

Medicines Management & Pharmacy Services (MMPS)

Clozapine

Clozapine is licensed for the treatment of schizophrenia in patients, who are either unresponsive or intolerant to other antipsychotics.

It is a “red” drug and only prescribed in secondary care.

Continuous blood monitoring is necessary for patients taking clozapine – see below.

GPs should document clozapine prescription in patient’s notes to avoid use of interacting drugs.

Dosage

Response usually seen with a dose in the range of 150mg – 900mg /day, when used alone

Lower doses required in the elderly, females and non-smokers

“**Clozaril**” (Novartis) brand of tablets is currently used in LYPFT. Patients receiving these tablets are registered with the Clozaril Patient Monitoring Service and results of all blood tests are held by them.

“**Denzapine**” suspension (Merz) is currently used in LYPFT for patients unable to swallow tablets. These patients are registered with the Denzapine Monitoring Service and results of all blood tests are held by them.

The monitoring services give advice relating to abnormal blood results.

Blood monitoring

Since clozapine can cause neutropenia and agranulocytosis, patients taking the drug need continuous blood monitoring.

White cell, neutrophil and platelet counts are required by the monitoring services for each blood sample.

Monitoring regime

Before beginning treatment

Weekly for the first 18 weeks of treatment

Two weekly for weeks 19 – 52

Four weekly after 52 weeks

Four weeks after discontinuing treatment

Blood results

Blood results are considered to be abnormal when:

White cell count $<3.5 \times 10^9/L$

Neutrophils $<2.0 \times 10^9/L$

Lower values apply to patients with benign ethnic neutropenia

Breaks in treatment

If a patient misses doses for >48 hours it is necessary to re-titrate.

The starting dose is 12.5 or 25mg daily gradually increased to the previous level. This can usually be done more rapidly than with an initial titration.

Blood monitoring frequency may also need adjusting – seek specialist advice.

Options for augmenting clozapine

Add **amisulpride** 400 – 800mg/day

Add **aripiprazole** 15 – 30 mg/day

Common adverse effects

Adverse effect	Treatment options
Sedation	Often troublesome initially. Give a smaller dose in the morning
Hypersalivation	Can be very troublesome at night Treat with hyoscine hydrobromide (Kwells) 300 micrograms up to three times a day
Constipation	Usually persists Treat with high fibre diet, bulk forming and stimulant laxative This can be a serious side-effect, which can be life threatening.
Hypertension	Low dose hypotensive sometimes required
Weight gain	Usually during the first year of treatment
Seizures	Related to dose and plasma level Usually treated with prophylactic sodium valproate
Tachycardia	Common in the early stages of treatment and usually benign. If persists at rest and associated with

	chest pain may indicate myocarditis – refer to cardiology team.
Neutropenia	See blood monitoring information above

Unlicensed uses of clozapine

Clozapine is used off licence for the treatment of behaviour disorder in patients with learning disabilities and for refractory bipolar disorder – see unlicensed use of licensed drugs.

Further information on clozapine is available at: [Clozaril 25mg and 100mg Tablets - Summary of Product Characteristics \(SPC\) - \(eMC\)](#) and [Denzapine 50mg/ml Oral Suspension - Summary of Product Characteristics \(SPC\) - \(eMC\)](#)

For further information: www.choiceandmedication.org/leedsandyorkpft

References

- (1) Maudsley Prescribing Guidelines; 11th edition; 2012
- (2) Clozaril Patient Monitoring Service; Novartis Pharmaceuticals UK Ltd
- (3) BNF 64; September 2012
- (4) Frith Guidelines 2008

Provenance

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