SUMMARY OF PRODUCT CHARACTERISTICS OF HYOSCINE BUTYL BROMIDE 10 MG FILM COATED TABLET

1. Name of the medicinal product

Hyoscine butyl bromide 10 mg film coated Tablet

2. Qualitative and quantitative composition

Each film coated tablet contains 10 mg of Hyoscine butyl bromide.

Pharmaceutical form

Film coated Tablet

White, circular biconvex film coated tablets plain on both sides.

3. Clinical particulars

3.1 Therapeutic indications

Indicated for:

The relief of spasm of the genito-urinary tract or gastro- intestinal tract and for the symptomatic relief of Irritable Bowel Syndrome.

3.2 Posology and method of administration

Oral administration only.

Adults: 2 tablets four times daily. For the symptomatic relief of Irritable Bowel Syndrome, the recommended starting dose is 1 tablet three times daily; this can be increased up to 2 tablets four times daily if necessary.

Children 6 - 12 years: 1 tablet three times daily.

No specific information on the use of this product in the elderly is available. Clinical trials have included patients over 65 years and no adverse reactions specific to this age group have been reported.

3.3 Contraindications

It is contraindicated in:

- Patients who have demonstrated prior hypersensitivity to hyoscine butylbromide or any other component of the product

- Myasthenia gravis

- Mechanical stenosis in the gastrointestinal tract

- Paralytical or obstructive ileus

- Megacolon

- Narrow angle glaucoma

3.4 Special warnings and precautions for use

In case severe, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting, or blood in stool, medical advice should immediately be sought.

It should be used with caution in conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure and in cardiac surgery where it may further accelerate the heart rate. Due to the risk of anticholinergic complications, caution should be used in patients susceptible to intestinal or urinary outlet obstructions.

Because of the possibility that anticholinergics may reduce sweating, it should be administered with caution to patients with pyrexia.

Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as it in patients with undiagnosed and therefore untreated narrow angle glaucoma. Therefore, patients should seek urgent ophthalmological advice in case they should develop a painful, red eye with loss of vision.

3.5 Interaction with other medicinal products and other forms of interaction

The anticholinergic effect of drugs such as tri- and tetracyclic antidepressants, antihistamines, quinidine, amantadine, antipsychotics (e.g. butyrophenones, phenothiazines), disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds).

Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both drugs on the gastrointestinal tract.

The tachycardic effects of beta-adrenergic agents may be enhanced.

3.6 Pregnancy and lactation

Pregnancy

There are limited data from the use of hyoscine butylbromide in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). As a precautionary measure it is not recommended during pregnancy.

Lactation

There is insufficient information on the excretion of hyoscine butylbromide and its metabolites in human milk. A risk to the breastfeeding child cannot be excluded. Use during breastfeeding is not recommended.

Fertility

No studies on the effects on human fertility have been conducted.

3.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Because of possible visual accommodation disturbances patients should not drive or operate machinery if affected.

3.8 Undesirable effects

Immune system disorders

Not known: anaphylactic shock, anaphylactic reactions, dyspnoea, other hypersensitivity

Cardiac disorders

Uncommon: tachycardia

Gastrointestinal disorders:

Uncommon: dry mouth

Skin and subcutaneous tissue disorders

Uncommon: skin reactions (e.g. urticaria, pruritus), abnormal sweating

Not known: rash, erythema

Renal and urinary disorders

Rare: urinary retention

3.9 Overdose

Symptoms:

Serious signs of poisoning following acute overdosage have not been observed in man. In the case of overdosage, anticholinergic effects such as urinary retention, dry mouth, reddening of theskin, tachycardia, inhibition of gastrointestinal motility and transient visual disturbances may occur, and Cheynes-Stokes respiration has been reported.

Therapy:

In the case of oral poisoning, gastric lavage with medicinal charcoal should be followed by magnesium sulfate (15%). Symptoms of overdosage respond to parasympathomimetics. For patients with glaucoma, pilocarpine should be given locally. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis, intubation and artificial respiration should be considered. Catheterisation may be required for urinary retention.

4. Pharmacological properties

4.1 Pharmacodynamic properties

Mechanism of action

It exerts a spasmolytic action on the smooth muscle of the gastrointestinal, biliary and genito-urinary tracts. As a quaternary ammonium derivative, hyoscine butylbromide does not enter the central nervous system. Therefore, anticholinergic side effects at the central nervous system do not occur. Peripheral anticholinergic action results from a ganglion-blocking action within the visceral wall as well as from an anti-muscarinic activity.

4.2 Pharmacokinetic properties

<u>Absorption</u>

As a quaternary ammonium compound, hyoscine butyl bromide is highly polar and hence only partially absorbed following oral (8%) or rectal (3%) administration. After oral administration of single doses of hyoscine butyl bromide in the range of 20 to 400 mg, mean peak plasma concentrations between 0.11 ng/mL and 2.04 ng/mL were found at approximately 2 hours. In the same dose range, the observed mean $AUC_{0\text{-}tz}$-values varied from 0.37 to 10.7 ng h/mL. The median absolute bioavailabilities of different dosage forms, i.e. coated tablets, suppositories and oral solution, containing 100 mg of hyoscine butyl bromide each were found to be less than 1%.

Distribution

Because of its high affinity for muscarinic receptors and nicotinic receptors, hyoscine butyl bromide is mainly distributed on muscle cells of the abdominal and pelvic area as well as in the intramural ganglia of the abdominal organs. Plasma protein binding (albumin) of hyoscine butyl bromide is approximately 4.4%. Animal studies demonstrate that hyoscine butyl bromide does not pass the blood-brain barrier, but no clinical data to this effect is available. Hyoscine butyl bromide (1 mM) has been observed to interact with the choline transport (1.4 nM) in epithelial cells of human placenta *in vitro*.

Metabolism and elimination

Following oral administration of single doses in the range of 100 to 400 mg, the terminal elimination half-lives ranged from 6.2 to 10.6 hours. The main metabolic pathway is the hydrolytic cleavage of the ester bond. Orally administered hyoscine butyl bromide is excreted in the faeces and in the urine. Studies in man show that 2 to 5% of radioactive doses are eliminated renally after oral and 0.7 to 1.6% after rectal administration. Approximately 90% of recovered radioactivity can be found in the faeces after oral administration. The urinary excretion of hyoscine butyl bromide is less than 0.1% of the dose. The mean apparent oral clearances after oral doses of 100 to 400 mg range from 881 to 1420 L/min, whereas the corresponding volumes of distribution for the same range vary from 6.13 to 11.3 x 10^5 L, probably due to very low systemic availability. The metabolites excreted via the renal route bind poorly to the muscarinic receptors and are therefore not considered to contribute to the effect of the hyoscine butyl bromide.

4.3 Preclinical safety data

In limited reproductive toxicity studies hyoscine butyl bromide showed no evidence of teratogenicity in rats at 200 mg/kg in the diet or in rabbits at 200 mg/kg by oral gavage or 50 mg/kg by subcutaneous injection. Fertility in the rat was not impaired at doses of up to 200 mg/kg in the diet.

5. Pharmaceutical particulars

5.1 List of excipients

Lactose BP

Maize starch BP

Povidone BP

Isopropyl alcohol BP

Magnesium stearate BP

FILM COATING

Hypromellose BP

Diethyl phthalate BP

Titanium dioxide BP

Isopropyl alcohol BP

Dichloromethane BP

Hard paraffin

Carnauba wax

Chloroform BP

5.2 Incompatibilities

None

5.3 Shelf life

3 years

5.4 Special precautions for storage

Store in a dry place below 30˚C. Protect from Light.

5.5 Nature and contents of container

PVC/Alu

5.6 Special precautions for disposal and other handling

No special requirements.

7 Registrant

Cosmos Limited

8 Manufacturer

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