1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

HY-PO-TONE 250 (film-coated tablet)

HY-PO-TONE 500 (film-coated tablet)

COMPOSITION

HY-PO-TONE 250:

Each film-coated tablet contains 250 mg methyldopa as anhydrous methyldopa.

Excipients:

Citric acid monohydrate, crospovidone, disodium edetate, iron oxide yellow (C.I. 77492), magnesium stearate, methocel, microcrystalline cellulose, povidone, polyethylene glycol, quinoline yellow aluminium lake (C.I. 47005), titanium dioxide (C.I. 77891)

Sugar free

HY-PO-TONE 500:

Each film-coated tablet contains 500 mg methyldopa as anhydrous methyldopa.

Excipients:

Citric acid anhydrous, crospovidone, disodium edetate, magnesium stearate, opadry II HP 58F22107 yellow, povidone, silicified microcrystalline cellulose

Sugar free

CATEGORY AND CLASS

A 7.1.3 Other hypotensives

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

The exact mechanism of pharmacological action is not known.

It may involve stimulation of central alpha-adrenergic receptors by a metabolite, alpha-methylnorepinephrine, thus inhibiting sympathetic outflow to the heart, kidneys and peripheral vasculature. Reduced peripheral resistance and plasma renin activity may also contribute to its effect.

Pharmacokinetic properties

After oral use methyldopa is variably and incompletely absorbed, apparently by an amino-acid active transport system. The mean bioavailability has been reported to be about 50 %. It is extensively metabolised and is excreted in urine mainly as unchanged medicine and the *O*-sulfate conjugate. It crosses the blood-brain barrier and is decarboxylated in the CNS to active alpha-methylnoradrenaline.

INDICATIONS

HY-PO-TONE is indicated in the treatment of essential hypertension.

CONTRAINDICATIONS

HY-PO-TONE is contraindicated in:

- Persons known to be hypersensitive to methyldopa or its excipients.

- Impaired kidney or liver function or with a history of liver disease.
- Mental depression.
- It should not be given to patients with acute liver disease.
- Phaeochromocytoma.
- Porphyria.
- Patients on therapy with monoamine oxidase inhibitors (MAOI).

WARNINGS AND SPECIAL PRECAUTIONS

It is advisable to do periodic blood counts and to perform liver function tests at intervals during the first 6 to 12 weeks of treatment or if the patient develops an unexpected fever. Patients taking HY-PO-TONE may produce a positive response to a direct antiglobulin test (Coombs' test); if blood transfusion is required, prior knowledge of a positive direct antiglobulin test (Coombs' test) reaction will aid cross-matching.

HY-PO-TONE may occasionally cause urine to darken because of the breakdown of the medicine or its metabolites.

Severe hypotension may occur during anaesthesia in patients being treated with HY-PO-TONE. The hypotensive effects may be diminished by sympathomimetics, imipramine and other tricyclic antidepressants and monoamine oxidase inhibitors.

Effects on ability to drive and use machines

HY-PO-TONE may cause sedation, usually transient, may occur 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.

INTERACTIONS

HY-PO-TONE may interfere with the measurement of urinary uric acid by the phosphotungstate method and serum glutamic-pyruvic transaminase by the colorimetric method. Methyldopa fluoresces at the same wavelengths as catecholamines and may cause erratic reports of elevated urinary catecholamine concentrations.

Severe hypotension may occur during anaesthesia in patients being treated with HY-PO-TONE. The hypotensive effects may be diminished by sympathomimetics, imipramine and other tricyclic antidepressants and monoamine oxidase inhibitors.

Lithium

When HY-PO-TONE and lithium are given concomitantly the patient should be monitored carefully for symptoms of lithium toxicity.

Other classes of medicines

The hypotensive effect of HY-PO-TONE may be diminished by sympathomimetics, phenothiazines, tricyclic antidepressants and MAOIs (see CONTRAINDICATIONS).

The combination of HY-PO-TONE with other potentially hepatotoxic medicines, particularly halothane, is not advisable.

HUMAN REPRODUCTION

Pregnancy:

The safety of HY-PO-TONE in pregnancy has not been established, as there are no adequate and well-controlled studies in pregnant women.

HY-PO-TONE crosses the placenta and reduced blood pressure has been reported in

infants born to mothers receiving HY-PO-TONE.

Lactating mothers:

Methyldopa is distributed into breast milk in small amounts. The safety of HY-PO-TONE in lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE

Doses of 250 mg two or three times daily during the first 48 hours. Thereafter, the daily dosage may be adjusted preferably at intervals of not less than 48 hours intervals until an adequate response has been achieved. The usual dose is from 500 mg to 2 g daily.

A suggested initial dose for children is 10 mg/kg body mass daily in divided doses.

SIDE EFFECTS

Blood and lymphatic system disorders:

Less frequent: Thrombocytopenia, leucopenia, granulocytopenia and haemolytic anaemia

A positive response to the direct antiglobulin test (Coombs' test) may occur in 10 % to 20 % of patients on prolonged therapy, usually without evidence of haemolysis.

Immune system disorders:

Less frequent: Drug fever may occur within the first few weeks of therapy and may be accompanied by eosinophilia and abnormal liver function tests. Jaundice with or without fever may occur.

It is advisable to take blood counts and to perform liver-function tests at intervals during the first 6 to 12 weeks of treatment or if the patient develops an unexplained fever.

Psychiatric disorders:

Less frequent: Psychic effects, nightmares

Nervous system disorders:

Frequent: Headache, drowsiness (drowsiness occurs commonly in the first 2 or 3 days and usually decreases spontaneously or as a result of a reduction in the dosage)

Less frequent: Depression, impaired mental acuity

Frequency unknown: Involuntary choreoathetotic movements have occurred in patients with severe bilateral cerebrovascular disease, Bell's palsy, Parkinsonism

Cardiovascular disorders:

Frequent: Oedema. (Mass gain and oedema may be diminished by the concomitant administration of a thiazide diuretic such as hydrochlorothiazide)

Less frequent: Bradycardia, postural hypotension (with associated weakness, dizziness, light-headedness), myocarditis

Frequency unknown: Aggravation of angina pectoris

Gastrointestinal disorders:

Frequent: Colitis, diarrhoea, nausea, pancreatitis

Frequency unknown: Salivary gland inflammation, black or sore tongue, constipation

Hepatobiliary disorders:

Less frequent: Liver damage may develop after long-term administration; fatal hepatic necrosis

Skin disorders:

Frequency unknown: Eczematous rashes and lichenoid and granulomatous skin eruptions

have occurred

Musculoskeletal disorders:

Frequency unknown: Mild arthralgia, myalgia

Renal disorders:

Frequency unknown: Uraemia

General disorders:

Less frequent: A condition resembling systemic lupus erythematosus, disorders of sexual function, hyperprolactinaemia (with breast enlargement, lactation), nasal stuffiness

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

See SIDE EFFECTS.

Symptoms

Acute overdose may produce acute hypotension with other responses attributable to brain and gastrointestinal malfunction (excessive sedation, weakness, bradycardia, dizziness, lightheadedness, constipation, distention, flatus, diarrhoea, nausea, vomiting).

Treatment

If overdosage occurs the stomach should be emptied by aspiration and lavage. Treatment is largely symptomatic, but if necessary, intravenous infusions may be given to promote urinary excretion, and pressor medicines given cautiously. Methyldopa is dialysable.

IDENTIFICATION

HY-PO-TONE 250: A round, pale yellow, film-coated biconvex tablet bearing a distinctive H-

P-T logo on one side, free from cracking, peeling or chipping.

HY-PO-TONE 500: A pale yellow, round, biconvex film-coated tablet, free from cracking, peeling or chipping.

PRESENTATION

HY-PO-TONE 250:

30 tablets are packed in a white polypropylene securitainer with or without a foam or rayon insert and sealed with a white low-density polyethylene securitainer cap.

100 tablets are packed in a white polypropylene securitainer with or without a foam or rayon insert and dessicant disc, which is sealed with a white low-density polyethylene securitainer cap.

500 tablets are packed in a white polypropylene securitainer with or without a foam insert and silica gel sachet, which is sealed with a white low-density polyethylene securitainer cap.

28, 56 and 84 tablets are packed into metallised patient ready packs which are sealed with lay-flat zips after filling and packed into clear polyethylene bags.

1 000 tablets are packed into clear polyethylene bags, into 5 l tins.

HY-PO-TONE 500:

100 tablets are packed in a white polypropylene securitainer together with a desiccant and sealed with a white low-density polyethylene cap.

500 tablets are packed in a white polypropylene securitainer together with a silica gel sachet

and foam insert and sealed with a white low-density polyethylene cap.

28 tablets are packed into metallised patient ready packs which are sealed with lay-flat zips and packed into polyethylene bags.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Keep the container tightly closed.

Protect from light and dispense in amber bottles.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

HY-PO-TONE 250: K/7.1.3/90

HY-PO-TONE 500: K/7.1.3/209

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Dates of registration:

HY-PO-TONE 250: 09 December 1977

HY-PO-TONE 500: 05 December 1977

Date of the most recent amendment to the professional information as approved by the Authority: 01 March 2013

Botswana:	S2
HY-PO-TONE 250:	B9322375
HY-PO-TONE 500:	B9322380

Namibia:	NS2
HY-PO-TONE 250:	90/7.1.3/00982
HY-PO-TONE 500:	90/7.1.3/00983

Zimbabwe:	P.P.10
HY-PO-TONE 250:	92/12.3.3/2603

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