td>
<td>Normal pt</td>
<td>Normal pt</td>
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<tr>
<td></td>
<td>3000-3500 (3.0x10⁹ - 3.5x10⁹)</td>
<td>1500-2000 (1.5x10⁹ - 2.0x10⁹)</td>
<td>&gt; 50 000/mm³ (50x10⁹/L)</td>
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<tr>
<td></td>
<td>BEN pt</td>
<td>BEN pt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2500-3000 (2.5x10⁹ - 3.0x10⁹)</td>
<td>1000-1500 (1.0x10⁹ - 1.5x10⁹)</td>
<td></td>
</tr>
<tr>
<td>RED</td>
<td>Normal pt</td>
<td>Normal pt</td>
<td>Normal pt</td>
</tr>
<tr>
<td></td>
<td>&lt; 3000 (&lt; 3.0x10^9)</td>
<td>&lt; 1500 (&lt; 1.5x10^9)</td>
<td>&lt;50 000/mm³ (50x10⁹/L)</td>
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<tr>
<td></td>
<td>BEN pt</td>
<td>BEN pt</td>
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<td>&lt; 2500 (&lt; 2.5x10^9)</td>
<td>&lt; 1000 (&lt; 1.0x10^9)</td>
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If the result is **GREEN**:

Continue clozapine and take blood sample at the next planned blood test date.

If result is **AMBER**:

- If the service user is clinically well and not experiencing any signs of neutropenia (flu like symptoms, sore throat and raised temperature) clozapine can still be administered.
- However the service user will have to have twice weekly full blood counts (FBC), in addition to physical observations until the result is ‘green’.
- Where blood test are carried out using Point Of Care Haematology i100 (PoCHi100), clinic staff will be aware immediately of the result. Pharmacist and clinic staff are notified by ZTAS via telephone call and Consultants are notified by fax.
- The service user should be advised to attend GP or A&E if they begin to feel unwell or experience signs or symptoms of neutropenia or agranulocytosis (sore throat, high temperature, flu like symptoms), between blood tests.

If result is **RED**:

- The service user must be informed and **CLOZAPINE STOPPED**.
- **No clozapine** should be given to service user.
- All physical observations should be carried out and staff should check if the service user is experiencing any flu like symptoms, high temperature, and sore throat. If the service user is experiencing any of these symptoms they should be advised to present at their local A+E service. Clinic staff will contact the A+E service to inform them of the relevant details and implications.
- Where possible, service user to be reviewed by RC or a senior doctor from his/her team, for review of mental and physical health and medication.
- Service user will need to have daily blood tests until 2 consecutive GREEN results are obtained. The service user will be advised to attend A&E or GP if physical health deteriorates.
- RC, clinic staff and pharmacist are notified by ZTAS via telephone call of RED result. (PoCHi 100 sites are aware of the result ).
- Red Alert Guidelines and Adverse Events forms are faxed by ZTAS to RC. These are to be completed by RC and return to ZTAS.
- If service user has an AMBER result after RED, 2 consecutive GREEN results MUST be obtained to restart Clozapine. However, service user will need to be re-titrated back on clozapine.
- If service user has two consecutive RED results, the service user will NOT be able to restart Clozapine and their name will be added to the clozapine non-rechallengable list. Service user must be seen immediately by a psychiatrist.
- If a service user is concerned about signs of infection outside working hours, they should immediately attend their local A&E Department or Walk-in clinic, stating that they had been taking clozapine.
4.2 Acute Intestinal Obstruction and Constipation

4.21 Clozapine has an anti-cholinergic effect, which may produce problems for service users treated with clozapine. Its anti-cholinergic properties may cause varying degrees of impairment or slowing of intestinal peristalsis ranging from constipation to intestinal obstruction, faecal impaction and paralytic ileus that may be fatal. Acute obstruction is a medical emergency.

At the earliest opportunity the service user should be counselled about constipation and that it is important that they report any constipation lasting more than 2 days to a healthcare professional as a matter of priority. They should also be counselled on methods to avoid constipation including maintaining an adequate fluid balance and eating a high fibre diet, which includes fruit and vegetables (‘five a day’).

Particular care is necessary in service users who are receiving concomitant medications known to cause constipation: especially those with anti-cholinergic properties such as other antipsychotic medications, antidepressants, and anti-parkinsonian treatments. Hyoscine Hydrobromide and pirenzapine are commonly prescribed for the treatment of clozapine induced hypersalivation and are anti-cholinergic in nature. They can therefore compound the problem. Careful management of this aspect of the Service User’s care is advised and it should be addressed during medical reviews and CPA meetings as it is on each attendance at the Clozapine Clinic. Service users who have a history of colonic disease or a history of lower abdominal surgery should be carefully monitored as this may exacerbate the risk of constipation.

4.22 Required monitoring:

- Whilst on the ward the service user will be asked whether they have opened their bowels/are constipated.
- At every clinic visit staff will enquire as to whether they have opened their bowels/are constipated.
- Clinical staff should also be alert for the symptoms of acute intestinal obstruction. These include abdominal distension, loss of appetite, pain, nausea/vomiting and faecal overflow (service users will report this as diarrhoea).

4.23 Management of Constipation

Advice/action should follow that set out in figure 1.

It may be possible to manage constipation using bulk forming laxatives and/or stimulants, such as; Fybogel, and senna.
Figure 1: Constipation Decision Making Algorithm

Day 1: Constipated without symptoms
- Ward/Clinic to provide healthy lifestyle advice
  - Take any laxatives as prescribed
  - Increase fruit, vegetable and fibre intake
  - Increase fluid intake to at least 2-3 litres per day
  - Increase activity levels
- Ward or Clinic to follow up by contacting service user the following day

Day 2 and 3: Constipated without symptoms
- Ward/Clinic contacts Care Coordinator to advise
- Care Coordinator/Clinic/Pharmacy facilitates GP appointment
- GP to review/prescribe laxatives and to advise Clinic/Care Coordinator of plan

Day 2 and 3: Constipated with Symptoms or Day 4 or beyond: Constipated with or without Symptoms
- Ward/Clinic contacts Care Coordinator and Consultant Psychiatrist to Advise
- Ward/Clinic contacts local acute Trust A+E or Fast Response Team. Full description of presentation and risks is given
- Ward or Clinic facilitates transfer to local acute Trust A+E or Fast Response team.
4.3 Myocarditis and Cardiomyopathy

4.3.1 Although very rare (<1/10,000), the use of clozapine is associated with an increased risk of myocarditis (especially during first 2 months) and cardiomyopathy.

4.3.2 Required Monitoring:
- Troponin level weekly for first 4 weeks of treatment.
- CRP weekly for first 4 weeks of treatment.
- Pre and post clozapine BP and pulse whilst service user remains on titration. Daily BP and pulse thereafter on the ward.
- BP and pulse to be monitored at every visit to the clozapine clinic.
- Clinical staff should be alert to symptoms of myocarditis or cardiomyopathy. These include palpitations, arrhythmias, chest pain and other signs and symptoms of heart failure (e.g. unexplained fatigue, dyspnoea, tachypnoea), or symptoms that mimic myocardial infarction. Other symptoms which may be present in addition to the above include flu-like symptoms.

4.3.3 Management of Cardiomyopathy/Myocarditis

If myocarditis or cardiomyopathy is suspected, clozapine should be promptly stopped and the service user immediately referred to a cardiologist/A+E.

Service users with clozapine-induced myocarditis or cardiomyopathy should not be re-exposed to clozapine.

4.4 Orthostatic hypotension and hypertension

4.4.1 Orthostatic hypotension, with or without syncope, can occur at any point of clozapine treatment. However, it is far more likely to become an issue during the initial titration of this drug, or when dose escalation is too rapid. For this reason clozapine initiation in ELFT follows 3 standardised titrations, depending on whether the service user is an inpatient, day patient, or community based patient. Outside of clozapine titrations, dose increases are limited to a maximum of 50mg per day. The risk of hypotension is enhanced by the concomitant use of benzodiazepines or any other psychotropic agents, so these need to be used with caution.

4.4.2 Hypertension can also occur commonly in the first 4 weeks of treatment with clozapine, although in some cases this may last longer.

4.4.3 Required Monitoring
- Pre and post clozapine BP whilst service user remains on titration. Daily BP thereafter on the ward.
- BP to be monitored at every visit to the clozapine clinic.

4.4.4 Management of hypotension

If a service user develops hypotension during clozapine titration, it may be
advisable to slow down the titration or in extreme cases stop it all together. The service use should be offered standard advice to deal with hypotension including advising them to take time to stand up and ensuring adequate fluid intake.

4.45 Management of hypertension

If a systolic reading of greater than 140 mmHg or a diastolic reading of greater than 90mmHg is recorded then the ward doctor should be notified (if inpatient) or the service user’s GP (if they are an outpatient).

4.5 Tachycardia

4.51 Tachycardia is very common in the early stages of clozapine treatment and usually benign. However, together with chest pain, symptoms of heart failure or flu like symptoms may be indicative of cardiomyopathy or myocarditis.

4.52 Required Monitoring:

- ECG prior to initiation
- Pre and post clozapine pulse whilst service user remains on titration. Daily manual pulse thereafter on the ward.
- Manual pulse to be monitored at every visit to the clozapine clinic.

4.53 Management of Tachycardia

If tachycardia occurs in combination with chest pain, shortness of breath or symptoms that resemble a Myocardial Infarction, staff should refer to section 4.3 on myocarditis and cardiomyopathy.

Any long-standing tachycardia should be investigated further, preferably by a cardiologist. If found to be a benign sinus tachycardia, it may be possible to treat this with a beta-blocker.

4.6 Pyrexia

4.61 Mild hyperthermia occurs in approximately 5% of service users, typically early in treatment and is usually not significant. However, pyrexia may also be indicative of an infection and rarely neutropenia or agranulocytosis.

4.62 Required Monitoring:

- Daily temperature whilst on titration and during inpatient stay.
- Temperature will be measured at clinical discretion of clozapine clinic staff whilst an outpatient, if service user appears unwell or there is cause for concern.

4.63 Management of Pyrexia

Any pyrexia should be medically examined and a full blood count should be performed as soon as possible. If the body temperature exceeds 38.5°C, clozapine should be stopped until the temperature drops. ZTAS should be contacted and their advice followed.
4.7 Diabetes and Impaired Glucose Tolerance

4.71 Clozapine has been strongly linked to hyperglycaemia and impaired glucose tolerance with as many as a third of patients developing diabetes after 5 years of treatment. There are also rare reports of diabetic ketoacidosis.

Most cases of diabetes are noted in the first 6 months. Diabetes associated with clozapine is not necessarily linked to obesity or to a family history of diabetes. However standard risk factors still apply and these include the above in addition to poor diet, lack of exercise, increased age and existing cardiovascular disease.

Use of clozapine in those with already established diabetes may also de-stabilise blood sugar control. Therefore, ELFT staff should closely monitor blood glucose levels following initiation of clozapine in diabetic service users.

4.72 Required Monitoring and Management of Suspected Diabetes or Glucose Intolerance

For service users screened as non-DM.

- Random Blood Glucose (using glucometer) should be monitored at every scheduled blood test for the duration of clozapine treatment. The GP will be notified of any abnormal results falling outside of the target range of 5-7 mmols/L and a note placed on RIO.
- If the service user refuses a random blood glucose test, clozapine can still be issued to them.

For service users with a diagnosis of DM.

- There is a need for a shared clinical plan with the GP monitoring and treating DM. The mental health team should not be treating DM.
- Blood glucose levels should be monitored in line with the service user’s normal schedule whilst on the ward.
- The clozapine clinic will perform 6 monthly random blood glucose checks using a glucometer whilst service users are in the community.
- Where blood glucose is outside the target range (5-8 mmols/L) referral should be made to the GP.

All service users should be monitored for symptoms of diabetes. These include rapid weight loss (5kg in one month), excessive thirst or increased urinary output. These symptoms should prompt an immediate random blood glucose and referral to the service user’s GP.
4.8 Weight Gain

4.81 Weight gain following clozapine is common and may be significant for some service users. Most weight gain tends to occur within the first year of treatment. This is extremely important as obesity is a risk factor for cardiovascular disease and the development of diabetes mellitus.

Service users need to be counselled from an early stage (preferably before starting treatment) regarding this adverse effect and standard advice applies.

4.82 Required monitoring:

- Weekly weight and BMI whilst on titration and an inpatient.
- Weight and BMI at every clinic appointment.

4.84 Management of Weight Gain

All service users whose BMI exceeds 30, or who are rapidly gaining weight should be referred to their GP for further investigation and/or treatment.

A referral to a Dietician may also be of use. It is often reported by Service Users that an increase in appetite occurs in the evening/after administration of nighttime dose of clozapine. However, it does also occur during the day. A frank discussion with the Service User and their carer if possible needs to take place regarding their diet and how best to manage their increased appetite. Snacking using fruit and vegetables is recommended as they are low in calorific value and are nutritious.
4.9 Seizures

4.91 Clozapine can lower the seizure threshold and this is a dose related side effect. The incidence of seizures increases with doses of clozapine greater than 600mg daily. However this can occur in doses under 600mg daily and staff should always be aware of this.

Some 2% of patients taking clozapine develop myoclonus, mostly orofacial myoclonus though it can occur in other parts of the body in particular the hands/lower arms.

(http://www.ninds.nih.gov/disorders/myoclonus/detail_myoclonus.htm)

Myoclonus is a sudden, involuntary jerking of a muscle or group of muscles. Myoclonic twitches or jerks usually are caused by sudden muscle contractions. The twitching cannot be controlled by the person experiencing it. In its simplest form, myoclonus consists of a muscle twitch followed by relaxation. These movements may represent myoclonic seizures, and increase the risk of the service user experiencing grand mal convulsions.

(http://www.epilepsysociety.org.uk/AboutEpilepsy/Whatisepilepsy/Seizures?qclid=CLD48IPqqUCFUoP4QodrGOuXQ#p)

4.92 Required Monitoring:

- Service user will be visually observed by staff whilst an inpatient.
- Clozapine clinic staff will enquire and also observe for any symptoms that resemble seizures/myoclonus at every visit to clinic.

4.93 Management of Seizures

Management consists of clozapine dose reduction or discontinuation, or cautious use of sodium valproate or lamotrigine. Sodium valproate is contraindicated if pregnancy is a possibility; Sodium valproate and lamotrigine are also associated with an increased risk of neutropenia/ agranulocytosis. Use of carbamazepine is contraindicated with clozapine.


Should a seizure occur, withhold clozapine for one day, restart at a lower dose. Those needing doses of clozapine that causes seizures may be prescribed sodium valproate at doses between 1000-2000mg /day, use of modified release preparations (Epilim Chrono) may aid concordance as it can be given once daily and may be better tolerated. Clozapine plasma levels may be useful as a rough guide to dosing – aim for a level of 0.35 – 0.5mg/L (Maudsley prescribing Guidelines, 10th edition).
### 4.10 Summary Matrix of Mandatory Monitoring Parameters for Clozapine Treatment in ELFT.

<table>
<thead>
<tr>
<th>Monitoring Parameter</th>
<th>Week of Clozapine Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>FBC+ differential</td>
<td>☑</td>
</tr>
<tr>
<td>Troponin level</td>
<td>☑</td>
</tr>
<tr>
<td>+ CRP</td>
<td>☑</td>
</tr>
<tr>
<td>BP and pulse</td>
<td>☑</td>
</tr>
<tr>
<td>Weight/Height (BMI)</td>
<td>☑</td>
</tr>
<tr>
<td>Temperature</td>
<td>Monitored daily whilst on titration and remains as inpatient. In community measured at clinical discretion if service user appears unwell or there is cause for concern.</td>
</tr>
<tr>
<td>Random Blood Glucose (Non-DM)</td>
<td>☑</td>
</tr>
<tr>
<td>Constipation</td>
<td>☑</td>
</tr>
<tr>
<td>Seizures</td>
<td>☑</td>
</tr>
</tbody>
</table>

* Beyond first year of treatment, all tests with exception of Troponin, CRP and temperature should be undertaken on a monthly basis.

**In the case of a treatment break, the blood test frequency will be altered. See section 11.0 for further details.
5.0 Other Side Effects associated with clozapine

5.1 Hypersalivation

5.11 Hypersalivation is a common side effect experienced by service users and is often given as a reason for wanting to stop clozapine. It usually occurs at night but can also occur during the day. It can be mild or excessive. It may be experienced frequently or intermittently.

5.12 Hypersalivation is usually treated with Hyoscine Hydrobromide (Kwells) which can be either chewed or left to dissolve in the mouth. Other treatments such as pirenzepine can also be used. Like clozapine these drugs also have an anti-cholinergic effect, which may increase the risk of constipation.

5.13 Other means of dealing with hypersalivation might include using two pillows to sleep with and wrapping pillows in towels. It may also be beneficial to raise the height of the pillows to sleep with. If hypersalivation is experienced during the day then chewing gum (sugar free) may be beneficial.

5.14 Clozapine-induced hypersalivation may be dose related and it may be worth the RC considering a dose reduction if possible although this needs to be considered with caution.

5.15 If the service user is not maintaining an adequate daily fluid balance of around 2-3 litres and they are also hypersalivating, then they may become dehydrated. Dehydration should be avoided as it can increase the risk of or worsen any constipation that might be experienced.

5.2 Dizziness

5.21 Dizziness is a common side effect experienced by service users and it can be very distressing. It can be postural in nature but it can also occur without any change in posture.

5.22 There are a number of reasons why service users taking clozapine may experience dizziness.

- Time of clozapine dose
- Dose of clozapine
- Dehydration
- Low blood pressure

5.23 Clozapine is always initially prescribed in twice daily doses after the first day. It may be that the morning dose is causing dizziness during the day and the RC should consider moving the majority of or the entire Clozapine dose to night time. As dizziness is a dose related side effect it may even be necessary to consider a dose reduction.
5.24 Dehydration can cause dizziness. If the service user is not maintaining an adequate daily fluid balance of around 2-3 litres then they may become dehydrated. Other possible factors that may contribute to dehydration are urinary frequency, hypersalivation and excessive perspiration. If the service user is not maintaining an adequate daily fluid balance of around 2-3 litres and they are also hypersalivating, then they may become dehydrated. Dehydration should be avoided as it can increase the risk of or worsen any constipation that might be experienced.

5.25 Low blood pressure can also cause dizziness. This may be pre-existing low blood pressure or it may be a dose related side effect of clozapine. If low blood pressure is apparent through observation then this should be made known to the RC and GP.

5.26 Sudden dizziness can cause falls and the service user should consider sitting and resting should dizziness occur.

5.27 Dizziness can occur if clozapine is also taken with other medications, especially anxiolytics or other anti-psychotic or antihypertensive medications.

5.3 Sedation

5.31 Generally experienced when first starting clozapine. However this can be ongoing. Clozapine is always initially prescribed in twice daily doses. It may be that the morning dose is causing sedation during the day and the RC should consider moving the majority of or the entire clozapine dose to night time. As sedation is a dose related side effect it may even be necessary to consider a dose reduction.

5.32 Sedation can also occur if clozapine is also taken with other medications, especially anxiolytics or other anti-psychotic medications.

5.4 Nausea/ Vomiting

5.41 Nausea is identified as being experienced by around 11% of service users (Flanagan. R.J, Side Effects of Clozapine and some other Psychoactive Drugs, 2008) and it can be very distressing. It is also reported that this most frequently occurs in the later stages of treatment; however service users do commonly report this within the first few months after starting Clozapine.

5.42 There are a number of reasons why service users taking Clozapine may experience nausea.

- Dose of clozapine
- Increase in food intake
- Delayed gastric emptying
- Hypersalivation/dehydration
5.43 As nausea is a dose related side effect it may even be necessary to consider a reduction in the dose of clozapine. This may reduce or stop the experience of nausea.

5.44 Clozapine is well known to cause increased appetite. It is important to discuss this side effect with service users prior to commencing and during treatment with clozapine in order to assist them with any lifestyle changes that they may need to make. A referral to a Dietician may also be of use.

5.45 Delayed gastric emptying can be as a result of a number of things, for instance; an increase in food intake, a high fat content in the diet, cigarette smoking and consumption of alcohol amongst others.

5.46 The service user should be encouraged to maintain a healthy diet; eating more slowly and changing portion size and meal frequency if required. They should also be encouraged to meet with their GP as they may require prescribing of anti-emetics or antacids.

5.47 Hypersalivation is a very common side effect of clozapine and can cause dehydration if an adequate daily fluid balance of around 2-3 litres is not maintained. If the service user is vomiting frequently this can contribute to any dehydration. Dehydration should be avoided as it can increase the risk of or worsen any constipation that might be experienced.

5.5 Dry mouth

5.51 This is often experienced in the morning when waking having hypersalivated throughout the night. However this can occur at other times of the day also and not in relation to hypersalivation. The Service User should be advised to maintain an adequate daily fluid balance of around 2-3 litres.

5.6 Urinary problems

5.61 Urinary frequency and urgency are often experienced; this can occur or abate at any time during Clozapine therapy. It can be increased in severity to the point of experiencing enuresis particularly at night-time. The Service User should be advised to attend their GP. Clinic staff should notify RC and GP if this occurs.

5.7 Pneumonia

5.71 There is anecdotal evidence that clozapine may be associated with an increased risk of chest infections, which may prove fatal. The proposed mechanism is unknown, but hypersalivation leading to pulmonary aspiration, impaired oesophageal peristalsis, use of antacids (reflecting upper GI problems), gastro-oesophageal reflux and smoking cessation (leading to increased clozapine levels) have all been implicated (Taylor et al, 2010; Taylor et al, 2009; Gulmez et al, 2007). The presence of asthma may exacerbate the risk of developing pneumonia.

5.72 Service users taking clozapine should be closely monitored for symptoms of chest infection and pneumonia (fever, aches and pains, breathlessness, wheeze, sputum production etc). Any purported risk
factor, such as a history of asthma, change in smoking habit, hypersalivation or upper GI symptoms, should be carefully noted and treatment commenced if indicated. Assessment should include measurement of temperature, pulse and blood pressure.

5.73 The development of a chest infection in patients taking clozapine should result in immediate treatment, including specialist referral if necessary. If pneumonia develops, consideration should be given to discontinuing clozapine sooner rather than later, particularly if it is suspected as being the causative agent. Alternative antipsychotics should be commenced. Amisulpride is associated with a low risk of pneumonia and a suitable alternative if clinically appropriate.

5.8 This is not an exhaustive list of side effects associated with clozapine. Staff should refer to either the BNF, Zaponex Summary of Product Characteristics, or Maudsley Prescribing guidelines for information on other side effects associated with clozapine and their management.
6.0 Preparing for Initiating Clozapine

6.1 Referring the service user to Clozapine Clinic

6.11 Service users cannot be initiated on clozapine until their referral to the clozapine clinic has been accepted. There is one [clozapine clinic referral form](#) used throughout the Trust for both inpatients and outpatients and this should be sent to the relevant Clozapine Clinic.

6.12 There are four clozapine clinics in operation in ELFT and their contact details are as follows:

<table>
<thead>
<tr>
<th>City and Hackney Clozapine Clinics</th>
<th>Newham Clozapine Clinic</th>
</tr>
</thead>
</table>
| Joan Johnson (Clozapine Manager), Pramodh Matadeen (Clozapine Nurse) | Matthew Oppong  
Clozapine/Asylum Manager & Primary Care Liaison Lead |
| Tel: 07813 114 619 | 115 Balaam Street |
| **South Clinic** (operating Mondays and Tuesdays) | London E13 8AF |
| Donald Winnicott Centre, Coates Road, London, E2 9AG | Tel: 020 8548 5181 |
| Tel: 020 7033 6100 Fax: 020 7033 6196 | Fax: 020 8548 5165 |
| **North Clinic** (operating Wednesdays and Thursdays) |  
Anita House, Wilmer Place, Stoke Newington, London, N16 0LN |
| Tel: 020 7275 1000 Fax: 020 7275 1100 |  
Matthew Oppong  
Clozapine/Asylum Manager & Primary Care Liaison Lead |

<table>
<thead>
<tr>
<th>Forensics Clozapine Clinics</th>
<th>Tower Hamlets Clozapine Clinic</th>
</tr>
</thead>
</table>
| **John Howard Centre** | Pete Healy  
Clozapine Clinic Manager |
| Curtis Reece  
Limehouse ward  
John Howard Centre | 54-86, Old Montague Street,  
LONDON, E1 5NN. |
| Tel: 0208 5102060 Fax: 0208 5102315 | Tel: 0207 426 2350 Mob: 07967 613 924 |
| **Wolfson House** |  
Alison Wright  
Clissold Ward |
| Tel: 0203 222 7133 Fax: 0203 222 7233 | Tel: 0207 426 2497 |

6.13 The following baseline tests must be carried out before a referral:

- Full blood count
- HbA1C and fasting blood glucose
- LFTs and U+Es
- Fasting lipids
- Weight
- Blood Pressure
- Pulse
- Temperature
- ECG
- CRP
- Troponin
6.14 All CPA/CRAM documents should be up to date on RiO and the Clozapine Clinic staff should be made aware of any active risk factors.

6.2 Registration with ZTAS

6.21 ELFT currently use the Zaponex™ brand of clozapine.

6.22 The Zaponex Treatment Access System (ZTAS) provides centralised monitoring of leukocyte and neutrophil counts which is mandatory for all service users in the UK treated with Zaponex.

6.23 Therefore, before any service user can be initiated on clozapine, they must be registered with ZTAS.

6.24 The ZTAS patient registration form should only be completed following the successful referral of the service user to the Clozapine Clinic. The completed form will only be sent to ZTAS after the clozapine pharmacist has clinically screened the service user’s existing medication and has approved treatment with clozapine.

6.25 The prescribing RC and clozapine pharmacist must be registered with ZTAS to enable them to prescribe and dispense Zaponex to the patient.
7.0 Initiating Clozapine

7.1 General Information

7.11 In ELFT, three initiation pathways are available depending on whether the service user is starting clozapine as an inpatient, day patient or outpatient.

7.12 The decision as to which initiation pathway is used is at the discretion of the ward or community based clinical teams within the borough, dependent on the service user's clinical circumstances and also the clinical resources available.

7.13 Clozapine titrations should generally be started at the beginning of the week. This is because the risk of serious adverse reactions is higher in the first few days of treatment. Staffing levels are generally higher during weekdays, providing the infrastructure to carry out enhanced monitoring and to also deal with any emergent serious adverse reactions. It is for this reason that the initiation of clozapine titrations at the end of the week or weekends is not recommended.

7.2 Providing Information to the service user and carer

7.21 Before treatment with clozapine, the service user should be given the following:

- An ELFT Clozapine information leaflet.
- A clear explanation of the requirement for blood tests, the duration and frequency of these.
- A clear explanation of potential adverse effects, especially constipation and what they should do if they experience these.
- An explanation of why adherence is important. What the service user must do if they have not taken clozapine for more than 48 hours.
- Contact numbers for the clozapine clinic. If the service user is titrating on the day patient or community pathways, they should also have emergency contact numbers for the ward/community team undertaking the titration.
7.3 Inpatient Titration

7.31 Summary of titration

Service user is initiated on clozapine on the ward as part of a normal inpatient admission.

7.32 Who is this titration suitable for?

This is the preferred method of clozapine titration and is suitable for all service users who meet the general inclusion criteria for treatment with clozapine.

7.33 Prescribing clozapine during titration

An inpatient clozapine titration should be prescribed using the Trust pre-printed clozapine titration sheet. This must be attached to the front of the service user’s drug chart and in the regular section of the drug chart ‘Clozapine-see titration sheet’ should be written. This will titrate the service user to a daily dose of 300mg in 17 days, although it should be noted that there is no standard dose of this drug, with some service users requiring smaller doses whilst others larger doses.

The ward doctor will review, at a minimum, once every week. The doctor will assess the service user’s progress, enquire into any adverse reactions to clozapine and manage any other anti-psychotic medication; cross-tapering etc. In some cases it may be necessary to slow or alter the titration regime (for example if the standard titration is too rapid, or if service user has developed complications during the titration). In such cases the blank clozapine titration sheet should be used and the titration dosing completed manually.

7.34 Monitoring to be carried out during titration period

<table>
<thead>
<tr>
<th>PHYSICAL OBSERVATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>All monitoring should be recorded on the clozapine titration sheet for the entire titration period.</td>
</tr>
</tbody>
</table>

Before every clozapine dose: Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered.

2 hours after every clozapine dose: Blood pressure (lying and standing), pulse and temperature.

Service user should be regularly prompted about constipation.

<table>
<thead>
<tr>
<th>BLOOD TESTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Blood Count plus differential, CRP and troponin levels will be organised by the Clozapine Clinic and taken on a weekly basis on the ward. CRP and troponin should only be continued weekly for the first 4 weeks of treatment.</td>
</tr>
</tbody>
</table>

Random Blood Glucose will be monitored by ward staff using a Glucometer on a weekly basis.

- For non-diabetic service users, any results greater than 7mmols/L should be reported to the ward doctor.
- With known diabetics any result outside of the range 5-8mmols/L should be reported to the ward doctor.
7.35 Supply and administration of clozapine during titration period

Clozapine will be ordered and dispensed weekly in accordance with the service user’s inpatient medication chart and following the receipt of a valid blood result as indicated by ZTAS – that is a ‘green’ or ‘amber’ result.

Nursing staff may only administer clozapine to a service user if the service user has their own labelled supply that has been issued by pharmacy. If the service user does not have their own labelled clozapine supply, the nurse must contact pharmacy and not administer another service user’s supply.

7.36 Leave from the ward during titration period

Days 1-6

It is recommended that the service user remains on the ward for the first week of titration. This is because many of the emergent adverse drug reactions are more likely to occur during the early stages of treatment.

Day 7-onwards

Leave from the ward is at the clinical discretion of the medical team. Service users must not be sent on leave until at least 2 hours after their clozapine dose. Physical observations should be within normal limits (or agreed limits) and they should be considered medically fit for leave.

The service user should ideally be accompanied by a carer or responsible adult when on leave. If overnight leave is required, there must be an adult at the service user’s home whilst they stay overnight.
7.4 Day patient Titration

7.41 Summary of titration

Service user technically remains an outpatient, but attends the ward during the day to take clozapine and for associated monitoring required during the course of the titration.

7.42 Who is this titration suitable for?

This titration is suitable for those service users who would normally be considered suitable for outpatient or community team care. It is expected that the clinician has given due consideration and discussed the pros and cons of initiating clozapine on a day patient basis taking into account medical co-morbidities that may present a risk during clozapine titration (for example epilepsy or problems with hypotension). There must also be an adult at the service user’s home (or the address where he or she would be residing) whilst they are on titration. There must also be access to an in-patient bed in the event that their mental or physical state deteriorates during the titration.

This titration is useful when it is not possible for the community team (Home Treatment Team or Assertive Outreach Team) to facilitate clozapine initiation for those service users who do not need to be inpatients.

7.43 Prescribing Clozapine During Titration

A day patient titration should be prescribed using the pre-printed clozapine day patient titration sheet. This must be attached to the front of the service user’s drug chart and in the regular section of the drug chart ‘Clozapine-see titration sheet’ should be written. This will titrate the service user to a daily dose of 300mg in 17 days, although it should be noted that there is no standard dose of this drug, with some service users requiring smaller doses whilst others larger doses.

The titration is almost identical to the inpatient titration, with the exception of the PM dose being administered at 18.00 rather than 22.00. This enables the service user to leave the ward in the evening.

The ward doctor will review, at a minimum, once every week. The doctor will assess the service user’s progress, enquire into any adverse reactions to Clozapine and manage any other anti-psychotic medication; cross- tapering etc. In some cases it may be necessary to slow or alter the titration regime (for example if the standard titration is too rapid, or if service user has developed complications during the titration). In such cases the blank clozapine day patient titration sheet should be used and the titration dosing completed manually.
7.44 Monitoring to be carried out during titration period

**PHYSICAL OBSERVATIONS**

All monitoring should be recorded on the clozapine titration sheet for the entire titration period.

**Before every clozapine dose:** Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered.

**2 hours after every clozapine dose:** Blood pressure (lying and standing), pulse and temperature.

Service user should be regularly prompted about constipation.

**BLOOD TESTS**

Full Blood Count plus differential, CRP and troponin levels will be organised by the Clozapine Clinic and taken on a weekly basis on the ward. CRP and troponin should only be continued weekly for the first 4 weeks of treatment.

Random Blood Glucose will be monitored by ward staff using a Glucometer on a weekly basis.

- For non-diabetic service users, any results greater than 7mmols/L should be reported to the ward doctor.
- With known diabetics any result outside of the range 5-8mmols/L should be reported to the ward doctor.

7.45 Supply and administration of clozapine during titration period

Clozapine will be ordered and dispensed weekly in accordance with the service user’s inpatient medication chart and following the receipt of a valid blood result as indicated by ZTAS – that is a ‘green’ or ‘amber’ result.

Nursing staff may only administer clozapine to a service user if the service user has their own labelled supply that has been issued by pharmacy. If the service user does not have their own labelled clozapine supply, the nurse must contact pharmacy and not administer another service user’s supply.

7.46 Leave from the ward

**Day 1**

The service user should arrive on the ward for 09.00, in order to receive their first dose of clozapine. They should remain on the ward until their physical observations are re-checked at 18.00. These should be within normal limits (or agreed limits) and they should be considered medically fit for leave. The service user should ideally be accompanied by a carer or responsible adult when on leave.

**Days 2-6**

The service user should arrive on the ward for 09.00, in order to receive their morning dose of clozapine. They should remain on the ward the entire day. They should not be sent on leave until at least 2 hours after their 18.00 clozapine dose. Physical observations should be within normal (or agreed) limits and they should be considered medically fit for
leave. The service user should ideally be accompanied by a carer or responsible adult when on leave.

Day 7-onwards

The service user should arrive on the ward for 09.00, in order to receive their morning dose of clozapine. They may be sent on leave 2 hours after their morning dose if their physical observations are within normal (or agreed) limits and they are considered medically fit.

The service user should return to the ward for 18.00 for their evening dose of clozapine. They must not be sent on leave until at least 2 hours after their clozapine dose. Physical observations should be within normal limits (or agreed limits) and they should be considered medically fit for leave.
7.5 Community Titration

7.51 Summary of titration

Service user is initiated on clozapine by the community team (Home Treatment or Assertive Outreach Team).

7.52 Who is this titration suitable for?

This titration is suitable for those service users who are considered suitable for community initiation. It is expected that the clinician has given due consideration and discussed the pros and cons of initiating clozapine in the community taking into account medical co-morbidities that may present a risk during clozapine titration (for example epilepsy or problems with hypotension).

There must also be an adult at the service user's home (or the address that he or she would be residing) for the entire time that they are on titration and they must consent to daily (and in the first 4 days twice daily) visits from the Home Treatment Team or Assertive Outreach Team coordinating the titration.

There must be access to an in-patient bed in the event that the service user's mental or physical state deteriorates during the initiation.

7.53 Prescribing Clozapine During Titration

Community clozapine titrations should be prescribed using the Trust pre-printed clozapine community titration sheet. This must be attached to the front of the service user’s community drug chart and in the regular section of the drug chart ‘Clozapine-see titration sheet’ should be written. This will titrate the service user to a daily dose of 175mg in 28 days, although it should be noted that there is no standard dose of this drug, with some service users requiring smaller doses and others larger doses.

The community team doctor will review, at a minimum, once every week. The doctor will be expected to assess the service user's progress, enquire into and review any adverse reactions to clozapine and manage any other anti-psychotic medication; cross-tapering etc.
MONITORING TO BE CARRIED OUT DURING TITRATION PERIOD

PHYSICAL OBSERVATIONS
Visits should be undertaken by at least one mental health practitioner who is competent at taking physical observations. All monitoring should be recorded on the Trust physical observation sheet.

DAYS 1-4

Before every clozapine dose: Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered.

2 hours after every clozapine dose: Blood pressure (lying and standing), pulse and temperature.

Service user should be regularly prompted about constipation.

DAYS 5-14

Clinical decision made by team as to frequency of monitoring based on previous physical observations.

If no concerns:

Before morning clozapine dose: Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered and evening dose of clozapine will be left as a TTA.

At night time: Member of HTT to phone service user and check how they are.

Service user should be regularly prompted about constipation.

If higher level of monitoring required:

Before morning clozapine dose: Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered.

Before night-time clozapine dose: Blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered.

Service user should be regularly prompted about constipation.

DAY 14 ONWARDS

Alternate day blood pressure (lying and standing), pulse and temperature. If observations are clinically appropriate, clozapine dose to be administered and TTA left for that evening and the following day.

Service user should be regularly prompted about constipation.

BLOOD TESTS

Full Blood Count plus differential, CRP and troponin levels will be organised by the Clozapine Clinic and taken on a weekly basis on the ward. CRP and troponin should only be continued weekly for the first 4 weeks of treatment.

Random Blood Glucose will be monitored by ward staff using a Glucometer on a weekly basis.

- For non-diabetic service users, any results greater than 7mmols/L should be reported to the ward doctor.
- With known diabetics any result outside of the range 5-8mmols/L should be reported to the ward doctor.
7.55 Supply and administration of clozapine during titration period

Clozapine will be ordered and dispensed weekly in accordance with the service user’s community medication chart and following the receipt of a valid blood result as indicated by ZTAS – that is a ‘green’ or ‘amber’ result.

Nursing staff may only administer clozapine to a service user if the service user has their own labelled supply that has been issued by pharmacy. If the service user does not have their own labelled clozapine supply, the nurse must contact pharmacy and not administer another service user’s supply.

8.0 Maintenance treatment with clozapine and further dose changes

8.1 Following the initial clozapine titration, the titration sheet should be filed in the service user’s medical notes and a new prescription of clozapine prescribed in the regular section of their drug chart. Any subsequent dose increases are limited to a maximum of 50mg a day, to reduce the risk of orthostatic hypotension and other complications. Any further dose increases do not require the enhanced monitoring associated with the titration period.

8.2 Clozapine will be ordered and dispensed weekly in accordance with the service user’s community medication chart and following the receipt of a valid blood result as indicated by ZTAS – that is a ‘green’ or ‘amber’ result.

8.3 Nursing staff may only administer clozapine to a service user if the service user has their own labelled supply that has been issued by pharmacy. If the service user does not have their own labelled clozapine supply, the nurse must contact pharmacy and not administer another service user’s supply.

9.0 Discharge Planning

9.1 When considering discharging the service user from the ward please ensure that:

- You have informed the Clozapine Clinic and the Pharmacy Department of impending discharge.
- That you are certain the service user has a follow up appointment with the Clozapine Clinic (Please see section 4.1 for clinic contact details). Preferably their first appointment should be once they have attained one week’s leave from the ward.
- That a discharge care plan and a comprehensive discharge summary is sent to the Clozapine Clinic and Pharmacy Dept.
- An outpatient clozapine prescription is completed and given to pharmacy so that the service user can receive a continued supply of clozapine post discharge. This prescription should only contain medicines that cannot be prescribed by the GP.

9.2 If at any time anyone involved in the service users care is concerned about side effects or any other aspect of their presentation, they should contact the Ward, Pharmacy Department and/or the Clozapine Clinic to seek further advice.
10.0 Outpatient Care and Prescribing

10.1 Following discharge, the clozapine clinic will coordinate all operational aspects around treatment with clozapine in the community. These will include undertaking and processing the required blood tests, undertaking necessary physical health monitoring, issuing medication and liaising with the relevant Mental Health team and GP where appropriate. For a full list of these aspects please refer to the Clozapine Clinic Standard Operating Procedure. The clozapine clinic does not take over any care coordinator responsibilities.

10.2 All outpatient prescribing is via clozapine outpatient prescription forms. These are held centrally at Mile End Pharmacy where prescriptions are dispensed. Medication is then sent to the relevant Clozapine Clinic for issue to the service user. Owing to the centralised location of the clozapine prescriptions, pharmacists may make dose alterations or other changes to these prescriptions following a written request from the prescriber with words to this effect.

11.0 Treatment Breaks

11.1 If a service user misses a single dose, the next dose should not be doubled. The service user should continue with their next prescribed dose as normal.

11.2 Clozapine must not be re-started at the original dose if there has been a treatment break of greater than 48 hours. Re-starting at the original dose after a treatment break could prove harmful to the service user.

11.2 The Clozapine Clinic will inform ZTAS of the treatment break. If the treatment break is greater than 3 days, the service user can revert to their original blood test frequency. If the treatment break was for 4 weeks or greater, the patient will require weekly monitoring for 18 weeks, before they can revert to their original blood test frequency.

11.3 Those service users who re-start clozapine will require re-titration to their original dose. The speed of this re-titration will be dependent on the duration of clozapine abstinence, the service user's mental state, medical co-morbidities as well as team specific operational factors.

11.4 Re-titration is service user specific and the Clozapine Clinic pharmacist and consultant psychiatrist should devise a suitable and appropriate re-titration prescription for each individual service user. In some cases it may be possible to undertake an accelerated re-titration (that is, faster than the standard titration set out in this policy). In such cases, the initial dose should still be 12.5mg once daily and if the service user experiences any adverse events the doctor should review and the titration be slowed.

12.0 Ceasing Treatment of Clozapine

12.1 The Clozapine Clinic should be informed when there are plans to discontinue clozapine. Where possible, clozapine should be gradually reduced over a period of at least 2 weeks to reduce the risk of psychotic and cholinergic rebound.
12.2 The Clozapine Clinic will contact ZTAS to notify them of the plan to discontinue clozapine.

12.3 Blood test monitoring will still need to continue for a further 4 weeks following ceasing clozapine.

13.0 Treating Out of Area Service Users with Clozapine

13.1 ELFT staff should use the following algorithm for dealing with out of area patients already established on clozapine.

13.2 Supplies of clozapine should be obtained from the service user’s local clozapine service.

13.3 In exceptional circumstances ELFT pharmacy may be able to supply up to 48 hours supply of clozapine until more can be obtained from the patient’s normal clozapine service. In some circumstances (for example long stay medical admission) it may be more appropriate to transfer the service user’s clozapine service over to ELFT. However this would require transfer of the service user’s psychiatric care over to a local consultant whilst they remain in the medical facility.

14.0 Service Users Going on Holiday

14.1 Owing to the mandatory MHRA requirement for blood tests there are limits to how much clozapine may be supplied to the service user. The amount that can be supplied will be dependent on the service user’s current frequency of blood tests:

<table>
<thead>
<tr>
<th>Frequency of Blood Test</th>
<th>Standard duration of time clozapine may be supplied for</th>
<th>Emergency duration of time clozapine may be supplied for if service user ‘late’</th>
<th>Total duration of time that clozapine may be supplied for</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/52</td>
<td>1/52</td>
<td>1/52</td>
<td>2/52</td>
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<tr>
<td>2/52</td>
<td>2/52</td>
<td>1/52</td>
<td>3/52</td>
</tr>
<tr>
<td>4/52</td>
<td>4/52</td>
<td>2/52</td>
<td>6/52</td>
</tr>
</tbody>
</table>

14.2 If the service user is planning to go on holiday for a time period greater than the duration of clozapine that can be supplied, they should see their psychiatrist. In this meeting a treatment plan for alternative antipsychotic treatment arrangements will need to be made. ELFT should have no further responsibility for organising supplies of medication beyond holiday durations of 8 weeks.

14.3 It may be advisable for service users to keep a cover letter from their consultant/Care Coordinator if they are carrying a large amount of medication, to avoid any issues with customs.

14.4 The Clozapine Clinic is unable to accept the results of blood tests for service users that have been taken and measured outside of the UK.

14.5 If a treatment break occurs, ZTAS should be informed as set out in section 11.0 of this policy.
15.0 Smoking, Smoking Cessation and Clozapine

15.1 Smoking reduces clozapine plasma levels by up to 50% depending on the number and type of cigarettes smoked.

15.2 This effect is unrelated to nicotine and is caused by polycyclic aromatic hydrocarbons (PAHs) present in tobacco smoke. PAHs increase activity of the cytochrome P450 system that is responsible for the metabolism of a number of commonly used psychotropics.

15.3 Following smoking cessation, the service user is no longer exposed to PAHs and metabolism of these psychotropics decreases, resulting in increased plasma levels. Plasma levels will rise regardless of whether a patient is treated with NRT, bupropion or varenicline.

15.4 If smoking cessation is planned a clozapine plasma level should be taken before smoking. On stopping smoking the clozapine dose should be reduced gradually (over a week) until around 75% dose reached. A clozapine plasma level should be repeated 1 week after stopping. Further dose reductions should be considered if necessary.

15.5 If the service user is re-starting smoking, the clozapine dose should be increased to ‘normal’ smoking dose over 1 week. A clozapine plasma level should then be taken and dose adjustments made if necessary.

15.6 For further information, staff should refer to the ELFT guidelines for smoking cessation pharmacotherapy.

16.0 Nursing Staff Responsibilities (Inpatient Units and Community Teams)

16.1 To ensure that all baseline and subsequent monitoring is carried out as set out in this policy.

16.2 To report any adverse effects or abnormal results to the medical team as appropriate.

16.3 To provide counselling and information to service users and carers as required.

16.4 To only administer clozapine to a service user if the service user has their own labelled supply that has been issued by pharmacy. If the service user does not have their own labelled clozapine supply, the nurse must contact pharmacy and not administer another service user’s supply.

16.5 To ensure that clozapine is not administered to service users who have not had clozapine for greater than 48 hours. The nurse should contact the doctor/clozapine clinic/pharmacy for further information.
17.0 Medical Responsibilities

17.1 To refer patients to the clozapine clinic by completing the ELFT clozapine clinic referral form together with the full baseline tests performed as set out in this policy.

17.2 To register the patient with ZTAS (named responsible consultant not the junior doctor's for a ward), take required baseline blood samples and send to the local haematology departments for analysis.

17.3 Once the patient has been discharged from the inpatient setting, a copy of the discharge summary, completed CPA documentation and risk assessment should sent to the clinic.

17.4 Responsible consultant to inform the clinic staff, pharmacy and G.P. of any changes in the dose of clozapine and other medications.

17.5 To review all patients as requested by the clinic staff.

17.6 Each patient attending the clinic should be reviewed by his or her responsible consultant /junior doctor every six months.

17.7 To inform clinic, pharmacy and G.P. when clozapine is to be discontinued.

17.8 To inform clinic if patient's care is transferred to/from another consultant.

18.0 Pharmacy Responsibilities

18.1 To be clinically responsible and oversee the safe and efficient dispensing and monitoring of clozapine for both in and out- patients.

18.2 To monitor the blood results for clozapine issued to wards using the ZTAS monitoring system.

18.3 To provide counselling and information to patients and carers as required.

18.4 To provide training to clinic and other relevant staff as required.

18.5 To hold clozapine outpatient prescriptions. To make changes to these prescriptions if necessary under the written instructions of the Responsible Consultant. To ensure that all prescriptions are current and obtain new ones as necessary.

19.0 Clozapine clinic responsibilities

19.1 Liaise and co-ordinate care with the patients, their carers and care coordinator, consultants, psychiatric registrars, GPs and in-patient nursing staff.

19.2 To check that the referral form is completed and accurate and baseline observations are complete and within range and act on these as appropriate.

19.3 To ensure that appropriate baseline and subsequent blood and physical health monitoring is carried out as set out in this policy.
19.4 To inform the respective GP of any new patient to the clinic and of the clinic contact details.

19.5 To liaise with the care coordinator, responsible consultant and/or SHO when concerned about the patient's mental health. Concerns about physical health should be addressed to the G.P and responsible consultant and care coordinator.

20.0 Training

20.1 The Clozapine Clinic Managers throughout the Trust are to provide training for the Trusts medicines management training days. This is to be carried out on a rotational basis.

20.2 The Clozapine Clinic Manager is to provide training to all Care Co-ordination teams, inpatient services and to all of the relevant supported housing projects throughout their borough on a yearly basis.

20.3 The Clinic will provide a training environment for student nurses and students of other disciplines, e.g. OT and pre-registration Pharmacy students.