Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dopagen Tablets 125 mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Methyldopa equivalent to 125 mg anhydrous methyldopa.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Yellow, film-coated tablets embossed ‘a’ on one face and ‘M/125’ on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of hypertension.

4.2 Posology and method of adminstration

Dopagen tablets are for oral administration only.

Adults:

The usual dose is 250 - 500mg daily with subsequent slow increments until optimal control is achieved. Maintenance dosage is usually 0.5 to 2.0 grams daily in divided doses. The maximum recommended daily dosage is 3 grams.

Children:

The usual initial dosage is 10mg/kg body weight daily in 2 to 4 divided doses with gradual increments until optimal control is achieved. The usual maintenance dose is 10 to 65mg/kg daily, but a maximum dose of 3g or 65mg/kg, whichever is less, should not be exceeded.

Elderly:

In older patients, syncope may be related to an increased sensitivity and to atherosclerosis and may be avoided by using lower doses.

4.3 Contraindications

1) Hypersensitivity to methyldopa or to any of the components in these tablets.
2) Active liver disease.
3) Depression.
4) Concurrent use of monoamine oxidase inhibitors (MAOIs).
5) Methyldopa is not recommended for the treatment of phaeochromocytoma.

4.4 Special warnings and precautions for use

Methyldopa may give rise to haemolytic anaemia, the occurrence of which necessitates stopping the drug and the initiation of appropriate therapy. Leucopenia and thrombocytopenia may also occur and regular monitoring of the haemopoietic state is essential during long-term therapy.

Methyldopa may give rise to a hepatic reaction which may be acute (severe hepatitis with jaundice) or chronic (active hepatitis with clear prodromal symptoms of fever, malaise, epigastric discomfort or pain, nausea, vomiting and colic, with an eosinophilia). Rising transaminase levels herald a hepatic reaction and baseline liver function tests and white blood cell counts should be established prior to commencement of therapy. Thereafter these tests should be carried out at intervals during the first 6 - 12 weeks of treatment and regularly (e.g. twice yearly) during long term treatment or whenever an unexplained pyrexia occurs.

The product should be introduced with caution in those with pre-existing liver dysfunction.

Methyldopa may give rise to a positive Coomb's test and may thus interfere with the x-matching of blood.

This product may give rise to systemic lupus erythematosus with a positive ANF test and also to involuntary choreoathetotic movement, the occurrence of either of which is an indication for drug withdrawal.

Methyldopa may cause darkening of the urine in some patients, and spuriously high amounts of catecholamines may give rise to a false positive diagnosis of phaeochromocytoma.

Tolerance to this product may occur.

Patients with impairment of renal function may respond to smaller doses of this agent.

If cerebral or myocardial infarction occurs during therapy with this agent, adjustment of dosage or temporary cessation may be required during the acute phase. Therapy with this agent should not be initiated during the acute phase of cerebral or myocardial infarction.

4.5 Interaction with other medicinal products and other forms of interaction

1) The hypotensive effects of this preparation are enhanced by other anti- hypertensive drugs, diuretics, alcohol and anaesthetic agents, and are modified by sympathomimetics, tricyclic antidepressants, phenothiazine derivatives and monoamine oxidase inhibitors. This should be borne in mind when relevant concomitant therapy is being considered. Interactions with haloperidol and lithium have been reported.
2) In the event that a patient requires anaesthesia, the anaesthetist should be informed of the use of the medication prior to the administration of a general anaesthetic, to permit his taking the necessary precautions.
3) The anti-hypertensive effects of methyldopa can be reduced by the concurrent use of ferrous sulphate and ferrous gluconate.

4.6 Pregnancy and lactation

Methyldopa crosses the placental barrier and appears in cord blood and breast milk. Although no obvious teratogenic effects have been reported, the possibility of foetal damage cannot be excluded and the drug should not be used during pregnancy and lactation unless considered essential by the physician.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Sedation, usually transient may occur during the initial period of therapy or whenever dosage is increased. The following reactions have been reported:

Central Nervous system:

Sedation (usually transient), headache, weakness, fatigue, paraesthesia, Parkinsonism, involuntary choreoathetotic movements, Bells' palsy.
Dizziness and lightheadedness, which may be associated with reduction in blood pressure. Nightmares, impaired mental activity, mild psychosis or depression.

Cardiovascular system:

Bradycardia, prolonged carotid sinus hypersensitivity, orthostatic hypotension, aggravation of angina pectoris. Oedema (discontinue methyldopa if oedema progresses or if signs of heart failure develop).

Gastrointestinal system:

Nausea, vomiting, diarrhoea or constipation. Colitis, pancreatitis, dry mouth, sialadenitis, soreness of blackness of the tongue.

Hepatic:

Liver disorders, including hepatitis, jaundice, abnormal liver function tests.

Haematological:

Haemolytic anaemia, bone marrow depression, leucopenia, granulocytopenia, thrombocytopenia, eosinophilia. A positive Coombs test and positive tests for antinuclear antibody, LE cells and rheumatoid factor.

Dermatological:

Skin rashes, including eczema or lichenoid eruption, toxic epidermal necrolysis

Immunological:

Allergic reactions, including drug-related fever and lupus like syndrome, pericarditis, myocarditis.

Musculoskeletal:

Arthralgia, myalgia.

Endocrine:

Hyperprolactinaemia, gynaecomastia, breast enlargement, lactation.

Genitourinary:

Amenorrhoea, impotence, decreased libido, failure of ejaculation, rise in blood urea.

Other:

Nasal stuffiness.

4.9 Overdose

Possible symptoms of acute overdosage include acute hypotension, bradycardia, weakness, nausea, vomiting and coma. There is no antidote to methyldopa and treatment is symptomatic and supportive.

In acute overdosage, the stomach should be emptied by aspiration and lavage. If necessary, intravenous infusions may be given to promote urinary excretion and pressor agents may be administered cautiously where indicated. Methyldopa is dialysable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Methyldopa is an antihypertensive agent. It acts centrally by stimulating alpha 2-adrenoceptors, resulting in a reduction in sympathetic tone and a fall in blood pressure.

5.2 Pharmacokinetic properties

Methyldopa is incompletely absorbed from the gut, reaches peak concentrations in plasma in 2 hours and is eliminated via the kidney as unchanged drug and conjugates: half-life ranges from 8 to 65 hours.

5.3 Preclinical safety data

No further relevant information other than that, which is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Colloidal anhydrous silica
Povidone
Magnesium stearate
Sodium starch glycollate Type A
Methylcellulose
Ethylcellulose
Diethylphthalate
Opaspray K-I-2119 (Contains Hydroxypropylcellulose, Titanium Dioxide E171, Tartrazine Lake E102).

6.2 Incompatibilities

None known.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep in original container to protect from light.

6.5 Nature and contents of container

Polypropylene securitainers with tamper evident polypropylene caps.
Pack sizes: 100, 500 and 1,000 tablets.

6.6 Instructions for use and handling

None.

7 MARKETING AUTHORISATION HOLDER

Antigen Pharmaceuticals Limited
Roscrea
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA 73/51/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14th November 1981.

Date of last renewal: 14th November 2001.

10 DATE OF REVISION OF THE TEXT

June 2002.