Clozapine Policy

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Author:	Dr Adnan Sharaf, Consultant Psychiatrist	
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The latest approved version of this document is online.
If the review date has passed, please contact the Author for advice.

Powys Teaching Health Board is the operational name of Powys Teaching Local Health Board
Bwrdd Iechyd Addysgu Powys yw enw gweithredol Bwrdd Iechyd Lleol Addysgu Powys

Version Control

Version	Summary of Changes/Amendments	Issue Date
1	Initial Issue	07/08/2024

Engagement & Consultation

Key Individuals/Groups Involved in Developing this Document

Role / Designation
Dr Adnan Sharaf – Consultant Psychiatrist

Circulated to the Following for Consultation

Date	Role / Designation
12/09/2023	Assistant Director of Mental Health and LD Services
12/09/2023	Head of Mental Health Operations
12/09/2023	Head of Mental Health Nursing, Quality and Safety
12/09/2023	Senior Nurse Managers
12/09/2023	Clinical Lead for Quality and Safety
12/09/2023	Consultant Psychiatrists
12/09/2023	Advanced Nurse Practitioners
10/10/2023	Service User
10/10/2023	Service User's relative

Evidence Base
Please list any National Guidelines, Legislation or Health and Care Standards relating to this subject area? https://www.nice.org.uk/guidance/qs80/chapter/quality-statement-4-treatment-with-clozapine https://www.nice.org.uk/guidance/ng71/chapter/Recommendations#pharmacological-management-of-non-motor-symptoms_section 1.5.17 https://www.nice.org.uk/guidance/cg178

Impact Assessments

Equality Impact Assessment Summary					
	No impact	**Adverse**	**Differentia**	**Positive**	**Statement** The aim of this policy is to allow effective treatment of psychosis with clozapine, in a safe manner which minimizes risks.
Age	x				
Disability				x	
Gender reassignment	x				
Pregnancy and maternity	x				
Race	x				
Religion/ Belief	x				
Sex	x				
Sexual Orientation	x				
Marriage and civil partnership	x				
Welsh Language	x				
Human Rights	x				

Risk Assessment Summary

Have you identified any risks arising from the implementation of this policy / procedure / written control document?

Clozapine is a drug associated with a number of side effects and risks. There is a risk to every individual who takes it. That risk is minimized by the use of the Zaponex Treatment Access System (ZTAS), as well as the input of the clinical teams to ensure adequate physical monitoring.

Have you identified any Information Governance issues arising from the implementation of this policy / procedure / written control document?

No

Have you identified any training and / or resource implications as a result of implementing this?

Any staff who are not familiar with clozapine but who are involved in the application of this policy will need to undergo appropriate training. Suitably equipped clinic space for physical health monitoring is essential.

1 - Policy Statement / Introduction

This document sets out the criteria to be followed by Powys Teaching Health Board (PTHB) staff for the prescribing, administration and monitoring of clozapine. PTHB strives for safe, effective prescribing and monitoring of medicines as an important means of maintaining patient safety. This document provides guidance for the use of clozapine in line with NICE quality statement 80:

Clozapine is the only drug with established efficacy in reducing symptoms and the risk of relapse for adults with treatment-resistant schizophrenia. It is licensed only for use in service users whose schizophrenia has not responded to, or who are intolerant of, conventional antipsychotic drugs.[1]

This document also provides guidance for the use of clozapine to treat psychosis in Parkinson's disease in line with NG71 to offer clozapine *to treat hallucinations and delusions in people with Parkinson's disease.*[2]

2 – Objectives

This document aims to guide staff in the safe initiation and maintenance of clozapine for inpatients and for long-term monitoring post-discharge.

This policy is intended to be read and applied by all staff who are involved in the prescribing, administration, monitoring and dispensing of clozapine.

3 – Definitions

- **CBT –** Cognitive Behavioural Therapy
- **CC –** Care Co-ordinator
- **CMHT –** Community Mental Health Team
- **CNS –** Central Nervous System
- **CPN –** Community Psychiatric Nurse
- **CTP –** Care and Treatment Plan
- **FBC –** Full Blood Count
- **PTHB** – Powys Teaching Health Board
- **SPC** – Summary of Product Characteristics
- **WARRN** – Wales Applied Risk Research Network
- **WCCIS** – Welsh Community Care Information System
- **ZTAS** – Zaponex Treatment Access Service

4 – Responsibilities

4.1 - Consultant Psychiatrist

- Be registered with the ZTAS.
- Be knowledgeable of the most up-to-date evidence regarding use of clozapine.
- Evaluate the risks and benefits on a case-by-case basis.

[1] https://www.nice.org.uk/guidance/qs80/chapter/quality-statement-4-treatment-with-clozapine

[2] https://www.nice.org.uk/guidance/ng71/chapter/Recommendations#pharmacological-management-of-non-motor-symptoms section 1.5.17

- Ensure (or delegate appropriately to a suitably qualified colleague) the patient is registered with the ZTAS.
- Ensure (or delegate appropriately to a suitably qualified colleague) that a full medical history has been taken, inclusive of treatment history and potential contra-indications to clozapine.
- Ensure (or delegate appropriately to a suitably qualified colleague) that baseline investigations have been carried out and are satisfactory prior to starting clozapine.
- Prescribe clozapine according to these guidelines.
- Ensure all red or amber results are communicated to the patient and team and acted upon.
- Monitor the patient's physical and mental health.
- Ensure a high standard of communication with the General Practitioner and in/out-patient teams. (see Appendix 1 and 2)
- Liaise with ZTAS as needed.

4.2 - Pharmacy Staff

- Timely dispensing of clozapine.
- Liaise with ZTAS as needed.
- Liaise with nursing and medical teams as appropriate.

4.3 - Nursing Staff/Care Co-ordinator

- Inpatient nurses should liaise with the Care Co-ordinator to arrange community follow-up and monitoring.The Care-Coordinator should be a member of the nursing staff in the vast majority of cases. There will be some situations (e.g. those who are conditionally discharged with a social supervisor) where deviations from this are needed. In those situations, the reasons for a non-CPN Care Co-ordinator must be clearly defined and recorded in the records. The person's Care Plan must clearly set out how the Care Coordinator will work jointly with a CPN including in the event of any concerns.
- Ensure the patient attends for blood monitoring.
- Monitor the patient's physical and mental health.
- Report any concerns to the Consultant.
- Ensure there is a valid prescription for clozapine, up to date CTP (which includes clear reference to the use of clozapine) and WARRN.

5 - Standards for Prescribing

The licensed indications for clozapine[3] are:

- Schizophrenia in patients unresponsive to, or intolerant of conventional anti-psychotic drugs.
- Psychosis in Parkinson's disease.

For those patients with schizophrenia who have not responded to conventional treatment, the following interventions should occur[4]:

[3] https://bnf.nice.org.uk/drug/clozapine.html

[4] https://www.nice.org.uk/guidance/cg178/chapter/1-Recommendations#subsequent-acute-episodes-of-psychosis-or-schizophrenia-and-referral-in-crisis-2 section 1.5.7.1

- Review the diagnosis.
- Establish that there has been adherence to anti-psychotic medication, prescribed at an adequate dose and for the correct duration.
- Review engagement with and use of psychological treatments and ensure that these have been offered according to this guideline. If family intervention has been undertaken, suggest CBT; if CBT has been undertaken, suggest family intervention for people in close contact with their families.
- Consider other causes of non-response, such as comorbid substance misuse (including alcohol), the concurrent use of other prescribed medication or physical illness.

Lack of response to conventional treatment is defined as [patients whose illness has not] *"responded adequately to treatment despite the sequential use of adequate doses of at least 2 different antipsychotic drugs. At least 1 of the drugs should be a non-clozapine second-generation antipsychotic*.[5]

	5.1 - Prescribing There are 3 brands of clozapine and their specific monitoring services in the UK: • The Zaponex Treatment Access System (ZTAS) monitors Zaponex©. • The Clozaril Patient Monitoring Service (CPMS) monitors Clozaril©. • The Denzapine Monitoring System (DMS) monitors Denzapine©. In PTHB Zaponex and the ZTAS are used. In the UK ZTAS is available 24 hours a day and can be contacted by telephone and/or email: Tel: (0207)365 58 42 Email: info@ztas.co.uk The initiation of clozapine in PTHB is restricted to consultant psychiatrists registered with the ZTAS. Nominated pharmacists and service users must also be registered. Registration forms are available on the ZTAS website[6]. All patients treated with clozapine must be under the care of a consultant psychiatrist. Prescribing responsibility must remain in secondary care and not be passed over the GP.
	5.2 - Consent Clozapine is usually given with informed consent of the service-user. The consent process must involve a discussion regarding side-effects and monitoring. For those detained under the Mental Health Act a valid consent to treatment form must be completed at the appropriate time.

[5] https://www.nice.org.uk/guidance/cg178/chapter/1-Recommendations#subsequent-acute-episodes-of-psychosis-or-schizophrenia-and-referral-in-crisis-2 section 1.5.7.2
[6] https://www.ztas.co.uk/

5.3 - Contra-Indications to Clozapine

The following are taken from the Zaponex© Summary of Product Characteristics (SPC)[7]:

- Hypersensitivity to the active substance or to any of the excipients, listed in section 6.1. (Section 6.1 lists the following: Lactose monohydrate, Povidone, Pregelatinized starch, Maize starch, Talc, Colloidal anhydrous silica, Magnesium stearate.)
- Patients unable to undergo regular blood tests.
- History of toxic or idiosyncratic granulocytopenia/agranulocytosis (with the exception of granulocytopenia / agranulocytosis from previous chemotherapy).
- History of clozapine-induced agranulocytosis.
- Impaired bone marrow function.
- 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; concomitant use of depot anti-psychotics is to be discouraged.

Clozapine treatment should not be started concurrently with substances known to cause agranulocytosis, i.e. bone marrow suppressants. **Please see Appendix 3.**

5.4 - Special Precautions for the Use of Clozapine

Refer to the SPC for a full set of special precautions in the use of clozapine.

- There are limited clinical data on exposed pregnancies. Caution should be exercised when prescribing to pregnant women. Prescription decisions should be made on an individual risk assessment.
- A withdrawal syndrome has been described in neonates exposed to clozapine in the third trimester. Consequently, newborns should be monitored carefully.
- Clozapine is excreted in breast milk and mothers receiving clozapine should not breast feed.
- In women of childbearing potential, a return to normal menstruation may occur as a result of switching from other anti-psychotics to clozapine. Care should be given to ensure contraception is discussed and adequate measures used if appropriate.

[7] https://www.medicines.org.uk/emc/medicine/30938#:~:text=The%20Zaponex%20Treatment%20Access%20System%20%28ZTAS%29%20was%20developed,suggests%20a%20mortality%20rate%20from%20agranulocytosis%20of%200.3%25.

- Use in the elderly requires a lower dose and a slower titration.
- The elderly are more susceptible to side effects.
- Smaller doses are needed to treat psychosis in Parkinson's disease.
- Patients with benign ethnic neutropenia should only be prescribed clozapine after consulting with a haematologist.
- Due to the risk of sedation and seizures, activities such as driving or operating heavy machinery should be avoided especially in the initiation period.

6 - Initiation of Clozapine Treatment

Clozapine is a complex treatment with significant side effects. It is beyond the scope of a policy to define which individual patients should and should not receive it. Each service user should be considered on an individual basis with a careful analysis of the risks and benefits. The decision to treat with clozapine should be made on an individual basis with the rationale for doing so, recorded in the patient records by the treating Consultant Psychiatrist. At this moment in time, community initiation is not available in PTHB.

The standards for community and in-patient safety and monitoring must be the same.

Prior to titration checks on physical health, safety criteria are mandatory. This can be facilitated using the Pre-initiation checklist which is seen at **Appendix 4**. This should be completed and recorded in the patient records.

There are 2 named dispensing pharmacies:
Primrose Pharmacy Talgarth – Serves Welshpool, Newtown and Ty Illtyd.

Prescriptions should be sent to:
Mr Stefan Fec, Pharmacist
Primrose Pharmacy
Garth House
High Street
Talgarth
Powys
LD3 0PF
Tel: 01874 712173
stefan.fec@wales.nhs.uk

Nevill Hall Hospital Pharmacy, ABUHB – Serves Felindre Ward, Clywedog Ward Ystradgynlais and the Hazels.

Prescriptions should be sent to:
Nevill Hall Hospital
Aneurin Bevan University Health Board
Brecon Road
Abergavenny
NP7 7EG
01873 732279
abb.mhhpharmacy@wales.nhs.uk

6.1 - Practicalities of Initiation

Initiation should start on a MONDAY. A green result must be obtained from ZTAS no more than 10 days before initiation begins.

On the first day observations should be taken
- Prior to the first dose
- 15 minutes after the first dose.
- Hourly for the first 6 hours.

Observations should be recorded on HB approved observations sheets and kept in the patient records.

The required observations are: lying and standing blood pressure, pulse and temperature. See **Appendix 5**

If observations are outside the following parameters, repeat them after 15 minutes.

Systolic blood pressure	<100mmHg or > 170mmHg
Diastolic blood pressure	<60mmHg or > 100mmHg
Pulse	>100bpm
Temperature	>38.4°C or <35.5°C

If still outside the above parameters, seek medical advice.

Refer to **APPENDIX 6** for the temperature advice algorithm.

Observations for subsequent doses:
Day 2-14: Observations as described above should be taken and recorded prior to the morning dose and 2 hours after the morning dose. A GASS monitoring form should be completed weekly. (**Appendix 7**)

Day 15-28: Observations as described above should be taken and recorded 2 hours after the morning dose.

Ongoing: Observations as described above and weight should be taken and recorded at the time of blood monitoring, i.e. in the clozapine clinic.

The rate of titration can vary and may reflect the degree of psychosis and the need for in-patient treatment. Reasons for varying the rate of titration should be clearly recorded in the patient records.

Most in-patients will be titrated using the regime and prescription chart in **Appendix 8**.

If a different titration regime is used, a non-standard prescription form is available in **Appendix 9**

These are signed by the prescriber and are sent to the pharmacy at:
Nevill Hall Hospital
Aneurin Bevan University Health Board

Brecon Road
Abergavenny
NP7 7EG

This is the registered pharmacy for in-patients and will have dispensing responsibilities.

The regime for treating psychosis in Parkinson's disease is available in **Appendix10** and is not variable in the first week. The prescription chart for psychosis in Parkinson's disease is available in **Appendix 11**.

The monitoring chart in **Appendix 5** should be used for both schizophrenia and for psychosis in Parkinson's disease.

When the patient is ready for discharge and is on a stable dose, responsibility for the monitoring will be handed over to the respective clozapine clinic and back to the CMHT.

7 - Clozapine Monitoring

Clozapine carries a well described risk of neutropenia and agranulocytosis.

Regular blood monitoring is a MANDATORY requirement for clozapine therapy. The purpose of this is to detect any haematological complications at an early stage and prevent service users developing serious and potentially life-threatening complications.

The service user must have a weekly full blood count for the first 18 weeks of treatment, then 2 weekly until the service user has been on clozapine for 1 year. After 1 year of treatment the service user can have a full blood count (FBC) every 4 weeks. The responsibility for this lies with the CMHT, and each CMHT must have arrangements in place for blood and physical health monitoring.

If a patient does not attend for their monitoring appointment, the Care Co-ordinator must be notified immediately.

If a patient has missed the regular day for their blood test and is close to being prohibited, a sample must be sent urgently to a local acute hospital laboratory. It is the responsibility of the community team to facilitate this if for out-patients or the inpatient team if still a ward patient. ZTAS must be updated with the result.

Results of the FBC must be uploaded to the ZTAS for a green/amber/red result to be generated.

Green Results:	OK to dispense and administer.
Amber Results:	Dispense and administer with caution. Twice weekly FBC until green (or red) result. Monitor Trends. Follow advice from ZTAS.
Red Result:	Stop clozapine immediately.

Remove all clozapine tablets from patient.
Contact ZTAS immediately.
Medical review of the patient is mandatory.
ZTAS will generate the details of the emergency procedure which must be followed.
Arrange daily FBC.
Arrange daily temp, BP and pulse.
Arrange for patient or carer to take temp at home if they feel unwell.
Instruct patient to report any symptoms suggestive of infections.
Consult a haematologist and/or physician if neutrophil count below 0.5 $x10^9$/L OR below 1.0 $x10^9$/L with a Temp > 38.5°C.

Service users should report to the hospital, the CMHT or their GP if they develop signs of infection or neutropenia. In these circumstances a full blood count should be arranged for URGENT analysis, the result of which should be discussed with the ZTAS. This discussion should take place as soon as the result is back and not wait until usual working hours.

Signs of infection/neutropenia include sore throat, temperature, mouth ulcers and unexplained bruising. Clinicians should have a low threshold for taking an urgent full blood count.

The following additional blood and physical health monitoring is required:

	Initial visit	4 wks	8 wks	12 wks	6 months	9 months	12 months	6 monthly thereafter	Annually thereafter
U&E	X						X		X
Fasting lipids	X			X	X	X	X		X
BMI	X	X	X	X	X	X	X		X
Waist (cm)	X	X	X	X	X	X	X		X
Fasting Glucose	X	X			X		X	X	
ECG	X						X		X
BP (L&S)	X	X	X	X	X		X		X
LFT	X								X
Trop T/I	X Weekly	X							
CRP	X Weekly	X							
CK	X								

Results should be shared in writing with the GP and recorded in the electronic notes system. If local arrangements are in place for phlebotomy to take place in GP surgeries, the responsibility for checking the results and updating the ZTAS lies with the mental health team.

Direct questioning regarding the presence of constipation should occur at every appointment for blood monitoring.[8] Consideration and a low threshold for prescription should be given to prophylactic use of stimulant laxatives such as senna. [9]

7.1 - Therapeutic Drug Monitoring

Routine monitoring is generally not needed but may be useful in these circumstances:

- Non-compliance is suspected.
- Response to an adequate dose is poor.
- High doses are being used.
- Concomitant hepatic enzyme inducers are being used.
- Change in smoking habit.

Higher plasma levels (>0.6mg/l) are associated with seizures and other adverse drug reactions.

The usual therapeutic dose is 0.35-0.6 mg/l.

Much lower levels are needed for psychosis in Parkinson's disease.

The blood sample should be at least 2mls collected in an EDTA tube. The sample must be taken before a morning dose or in the morning after an evening dose – a trough sample. Sampling less than 6 hours post dose would make the results difficult to interpret.

7.2 - Cigarette Smoking

Clozapine levels can change significantly when a patient starts smoking. Here the blood levels are reduced. If a patient stops smoking, then the blood levels can increase.

Switching to e-cigarettes (*vapes*)and nicotine patches can have the same effect as stopping smoking – i.e. risking clozapine toxicity.[10]

Blood levels can change quickly and continue for 2-3 weeks.

Starting smoking risks less toxicity but equally can lead to less effective treatment.

If a patient stops smoking, decrease the dose by 30-40% at the time of stopping smoking and recheck levels in 2 weeks.

[8] https://www.ztas.com/PDF/FS_Constipation_jan2023.pdf

[9] Every-Palmer, S., Ellis, P.M. Clozapine-Induced Gastrointestinal Hypomotility: A 22-Year Bi-National Pharmacovigilance Study of Serious or Fatal 'Slow Gut' Reactions, and Comparison with International Drug Safety Advice. CNS Drugs 31, 699–709 (2017). https://doi.org/10.1007/s40263-017-0448-6

[10] https://www.ztas.com/PDF/MI.A02.S01-%20FAQv4_2020.pdf

7.3 - Clozapine: Norclozapine Levels

A clozapine: norclozapine ratio should normally be approximately 1.5 (clozapine 1:0.66 norclozapine). This ratio may be affected by poor compliance, fast or slow metabolism, incorrect sampling and concomitant administration of hepatic enzyme-inducing drugs.

A low clozapine level and a low ratio may indicate recent partial non-compliance.

A ratio closer to 1 (clozapine 1: >0.66 norclozapine) may indicate poor compliance, fast metabolization of clozapine, enzyme-inducing drugs or tobacco smoking.

A ratio closer to 2 (clozapine 1: <0.66 norclozapine) can indicate that either the patient has only been partially compliant in the last few days or that they are a slow metaboliser of clozapine or that a true trough sample has not been generated.

7.4 - Laboratory

Blood for FBC and blood levels is processed at Magna Laboratories Ltd:
(0)1989 763333
https://magnalabs.co.uk/
info@magnalabs.co.uk

Forms and consumables can be ordered on the website.

8 - Treatment Breaks

If clozapine has not been taken for more than 48 hours, then it must be re-titrated.

For those on weekly FBC:
If the time off clozapine is less than 48 hours, no change to monitoring is needed.
If the time off clozapine is greater than 48 hours, contact ZTAS for advice.

For those on fortnightly or monthly FBC:
If the time off clozapine is less than 48 hours, no change to monitoring is needed.
If time off clozapine is greater than 48 hours, contact ZTAS for advice.

If there is any doubt about monitoring requirement always seek advice from ZTAS.

9 - Serious Adverse Events

Adverse reactions should be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA). Electronic submissions can be made at www.mhra.gov.uk/yellowcard. Paper submissions can still be made via the yellow forms in the BNF which can be sent free of postal charges. The major groups of side effects are detailed below:

Neutropenia/agranulocytosis:

- Particular attention should be paid to signs of infection such as sore throat, pyrexia and flu-like symptoms.
- ZTAS provides guidance on how to manage these situations as well as the information in this policy.
- The ZTAS guidance should take priority.

Pyrexia:

- 5% of patients will experience transient temperature elevations above 38°C.
- The peak incidence is within the first 3 weeks of treatment.
- See Appendix 6.
- In the presence of a high fever consider the possibility of neuroleptic malignant syndrome.

Cardiovascular Events:

- There is an increased risk of pulmonary embolism.
- Cardiomyopathy and myocarditis (fatal cases have been described) have been associated with clozapine use and the risk is highest in the first 2 months of treatment.
- Signs of cardiac complications are persistent tachycardia at rest, palpitations and chest pain. Examination may reveal arrhythmias or signs of heart failure. Clozapine should be immediately discontinued. Referral to a cardiologist should be made.
- The patient should not be re-exposed to clozapine.
- The risk of postural hypotension can be minimised by a slow titration and spreading out the dose throughout the day.

Seizures:

- Clozapine lowers the seizure threshold.
- A seizure disorder may occur, especially in those on high doses.
- Prophylactic Valproate **[note risk of teratogenicity]** or lamotrigine can be used in high-risk individuals.
- Carbemazepine can cause bone marrow suppression and should not be used.
- Prophylactic anti-convulsants should be considered for those on doses of 600mg /24 hours or more.

Acute intestinal Obstruction:

- Clozapine can cause constipation due to slowing of peristalsis.
- Obstruction can be caused by a paralytic ileus.
- Acute obstruction is a surgical emergency characterised by pain, abdominal distension and vomiting. When suspected, a medical review is needed and surgical referral if appropriate.

Diabetes and Impaired Glucose Tolerance:

- Clozapine has been strongly linked to hyperglycaemia, impaired glucose tolerance and diabetic ketoacidosis.
- Up to one third of patients will develop diabetes after 5 years of treatment, the majority will do so in the first 6 months.
- Baseline screening and regular monitoring of glucose is essential.
- Abnormal random blood glucose monitoring should prompt a fasting sample.

Common Side Effects:

- Constipation, tachycardia, drowsiness, sedation, blurred vision, headache, tremor, rigidity, akathisia, convulsions, extrapyramidal side-effects, nausea, vomiting, anorexia, dry mouth, urinary incontinence or retention, weight gain, hypertension postural hypotension, syncope, disturbance in temperature regulation, sweating, fatigue, fever, elevated LFTs and dysarthria.
- This list is not exhaustive. For further details please see the Zaponex SPC.
- Consider using a GASS[11] monitoring form to assess side effects. (**Appendix 5**)
- Beware of "overshadowing." Not every symptom will be attributable to clozapine, and it is vital not to miss symptoms of unrelated physical health conditions or side effects of other drugs.

Management of Adverse Effects

Neutropenia/Agranulocytosis:

- Usually occurs in first 18 weeks but can happen at any time.
- **STOP CLOZAPINE.**
- See *"Red Result"* above. Daily FBC until green result. Discuss with haematologists. Low threshold for admission.

Hypersalivation:

- Usually happens in first few months.
- May persist.
- Worse at night.
- Hyoscine (Kwells) 300mcg at night. Hyoscine patches as an alternative.
- Treatment may not be needed if not problematic for patient.
- Beware anti-cholinergics in the elderly or those with cognitive impairment.

Sedation:

- Usually in first 4 weeks.
- May persist but usually wears off.
- Give smaller dose in the mornings.
- Reduce dose if necessary.
- May need single night-time dose.
- Consider plasma level monitoring.

Constipation:

- Usually persists.
- High-fibre diet.
- Bulk forming laxatives.
- Stimulants – ensure not obstructed before using a stimulant.

Hypotension:

- First 4 weeks.
- Postural.
- Advise patient to take time standing up.
- Reduce dose or rate of titration.
- If persistent, consider if a sign of cardiac complication/PE/sepsis or other systemic disease.

[11] https://www.researchgate.net/publication/281574111_GASS_scale_instructions-2

Hypertension:
- First 4 weeks, sometimes longer.
- Monitor closely and decrease rate of titration.
- Consider anti-hypertensives.

Tachycardia:
- First 4 weeks but can often persist.
- Exclude serious illness, i.e. myocarditis, PE, sepsis.
- If associated with chest pain, fever, hypotension or shortness of breath, refer to a physician urgently.
- If serious illness is excluded, slow down rate of titration if possible or consider small dose of beta blocker.

Weight gain:
- Often in the first year of treatment
- Common and can be profound.
- Dietary counselling is essential.
- May be more effective if given before weight gain occurs.
- Some evidence for use of metformin.

Fever:
- Usually in first 3 weeks.
- See Appendix 6.
- Consider myocarditis or sepsis.

Seizures:
- Dose dependent.
- Incidence rises above 600mg/day or plasma level >0.6mg/l.
- Consider prophylactic sodium valproate. (1-2g/day).
- **BEWARE RISK of TERATOGENICITY.**
- After a seizure withhold clozapine for one day, restart at reduced level and give valproate.
- Lamotrigine can be used if valproate contra-indicated.

Hyperglycaemia:
- Can happen at any time.
- Risk factors will be evident.
- Diagnose diabetes if present.
- Seek expert help in managing diabetes.

Nausea:
- Usually in first 6 weeks.
- Use anti-emetics.
- Avoid dopamine antagonists.

Nocturnal enuresis:
- May occur at any time.
- Try changing dose regime.
- Avoid fluids/caffeine/alcohol at bedtime.
- Desmopressin has been used – risk of hypoglycaemia.

10 - Monitoring Compliance, Audit & Review

This document will be reviewed every three years or earlier should audit results or changes to legislation / practice within PTHB indicate otherwise.

11 - References / Bibliography

- Psychosis and Schizophrenia in Adults, February 2015. https://www.nice.org.uk/guidance/qs80/chapter/quality-statement-4-treatment-with-clozapine

- Parkinson's Disease in Adults, July 2017 https://www.nice.org.uk/guidance/ng71/chapter/Recommendations#pharmacological-management-of-non-motor-symptoms section 1.5.17

- https://bnf.nice.org.uk/drug/clozapine.html

- https://www.nice.org.uk/guidance/cg178/chapter/1-Recommendations#subsequent-acute-episodes-of-psychosis-or-schizophrenia-and-referral-in-crisis-2 section 1.5.7.1

- https://www.nice.org.uk/guidance/cg178/chapter/1-Recommendations#subsequent-acute-episodes-of-psychosis-or-schizophrenia-and-referral-in-crisis-2 section 1.5.72

- https://www.clozaril.co.uk/scrLogon.asp

- https://www.medicines.org.uk/emc/medicine/30938#:~:text=The%20Zaponex%20Treatment%20Access%20System%20%28ZTAS%29%20was%20developed,suggests%20a%20mortality%20rate%20from%20agranulocytosis%20of%200.3%25.

- https://www.ztas.com/PDF/FS_Constipation_jan2023.pdf

- Every-Palmer, S., Ellis, P.M. Clozapine-Induced Gastrointestinal Hypomotility: A 22-Year Bi-National Pharmacovigilance Study of Serious or Fatal 'Slow Gut' Reactions, and Comparison with International Drug Safety Advice. CNS Drugs 31, 699–709 (2017). https://doi.org/10.1007/s40263-017-0448-6

- https://www.ztas.com/PDF/MI.A02.S01-%20FAQv4_2020.pdf

- https://www.researchgate.net/publication/281574111_GASS_scale_instructions-2

- https://www.researchgate.net/publication/5315035_A_new_self-rating_scale_for_detecting_atypical_or_second-generation_antipsychotic_side_effects

Appendix 1 - (send with appendix 2)

Dr xxxxx
Xxxx Surgery

Re Patient xxxxxxxxxxxx
Address

Felindre Ward/CMHT*
Address
Date

Dear Dr

This patient has been started on clozapine to treat the psychotic features of Schizophrenia/Parkinson's disease *. Please make a note of the prescription in your records and in the treatment history.

Please note that prescribing and monitoring responsibility for this drug lies with the CMHT. Please do NOT mark it for prescription within Primary Care.

The drug will be prescribed by Dr XXXXX, the supervising Consultant.
It will be dispensed by:*

Mr Stefan Fec, Pharmacist
Primrose Pharmacy
Garth House
High Street
Talgarth
Powys
LD3 0PF
Tel: 01874 712 173

Nevill Hall Hospital Pharmacy
Aneurin Bevan University Health Board
Brecon Road
Abergavenny
NP7 7EG

Tel 01873 732279

No other pharmacy will dispense the drug. The CMHT in Newtown/Welshpool/Brecon/ Llandrindod Wells/Ystradgynlais * will be responsible to delivering the drug to the patient.

There are significant risks of neutrophilia and agranulocytosis. For this reason a Full blood count is needed weekly for the first 18 weeks, then fortnightly for the rest of the year, after a year of treatment the monitoring is done monthly. The responsibility for this is with the CMHT and NOT primary care.

There are also significant other risks including severe constipation and hypersalivation. I have enclosed an information leaflet regarding these risks and commonly used strategies to treat them. If there is any doubt please contact the supervising Consultant.

* = Delete as appropriate

Dr XXXXX
Consultant in Psychiatry
GMC No: XXXXXX

Tel:

Appendix 2

CLOZAPINE INFORMATION FOR GP AND OTHER HEALTH PROFESSIONALS

This document must be filed prominently in the patient's primary care notes
Clozapine for GPs and other health professionals
A medicine for schizophrenia, and psychosis in Parkinson's disease

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Ensure that clozapine is added to the electronic patient's medication list (GP) but not for issuing
Perform annual primary care review (GP)
Urgent full blood count if signs of infection inc. sore throat & flu symptoms
Clozapine can cause constipation; if untreated may lead to fatal complications
Do not restart if there has been a break of >48hours between doses
Check drug interactions
Stopping smoking can increase clozapine levels; be alert to smoking status
Increased risk of myocarditis or cardiomyopathy may be fatal in rare cases

This document provides important information with respect to the prescribing of clozapine. Clozapine is prescribed, monitored and supplied by the CMHT, not the GP. **However, familiarity with the contents of this document will serve to protect patients treated with clozapine from adverse events associated with its use.**

Clozapine is indicated in Schizophrenia and psychotic disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed.

The Zaponex® brand of clozapine is prescribed in Powys Teaching Health Board. In Parkinson's the average effective dose is usually between 25 and 37.5 mg/day, though it is licensed up to 100mg/day. In Schizophrenia higher doses are used in a BD regime and may be augmented by other anti-psychotics.

Dose initiation and breaks in treatment
Since many of the adverse effects of clozapine are dose-dependent and associated with speed of titration, therapy is started at a low dose (12.5mg once a day) and increased slowly. If the patient has not taken clozapine for greater than **48 hours** advise that the usual dose **must not** be resumed. The Responsible Consultant must be contacted urgently as the dose must be re-titrated from 12.5mgmg/day. Please report any concerns regarding non-adherence with treatment to the Supervising Consultant at the CMHT.

Monitoring
All patients receiving clozapine in Powys must be monitored physically by the CMHT as per the Health Board's monitoring guidelines. In addition, white cells and neutrophils are checked each week, fortnight or 4-weeks depending on the specification of the Zaponex Treatment Access System (ZTAS). Clozapine increases the incidences of diabetes and cardiac events in a group already at increased risk.

Smoking
Smoking tobacco reduces plasma levels of clozapine by up to 50% so smokers may need higher doses. Likewise, patients who stop smoking may experience a 50% increase in plasma level; there have been case reports of adverse effects in patients taking clozapine when they have stopped smoking. This effect is related to inhalation of tobacco smoke and is **independent of any NRT product** used including e-cigarettes (vape).
If your patient wants to quit/cut down smoking inform the psychiatric team. Side effects of clozapine should be reviewed regularly during the period of cutting down.

Interactions
Clozapine is contraindicated with

- other medicines with a substantial potential to depress bone marrow function (e.g. carbamazepine, carbimazole).

Clozapine is cautioned with:

- other medicines with anticholinergic effects (additive effect) e.g. some drugs for urinary incontinence - be aware of potential additive constipation burden
- other medicines with hypotensive effects (additive effect)
- erythromycin and ciprofloxacin; may increase clozapine levels and are associated with additive QTc risks
- alcohol, due to potential for sedation
- benzodiazepines, due to increased risk of circulatory collapse.

Try to avoid antibiotics with potential to cause e.g. blood dyscrasias eg cephalosporins, trimethoprim and nitrofurantoin.
This is not an exhaustive list. Please see BNF and summaries of product characteristics for further information.

GPs should liaise with the CMHT if there are any identified physical health concerns that may impact on treatment.

Adverse effects Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), including isolated reports.

Adverse effect	Incidence	Action
Anticholinergic effects- constipation	Very common	Act promptly and treat actively when constipation is recognised. **This side effect must not be ignored. Constipation can lead to clozapine toxicity and deaths have occurred as a result of paralytic ileus and perforation.**
dry mouth	Common	Advise symptomatic relief. May be a sign of too high dose, consider informing Supervising Specialist
blurred vision	Common	May be a sign of too high dose, consider informing Supervising Consultant. Careful supervision is indicated in the presence of narrow-angle glaucoma.
urinary retention (incontinence can also occur)	Common	Manage in consultation with Supervising Specialist and urologist. Acute retention may need emergency catheterisation and hospital admission.
Pyrexia (see myocarditis/ cardiomyopathy)	Common	More common at beginning of treatment and can be of no clinical significance, resolving spontaneously after a few days. However, evaluate carefully to rule out possibility of infection, agranulocytosis or myocarditis (see below). Pneumonia is a rare reaction to clozapine. **Take urgent full blood count with differential and inform Supervising Consultant if abnormal.** In the presence of high fever the possibility of neuroleptic malignant syndrome (NMS) must be considered. If count is satisfactory and temperature no more than 38.5°C, clozapine may continue. If fever is >38.5°C or persistent, the clinician may wish to consider withholding clozapine until the fever subsides.
Hypersalivation	Very common	Extra pillows at night/daytime chewing gum may help. Liaise with specialist to consider dose reduction. May be treated with hyoscine hydrobromide (Kwells); suck and swallow a 300mcg tablet up to three times a day. Unlicensed.
Nausea and vomiting	Common	More common early in treatment- slowing the titration or reducing the dose may help. Avoid prochlorperazine, metoclopramide and domperidone. Antacids and Ranitidine may be of benefit. If necessary, consider

		cyclizine with caution for additive drowsiness and antimuscarinic effects (care with constipation) or ondansetron (unlicensed) with caution for additive QTc risks, other medicines which may prolong QTc and cardiac history.
Sedation	Very common	Manipulation of dosage times may alleviate daytime sedation. Dose may be too high. Inform Supervising Consultant.
Hypertension, postural hypotension, syncope	Common	Dose may have been increased too quickly or dose is too high. Inform Supervising Consultant.
Tachycardia (see myocarditis/ cardiomyopathy)	Very common	More common at beginning of treatment. Dose may have been increased too quickly or dose is too high. Inform Supervising Consultant. Where persistent and clinically appropriate consider management with a beta-blocker.
Weight gain	Common	Lifestyle advice. Referral to dietician may be appropriate. Ensure physical monitoring as per the Health Board's monitoring guidelines for antipsychotics (e.g. glucose, lipids).
Seizures/convulsions/ myoclonic jerks	Common	More common with higher doses of clozapine. May be a sign of toxicity. Inform Supervising Consultant immediately.
Agranulocytosis/ neutropenia (patient may report symptoms of infection, e.g., flu-like symptoms, sore throat, high temperature)	Uncommon/ common	Urgent full blood count indicated. Inform Supervising Consultant immediately. Clozapine to be discontinued if WCC<$3.5x10^9$/L or ANC<$2.0x10^9$/L.
Myocarditis/ Cardiomyopathy	Rare/Very rare	If myocarditis or cardiomyopathy suspected clozapine should be stopped and patient referred to cardiologist. Suspect in patients who have persistent tachycardia at rest, particularly during the first two months, palpitations, arrhythmias, chest pain, and other signs/symptoms of heart failure or symptoms that mimic MI. Flu-like symptoms may also be present. Inform Supervising Consultant.

Appendix 3: Interactions with Other Medicinal Products and Other Forms of Interactions

This list is not exhaustive.
Please refer to the manufacturers SPC and/or refer to a pharmacist.

Bone marrow suppressants (e.g. carbamazepine, chloramphenicol), sulphonamides (e.g. co-trimoxazole), pyrazolone analgesics (e.g. phenylbutazone), penicillamine, cytotoxic agents and long-acting depot injections of antipsychotics.
Interact to increase the risk and/or severity of bone marrow suppression.
Clozapine must not be used concomitantly with other agents having a well known potential to suppress bone marrow function (see contra-indications).

Benzodiazepines
Concomitant use may increase risk of circulatory collapse, which may lead to cardiac and/or respiratory arrest.
Whilst the occurrence is rare, caution is advised when using these agents together. Reports suggest that respiratory depression and collapse are more likely to occur at the start of this combination or when Clozapine is added to an established benzodiazepine regimen.

Anticholinergics
Clozapine potentiates the action of these agents through additive anticholinergic activity.
Observe patients for anticholinergic side-effects, e.g. constipation, especially when using to help control hypersalivation.

Antihypertensives
Clozapine can potentiate the hypotensive effects of these agents due to its sympathomimetic antagonistic effects.
Caution is advised if Clozapine is used concomitantly with antihypertensive agents. Patients should be advised of the risk of hypotension, especially during the period of initial dose titration.

Alcohol, MAOIs, CNS depressants, including narcotics and benzodiazepines
Enhanced central effects. Additive CNS depression and cognitive and motor performance interference when used in combination with these substances.
Caution is advised if Clozapine is used concomitantly with other CNS active agents. Advise patients of the possible additive sedative effects and caution them not to drive or operate machinery.

Highly protein bound substances (e.g. warfarin and digoxin)
Clozapine may cause an increase in plasma concentration of these substances due to displacement from plasma proteins.
Patients should be monitored for the occurrence of side effects associated with these substances, and doses of the protein bound substance adjusted, if necessary.

Phenytoin
Addition of phenytoin to Clozapine regimen may cause a decrease in the clozapine plasma concentrations.
If phenytoin must be used, the patient should be monitored closely for a worsening or recurrence of psychotic symptoms.

Lithium
Concomitant use can increase the risk of development of neuroleptic malignant syndrome (NMS).
Observe for signs and symptoms of NMS.

CYP1A2 inducing substances (e.g. omeprazole)
Concomitant use may decrease clozapine levels
Potential for reduced efficacy of clozapine should be considered.

CYP1A2 inhibiting substances e.g. fluvoxamine, caffeine, ciprofloxacin, perazine or hormonal contraceptives (CYP1A2, CYP3A4, CYP2C19)
Concomitant use may increase clozapine levels
Potential for increase in adverse effects. Care is also required upon cessation of concomitant CYP1A2 or CYP3A4 inhibiting medications as there may be a decrease in clozapine levels. The effect of CYP2C19 inhibition may be minimal.

Appendix 4: Pre-initiation Checklist

Name: ZTAS Number:
DOB:
WCCIS number:
NHS Number:
Address:

Consultant Psychiatrist:

Nominated initiation centre:

Pre-initiation Checklist

1.	Diagnosis confirmed as treatment resistant schizophrenia/psychosis in Parkinson's.	Y/N
2.	Pre-initiation mental state examination including suicidality recorded in wccis?	Y/N
3.	Contraindications to clozapine are ABSENT	Y/N
4.	Information regarding treatment and risks given to service user?	Y/N
5.	Service user agreeable and consenting to the use of Clozapine?	Y/N
6.	Physical health acceptable?	Y/N
7.	Physical examination recorded in WCCIS?	Y/N
8.	Record of past medical history and treatment history from GP seen and noted?	Y/N
9.	Smoking status noted in WCCIS?	Y/N
10.	Carer support at home?	Y/N
11.	Cautions to clozapine have been considered?	Y/N
12.	Drug interactions have been considered?	Y/N
13.	Adherence to oral medication felt to be likely?	Y/N
14.	Service user aware of the need for 6-hour monitoring period on day one?	Y/N
15.	Service user is aware of physical health monitoring for 4-week initiation period	Y/N
16.	Service user is aware of and agrees to regular blood monitoring	Y/N
17.	Service user advised to drive and not to drink alcohol	Y/N
18.	Service user has been given health advice regarding possible weight gain	Y/N
19.	GP has been informed of treatment with clozapine	Y/N
20.	Patient has been registered with ZTAS	Y/N
21.	Result of pre-initiation FBC	
22.	Interpretation of pre-initiation ECG	
23.	Result of pre-initiation blood glucose	
24.	Baseline weight/BMI	
25.	Pre-initiation Blood Pressure	
26.	Result of pre-initiation urea and electrolyes	
27.	Result of pre-initiation liver function tests	
28.	Result of pre-initiation lipid profile	
29.	Result of pre-initiation CK	
30.	Result of pre-initiation CRP	

Appendix 5: Clozapine Titration Observation Chart

Name:	Consultant:
Date of Birth:	ZTAS No:
Address:	Service User contact telephone number:

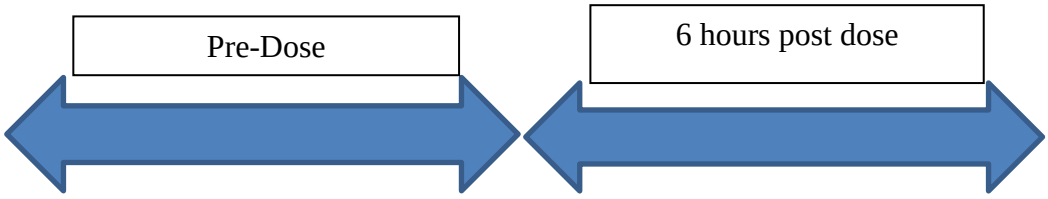
First dose: **6.25mg or 12.5mg**

Date given:

Time given: **10am**

First dose	Pre dose	15 mins after	1 hour after	2 hours after	3 hours after	4 hours after	5 hours after	6 hours after
Pulse								
Lying BP								
Standing BP								
Temp								

Day 2 -14: obs before/after morning dose



Day & Date	Dose	Lying bp	Standing bp	Pulse	Temp	Lying BP	Standing BP	Pulse	Temp
2									
3									
4									
5									
6									
7 Blood test									
8									
9									
10									
11									
12									
13									
14Blood test									

Day 14-28 (observations done 6 hours after morning dose) Give at 10am

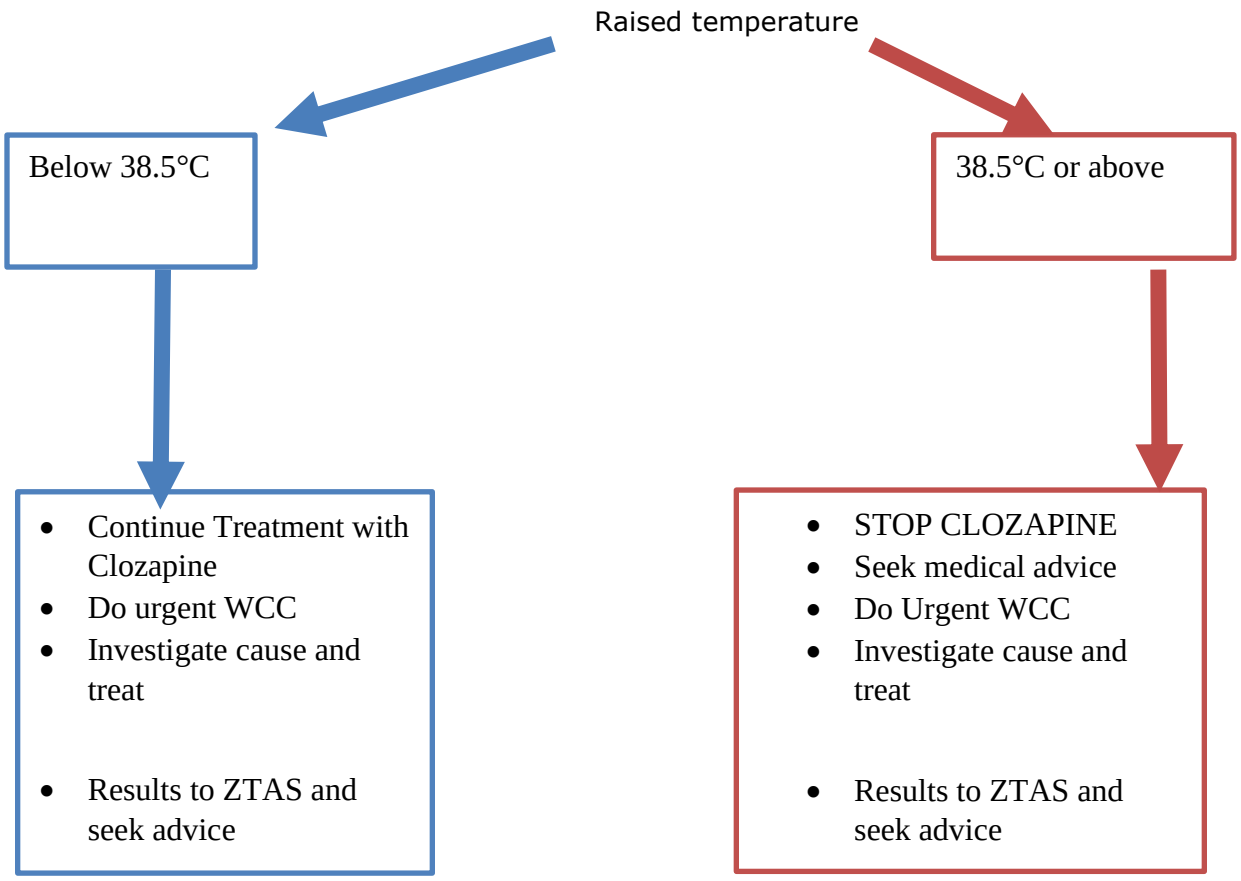
Day & Date	Dose	Lying BP	Standing BP	Pulse	Temp
15					
16					
17					
18					
19					
20					
21 Blood test					
22					
23					
24					
25					
26					
27					
28 Blood test					

Day 28 Onwards Observations done at the same time as FBC monitoring.

When to refer to a prescriber:

- Patient is clearly over-sedated – contact prescriber immediately
- Postural blood pressure drop of more than 30mmHg – contact prescriber immediately
- Temperature rises above 38 °C – contact prescriber immediately if an infection is suspected or there are large temperature changes. If changes are slow, monitor and inform a prescriber as soon as possible
- Pulse is over 100bpm – contact prescriber immediately if associated with chest pain. If no other worrying symptoms, inform prescriber at next meeting or sooner if possible.
- Any intolerable adverse effects – inform prescriber as soon as possible

Appendix 6: Temperature Advice Algorithm



Appendix 7: Glasgow Anti-Psychotic Side Effect Scale

Glasgow Antipsychotic Side-effect Scale (GASS)

Name: **Age:** **Sex: M / F**

Please list current medication and total daily doses below:

This questionnaire is about how you have been recently. It is being used to determine if you are suffering from excessive side effects from your antipsychotic medication.
Please place a tick in the column which best indicates the degree to which you have experienced the following side effects.
Also tick the **end or last** box if you found that the side effect was distressing for you. *© Waddell & Taylor, 2007*

Over the past week:	*Never*	*Once*	*A few times*	*Everyday*	*Tick this box if distressing*
1. I felt sleepy during the day					
2. I felt drugged or like a zombie					
3. I felt dizzy when I stood up and/or have fainted					
4. I have felt my heart beating irregularly or unusually fast					
5. My muscles have been tense or jerky					
6. My hands or arms have been shaky					
7. My legs have felt restless and/or I couldn't sit still					
8. I have been drooling					
9. My movements or walking have been slower than usual					
10. I have had uncontrollable movements of my face or body					
11. My vision has been blurry					
12. My mouth has been dry					
13. I have had difficulty passing urine					
14. I have felt like I am going to be sick or have vomited					
15. I have wet the bed					
16. I have been very thirsty and/or passing urine frequently					
17. The areas around my nipples have been sore and swollen					
18. I have noticed fluid coming from my nipples					
19. I have had problems enjoying sex					
20. **Men only:** I have had problems getting an erection					

Tick yes or no *for the* ***last <u>three months</u>***	*No*	*Yes*	*Tick this box if distressing*
21. **<u>Women only</u>**: I have noticed a change in my periods			
22. **<u>Men and women</u>**: I have been gaining weight			

<u>Staff Information</u>

1. Allow the patient to fill in the questionnaire themselves. All questions relate to the previous week.

2. Scoring

   For questions 1-20 award 1 point for the answer “once”, 2 points for the answer “a few times” and 3 points for the answer “everyday”.
   Please note zero points are awarded for an answer of “never”.

   For questions 21 and 22 award 3 points for a “yes” answer and 0 points for a “no”.

   Total for all questions=

3. For male and female patients a score of: 0-21 absent/mild side effects
   22-42 moderate side effects
   43-63 severe side effects

4. Side effects covered include: 1-2 sedation and CNS side effects
   3-4 cardiovascular side effects
   5-10 extra pyramidal side effects
   11-13 anticholinergic side effects
   14 gastro-intestinal side effects
   15 genitourinary side effects
   16 screening question for diabetes mellitus
   17-21 prolactinaemic side effects
   22 weight gain

The column relating to the distress experienced with a particular side effect is not scored, but is intended to inform the clinician of the service user’s views and condition.

Appendix 8: Clozapine Prescription Chart (Schizophrenia)

GIG CYMRU NHS WALES
Bwrdd Iechyd Addysgu Powys
Powys Teaching Health Board

This chart should only be used for inpatients starting clozapine.
This chart must be attached to the standard prescription chart which must be endorsed "Clozapine as per Titration Chart"
Once on a maintenance dose, clozapine should be prescribed on the standard chart.

Name: Date of Birth:

ZTAS number: Hospital Number:

Consultant:

Date	Prescriber name and signature	Drug	AM dose	Given by	PM dose	Given by
		Clozapine	12.5mg		nil	
		Clozapine	12.5mg		12.5mg	
		Clozapine	12.5mg		25mg	
		Clozapine	25mg		25mg	
		Clozapine	25mg		50mg	
		Clozapine	25mg		75mg	
		Clozapine	25mg		75mg	
Blood test		Clozapine	50mg		75mg	
		Clozapine	50mg		100mg	
		Clozapine	50mg		100mg	
		Clozapine	50mg		125mg	
		Clozapine	100mg		100mg	
		Clozapine	100mg		125mg	
		Clozapine	100mg		150mg	
Blood Test		Clozapine	100mg		175mg	
		Clozapine	100mg		200mg	

Appendix 9: Non-Standard Clozapine Prescription Chart (Schizophrenia)

GIG CYMRU NHS WALES
Bwrdd Iechyd Addysgu Powys
Powys Teaching Health Board

This chart should only be used for those starting clozapine.
Chart must be attached to the standard prescription chart which must be endorsed "Clozapine as per Titration Chart"
Once on a maintenance dose, clozapine should be prescribed on the standard chart.

Name: Date of Birth:

ZTAS number: Hospital Number:

Consultant:

Date	Prescriber name and signature	Drug	AM dose	Given by	PM dose	Given by
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
Blood test		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
		Clozapine				
Blood test		Clozapine				
		Clozapine				

Appendix 10: Suggested Schedule for Psychosis in Parkinson's Disease

Week 1: 6.25mg once a day.
Week 2: 6.25mg once a day with medical review on day 7-10.

Significantly lower doses are needed in this patient group and 6.25mg may be sufficient. Doses above 50mg are rarely needed. Doses for weeks 3 and 4 will need to be dictated by clinical response. The dose should be increased by no more than 6.25mg each time and should not be done more frequently than weekly.

Appendix 11: Clozapine Titration Prescription Chart (Psychosis in Parkinsons Disease)

Patient name:

Consultant:

WCCIS number:

DOB:

ZTAS number:

Day	Date	Drug	Dose	Dose time (10am)	Nurse signature
Monday Blood test *		Clozapine	6.25mg		
Tuesday		Clozapine	6.25mg		
Wednesday		Clozapine	6.25mg		
Thursday		Clozapine	6.25mg		
Friday		Clozapine	6.25mg		
Saturday		Clozapine	6.25mg		
Sunday		Clozapine	6.25mg		
Monday Blood test		Clozapine	6.25mg		
Tuesday		Clozapine			
Wednesday		Clozapine			
Thursday		Clozapine			
Friday		Clozapine			
Saturday		Clozapine			
Sunday		Clozapine			

Prescribers Name:
Prescribers Signature:
Date:

* Blood test not needed on Day 1 but every Monday after that for 18weeks and then as per monitoring standards. A green result is needed from the preceding 10 days for treatment to start on day 1.