Clozapine quick reference

Information for Doctors

Clozapine

Clozapine can be effective when other antipsychotics have failed. There is a high risk that mental health symptoms will return if treatment is interrupted. There is a risk of agranulocytosis. Patients with signs or symptoms of infection need an immediate full blood count.

Other important side effects can include:

- Sedation
- Constipation
- Hypersalivation
- Metabolic disturbances
- Myocarditis and cardiomyopathy
- Epileptic seizures
- Nocturnal urinary incontinence

Some drugs and substances can interact with clozapine

Avoid drugs with the potential for bone marrow suppression or constipation. Some drugs and substances can increase or reduce clozapine serum levels, especially liver enzyme inhibitors or inducers. Clozapine serum levels can be affected adversely by cigarettes and caffeine.

Agranulocytosis

KEY ACTION: Regular full blood counts: Every week for the first 18 weeks and then every four weeks thereafter. Request that copy of the results be sent to the dispensing pharmacy and Clozaril Carelink Plus Patient Monitoring System. **Please see over the page for guidance on interpreting the results.**

Interruption of treatment

KEY ACTION: Resume at the usual dose unless more than two days of doses have been missed. If greater than 48 hours, contact the Clozapine Clinic and relevant Specialist Mental Health Service (SMHS) team as restarting treatment will need to be supervised by the SMHS.

Sedation

KEY ACTION: Commonly occurs on initiation. Consider slowing down the initial dose titration, reducing the dose or shifting more of the dose to night-time. Consider additive effect of other sedating medications.

Constipation

KEY ACTION: Clozapine is very constipating. Patients should be pro-actively managed and started on regular docusate and senna (Laxsol™) when they start clozapine. Follow the Porirua protocol to manage constipation which is available on Health Pathways. Avoid prescribing other medications that cause constipation.

Hypersalivation

KEY ACTION: Treatment is often successful. Prescribing benzatropine (1-2mg daily), atropine eye drops 1% orally (1-2 drops) at night or Scopaderm™ patches may be effective but increase the risk of constipation.

Metabolic disturbances

KEY ACTION: Monitor for weight gain, lipid abnormalities and diabetes mellitus at baseline, three-monthly after starting, then annually (or more frequently if indicated). Primary care should lead with any indicated treatment.

Myocarditis and cardiomyopathy

KEY ACTION: Myocarditis most commonly occurs in the first four - eight weeks of treatment. Urgently investigate signs/symptoms of any adverse cardiac effects including unexplained fatigue, fever, chest pain, palpitations, and shortness of breath (e.g. ECG, FBC, troponin, CRP, chest x-ray and possible cardiology referral). If myocarditis is suspected immediately withdraw clozapine and contact the Mental Health Team. Cardiomyopathy may occur later and present similar to heart failure. It is thought to be associated with a sustained increased in heart rate (>100bpm).

Epileptic seizures

KEY ACTION: These are uncommon and generally occur only at high levels. If seizures occur, contact the Mental Health Team. Clozapine does not necessarily need to be stopped as addition of sodium valproate will usually be effective.

Nocturnal urinary incontinence

KEY ACTION: Advise reduction of caffeine and fluid in the evening. Encourage voiding prior to bedtime. Treatment with oxybutynin, solifenacin or desmopressin may be effective. Please let the Mental Health Team know if this is a problem.

Drug interactions

KEY ACTION: Avoid drugs with the potential for bone-marrow suppression. The most common examples are co-trimoxazole, trimethoprim and carbamazepine. Some drugs and substances increase or reduce serum levels of clozapine, especially liver enzyme inducers and inhibitors (e.g. erythromycin and ciprofloxacin). Care needs to be taken if co-prescribing.

Chemicals in cigarette smoke (not nicotine) can lower clozapine serum levels so sudden smoking cessation can cause a large rise in serum levels with associated toxicity.

Caffeine if consumed in large amounts can raise clozapine serum levels so sudden cessation of regular caffeine can cause a decrease in clozapine levels and possible return of mental health symptoms.

Monitoring of haematological values in patients taking clozapine

Situation	Haematological values	Monitoring required
Systemically unwell, fever or sore throat.		Repeat FBC at once.
Red result	WBC is less than $3.0x10^9$/L or the neutrophil count is less than $1.5x10^9$/L.	Discontinue clozapine immediately. Perform daily FBC until haematological recovery has occurred. The patient must be closely monitored, especially for any signs of infection. *
Amber result	WBC drops to between 3.0-$3.5x10^9$/L and/or the neutrophil count drops to between 1.5-$2.0x10^9$/L.	Repeat FBC (within 2-3 days) and continue twice a week until the WBC returns to above 3.5 $x10^9$/L and the neutrophil count is above 2.0 $x10^9$/L.
Any point during treatment.	WBC or neutrophils show a drop of $3.0x10^9$/ L or more from baseline or a single drop of $3.0x10^9$/L or more.	Repeat FBC (within 2-3 days if weekly or within a week if monthly).
Any point during treatment.	Three consecutive drops of the WBC or neutrophil count.	Repeat FBC where clinically appropriate.
Any point during treatment.	Eosinophil count rises above $3.0x10^9$/L.	Discontinue clozapine immediately Clozapine should only be restarted after the count is below $1.0x10^9$/L. *
Any point during treatment.	Platelet count falls below $50x10^9$/L.	Discontinue clozapine immediately and follow health pathways. Clozapine should not normally be reinitiated. However, if consideration is being given to reinitiate clozapine the patient's platelet count must be greater than $100x10^9$/L, and a haematologist must be consulted. *
The patient refuses a blood test at any stage of treatment and cannot be persuaded to reconsider.		Clozapine must be discontinued. The patient's physical condition must be monitored for at least one month following discontinuation. Ideally the FBC should also continue to be monitored for a period of one month following discontinuation. * * Also, ensure contact with SMHS for follow-up.

Contacts:

For general advice phone Specialist Mental Health Service

(03) 337-7969 ext 54033

Urgent after-hours 0800-920-092

Blood collection, collation and dissemination of results is coordinated by a system involving pharmacies, all the pathology laboratories, and mental health teams, and is backed up by a monitored database called Clozaril Carelink Plus.

Should you have any queries about the database or results for one of your patients freephone:

Clozaril Carelink Plus: 0800 535 020