Livewell Southwest

Clozapine Policy for Mental Health Staff and GP Practice Staff

Version No 2:2

Notice to staff using a paper copy of this guidance

The policies and procedures page of LSW intranet holds the most recent version of this document and staff must ensure that they are using the most recent guidance.

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2.1	Updated	08/2015	Mental Health Pharmacist	Updated to include change of dispensing pharmacy and contact details.
2.2	Ratified	2/10/15	MGG	All changes accepted

Contents

Clozapine Policy for Mental Health Staff and GP Practice Staff

1. Introduction

1.1 Clozapine is an atypical antipsychotic that was first introduced in the 1960's. It has been shown to be very effective for schizophrenia, including that unresponsive to other antipsychotics, but was withdrawn from the UK market in the 1970's following fatal cases of agranulocytosis. It was re-introduced in the late 1980's but can only be prescribed for treatment resistant schizophrenia (or psychotic disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed) and to patients who are registered with an approved monitoring service and with regular blood monitoring.

1.2 In Plymouth patients will be registered with the **Clozaril® Patient Monitoring Service (CPMS)** if taking clozapine tablets or with the Denzapine® Monitoring Service (DMS) if taking clozapine suspension.

1.3 Clozapine can only be prescribed by doctors and dispensed by pharmacies that are registered with CPMS and / or DMS. Within the South and West Devon Formulary clozapine is listed as a "hospital only drug" and is therefore prescribed by psychiatrists and dispensed by LSW pharmacy.

1.4 However, Mental Health Services are keen to make Clozapine as accessible to patients as possible and, for some patients, allowing them to attend their GP Practice for blood tests and/or for collecting their Clozapine supplies can have a positive effect on the patient's compliance with treatment. **However, there are risks to taking Clozapine and it is important that GP Practice staff are aware of these risks and are willing, and adequately supported, to take on this role.**

2. Overall aim of the policy

2.1 This policy aims to give the necessary information to allow Mental Health Staff to initiate and to continue to prescribe Clozapine safely, and to plan and monitor the patient's ongoing care, which may involve their GP Practice.

2.2 It outlines the responsibilities of both Mental Health Staff and GP Practice staff for those patients that are to have blood samples taken and/or to collect their Clozapine supplies from their GP Practice, and contains a formal agreement to be signed for each patient. It also aims to give the necessary information to GP Practice staff so that they are aware of the issues around Clozapine and are willing to take on this role.

3. Objectives that build toward the overall aim of the policy

3.1 To reduce risk to patients. To give adequate information and support to GP Practice staff.

4. Description of how you will measure its effectiveness

4.1 Monitoring of problems and errors via Clozapine Pharmacy Technician.

4.2 Feedback from GP Practice staff and Mental Health staff.

5. Workforce Planning Issues

5.1 For Mental Health staff it remains necessary to continue the delivery of Clozapine until patients have been on the medication for at least 18 weeks. This is now well embedded within service provision and mental health community team managers are aware of its workforce implications.

5.2 GP Practice staff already deal with Clozapine on an informal basis and this policy has hopefully had a positive impact on the service they are already providing.

6. Clozapine General Information

6.1 Blood Monitoring Requirements

6.1.1 Neutropenia and agranulocytosis are potentially serious adverse reactions to clozapine. They are generally reversible on stopping clozapine but may be fatal.

6.1.2 Around 2.7% of patients treated with clozapine will develop neutropenia.
Of these half occur within the first 18 weeks and three quarters within the first year.

6.1.3 Around 0.8% of patients treated with clozapine will develop agranulocytosis [(5)].
Of these 70% are within the first 18 weeks.
When a monitoring service is not used the mortality rate from agranulocytosis is 0.3%, compared to 0.01% when the Clozapine Patient Monitoring Service is used [(1)]

6.1.4 At each consultation, a patient receiving Clozapine must be reminded to contact the treating physician immediately if any kind of infection begins to develop. Particular attention should be paid to flu-like complaints such as fever or sore throat and to other evidence of infection, which may be indicative of neutropenia. Patients and their caregivers must be informed that, in the event of any of these symptoms, they must have a blood cell count performed immediately.

6.1.5 Clozapine patients must have their **WBC** (white blood cell count) and **ANC** (absolute neutrophil count) regularly monitored for the whole time they are taking Clozapine.

The frequency of monitoring is:

- One blood test within the 10 days prior to starting Clozapine
- At least weekly for the first 18 weeks
- At least every 2 weeks from weeks 19 to 52
- At least every 4 weeks thereafter
- After discontinuing Clozapine - at current frequency for a further 4 weeks (or as advised by CPMS following a RED blood result)
- Frequency of monitoring may change following a treatment break – this will be advised by CPMS

6.1.6 The cost of monitoring the blood counts is factored into the price of Clozaril® tablets (or Denzapine® suspension). **Therefore please ensure that CPMS (or DMS as appropriate) are used for this purpose**. The Derriford combined labs should only be used in an emergency e.g. if insufficient time available until patient status goes RED (see section 14.2).

6.1.7 The patient can only receive medication if they have a current normal WBC and ANC registered on the CPMS computer system and medication can only be dispensed for the duration of time between the required blood tests.

6.1.8 CPMS / DMS can be helpful with answering patient specific enquiries.

6.2 Clozapine Patient Monitoring Service (CPMS) or Denzapine Monitoring Service (DMS) Blood Results

A traffic-light system is used:

	WBC mm^3 /L	**ANC** mm^3 / L	**Action**
Green:	≥ 3500 (≥ $3.5x10^9$)	≥ 2000 (≥ $2.0x10^9$)	Continue Clozapine treatment and normal schedule for blood tests
Amber:	3000-3500 ($3.0x10^9$ - $3.5x10^9$)	1500-2000 ($1.5x10^9$ - $2.0x10^9$)	Continue Clozapine treatment, sample blood twice weekly until counts stabilise or increase. CPMS / DMS will be able to advise further Monitor patient medically
Red:	< 3000 (< $3.0x10^9$)	< 1500 (< $1.5x10^9$)	Immediately stop Clozapine treatment, sample blood daily until haematological abnormality is resolved, monitor for infection. Admission to general hospital may be required. The patient will be de-registered from the CPMS / DMS system and will not be able to receive Clozapine in the future (unless by special agreement with CPMS / DMS).

6.3 Myocarditis and cardiomyopathy [5]

Many of the symptoms of myocarditis and / or cardiomyopathy occur in patients on clozapine who are not developing myocarditis.

Estimates of the incidence vary greatly but the risk of fatal myocarditis / cardiomyopathy may be as high as 1 in 1000 patients treated with clozapine.

Myocarditis or cardiomyopathy should be suspected in patients who experience persistent tachycardia at rest, especially in the first 2 months of treatment, and/or palpitations, arrhythmias, chest pain and other signs and symptoms of heart failure (e.g. unexplained fatigue, dyspnoea, tachypnoea) or symptoms that mimic myocardial infarction.

If myocarditis or cardiomyopathy is suspected, clozapine treatment should be promptly stopped and the patient immediately referred to a cardiologist.

Patients who develop clozapine-induced myocarditis or cardiomyopathy should not be re-exposed to clozapine.

Clozapine is associated with an increased risk of myocarditis which has, in rare cases, been fatal.

The increased risk of myocarditis is greatest in the first 2 months of treatment. The median occurrence is at 3 weeks. But it may occur at any time during clozapine treatment.

Symptoms of myocarditis: tachycardia, fever, flu-like symptoms, fatigue, dyspnoea (with increased respiratory rate), chest pain.

Signs of myocarditis: ECG changes (ST depression), enlarged heart on radiography/echo, eosinophilia.

Suggested monitoring protocol for suspected myocarditis[5]

Time	**Parameter**
Baseline	Pulse
	Temperature
	Respiratory rate
	C reactive protein
	Troponin
	Echocardiography (if available)
Daily	Pulse
	Temperature
	Respiratory rate
Days 7, 14, 21 and 28	C reactive protein
	Troponin

Action

If CRP >100mg/l and troponin > twice upper limit of normal (2 x ULN)	Stop clozapine
	Repeat echocardiography
If fever + tachycardia + raised CRP or troponin (but less than 2 x ULN)	CRP and troponin daily

Fatal cases of cardiomyopathy have also been reported rarely. The median time for the occurrence of cardiomyopathy is 9 months. But it may occur at any time during clozapine treatment.

The presentation of cardiomyopathy varies. Cardiomyopathy should be suspected in any patient showing signs of heart failure. Any reported symptoms of palpitations, sweating and breathing difficulties should be taken seriously and closely investigated.

6.4 Common or Very Common (as per SPC) Side-effects of Clozapine and what to do about them

At each review patients should be asked about side-effects.

Side-effect	Comments	Action
Cardiovascular		
Tachycardia	Very common in the early stages of treatment but may persist. Usually benign but see section 6.3 above re: myocarditis	If present at rest and associated with fever / hypotension / chest pain may indicate myocarditis – see section 6.3 above. Benign sinus tachycardia can be treated with atenolol (starting dose 25mg od – assuming no contra-indications)
ECG changes	QTc interval may be extended (in common with other antipsychotics) ST depression in myocarditis	Pre-treatment, after dose increase and at least yearly ECG in patients with known CVD or a family history of QTc interval prolongation. Avoid combination with other drugs known to extend QTc interval.[1,5]
Hypertension	Most commonly in first 4 weeks but may persist	Monitor closely. Increase dose as slowly as necessary Antihypertensive treatment may be required (refer to latest guidelines)
Postural hypotension	Most commonly during first 4 weeks	Advise patient to stand and sit up slowly. Slow the rate of titration or reduce the dose
Dizziness / Syncope		
Immune system		
Leukopenia/decreased WBC/neutropenia	See section 6.2.1 above	
Eosinophilia		Clozapine should be discontinued if the eosinophil count rises to >3 x 10^9/L and only restarted when it falls below 1 x 10^9/L
Leukocytosis		
Anticholinergic (avoid combination with other anticholinergics if possible)		
Blurred vision/ glaucoma	Caution in patients with narrow angle glaucoma	Blurred vision may impair driving / skilled tasks
Urinary retention	Caution in patients with prostatic enlargement	
Constipation	Should be taken seriously due to the risk of paralytic ileus. There have been deaths reported due to clozapine related constipation.	All patients should be advised to follow a high fibre diet. If any signs of constipation use a bulk forming laxative (Ispaghula husk) and a stimulant (senna or bisacodyl) in combination.
Dry mouth		

CNS		
Sedation / drowsiness / fatigue	Most commonly in the first few months. Usually wears off but may persist to some extent	Give a smaller dose in the morning (night load). Check plasma level
Headache		Simple analgesia
Tremor, rigidity, akathisia, extrapyramidal symptoms	Although clozapine the least likely of the antipsychotics to cause these	
Seizures/convulsions/myoclonic jerks	Dose and plasma level related	Consider prophylactic lamotrigine, topiramate or valproate* if on high dose or plasma level >500microgram/L After a seizure withhold clozapine for one day; restart at a reduced dose and give lamotrigine, topiramate or valproate*. * use lamotrigine if poor response to clozapine, topiramate if weight loss is required, valproate if schizoaffective. Valproate should not be used in women of child bearing potential unless other options not suitable
fever, benign hyperthermia, disturbances in sweating/temperature regulation	Usually benign	Rule out the possibility of an underlying infection or the development of agranulocytosis. In the presence of high fever, the possibility of **neuroleptic malignant syndrome** (NMS) must be considered.
GI tract		
Hypersalivation	May persist beyond the first few months but may wear off. Can be most troublesome at night.	Try hyoscine hydrobromide 300 microgram (up to three times a day but less frequently may be sufficient). This is an off-label use of this medication. It is also an anticholinergic (see 6.4). The tablets should be sucked or chewed before swallowing. There are many other options but the evidence is base is poor.
Nausea, vomiting	Usually during first 6 weeks	Avoid anti-emetics if possible (prochlorperazine and

		metoclopramide increase risk of EPSE; domperidone and ondansetron increase risk of QTc interval prolongation that can also occur with clozapine; cyclizine may increase anticholinergic and sedative effects of clozapine).
Anorexia		
Urinary incontinence	May affect 1 in 5 people taking clozapine May occur at any time, may resolve spontaneously but may persist	Try altering dose schedule Avoid fluids before bedtime In severe cases desmopressin usually helps but is not without its own risks Anti-cholinergic agents may work but evidence is weak and note anti-cholinergic effects of clozapine
Other		
Weight gain	Usually during first year of treatment	Lifestyle advice (re diet and exercise) should be given to all patients when starting clozapine
Elevated LFTs	Check LFTs for patients with symptoms of liver dysfunction e.g. nausea, vomiting, anorexia[1]	Suspend treatment if LFTs > 3 x Upper limit of normal or if jaundice occurs.[1]

Advice about side-effects and their management can also be sought from the LSW mental health pharmacists and / or CPMS.

6.5 Clinically Important Drug Interactions[7]

- Increased risk of **bone marrow suppression** if given with other drugs that also have this effect (e.g. carbamazepine, chloramphenicol, co-trimoxazole, penicillamine, cytotoxic agents and antipsychotic depot injections). Avoid concomitant use.
- **Benzodiazepines** – a rare but potentially serious interaction that may increase risk of circulatory collapse. More likely at start of combination or when Clozapine is added to an established benzodiazepine regimen.
- **Antihypertensives** – can potentiate antihypertensive effect.
- **Anticholinergic drugs e**.g. tricyclic antidepressants, some antipsychotics, hyoscine, procyclidine, oxybutinin – additive anticholinergic effects (especially constipation) – use with caution and monitor.
- **Highly protein-bound drugs** (e.g. warfarin and digoxin) - Clozapine may cause increase in plasma concentrations due to displacement from plasma proteins.
- **Lithium** – increased risk of neuroleptic malignant syndrome (NMS).
- **Selective Serotonin Reuptake Inhibitors (SSRIs):**

    - **Fluvoxamine** – may significantly increase plasma Clozapine levels due to enzyme inhibition (CYP1A2) – avoid concomitant use. A lesser effect is seen with fluoxetine and paroxetine – use with caution.

- **Citalopram / Escitalopram** – now contra-indicated with other drugs that can extend QTc interval, this includes clozapine. If combination with an SSRI is necessary either use sertraline instead or monitor the ECG.

- **Tobacco and cannabis smoking –** significantly reduce plasma Clozapine levels due to enzyme induction by polycarbons in the smoke. Risk of toxic levels if a patient stops smoking – monitor plasma levels.

- **Caffeine** – increases plasma Clozapine levels. A 5 day caffeine-free period may result in up to a 50% fall in plasma Clozapine levels – though the effect is variable between individuals - dose adjustment may be required if there is a change in caffeine-drinking habit.
- CYP1A2 inducers e.g. phenytoin, omeprazole, tobacco smoke – may reduce plasma clozapine levels.
- CYP1A2 inhibitors e.g. cimetidine, ciprofloxacin – may increase plasma clozapine levels.
- Alcohol The SPC for Clozaril® advises avoidance of alcohol.[1] If alcohol is consumed by a patient on clozapine there is likely to be increased sedation and greater impairment of the ability to drive or perform skilled tasks.[7]

6.6 **For more detailed information** on Clozapine consult the current version of the BNF (paper copy or on-line at www.bnf.org) or the Clozapine Summary of Product Characteristics (available from Novartis, or on-line at www.medicines.org.uk).

There is additional written information for prescribers and staff available from CPMS (Tel. 0845 769 8269). The mental health pharmacists at LSW can also be contacted for advice.

7. Before Starting a Patient on Clozapine

7.1 Prescriber (Consultant Psychiatrist or deputy) to ensure that they are registered with CPMS (or DMS for clozapine suspension).

7.2 Prescriber to contact CPMS to check whether the patient has previously taken clozapine and whether there are any contraindications to do so again (e.g. previous serious adverse event). CPMS will provide a Patient Registration Number and an information pack.

7.3 If the patient is not able to swallow tablets then clozapine suspension (Denzapine® 50mg / ml) may be prescribed. In this case the patient will need to be registered with DMS not CPMS. Patients **cannot** be registered with both CPMS and DMS.

7.4 Patient to have a full blood count, a physical health history and a physical examination (including an ECG, weight, BMI and waist measurement, fasting plasma lipids and glucose and liver function tests).

7.5 Absolute contra-indications to clozapine are:

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

• Patients unable to undergo regular blood tests.

• History of toxic or idiosyncratic granulocytopenia / agranulocytosis (with the exception of granulocytopenia/agranulocytosis from previous chemotherapy). - Patients who have low WBC counts because of benign ethnic neutropenia should be given special consideration and may only be started on Clozapine with the agreement of a haematologist.

• History of Clozapine-induced agranulocytosis.

• Impaired bone marrow function - Patients with a history of primary bone marrow disorders may be treated only if the benefit outweighs the risk. They should be carefully reviewed by a haematologist prior to starting Clozapine.

• Uncontrolled epilepsy.

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

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

• Severe renal or cardiac disorders (e.g. myocarditis).

• Active liver disease associated with nausea, anorexia or jaundice; progressive liver disease, hepatic failure.

• Paralytic ileus.

• Clozapine treatment must not be started concurrently with substances known to have a substantial potential for causing agranulocytosis.

7.6 Inform the patient's GP. It is good practice for the GP Practice to include clozapine on the patient medication record for information and appropriate alerts.

7.7 Decide where and by whom ongoing blood tests will be taken.

7.8 Decide how the patient will receive continuing supplies of clozapine.

7.9 Decide who will monitor the patient during the first 18 weeks (see below). The patient should have a Care Co-ordinator (or someone responsible for co-ordinating their care) to ensure ongoing monitoring and support for the patient and any other agency involved.

7.10 Inform the clozapine Pharmacy Technician (LSW pharmacy based at Glenbourne tel. 01752 439006 or internal 39006) of new patient details, including patient name, NHS number, prescriber, care co-ordinator, who will be taking bloods and delivery details.

If any of 7.7 to 7.9 are to involve the GP Practice or another Mental Health Team then this decision must be made with their full agreement and co-operation. A clozapine Agreement Form (see Appendix 6) must be completed for the involvement of a GP Practice.

There are two Integrated Care Pathways available on SystmOne:

ICPCL for the Initiation of Clozapine
ICPCLRT for the Re-Titration of Clozapine®

These can be located by creating a letter through the communications and letters function on SystmOne – both ICPs are available as letter templates.

If the Home Treatment Team (HTT) are to be involved in this process they must be contacted at the out-set (01752 314033 or internal 41033). There is a separate HTT Referral Process

8. The first 18 weeks

8.1 The first 18 weeks of Clozapine treatment are considered to be the greatest risk for neutropenia and agranulocytosis (70% of cases), hence the weekly blood monitoring requirements. It is also the time when many of the other side-effects emerge and when non-adherence to treatment is likely to be greatest. Also, suicide risk is known to be increased early in the course of schizophrenia and during hospitalisation or shortly after discharge[8].

8.2 For these reasons, patients should be monitored very closely by Mental Health Services during this time. Patients may attend their GP Practice for blood tests (with agreement of the Practice) but the Care Co-ordinator (or designated person) must remain in close contact with the patient and GP Practice to ensure that the patient attends for blood tests, and intervene where necessary.

8.3 Arrangements must be in place for the delivery of medication to the patient by the mental health service, and for monitoring of concordance, effect and side-effects. Medication cannot be delivered to the GP surgery for the patient to collect during the 1st 18 weeks of treatment.

9. Information for Patients

9.1 All patients should be provided with a Clozapine Patient Information leaflet which should be explained to them by a nurse, doctor or pharmacist. These leaflets are available via http://patient.info/medicine/clozapine-clozaril-denzapine-zaponex

9.2 There is a DVD titled “A Journey into Light”. These can be obtained from CPMS (tel. 0845 769 8269) or there may be copies available from the Clinical Pharmacy Team (tel. 01752 439006).

9.3 All patients should be offered the opportunity to meet with a specialist mental health pharmacist which can be arranged via the ward / unit or by calling the Clinical Pharmacy Team.

Remember that the patient may not be able to understand and retain information at the point of starting clozapine It may be necessary to re-discuss the information once the patient is stable on clozapine.

10. Prescribing Clozapine

10.1 Writing Prescriptions

10.1.1 Clozapine can only be prescribed by doctors and dispensed by pharmacists who are registered with **CPMS (or DMS for suspension)**. Within the South and West Devon Formulary it is listed as a “hospital only drug” and can therefore only be prescribed by psychiatrists and within the Plymouth area only be dispensed by LSW pharmacy (areas outside of Plymouth e.g. falling under Devon Partnership Trust will be supplied by Derriford Hospital pharmacy).

10.1.2 When Clozapine treatment is first initiated the dose must be started low and gradually increased over 3 to 4 weeks to reduce the risk of side-effects. During this titration phase the prescription should be written using the **Standard Regimen for Inpatient Clozapine Titration which** is provided in Appendix 1 and should be completed in the titration section of the mental health in-patient prescription chart. The whole of the prescription chart must be faxed to LSW

Pharmacy (01752 430910 or internal 30910) for the attention of the clozapine technician **at least 24 hours before the first dose is due.**

10.1.3 Once a maintenance dose of clozapine is reached, the prescription should be written on either a mental health in-patient drug chart (for wards / units where these are used) or a **Clozapine Maintenance Prescription Form** (See Appendix 2). Prescription forms must be faxed to LSW Pharmacy by the end of the Tuesday of the dispensing week at the latest.

10.1.4 A **Clozapine Maintenance Prescription** is valid for a maximum of six dispensings (initial dispensing followed by five repeats). A new prescription must be written and faxed to LSW Pharmacy once this limit is reached.

10.1.5 A new **Clozapine Maintenance Prescription** must be written when a patient moves to the care of a new consultant or team.

10.2 Switching from other antipsychotics

10.2.1 The individual circumstances should be considered when switching a patient to clozapine from another antipsychotic. This will include:

- The patient's mental state
- Drug interactions
- Additive side-effects

10.2.2 Oral sertindole, pimozide and ziprasidone must be stopped before starting clozapine.[5]

10.2.3 In general other oral antipsychotics can be cautiously cross tapered with clozapine.

10.2.4 For patients on depots the depot must be stopped and the clozapine titration should start the day the next depot would have been due.

10.2.5 Risperidone Long Acting Injection should be stopped 4-6 weeks before clozapine is started (if necessary oral risperidone can be used to "bridge"). This recommendation is based on the fact that therapeutic blood levels of risperidone are maintained for 4-6 weeks after the last injection[9.]

10.2.6 The aim should ultimately be for antipsychotic monotherapy apart from in exceptional cases where clozapine monotherapy has not been successful and a therapeutic trial of augmentation with a second antipsychotic is justified (see ref 5 p. 66-67).

10.3 Dose / initiating clozapine - Treatment resistant schizophrenia

10.3.1 In-patients (see appendix 1): Start with 12.5mg given once on the first day, then increase slowly in increments of 25 to 50 mg to a dose of up to 300 mg/day within 2 to 3 weeks. Thereafter, if required, the daily dose may be increased in increments of 50 to 100 mg at half-weekly or, preferably, weekly intervals. In most patients, antipsychotic efficacy can be expected with 200 to 450 mg/day given in divided doses.

10.3.2 **Outpatient Initiation:** a slower titration dose to that normally used for in-patient initiation should be used. The dosing schedule should be tailored to the individual circumstances, to include first dose in hospital with 6 hourly monitoring, then the patient to be seen once or twice daily.

Dosage increases should not be made at weekends unless there is the same service support as on weekdays. A once daily dose may be used for the first week, changing to twice daily in the second week if this is preferable. The patient must been seen twice a day (or for each dose) during the titration phase.

10.3.3 The following are suggested target doses following the initial titration:

Female non-smokers: 250mg /day
Female smokers: 450mg / day
Male non-smokers: 350mg / day
Male smokers: 550mg / day

10.3.4 There is substantial individual variation and the dose should be guided based on response and side-effects.

10.3.5 To obtain full therapeutic benefit, a few patients may require larger doses (the maximum dose 900 mg/day).

10.3.6 The total daily dose should be given as two divided doses, with a larger proportion in the evening if sedation is a problem.

10.3.7 Daily doses of up to 200mg may be given once a day in the evening.

10.4 Use in the elderly:

Start with 12.5 mg given once on the first day, with subsequent dose increments restricted to 25 mg/day.

10.5 Psychotic disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed[1, 5]:

The starting dose is recommended to be 6.25mg (1/4 tablet) and must not exceed 12.5 mg/day taken in the evening. Subsequent dose increases must be by 12.5 mg increments, with a usual maintenance dose of 25mg daily. The maximum dose is 50 mg daily and should not be attained until at least the end of week 2. If a dose of 50 mg, given for at least one week, fails to provide a satisfactory therapeutic response, dosage may be cautiously increased by increments of 12.5 mg/week. The absolute maximum dose of 100 mg/day must never be exceeded.

11. Monitoring of Physical Health

11.1 During initiation the following physical observations should be made:

- Blood pressure lying down
- Blood pressure standing up
- Pulse
- Temperature

11.2 Frequency

- 1st day of clozapine treatment: Before administering the first dose and then hourly for 6 hours following the first dose check:
- Days 2-14 of clozapine titration check twice a day:

- Day 14 onwards check on alternate days until stable dose reached
- Subsequently at time of blood monitoring

11.3 The prescriber should be informed if the following are observed:

- Postural drop of >30mm/Hg
- Pulse >100bpm
- Temperature >38˚C
- Over-sedation
- Other intolerable adverse effects

11.4 The following monitoring is also recommended (after baseline measurements):

- Weight, BMI and waist circumference, lipids and glucose: baseline, then 3 monthly for 1st year, then yearly thereafter.
- Hyperglycaemia should be managed but where the active medical management of this fails discontinuation of clozapine should be considered.
- Liver function tests: baseline, 4-6months, 12 months. If LFTs rise to >3 time the upper limit of normal then clozapine should be stopped and clozapine only restarted once LFTs are normal. In such cases LFTs should be closely monitored.

12. Clozapine Plasma Level Monitoring

12.1 Clozapine Plasma Levels can be useful for determining recent compliance or for optimising treatment (if a patient is experiencing side-effects or a lack of efficacy). Plasma levels will be monitored by mental health services only. A charge is made for plasma level monitoring and will be invoiced directly to the requesting unit.

12.2 Use the same blood-taking equipment that is supplied for the white blood cell count. However, the samples for plasma levels are sent to KingsPath (not CPMS) - request forms and pre-paid envelopes are available from CPMS and can be requested from LSW pharmacy team members. Please note this cannot be processed at Derriford Combined labs.

12.3 A trough plasma level should be taken (i.e. immediately before the next dose is due) and information included on the request form as to the dose of clozapine prescribed and when the last dose was taken.

12.4 Clozapine takes 2-3 days to reach steady state so samples for assessing plasma levels should not been taken until day 4 of a stable dose.

12.5 A plasma level of 350 microgram / L should be aimed for to ensure an adequate trial, but some patients will respond with a lower plasma level, and others may require a higher plasma level (up to 500 microgram / L).

12.6 Results should be available via Kingspath online results service within 1-2 days of sample receipt. Email pathologyi.t@kch.nhs.uk to register.

12.7 Results include clozapine and norclozapine (the active metabolite of clozapine) levels. The significance of norclozapine is unclear but the ratio of clozapine / norclozapine may aid the assessment of recent compliance[5.]

12.8 Many side-effects are related to the plasma level.

13. Treatment Breaks or Stopping Clozapine

13.1 If, at any point during their treatment, there is a treatment break for longer than 48 hours, the Clozapine must be re-introduced at a lower dose and gradually increased back to the treatment dose. **The patient must not re-start their Clozapine at the previous dose.**

13.2 Mental Health Services must inform:

- the Clozapine Technician (by telephone)
- CPMS (or DMS for suspension)
- GP Practice (if involved).

13.3 **Table of dosing and monitoring following treatment breaks[2]**

Note: The table below is based on the advice from CPMS. For patients using DMS the advice differs slightly.

Duration of treatment break	**Dosing**	**Monitoring**	
		Weekly	**2 weekly or 4 weekly**
< 48 hours	Continue with prescribed dose	Continue with normal monitoring schedule	Continue with normal monitoring schedule
> 48 hours <4 whole days	Re-titration required*	Continue with normal monitoring schedule	Continue with normal monitoring schedule
> 48 hours < 7 days	Re-titration required*	Continue with normal monitoring schedule	Weekly for 6 weeks then back to previous monitoring frequency
> 7 days < 28 days	Full re-titration required	Re-start 18 weeks of weekly monitoring	Weekly for 6 weeks then back to previous monitoring frequency
28 days or more	Full re-titration required	Re-start 18 weeks of weekly monitoring	Re-start 18 weeks of weekly monitoring

* Start at 12.5mg once or twice on the first day. May be possible to re-titrate at faster rate than initial titration.

13.4 Stopping Clozapine

Except where the urgent cessation of clozapine is required (see above), it is recommended that clozapine is gradually withdrawn (slow taper down over 3 weeks) to reduce the risk of withdrawal reactions (e.g. recurrence of psychotic symptoms and cholinergic rebound)[5].

14. Taking Blood Samples

14.1 Blood sampling equipment is provided by CPMS / DMS (including pre-paid envelopes for posting blood samples directly to CPMS / DMS). The cost for this service is included in the contract price for Clozaril® / Denzapine® and should be used under normal circumstances.

14.2 In an emergency (i.e. if the blood sample will not reach CPMS / DMS in time by 1st class post) or under other circumstances (after discussion with the Clozapine Pharmacy Technician) blood samples can be sent to Derriford Combined Labs but this will incur the usual charge and will increase pharmacy time in chasing-up the results for CPMS. **The Clozapine Pharmacy**

Technician must be informed if the blood sample has been sent to Derriford Combined Labs. The clozapine technician will need to check the Derriford combined labs results system and enter the full blood count results into the CPMS / DMS system.

14.3 If the GP Practice has agreed to take blood samples, their details will be registered with CPMS / DMS by the Psychiatrist. They will then receive an Information Pack and blood sampling equipment (including pre-paid envelopes for posting blood samples to CPMS /DMS). The GP Practice will also be alerted if a RED blood result is received (in addition to the Psychiatrist and Clozapine Pharmacy Technician). It is the responsibility of the Psychiatrist to take the appropriate action necessary following a red blood result.

14.4 CPMS / DMS will advise both the prescriber and the Clozapine Pharmacy Technician when monitoring frequency changes. The prescriber should inform the Care Co-ordinator (or designated person), and the GP Practice if involved.

14.5 Blood samples should be taken according to the following schedule:
NB: GP Practice staff should not be expected to take blood samples at weekends

Frequency of blood monitoring	**Weekly**	**2 weekly**		**4 weekly**			
Week of cycle:	**Week 1-4**	**Week 1**	**Week 2**	**Week 1**	**Week 2**	**Week 3**	**Week 4**
Sunday							
Monday			} Blood			} Blood	
Tuesday	Blood sample taken		sample taken			sample taken	
Wednesday							
Thursday / Friday	Dispense one week's supply of medication		Dispense two week's supply of medication				Dispense four week's supply of medication
Friday / Saturday	Start new supply of medication		Start new supply of medication				Start new supply of medication

15. Notification from CPMS / DMS of late/missed blood test or amber/red alert

15.1 If a blood test is not registered on the CPMS / DMS system by the due date, CPMS / DMS will fax an "Overdue Notification" to the consultant registered with CPMS for that patient, and also to LSW Pharmacy and the patient's GP (if they are registered as the blood sampling site with CPMS / DMS). The fax will inform them of the last date on which the patient can take Clozapine unless a blood test result is sent to CPMS.

15.2 If a blood test is still not registered on the CPMS / DMS system then a "Clozapine Prohibited" notice will be faxed on the last day that the patient is allowed to take Clozapine.

15.3 If the blood sample is sent to Derriford Combined Labs instead of CPMS / DMS, the Clozapine Pharmacy Technician has to look for the test result and manually enter the result on the CPMS system. The consultant should therefore check with the Clozapine Pharmacy Technician before acting on an alert.

Monitoring Frequency	Sample Due Day*	Overdue Notification Notification Alert faxed on this day	Maximum cover from date of last sample	Clozapine prohibited on day Notification Alert faxed on this day
WEEKLY	7	10	10	11
2-WEEKLY	14	20	21	22
4-WEEKLY	28	36	42	43
Status on CPMS / DMS	ACTIVE	ACTIVE	ACTIVE	PROHIBITED

* assumes 1st sample taken on day 0.

15.4 If an amber or red test result is registered on the CPMS / DMS system an alert will be faxed to the consultant registered with CPMS /DMS for that patient, and also to LSW Pharmacy and the patient's GP (if they are registered as the blood sampling site with CPMS /DMS). The fax will inform the consultant of the action to be taken and the consultant must act immediately on this information.

15.5 It is very important that CPMS have the correct information registered for each so that the faxes are sent to the correct person. See Section 18.

16. Dispensing Clozapine

16.1 All Clozapine supplies for patients in Plymouth (under LSW mental health services) are dispensed by LSW pharmacy based at the Glenbourne unit. Patients falling under other mental health services in the area (e.g. Devon Partnership Trust) will be supplied via Derriford Hospital pharmacy.

16.2 The LSW pharmacy clozapine service is available Monday – Friday 9am-5pm, outside of these hours emergency supplies will be provided by Derriford Hospital pharmacy who can be contacted via Derriford Hospital switchboard.

16.3 Supplies are issued on a Friday (unless as agreed by prior arrangement with the Clozapine Pharmacy Technician) and are for a duration of one, two or four weeks corresponding to the blood monitoring frequency for the patient.

16.4 The patient can only receive medication if they have a current Green or Amber blood result registered on the CPMS or DMS computer system. **This blood result must be available to the Clozapine Pharmacy Technician by the Thursday before the medication is due at the very latest.** It is therefore extremely important that the blood test is taken in plenty of time taking account of the maximum validity (See Section 15.3). If there is going to be a problem obtaining a blood result in time, the patient's Care Co-ordinator (or designated person) or Psychiatrist must be contacted for advice.

16.5 In general clozapine will be supplied as 25mg and 100mg tablets. If a liquid is required this should be obtained as Denzapine® suspension 50mg / ml, this product is supplied with 1ml and 10ml oral syringes (1ml syringe for doses of 50mg or less, 10ml syringe for higher doses). The patient and prescriber will need to be registered with DMS.

16.6 Clozapine tablets will normally be dispensed in cartons. If a compliance aid is required then pharmacy should be contacted to discuss the most suitable options. The majority of patients will be supplied with a sealed Venalink® blister pack.

16.7 For patients using Medidose boxes empty devices can be sent back to LSW Pharmacy for re-filling via the internal post (N.B. they must be empty of all medication). If the Medidose is not returned or not returned in a reusable condition, the unit/team will be charged for a new Medidose.

17. Control of Clozapine Supplies

17.1 Clozapine can be a dangerous drug if taken incorrectly. There is a particular risk:

- In clozapine-naive persons
- When taken in a standard dose following a treatment break of longer than 48 hours
- When taken by a person with low WBC or ANC
- If taken in overdose

17.2 **Clozapine supplies must only be used for the person for whom they have been dispensed.** In addition, they must only be used by that person during the treatment period for which they have been dispensed (unless otherwise directed by the Clozapine Pharmacy Technician).

17.3 **If there is any medication left unused at the end of a treatment period, or any excess medication found (e.g. at a patient's home, on an inpatient unit, at a GP Practice etc.) it must be returned to the Clozapine Pharmacy Technician for disposal. This is to reduce the risk of misuse or overdose.**

17.4 If a patient is short of medication the Clozapine Pharmacy Technician must be contacted for advice.

18. Change of Patient Details

18.1 It is very important that both CPMS and the Clozapine Pharmacy Technician are informed if a patient changes any of their personal details or changes Consultant, GP, Care Co-ordinator (or designated person) or Mental Health Team. This includes discharge from, or transfer between, a ward or inpatient unit. When appropriate a new clozapine maintenance prescription must be written (see section 10).

18.2 If the patient has been having blood tests or collecting medication from their GP Practice the Care Co-ordinator (or designated person) must be informed if the patient transfers to a new Practice. This is the responsibility of both the current Practice and the new Practice as it is not always a planned process. The Care Co-ordinator (or designated person) should inform all necessary persons (see above) of the change.

18.3 The patient should also be made aware of the need to inform their Care Co-ordinator (or designated person) if they change any of their personal details or move to a new GP Practice.

19. Glossary

ANC	Absolute Neutrophil Count
BMI	Body Mass Index (weight in kg / height in metres squared)
BNF	British National Formulary
CPMS	Clozapine Patient Monitoring Service – provides mandatory monitoring for patients prescribed Clozapine tablets
CYP1A2	Cytochrome P450 enzyme mainly responsible for metabolising clozapine in the liver.
DMS	Denzapine Monitoring Service – mandatory monitoring for patients prescribed clozapine suspension.
HTT	Home Treatment Team
ICP	Integrated Care Pathway
LSW	Livewell Southwest
QTc interval	The corrected QT interval in the electrocardiogram. When extended in carries a risk of ventricular arrhythmias and torsaides de pointes
SPC	Summary of Product Characteristics. Contains prescribing and safety information for each licensed drug. Produced by the drug manufacturer. Available online at medicines.org.uk
WBC	White Blood cell Count

Approval by Medicines Governance Group (MGG)

Chief Pharmacist (Chair of MGG)

Name: Steve Cooke

Signature:…

Date: 20th November 2015

Final Approval by Livewell Southwest

Director of Professional Practice, Safety and Quality

Name: Geoff Baines

Signature

Date: 30th November 2015

Appendix 1

Standard Regimen for Inpatient Clozapine Titration

CLOZAPINE ORAL TABLETS / ORAL SUSPENSION (50mg / ml)*

Week No. 1	Time	Dose	mls susp	Week No.2	Time	Dose	mls susp
Day 1	0800	12.5mg	0.25	Day 1	0800	75mg	1.5
	(Test dose)				2200	100mg	2.0
Day 2	0800	12.5mg	0.25	Day 2	0800	100mg	2.0
	2200	12.5mg	0.25		2200	100mg	2.0
Day 3	0800	25mg	0.5	Day 3	0800	100mg	2.0
	2200	25mg	0.5		2200	125mg	2.5
Day 4	0800	25mg	0.5	Day 4	0800	100mg	2.0
	2200	50mg	1.0		2200	150mg	3.0
Day 5	0800	50mg	1.0	Day 5	0800	100mg	2.0
	2200	50mg	1.0		2200	175mg	3.5
Day 6	0800	50mg	1.0	Day 6	0800	100mg	2.0
	2200	75mg	1.5		2200	200mg	4.0
Day 7	0800	50mg	1.0	Day 7	0800	100mg	2.0
	2200	100mg	2.0		2200	200mg	4.0

*Clozapine suspension (Denzapine®) is presented as 50mg / ml (12.5mg / 0.25ml) suspension in 100ml bottles. A 1ml and a 10ml oral syringe are provided. For doses up to and including 50mg the 1ml syringe should be used. For doses over 50mg the 10.0ml syringe should be used.

Complete the Clozapine initiation page contained within the mental health prescription chart. Send or fax the whole of the prescription chart to LSW Pharmacy 430910 (internal 30910).

Appendix 2

Maintenance Clozapine Prescription

Name…… Address…… …… Hospital No……DoB ……. NHS Number…….. CPMS / DMS No……. Care Co-ordinator, if known (or designated person)…….. Mental Health Team:…….. Consultant……...	Dispensing week (pharmacy to complete): Monitoring Frequency (please circle): Weekly / 2-weekly / 4-weekly Compliance aid required (please circle): Yes / No (For new patients requiring a compliance aid please contact the pharmacy clozapine team (4)39006 to discuss requirements) Delivery Location:
PLEASE SUPPLY A NEW PRESCRIPTION WHEN DOSE(S)/DRUGS CHANGE SEND PRESCRIPTION TO LSW PHARMACY, KEEPING A COPY FOR PATIENT'S NOTES ALL PRESCRIPTIONS ARE VALID FOR 6 DISPENSINGS UNLESS OTHERWISE SPECIFIED.	
Quantity required (as per blood sampling frequency) (please circle) one week two weeks four weeks	
Repeat dispensing (please circle) **0 1 2 3 4 5**	

Code	Drug Name	Tablets/ susp	Dose	Frequency (times if Medidose)	Duration (if appropriate)	Prescriber's Initials
A	**CLOZAPINE**					
B	**CLOZAPINE**					
C						
D						
E						
F						
G						

Prescriber's Signature ……..Date…… Unit……..……

Print Name…….. ***Contact Number ……***

Pharmacy Use:

1st Disp. Date……. Quantity: Disp. by: Check by:	2nd Disp. Date…… Quantity: Disp. by: Check by:	3rd Disp. Date…….. Quantity: Disp. by: Check by:
4th Disp. Date……. Quantity: Disp. by: Check by:	5th Disp. Date……. Quantity: Disp. by: Check by:	6th Disp. Date……. Quantity: Disp. by: Check by:

Facsimile Transmission

Clozapine
For Urgent Attention

From: **Name** **Address** **Tel. No.** **Fax No.**	**To:** **Name** **Address** **Fax. No.**

Information for IMMEDIATE ATTENTION:

Number of pages (including this sheet):

Team Address

GP Practice Address

Dear

Re: Patient name
Date of Birth NHS Number

The above patient, who is registered with your Practice, is to be started on treatment with the antipsychotic Clozapine which requires regular blood monitoring for white blood cell count and absolute neutrophil count. He/she would find it helpful to be able to attend your GP Practice for the following:

a. ***To have regular blood samples taken** (The frequency is weekly for the first 18 weeks, then every two weeks for the next 34 weeks, then monthly thereafter. Equipment and pre-paid envelopes will be supplied, and Mental Health Services will inform you when the frequency changes).

b. ***To collect their Clozapine supplies** (this can only start when the patient is on 2-weekly blood monitoring. Clozapine dispensed for the patient will be sent to your Practice from LSW Pharmacy and will correspond to the blood monitoring frequency).

***Delete as applicable**

We are writing to request whether you would be happy to be involved in this way. We have enclosed Information on Clozapine, a Clozapine Agreement Form and two flow diagrams detailing the process.

If you are happy to be involved please would you complete the Agreement Form and return it to the address above.

The following people can be contacted if you wish to discuss this or have any concerns:

Psychiatrist		Tel.
Care Co-ordinator (or designated contact)		Tel.

Yours faithfully,

Appendix 5

Information on Clozapine Blood Monitoring and Issue of Medication for GP Practice Staff

Clozapine is an atypical antipsychotic that was first introduced in the 1960's. It has been shown to be **very effective** for schizophrenia, including that unresponsive to other antipsychotics, but was withdrawn from the UK market in the 1970's following fatal cases of agranulocytosis. It was re-introduced in the late 1980's but can only be used under the following conditions:

- Prescribed only for treatment resistant schizophrenia (or psychotic disorders occurring during the course of Parkinson's disease), in cases where standard treatment has failed
- Patients must be registered with the Clozaril Patient Monitoring Service (CPMS) or Denzapine® Monitoring Service (DMS) for clozapine suspension.
- Patients must have regular monitoring of white blood cell count and absolute neutrophil count at designated frequencies
- Prescribers and dispensing pharmacists must be registered with CPMS / DMS (**within Plymouth Area this means prescribed by psychiatrists and dispensed by LSW pharmacy** – GPs will not be able to prescribe Clozapine)

Mental Health Services in Plymouth are keen to make Clozapine as accessible to patients as possible. For some patients allowing them to attend their GP Practice for blood tests and/or for collecting their Clozapine supplies can have a positive effect on the patient's compliance with treatment.

However, there are risks to taking Clozapine and it is important that GP Practice staff are aware of these risks and are willing, and adequately supported, to take on this role. With this in mind the following conditions have been imposed:

- GP Practice staff must only be involved with their prior agreement and an Agreement Form must be completed for each patient detailing roles and responsibilities of both GP Practice Staff and Mental Health Staff
- The patient should have a named Care Co-ordinator, or designated person, whom the GP Practice can contact to discuss any concerns. Names and contact details of mental health staff will be included on the GP Agreement Form
- Patients will not be allowed to collect their Clozapine supplies from the GP Practice during the first 18 weeks of treatment. Mental Health Staff will have to make arrangements for the supply of medication to the patient during this time
- During the first 18 weeks of treatment the patient may attend their GP Practice for blood tests but their Care Co-ordinator (or designated person) must remain in close contact with the patient and GP Practice to ensure that the patient attends, and intervene where necessary
- GP Practice Staff must follow the procedures for blood monitoring and collection of Clozapine supplies (see Clozapine Policy for Mental Health Staff and GP Practice Staff)
- GP Practice staff must inform the Care Co-ordinator (or designated person) if there are concerns with the patient or the patient does not collect their Clozapine

If a GP Practice agrees to be involved in the blood monitoring and/or issue of medication for a patient, the following form must be completed (one for each patient). This form can be separated from the main body of the guideline but a copy of the complete guideline must be available at the GP Practice for information.
The full version of the LSW "Clozapine Policy for Mental Health Staff and GP Practice Staff" is available on the Livewell Southwest Website and on LSWnet (under Policies and Procedures)

Appendix 6

Clozapine Agreement Form between Mental Health Services and GP Practice Staff

Patient Details

Patient Name		Date of Birth
NHS number	CPMS / DMS Number	Hospital Number

GP Practice Details

Surgery Name & Address Tel. No.	GP Name Practice Manager

Roles and Responsibilities of GP Practice Staff

GP Practice Staff agree to undertake the following:

Taking Blood Samples YES / NO Start Date ……	Arranging appointments with the patient Taking blood samples in a timely manner and in accordance with CPMS / DMS guidelines (See Section 14 in main body of Policy for information on blood tests)
Issuing Clozapine Supplies to patient after the first 18 weeks of treatment* YES / NO Start Date ……..	Accepting delivery of the patient's Clozapine supplies from Derriford Pharmacy. Storing the medication in a secure place (preferably a locked cupboard) while waiting collection by the patient Issuing each supply to the patient for the corresponding treatment period only (as stated on the pack) Alerting the Care Co-ordinator (or designated person) if the patient does not collect the Clozapine supply during the treatment period. Returning uncollected supplies to the Clozapine Pharmacy Technician (telephone first) ***The patient will NOT be allowed to collect their medication from the GP surgery during the first 18 weeks of treatment**
Other responsibilities	It is good practice for the GP Practice to include clozapine on the patient medication record for information and appropriate alerts. Inform the Care Co-ordinator (or designated person) if the patient transfers to another GP Practice

Issuing Clozapine Supplies to the Patient

Clozapine supplies will be received in a brown bag, labelled as below:

Patient Name Treatment Issue Date……	If not collected by …….. do not issue to patient. Contact Care Co-ordinator (or designated person) URGENTLY.

The supply must only be issued to the patient before the "If not collected by" date stated on the label. If the supply has not been collected the Care Co-ordinator (or designated person) must be contacted urgently. They will advise on the action to be taken. If the Care Co-ordinator cannot be contacted then an urgent referral should be made to Mental Health Matters (Tel 0300 330 5476).

Patient Name	**NHS Number**	**CPMS / DMS Number**

Responsibilities of Mental Health Staff

	Responsibility
Psychiatrist Name Team Contact number	Registration of self and patient with CPMS / DMS. Arranging initial blood test and physical check (including ECG). Liaising with patient and GP Practice concerning any blood frequency changes. Taking appropriate action on red or amber blood results. Taking action on information from CPMS / DMS concerning overdue blood tests. Prescribing Clozapine. Prescribing any dose changes and letting relevant people know. Monitoring patient's mental health. Updating patient information with CPMS / DMS and the Clozapine Pharmacy Technician
Care Co-ordinator or designated person Name Team Contact number	Monitoring patient's mental health. Arranging supply of Clozapine to the patient during the first 18 weeks of treatment. Encouraging patient to attend for blood tests at the required time. Liaising with GP practice to ensure patient's compliance with medication and arrangements for blood tests and collecting medication. Collecting unused Clozapine supplies from patient's home and arranging return to pharmacy. Informing the Clozapine Pharmacy Technician and psychiatrist if the patient stops taking their medication. Informing the GP Practice and Clozapine Pharmacy Technician if there is a change of Care Co-ordinator (or designated person) or psychiatrist
Clozapine Pharmacy Team Contact number **01752 439006**	Checking blood status on CPMS / DMS. Informing Care Co-ordinator (or designated person) or GP Practice if blood test is overdue or extra tests are required Dispensing Clozapine and arranging delivery to GP Practice. Liaising with GP practice and mental health staff. Arranging destruction of returned Clozapine. Advice and support to Mental Health Staff and GP Practice staff as required.
Derriford Pharmacy On call service Contact via **Derriford Hospital switchboard.**	Emergency contact out of hours (evenings or weekends) for urgent clinical or supply queries.

Support for GP Practice Staff

GP Practice Staff can contact any of the staff detailed above for help and advice on Clozapine.

Signed on behalf of GP Practice
(by Clinical Governance or Prescribing Lead)

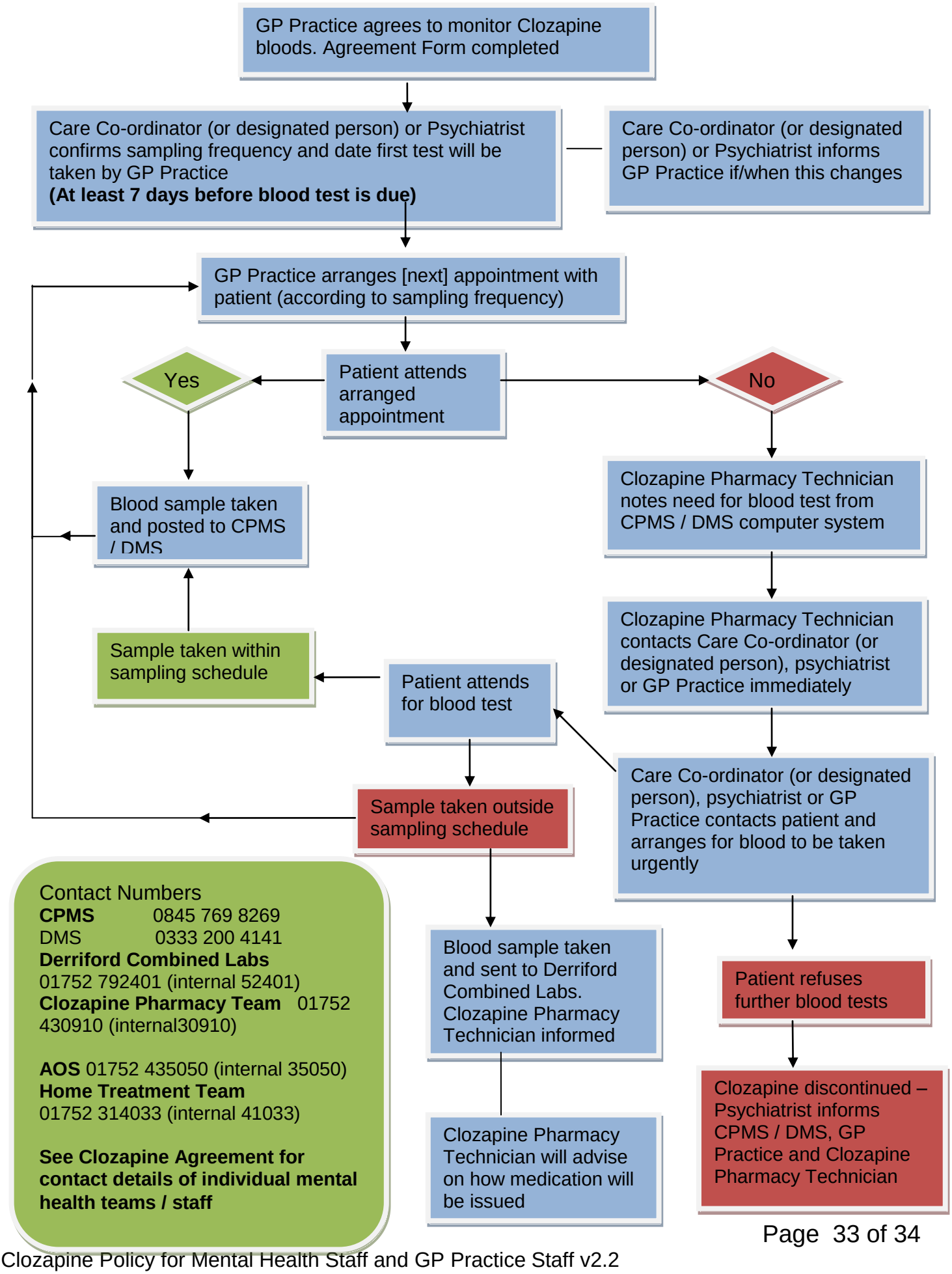
Signed…… Date……
Name……
Designation……

Signed on behalf of Mental Health Services
(by psychiatrist or Care Co-ordinator)

Signed…… Date……
Name……
Designation……..

Once completed, the original document should be stored in the patient's current hospital Mental Health notes. In addition, one copy should be kept by the GP Practice and one copy sent / faxed to the Clozapine Pharmacy Technician (Fax 01752 430910)

GP Blood Tests for Clozapine Patients



GP Clozapine Supplies for Patients