

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

Tablet

CAUTIONARY AND ADVISORY LABELS 2

▶ **Aripiprazole (Non-proprietary)**

Aripiprazole 5 mg Aripiprazole 5mg tablets | 28 tablet [PoM] £96.04 DT = £1.36

Aripiprazole 10 mg Aripiprazole 10mg tablets | 28 tablet [PoM] £96.04 DT = £1.36

Aripiprazole 15 mg Aripiprazole 15mg tablets | 28 tablet [PoM] £96.04 DT = £1.57

Aripiprazole 30 mg Aripiprazole 30mg tablets | 28 tablet [PoM] £192.08 DT = £13.94

▶ **Arpya** (Torrent Pharma (UK) Ltd)

Aripiprazole 5 mg Arpya 5mg tablets | 28 tablet [PoM] £96.04 DT = £1.36

Aripiprazole 10 mg Arpya 10mg tablets | 28 tablet [PoM] £96.04 DT = £1.36

Aripiprazole 15 mg Arpya 15mg tablets | 28 tablet [PoM] £96.04 DT = £1.57

Aripiprazole 30 mg Arpya 30mg tablets | 28 tablet [PoM] £192.08 DT = £13.94

Oral solution

CAUTIONARY AND ADVISORY LABELS 2

▶ **Aripiprazole (Non-proprietary)**

Aripiprazole 1 mg per 1 ml Aripiprazole 1mg/ml oral solution sugar-free | 150 ml [PoM] £101.20

Aripiprazole 1mg/ml oral solution | 150 ml [PoM] £102.90 DT = £99.55

▶ **Abilify** (Otsuka Pharmaceuticals (U.K.) Ltd)

Aripiprazole 1 mg per 1 ml Abilify 1mg/ml oral solution | 150 ml [PoM] £102.90 DT = £99.55

Orodispersible tablet

CAUTIONARY AND ADVISORY LABELS 2

▶ **Aripiprazole (Non-proprietary)**

Aripiprazole 10 mg Aripiprazole 10mg orodispersible tablets sugar-free | 28 tablet [PoM] £96.04 DT = £65.69

Aripiprazole 15 mg Aripiprazole 15mg orodispersible tablets sugar-free | 28 tablet [PoM] £96.04 DT = £65.69

F 260

02-Jul-2018

Clozapine

- **DRUG ACTION** Clozapine is a dopamine D₁, dopamine D₂, 5-HT_{2A}, alpha₁-adrenoceptor, and muscarinic-receptor antagonist.

INDICATIONS AND DOSE**Schizophrenia in patients unresponsive to, or intolerant of, conventional antipsychotic drugs**▶ **BY MOUTH**

- ▶ Child 12–17 years (under expert supervision): 12.5 mg 1–2 times a day for day 1, then 25–50 mg for day 2, then increased, if tolerated, in steps of 25–50 mg daily, dose to be increased gradually over 14–21 days, increased to up to 300 mg daily in divided doses, larger dose to be taken at night, up to 200 mg daily may be taken as a single dose at bedtime; increased in steps of 50–100 mg 1–2 times a week if required, it is preferable to increase once a week; usual dose 200–450 mg daily, max. 900 mg per day, if restarting after interval of more than 48 hours, 12.5 mg once or twice on first day (but may be feasible to increase more quickly than on initiation)—extreme caution if previous respiratory or cardiac arrest with initial dosing

- **UNLICENSED USE** Not licensed for use in children under 16 years.

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: CLOZAPINE: REMINDER OF POTENTIALLY FATAL RISK OF INTESTINAL OBSTRUCTION, FAECAL IMPACTION, AND PARALYTIC ILEUS (OCTOBER 2017)

Clozapine has been associated with varying degrees of impairment of intestinal peristalsis—see Cautions and

Contra-indications for further information. Patients and their carers should be advised to seek immediate medical advice before taking the next dose of clozapine if constipation develops.

- **CONTRA-INDICATIONS** Alcoholic and toxic psychoses · bone-marrow disorders · coma · drug intoxication · history of agranulocytosis · history of circulatory collapse · history of neutropenia · paralytic ileus · severe cardiac disorders (e.g. myocarditis) · severe CNS depression · uncontrolled epilepsy

- **CAUTIONS** Susceptibility to angle-closure glaucoma · taper off other antipsychotics before starting

CAUTIONS, FURTHER INFORMATION

- ▶ **Agranulocytosis** Neutropenia and potentially fatal agranulocytosis reported. Leucocyte and differential blood counts must be normal before starting; monitor counts every week for 18 weeks then at least every 2 weeks and if clozapine continued and blood count stable after 1 year at least every 4 weeks (and 4 weeks after discontinuation); if leucocyte count below 3000/mm³ or if absolute neutrophil count below 1500/mm³ discontinue permanently and refer to haematologist. Patients who have a low white blood cell count because of benign ethnic neutropenia may be started on clozapine with the agreement of a haematologist. Avoid drugs which depress leucopoiesis; patients should report immediately symptoms of infection, especially influenza-like illness.

- ▶ **Myocarditis and cardiomyopathy** Fatal myocarditis (most commonly in first 2 months) and cardiomyopathy reported.

- Perform physical examination and take full medical history before starting
- Specialist examination required if cardiac abnormalities or history of heart disease found—clozapine initiated only in absence of severe heart disease and if benefit outweighs risk
- 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

▶ **Uncommon** Fall

- ▶ **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