



<b>Brand Name</b> : DOPAMET TABLETS	2021
<b>Generic Name</b> : Methyldopa Tablets BP 250 mg	
<b>Module 1</b> Administrative Information and Product Information	<b>Confidential</b>
<b>1.5</b> Product Information	

## 1.5 PRODUCT INFORMATION

### 1.5.1 Prescribing information (Summary of products characteristics)

#### SUMMARY PRODUCT CHARACTERISTICS

#### 1. Name of drug product:

DOPAMET TABLETS (Methyldopa Tablets BP 250 mg)

#### 2. Qualitative and Quantitative Composition:

Each film coated tablet contains: Methyldopa Tablets BP 250 mg

#### 3. Pharmaceutical form:

White, circular, flat, biconvex tablets, having "UG" on one side and other side plain of each tablets.

#### 4. Clinical particulars:

##### 4.1 Therapeutic Indications:

##### 1. Therapeutic indications

Treatment of hypertension

##### 4.2 Posology and method of administration

##### *Posology*

*Use in adults and children over 12 years*

*Initial dosage:* Usually 250mg two or three times a day, for two days.

*Adjustment:* Usually adjusted at intervals of not less than two days, until an adequate response is obtained. The maximum recommended daily dosage is 3g.

Many patients experience sedation for two or three days when therapy with Methyldopa is started or when the dose is increased. When increasing the dosage, therefore, it may be desirable to increase the evening dose first. Withdrawal of Methyldopa is followed by return



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of hypertension, usually within 48 hours. This is not complicated generally by an overshoot of blood pressure.

#### *Patients with renal impairment*

Methyldopa is largely excreted by the kidney, and patients with impaired renal function may respond to smaller doses.

#### *Other antihypertensives*

Therapy with Methyldopa may be initiated in most patients already on treatment with other antihypertensive agents by terminating these antihypertensive medications gradually, as required. Following such previous antihypertensive therapy, Methyldopa should be limited to an initial dose of not more than 500mg daily and increased as required at intervals of not less than two days.

When Methyldopa is given to patients on other antihypertensives the dose of these agents may need to be adjusted to effect a smooth transition.

When 500mg of Methyldopa is added to 50mg of hydrochlorothiazide, the two agents may be given together once daily.

*Paediatric population: Children under 12 years:* Initial dosage is based on 10mg/kg of bodyweight daily in 2-4 oral doses. The daily dosage is then increased or decreased until an adequate response is achieved. The maximum dosage is 65mg/kg or 3g daily, whichever is less.

*Elderly:* The initial dose in elderly patients should be kept as low as possible, not exceeding 250mg daily. An appropriate starting dose in the elderly would be 125mg twice daily increasing slowly as required, but not to exceed a maximum daily dosage of 2g. Syncope in older patients may be related to an increased sensitivity and advanced arteriosclerotic vascular disease. This may be avoided by lower doses.

#### *Method of Administration*

For oral administration.

#### **4.4 Special warnings and precautions for use**

Acquired haemolytic anaemia has occurred rarely. Should symptoms suggest anaemia, haemoglobin and/or haematocrit determinations should be made. If anaemia is confirmed, tests should be done for haemolysis; if haemolytic anaemia is present Methyldopa should be discontinued. Stopping therapy with or without giving a corticosteroid, has usually brought prompt remission. Rarely, however, deaths have occurred.

Some patients on continued therapy with methyldopa develop a positive Coombs test. From the reports of different investigators, the incidence averages between 10% and 20%. A positive Coombs test rarely develops in the first six months of therapy, and if it has not developed within twelve months, it is unlikely to do so later on continuing therapy. Development is also dose-related, the lowest incidence occurring in patients receiving 1g or less of methyldopa per day. The test becomes negative usually within weeks or months of stopping methyldopa.



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Prior knowledge of a positive Coombs reaction will aid in evaluating a cross-match for transfusion. If a patient with a positive Coombs reaction shows an incompatible minor cross-match, an indirect Coombs test should be performed. If this is negative, transfusion with blood compatible in the major cross-match may be carried out. If positive, the advisability of transfusion should be determined by a haematologist.

Reversible leucopenia with primary effect on granulocytes has been reported rarely. The granulocyte count returned to normal on discontinuing therapy. Reversible thrombocytopenia has occurred rarely.

Occasionally, fever has occurred within the first three weeks of therapy, sometimes associated with eosin



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Rarely, when urine is exposed to air after voiding, it may darken because of breakdown of methyldopa or its metabolites.

This medicine contains sunset yellow (E110) which may cause allergic reactions.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

*Alcohol:* concomitant use may enhance the hypotensive effect.

*Alprostadil:* concomitant use may enhance the hypotensive effect.

*Anaesthetics:* as concomitant use may enhance the hypotensive effect, patients may require reduced doses of anaesthetics when on methyldopa. If hypotension does occur during anaesthesia, it can usually be controlled by vasopressors.

*Antidepressants:* concomitant use may enhance the hypotensive effect. Concomitant use with MAOIs should be avoided.

*Antihypertensives:* when Methyldopa is used with other antihypertensive drugs, potentiation of antihypertensive action may occur. The progress of patients should be carefully followed to detect side reactions or manifestations of drug idiosyncrasy.

*Antipsychotics:* concomitant use can increase the risk of extrapyramidal effects and enhance the hypotensive effect. In addition, phenothiazines may have additive hypotensive effects.

*Beta-blockers:* concomitant use may enhance the hypotensive effect.

*Calcium-channel blockers:* concomitant use may enhance the hypotensive effect.

*Diuretics:* concomitant use may enhance the hypotensive effect.

*Dopaminergics:* concomitant use may antagonise the antiparkinsonian effect of this type of medicine. Concomitant use with levodopa or entacapone may enhance the hypotensive effect.

*Iron:* concomitant use may reduce the hypotensive effect. Several studies demonstrate a decrease in the bioavailability of methyldopa when it is ingested with ferrous sulfate or ferrous gluconate. This may adversely affect blood pressure control in patients treated with methyldopa.

*Lithium:* when methyldopa and lithium are given concomitantly the patient should be monitored carefully for symptoms of lithium toxicity. Neurotoxicity may occur without increased plasma-lithium concentration.

*Moxisylyte:* concomitant use may enhance the hypotensive effect.

*Muscle relaxants:* concomitant use with baclofen and tizanidine may enhance the hypotensive effect.

*Nitrates:* concomitant use may enhance the hypotensive effect.



#### 4.6 Pregnancy and lactation

##### *Pregnancy*

Methyldopa has been used under close medical supervision for the treatment of hypertension during pregnancy. There was no clinical evidence that methyldopa caused foetal abnormalities or affected the neonate.

Published reports of the use of methyldopa during all trimesters indicate that if this drug is used during pregnancy the possibility of foetal harm appears remote.

Methyldopa crosses the placental barrier and appears in cord blood.

Although no obvious teratogenic effects have been reported, the possibility of foetal injury cannot be excluded and the use of the drug in women who are, or may become pregnant requires that anticipated benefits be weighed against possible risks.

##### *Breast-feeding*

Methyldopa appears in breast milk. The use of the drug in breast-feeding mothers requires that anticipated benefits be weighed against possible risks.

#### 4.7 Effects on ability to drive and use machines

Methyldopa may cause sedation, usually transient, during the initial period of therapy or whenever the dose is increased. If affected, patients should not carry out activities where alertness is necessary, such as driving a car or operating machinery.

#### 4.8 Undesirable effects

Sedation, usually transient, may occur during the initial period of therapy or when 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.

The following convention has been utilised for the classification of frequency: Very common ( $\geq 1/10$ ), common ( $\geq 1/100$  and  $< 1/10$ ), uncommon ( $\geq 1/1000$  and  $< 1/100$ ), rare ( $\geq 1/10,000$  and  $< 1/1000$ ), very rare ( $< 1/10,000$ ) and not known (cannot be estimated from the available data).

System Organ Class	Adverse event term	Frequency
Infections and infestations	Sialadenitis	Not known
Blood and lymphatic system disorders	Haemolytic anaemia, bone marrow failure, leucopenia, granulocytopenia, thrombocytopenia, eosinophilia	Not known
Endocrine disorders	Hyperprolactinaemia	Not known
Psychiatric disorders	Psychic disturbances including nightmares, reversible mild psychoses or depression, decreased libido	Not known



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Nervous system disorders	Sedation (usually transient), headache, paraesthesia, Parkinsonism, Bell's palsy, choreoathetosis, mental impairment, carotid sinus syndrome, dizziness, symptoms of cerebrovascular insufficiency (may be due to lowering of blood pressure)	Not known
Cardiac disorders	Bradycardia, angina pectoris, myocarditis, pericarditis, atrioventricular block	Not known
Vascular disorders	Orthostatic hypotension (decrease daily dosage)	Not known
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Not known
Gastrointestinal disorders	Nausea, vomiting, abdominal distension, constipation, flatulence, diarrhoea, colitis, dry mouth, glossodynia, tongue discolouration, pancreatitis	Not known
Hepatobiliary disorders	Liver disorders including hepatitis, jaundice	Not known
Skin and subcutaneous tissue disorders	Rash (eczema, lichenoid eruption), toxic epidermal necrolysis, angioedema, urticaria	Not known
Musculoskeletal and connective tissue disorders	Lupus-like syndrome, mild arthralgia with or without joint swelling, myalgia	Not known
Reproductive system and breast disorders	Breast enlargement, gynaecomastia, amenorrhoea, lactation disorder, erectile dysfunction, ejaculation failure	Not known
General disorders and administration site conditions	Asthenia, oedema (and weight gain) usually relieved by use of a diuretic (discontinue methyldopa if oedema progresses or signs of heart failure appear), pyrexia	Not known
Investigations	Positive Coombs test, positive tests for antinuclear antibody, LE cells, and rheumatoid factor, abnormal liver function tests, increased blood urea	Not known





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### 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 Yellow Card Scheme; website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

### **4.9 Overdose**

Acute overdosage may produce acute hypotension with other responses attributable to brain and gastrointestinal malfunction (excessive sedation, weakness, bradycardia, dizziness, light-headedness, constipation, distension, flatus, diarrhoea, nausea and vomiting).

If ingestion is recent emesis may be induced or gastric lavage performed. There is no specific antidote, but Methyldopa is dialysable.

Treatment is largely symptomatic but if necessary intravenous infusion may be given to promote urinary excretion and pressor agents given cautiously.

Special attention should be directed towards cardiac rate and output, blood volume, electrolyte balance, paralytic ileus, urinary function and cerebral activity. Administration of sympathomimetic agents may be indicated. When chronic overdosage is suspected Methyldopa should be discontinued.

## **5. Pharmacological properties**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antiadrenergic agents.

ATC code: C02AB

#### *Mechanism of action*

It appears that several mechanisms of action account for the clinically useful effects of methyldopa and the current generally accepted view is that its principal action is on the central nervous system. 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 has been shown to cause a net reduction in the tissue concentration of serotonin, dopamine, epinephrine (adrenaline) and norepinephrine (noradrenaline).

### **5.2 Pharmacokinetic properties**

#### *Absorption*

Absorption of oral methyldopa is variable and incomplete.

#### *Distribution*

Bioavailability after oral administration averages 25%.



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### *Biotransformation*

Peak concentrations in plasma occur at two to three hours, and elimination of the drug is biphasic regardless of the route of administration. Plasma half-life is  $1.8 \pm 0.2$  hours.

### *Elimination*

Renal excretion accounts for about two thirds of drug clearance from plasma.

## **5.3 Preclinical safety data**

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

## **6. Pharmaceutical particulars**

### **6.1 List of excipients**

Also contains: polyvidone, sodium edetate, magnesium stearate, crospovidone, precipitated silica, macrogol, talc, E104, E110, E132, E171, E172, E330, E460, E464.

### **6.2 Incompatibilities**

None known.

### **6.3 Shelf life**

#### *Shelf-life*

Three years from the date of manufacture.

#### *Shelf-life after dilution/reconstitution*

Not applicable.

#### *Shelf-life after first opening*

Not applicable.

### **6.4 Special precautions for storage**

Store below 25°C in a dry place.

Protect from light.

### **6.5 Nature and contents of container**

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene containers and snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass containers with screw caps.

The product may also be supplied in blister packs in cartons:

- a) Carton: Printed carton manufactured from white folding box board.
- b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-7g/M<sup>2</sup> PVC and PVdC compatible heat seal lacquer on the reverse side.

Pack size: 28s, 56s, 60s, 84s, 100s, 112s, 120s, 168s, 180s, 250s, 500s, 1000s.





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Product may also be supplied in bulk packs, for reassembly purposes only, in polybags contained in tins, skillets or polybuckets filled with suitable cushioning material. Bulk packs are included for *temporary* storage of the finished product before final packaging into the proposed marketing containers.

Maximum size of bulk packs: 50,000.

## 6.6 Special precautions for disposal and other handling

Not applicable.

## Administrative Data

### 7. Marketing authorization holder

Accord-UK Ltd

(Trading style: Accord)

Whiddon Valley

Barnstaple

Devon

EX32 8NS

### 8. Marketing authorization number

PL 0142/0093

## 6. Pharmaceutical particulars:

### 6.1 List of Excipients:

Micro Crystalline Cellulose Powder	BP
Di Sodium E.D.T.A.	BP
Poly Vinyl Pyrrolidone K-30	BP
Iso Propyl Alcohol	BP
Talcum	BP
Sodium Starch Glycolate	BP
Colloidal Silicon Dioxide	BP
Magnesium Sterate	BP
Colour Instamoistshield A21D00582 Yellow	BP
Iso propyl Alcohol	BP
Methylene Dichloride	BP

### 6.2 Incompatibilities:

None Reported

### 6.3 Shelf-Life:

36 months from the date of manufacture.



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**6.4 Special Precautions for Storage:**

Store under normal storage conditions (15°C-30°C) Protect from light.

**6.5 Nature and Contents of Container:**

1000 tablets packed in one Jar. Such jar packed in unit jar along with its package insert. Such jar packed in export worthy shipper.

**6.6 Special precautions for disposal:**

None reported.

**7. Registrant:**

**AGOG PHARMA LTD.**

Plot No. 33, Sector II,  
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Co-Op. Estate Ltd., Gauraijada,  
Vasai (E), Dist. Thane,  
India.

**8. Manufacturer:**

**AGOG PHARMA LTD.**

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**9. Date of revision of the text :**