NHS
Northumberland, Tyne and Wear
NHS Foundation Trust

Appendix 1 - Monitoring requirements for patients prescribed CLOZAPINE

Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Weight / BMI (Waist measurement where possible)	Clozapine can cause weight gain and this can contribute to an increased risk of cardiovascular and metabolic problems NICE guidance recommends that these results are plotted on a chart (Refs 1,5,6)	✓	Weight / BMI at baseline and then weekly for first six weeks. Then monthly at clozapine clinics.	
Urea and electrolytes (including creatinine or estimated GFR)	Patients with renal impairment may have reduced capacity to excrete clozapine and dose reductions may be required. Hypokaleamia is linked to QTc lengthening and other ECG abnormaliites (Ref 1)	✓		✓
Lipids (Total cholesterol, HDL cholesterol, Total/LDL cholesterol ratio, Triglycerides – fasting sample if possible)	Clozapine can cause small adverse changes in lipid profiles. Triglyceride levels can rise during periods of weight gain (Ref 1,5,6)	✓	✓	✓
Liver function (Bilirubin, Alk Phos, ALT, Albumin, Total protein, Gamma-GT)	Patients with hepatic impairment may have reduced capacity to metabolise clozapine and dose reductions may be required. Drug induced liver damage can be due to direct dose related hepatotoxicity or hypersensitivity reactions. Risk factors for drug induced hepatotoxicity include - ↑age, female gender, alcohol, prescribed enzyme inducing drugs, obesity (Ref 1)	✓	✓	✓
Full Blood Count (Hb, WBC, Platelets)	Clozapine can cause neutropenia +/- agranulocytosis.	✓	WBC, platelets, neutrophils – weekly for 18 weeks, fortnightly for 1 yr, then 4-weekly throughout treatment + FBC annually	
Glucose regulation (Fasting blood glucose (FBG), random blood glucose (RBG) or HbA_{1c}	Clozapine can increase the risk of developing diabetes (Ref 1,5,6)	✓	✓	✓

Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Blood Pressure (lying or sitting, then on standing) **and pulse**	Hypotension is a side effect of clozapine, and it is important to monitor this during periods of initation and stabilisation. Tachycardia is an ↑ risk for the first 2 months. Monitor for myocarditis/ cardiomyopathy (palpitations, arrythmias and chest pain) and other signs and symptoms of heart failure.	✓	At baseline and frequently during dose titration (see clozapine pack + RiO documentation) Then monthly at clozapine clinics.	
Respiration	Respiratory rate during initiation monitoring, and with addition of other drugs which may lower respiratory rate (e.g. lorazepam)	✓	Assessed informally, monthly at clozapine clinics	
Cardiovascular risk assessment	Compared with the general population, people with schizophrenia are at greater risk of dying from heart disease. CV risk must be monitored long term based on the QRISK-2 tool and managed in accordance with NICE / local clinical guidelines.	✓		✓
ECG (QTc interval)	Clozapine may occasionally be associated with ECG changes and prolongation of the QT interval. (Ref 1,5,6) **Please refer to NTW Guidelines for the Management of QTc Prolongation in Adults Prescribed Antipsychotics** **AMPH-PGN-06 - Appendix 3 - QTc Prolongation-Adults**	**All inpatients should have an ECG on admission.** ECGs should be performed at baseline and at least annually **when clinically indicated.** Factors that determine if ECG monitoring is indicated: • If the patient has a family history of cardiovascular disease (e.g. known ischaemic / structural heart disease QT prolongation) • If physical examination identifies cardiovascular risk factors (e.g. irregular pulse) • If a patient is on high dose antipsychotic therapy (HDAT) (see PPT PGN 10) • If a patient is on other drugs known to cause ECG abnormalities (e.g. Tricyclic antidepressants, erythromycin, anti-arrhythmics – see BNF for further information) • If the patient has factors which may predispose to arrhythmias including: - Electrolyte abnormalities – hypokalaemia, hypocalcaemia, hypomagnesaemia - Systemic disease – liver disease, renal disease, hypothyroidism		
Smoking status	Smoking cessation results in increased clozapine plasma levels. Smoking is linked to increased cardiovascular risk.	✓	Assessed monthly at clozapine clinics	

Test/ Measurement	Why is it important?	Baseline	3 months after initiation	Annually
Prolactin	Clozapine does not usually increase prolactin levels. A baseline should be taken to quantify the effect, should symptoms occur.	✓	Only if symptoms of hyperprolactinaemia occur (menstrual disturbance, galactorrhoea, gynaecomastia, sexual dysfunction), consider other possible causes.	
Creatine Kinase	Clozapine (when associated with seizures) can raise levels	✓	At baseline + If NMS suspected	
Pregnancy test		If there is any uncertainty about the possibility of pregnancy, a urine pregnancy test should be carried out		
Bowel habits	There is a risk of severe constipation (a potentially life threatening complication of clozapine that can lead to intestinal obstruction, faecal impaction, paralytic ileus and ultimately death) Refer to PGN section 4.7 for advice on management	✓	Check bowel habits monthly at clozapine clinics	
Review of the side effects of drug treatment efficacy and adherence	Refer to the clozapine specific side effect monitoring scale (Rio document)	Before treatment the side effects the patient is least willing to tolerate should be assessed	On review, at dose changes + annually (minimum): Efficacy, patient adherence + side effects should be assessed. Including: - EPSE, akathisia, dystonia and tardive dyskinesia - Very common side effects eg. Sedation, hypersalivation - Serious adverse effects eg arrhythmias, seizures, severe constipation	
Lifestyle Review	Poor diet and a sedentary lifestyle are linked to increased cardiovascular risk (Ref 5)	✓	✓	✓
Clozapine plasma level	Side effects that are thought to be dose related include seizures and gastrointestinal hypomotility	Refer to PPT-PGN-05 Safe Prescribing of Clozapine for guidance on additional checks		✓
Drug screening		If indicated by history or clinical picture		

References
[1] Maudsley Prescribing Guidelines 2015 [2] SPC of clozapine, available at www.medicines.org.uk [3] BNF, March 2015
[4] Royal College of Psychiatrists Consensus Statement on high dose antipsychotic prescribing May 2006 [5] Lester UK Adaptation Positive Cardio metabolic Health Resource June 2014 - www.rcpsych.ac.uk/quality/NAS/resources [6] NICE Guidelines CG178 – Psychosis and Schizophrenia in Adults – February 2014