SUMMARY OF PRODUCT CHARACTERISTICS
DOPAZEN 250 (Methyldopa Tablets 250 mg)

1. NAME OF THE MEDICINAL PRODUCT

DOPAZEN 250 (Methyldopa Tablets BP 250 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains methyldopa BP equivalent to anhydrous methyldopa 250 mg.

Excipients with known effect:

Each tablet contains 30 mg lactose (as lactose monohydrate). For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Dark yellow coloured, circular, biconvex film-coated tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of moderate to severe hypertension.

4.2 Posology and method of administration

Adults

Initially 250 mg 2–3 times daily for 2 days, then adjusted at intervals of at least 2 days until an adequate response is obtained. Maximum dose: 3 g daily. Usual effective dose: 500 mg to 2 g daily. When increasing the dosage, it may be desirable to increase the evening dose first, to minimise initial sedation. Withdrawal of methyldopa is followed by return of hypertension, usually within 48 hours, without overshoot.

Patients on other antihypertensives

When initiating methyldopa in patients already on other antihypertensives, those agents should be reduced gradually as required. Methyldopa should be limited to an initial dose of not more than 500 mg daily and increased at intervals of not less than 2 days. When 500 mg of methyldopa is added to 50 mg of hydrochlorothiazide, the two agents may be given together once daily.

Renal impairment

Methyldopa is largely excreted by the kidney; patients with impaired renal function may respond to smaller doses. Dialysis removes methyldopa; hypertension may recur after dialysis.

Elderly patients

Initial dose should be kept as low as possible, not exceeding 250 mg daily; an appropriate starting dose is 125 mg twice daily, increased slowly as required but not exceeding 2 g daily. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

Children

10 mg/kg body weight daily in 2–4 divided doses, adjusted or decreased until adequate response is achieved. Maximum: 65 mg/kg body weight or 3 g per day, whichever is less.

Method of administration

Oral.

4.3 Contraindications

- Hypersensitivity to methyldopa or to any of the excipients listed in section 6.1 (including hepatic disorders associated with previous methyldopa therapy).
- A history of depression.
- Active hepatic disease such as acute hepatitis and active cirrhosis.

- Concomitant therapy with MAOIs.
- Porphyria.
- Methyldopa is not recommended for the treatment of catecholamine-secreting tumours such as phaeochromocytoma or paraganglioma.

4.4 Special warnings and precautions for use

Haematological effects

Acquired haemolytic anaemia has occurred rarely. If symptoms suggest anaemia, haemoglobin and/or haematocrit should be measured. If haemolytic anaemia is confirmed, methyldopa should be discontinued. Stopping therapy, with or without a corticosteroid, has usually brought prompt remission, though deaths have occurred rarely.

A positive Coombs test develops in 10–20% of patients on continued therapy; it rarely develops within the first 6 months and is dose-related. If a patient with a positive Coombs reaction requires transfusion, appropriate compatibility testing should be performed. Reversible leucopenia (primarily granulocytes) and reversible thrombocytopenia have been reported rarely.

Hepatic effects

Fever has occasionally occurred within the first 3 weeks of therapy, sometimes associated with eosinophilia or abnormal liver function tests. Jaundice with or without fever, usually within the first 2–3 months, may be consistent with cholestasis. Rare cases of fatal hepatic necrosis have been reported. Liver function tests and a full blood count are advisable before therapy and at intervals during the first 6–12 weeks of therapy, or whenever unexplained fever occurs. If fever, abnormal liver function or jaundice occurs, therapy should be withdrawn; if related to methyldopa, parameters will return to normal. Methyldopa should not be used again in these patients. Use with caution in patients with a history of liver disease.

Anaesthesia

Patients may require reduced doses of anaesthetics when on methyldopa. If hypotension occurs during anaesthesia, it can usually be controlled by vasopressors. The adrenergic receptors remain sensitive during methyldopa treatment.

Neurological effects

Rarely, involuntary choreoathetotic movements have been observed during methyldopa therapy in patients with severe bilateral cerebrovascular disease; therapy should be discontinued if these movements occur. Methyldopa should be used with extreme caution in patients, or in near relatives of patients, with hepatic porphyria.

Laboratory test interference

Methyldopa may interfere with: urinary uric acid measurement (phosphotungstate method); serum creatinine (alkaline picrate method); and AST (SGOT) by colorimetric method. Methyldopa fluoresces at the same wavelengths as catecholamines; spuriously high amounts of urinary catecholamines may be reported, interfering with a diagnosis of phaeochromocytoma or paraganglioma. Methyldopa does not interfere with VMA measurements. When urine is exposed to air after voiding, it may rarely darken because of breakdown of methyldopa or its metabolites.

Lactose content

This product contains 30 mg lactose per tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Other antihypertensives (potentiation):

When methyldopa is used with other antihypertensives, potentiation of antihypertensive action may occur. Concurrent use of verapamil and methyldopa can intensify sinus bradycardia. Concomitant administration with thiazide diuretics, other antihypertensives, general anaesthetics and levodopa enhances the antihypertensive effect.

Drugs diminishing antihypertensive effect:

The antihypertensive effect of methyldopa may be diminished by sympathomimetics, tricyclic antidepressants, phenothiazine derivatives and MAOIs. Phenothiazines may have additive hypotensive effects and may also increase the toxicity of haloperidol.

MAOIs (contraindicated):

MAOIs should be discontinued before treatment with methyldopa.

Lithium:

When methyldopa and lithium are given concomitantly, the patient should be carefully monitored for symptoms of lithium toxicity.

Iron:

Several studies demonstrate a decrease in bioavailability of methyldopa when ingested with ferrous sulphate or ferrous gluconate; this may adversely affect blood pressure control. Avoid co-administration if possible.

4.6 Fertility, pregnancy and lactation

Pregnancy

Methyldopa has been used under close medical supervision for the treatment of hypertension during pregnancy. Published reports indicate no foetal harm when used during pregnancy; the possibility of foetal harm appears remote. Use in pregnancy requires that anticipated benefits be weighed against possible risks.

Breast-feeding

Methyldopa crosses the placental barrier and is present in cord blood and breast milk. Although no obvious teratogenic effects have been reported, the possibility of foetal injury cannot be excluded. The use of the drug in women who are, or may become, pregnant or who are breast-feeding requires careful consideration of risk/benefit.

Fertility

No specific fertility data available.

4.7 Effects on ability to drive and use machines

Caution should be observed when driving or operating machinery, as methyldopa therapy may result in drowsiness, dizziness, light-headedness and, rarely, involuntary choreoathetotic movements in patients with severe cerebrovascular disease. Patients should be advised accordingly on initiation of therapy and/or dose increases.

4.8 Undesirable effects

Summary of the safety profile

Sedation (usually transient) may occur during the initial period of therapy or whenever the dose is increased. Headache and asthenia or weakness may be noted as early and transient symptoms. The frequencies of all adverse reactions are 'not known' (cannot be estimated from available data).

System Organ Class	Adverse Event	Frequency
Cardiac disorders	Bradycardia, aggravation of angina pectoris, myocarditis, pericarditis, AV block	Not known
Blood and lymphatic	Haemolytic anaemia, bone marrow depression, leucopenia, granulocytopenia, thrombocytopenia, eosinophilia	Not known
Nervous system	Sedation (usually transient)*, headache**, paraesthesia, Parkinsonism, VIIth nerve paralysis, choreoathetosis*, mental impairment, carotid sinus syndrome, dizziness*, lightheadedness*, symptoms of cerebrovascular insufficiency	Not known
Psychiatric	Nightmares, reversible mild psychoses or depression, decreased libido	Not known
Respiratory	Nasal stuffiness	Not known
Gastrointestinal	Nausea, vomiting, abdominal distension, constipation, flatus, diarrhoea, colitis, mild dry mouth, glossodynia, sore or black tongue, pancreatitis	Not known
Skin	Rash (eczema or lichenoid eruption), toxic epidermal necrolysis, angioedema, urticaria	Not known
Musculoskeletal	Lupus-like syndrome, mild arthralgia with or without joint swelling, myalgia	Not known
Endocrine	Hyperprolactinaemia	Not known
Vascular	Orthostatic hypotension (decrease daily dosage)	Not known

System Organ Class	Adverse Event	Frequency
General	Asthenia or weakness**, oedema (and weight gain), drug-related fever	Not known
Hepatobiliary	Hepatitis, jaundice	Not known
Reproductive	Breast enlargement, gynaecomastia, amenorrhoea, lactation, impotence, failure of ejaculation	Not known
Infections	Sialadenitis	Not known
Investigations	Positive Coombs test, positive ANA/LE cells/rheumatoid factor; abnormal LFTs, raised blood urea	Not known

** Sedation, usually transient, may occur during the initial period of therapy or whenever the dose is increased. If affected, patients should not attempt to drive or operate machinery.*

*** Headache, asthenia or weakness may be noted as early and transient symptoms.*

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose

Symptoms

Acute hypotension, sedation, weakness, bradycardia, dizziness, gastrointestinal disturbances, light-headedness, constipation, distension, flatus, diarrhoea, nausea and vomiting.

Treatment

Stomach emptying by aspiration, lavage or emesis if ingestion is recent. There is no specific antidote. Methyldopa is dialyzable. Treatment is symptomatic. Intravenous infusion may be given to promote urinary excretion; pressor agents (metaraminol or noradrenaline) may be given. Monitor cardiac rate and output, blood volume, electrolyte balance, paralytic ileus, urinary function and cerebral activity. If chronic overdosage is suspected, methyldopa should be discontinued.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiadrenergic agents, centrally acting. ATC code: C02AB.

The antihypertensive effect of methyldopa is probably due to its metabolism to alpha-methylnoradrenaline, which lowers arterial pressure by stimulation of central inhibitory alpha-adrenergic receptors, false neurotransmission and/or reduction of plasma renin activity. Methyldopa causes a net reduction in the tissue concentration of serotonin, dopamine, epinephrine (adrenaline) and norepinephrine (noradrenaline).

5.2 Pharmacokinetic properties

Methyldopa is incompletely absorbed from the gastrointestinal tract. The bioavailability of an oral dose averages 25% (±16%); peak plasma levels occur 2–3 hours after administration. Extensively metabolised through pathways common to the catecholamines using dopa decarboxylases and dopamine β-hydroxylase. Partly conjugated mainly to the o-sulphate and excreted by the kidneys. Elimination half-life is 1.8 ± 0.2 hours. Methyldopa crosses the placental barrier; detectable quantities are present in the liver and kidneys. Renal excretion accounts for approximately two-thirds of drug clearance from plasma.

5.3 Preclinical safety data

No specific preclinical safety data are reported by the applicant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

No.	Excipient
1	Lactose monohydrate (excipient with known effect — 30 mg per tablet)

No.	Excipient
2	Maize starch
3	Microcrystalline cellulose
4	Citric acid
5	Sodium EDTA
6	Povidone K-30 (PVP K-30)
7	Isopropyl alcohol
8	Purified talc
9	Magnesium stearate
10	Colloidal anhydrous silica
11	Croscarmellose sodium
12	Iron oxide yellow (E172) — colour coat
13	Methylene dichloride

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store at a temperature not exceeding 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container
10 tablets in ALU-PVC amber coloured blister; 10 such blisters packed in a printed carton with package insert. Pack size: 100 tablets.

6.6 Special precautions for disposal and other handling
No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
ZAIN PHARMA LTD.
Plot No. 209/13741, Colchester Park,
Go-Down No. 1, 2, 3, Off Mombasa Road,
Behind Nice and Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)
H2026/CTD12757/26947

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION
17.12.2025

10. DATE OF REVISION OF THE TEXT
17.12.2025