

Persistent tachycardia especially in first 2 months should prompt observation for other indicators for myocarditis or cardiomyopathy

If myocarditis or cardiomyopathy suspected clozapine should be stopped and patient evaluated urgently by cardiologist

Discontinue permanently in clozapine-induced myocarditis or cardiomyopathy

- ▶ **Intestinal obstruction** Impairment of intestinal peristalsis, including constipation, intestinal obstruction, faecal impaction, and paralytic ileus, (including fatal cases) reported. Clozapine should be used with caution in patients receiving drugs that may cause constipation (e.g. antimuscarinic drugs) or in those with a history of colonic disease or lower abdominal surgery. It is essential that constipation is recognised and actively treated.

● **INTERACTIONS** → Appendix 1: clozapine

● **SIDE-EFFECTS**

- ▶ **Common or very common** Appetite decreased · eosinophilia · fatigue · fever · headache · hypertension · leucocytosis · muscle complaints · nausea · oral disorders · postural hypotension (dose-related) · speech impairment · sweating abnormal · syncope · temperature regulation disorders · urinary disorders · vision blurred
- ▶ **Rare or very rare** Anaemia · cardiac arrest · cardiac inflammation · cardiomyopathy · circulatory collapse · confusion · delirium · diabetes mellitus · dyslipidaemia · dysphagia · gastrointestinal disorders · glucose tolerance impaired · hepatic disorders · hyperglycaemia · increased risk of infection · intestinal obstruction (including fatal cases) · ketoacidosis · nephritis tubulointerstitial · obsessive-compulsive disorder · pancreatitis · pericardial effusion · respiratory disorders · restlessness · sexual dysfunction · skin reactions · thrombocytopenia · thrombocytosis
- ▶ **Frequency not known** Angina pectoris · angioedema · chest pain · cholinergic syndrome · diarrhoea · gastrointestinal discomfort · hypersensitivity vasculitis · muscle weakness · myocardial infarction · nasal congestion · pseudophaeochromocytoma · renal failure · systemic lupus erythematosus (SLE)

SIDE-EFFECTS, FURTHER INFORMATION Hypersalivation associated with clozapine therapy can be treated with hyoscine hydrobromide [unlicensed indication], provided that the patient is not at particular risk from the additive antimuscarinic side-effects of hyoscine and clozapine.

● **PREGNANCY** Use with caution.

● **BREAST FEEDING** Avoid.

● **HEPATIC IMPAIRMENT** Manufacturer advises caution—monitor liver function (discontinue if liver enzymes are greater than 3 times the upper limit of normal or jaundice occurs); avoid in symptomatic or progressive impairment and in hepatic failure.

● **RENAL IMPAIRMENT** Avoid in severe impairment.

● **MONITORING REQUIREMENTS**

- ▶ Monitor leucocyte and differential blood counts. Clozapine requires differential white blood cell monitoring weekly for 18 weeks, then fortnightly for up to one year, and then monthly as part of the clozapine patient monitoring service.
- ▶ Close medical supervision during initiation (risk of collapse because of hypotension and convulsions).
- ▶ Blood lipids and weight should be measured at baseline, at 3 months (weight should be measured at frequent intervals during the first 3 months), and then yearly with antipsychotics. Patients taking clozapine require more frequent monitoring of these parameters: every 3 months for the first year, then yearly.
- ▶ Fasting blood glucose should be measured at baseline, at 4–6 months, and then yearly. Patients taking clozapine

should have fasting blood glucose tested at baseline, after one month's treatment, then every 4–6 months.

- ▶ Patient, prescriber, and supplying pharmacist must be registered with the appropriate Patient Monitoring Service—it takes several days to do this.
- **TREATMENT CESSATION** On planned withdrawal reduce dose over 1–2 weeks to avoid risk of rebound psychosis. If abrupt withdrawal necessary observe patient carefully.
- **DIRECTIONS FOR ADMINISTRATION** Shake oral suspension well for 90 seconds when dispensing or if visibly settled and stand for 24 hours before use; otherwise shake well for 10 seconds before use. May be diluted with water.
- **PRESCRIBING AND DISPENSING INFORMATION** Clozapine has been used for psychosis in Parkinson's disease in children aged 16 years and over.
- **PATIENT AND CARER ADVICE** Patients or carers should be given advice on how to administer clozapine oral suspension.

● **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug. Forms available from special-order manufacturers include: oral suspension, oral solution

Oral suspension

CAUTIONARY AND ADVISORY LABELS 2, 10

▶ **Denzapine** (Britannia Pharmaceuticals Ltd)

Clozapine 50 mg per 1 ml Denzapine 50mg/ml oral suspension sugar-free | 100 ml [PoM](#) £39.60

Tablet

CAUTIONARY AND ADVISORY LABELS 2, 10

▶ **Clozaril** (Mylan)

Clozapine 25 mg Clozaril 25mg tablets | 28 tablet [PoM](#) £3.02 (Hospital only) | 84 tablet [PoM](#) £8.40 (Hospital only) | 100 tablet [PoM](#) £10.00 (Hospital only)

Clozapine 100 mg Clozaril 100mg tablets | 28 tablet [PoM](#) £12.07 (Hospital only) | 84 tablet [PoM](#) £33.60 (Hospital only) | 100 tablet [PoM](#) £39.00 (Hospital only)

▶ **Denzapine** (Britannia Pharmaceuticals Ltd)

Clozapine 25 mg Denzapine 25mg tablets | 84 tablet [PoM](#) £16.64 | 100 tablet [PoM](#) £19.80

Clozapine 50 mg Denzapine 50mg tablets | 100 tablet [PoM](#) £39.60
Clozapine 100 mg Denzapine 100mg tablets | 84 tablet [PoM](#) £66.53 | 100 tablet [PoM](#) £79.20

Clozapine 200 mg Denzapine 200mg tablets | 100 tablet [PoM](#) £158.40

▶ **Zaponex** (Leyden Delta B.V.)

Clozapine 25 mg Zaponex 25mg tablets | 84 tablet [PoM](#) £8.28 | 500 tablet [PoM](#) £48.39

Clozapine 100 mg Zaponex 100mg tablets | 84 tablet [PoM](#) £33.88 | 500 tablet [PoM](#) £196.43

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Olanzapine

● **DRUG ACTION** Olanzapine is a dopamine D₁, D₂, D₄, 5-HT₂, histamine-1₁, and muscarinic-receptor antagonist.

● **INDICATIONS AND DOSE**

Schizophrenia | Combination therapy for mania

▶ BY MOUTH

▶ Child 12–17 years (under expert supervision): Initially 5–10 mg daily, adjusted according to response, usual dose 5–20 mg daily, doses greater than 10 mg daily only after reassessment, when one or more factors present that might result in slower metabolism (e.g. female gender, non-smoker) consider lower initial dose and more gradual dose increase; maximum 20 mg per day

Monotherapy for mania

▶ BY MOUTH

▶ Child 12–17 years (under expert supervision): 15 mg daily, adjusted according to response, usual dose 5–20 mg daily, doses greater than 15 mg daily only after reassessment, when one or more factors continued →