# SUMMARY OF PRODUCT CHARACTERISTICS

**1. Name of the medicinal product**

Hyospan Syrup

**2. Qualitative and quantitative composition**

Each 5ml contains hyoscine butyl bromide 5. 0 mg.

**3. Pharmaceutical form**

Syrup

**4. Clinical particulars**

**4.1 Therapeutic indications**

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

**4.2 Posology and method of administration**

Hyospan Syrup is for oral administration only.

Adults: 20ml four times daily. For the symptomatic relief of Irritable Bowel Syndrome, the recommended starting dose is 10ml three times daily, this can be increased up to 20ml four times daily if necessary.

Children 6 - 12 years: 10ml 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.

Hyospan Syrup should not be taken on a continuous daily basis or for extended periods without investigating the cause of abdominal pain.

**4.3 Contraindications**

Hyospan Syrup is contraindicated in:

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

- Myasthenia gravis

- Mechanical stenosis in the gastrointestinal tract

- Paralytical or obstructive ileus

- Megacolon

- Narrow angle glaucoma

**4.4 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.

Hyospan Syrup should be used with caution in conditions characterized 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, Hyospan Syrup should be administered with caution to patients with pyrexia.

Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as Hyospan Syrup 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 whilst or after taking Hyospan Syrup.

Additional warnings for the Patient Information Leaflet (in relation to the Irritable Bowel Syndrome Indication)

Special warnings if you are taking Hyospan for Irritable Bowel Syndrome

If this is the first time you have had symptoms of Irritable Bowel Syndrome, consult your doctor before using any treatment.

If any of the following apply to you do not take Hyospan. It may not be the right treatment for you. See your doctor as soon as possible.

• You are aged 40 years or over

• You have passed blood from the bowel

• You are feeling sick or vomiting

• You have lost your appetite or lost weight

• You are looking pale and feeling tired

• You are suffering from severe constipation

• You have a fever

• You have recently travelled abroad

• You have abnormal vaginal bleeding or discharge

• You have difficulty or pain passing urine

Consult your doctor if you have developed new symptoms, or if your symptoms worsen, or if they do not improve after 2 weeks of treatment.

**4.5 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) may be intensified by Hyospan Syrup.

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 by Hyospan Syrup.

**4.6 Fertility, pregnancy and lactation**

Pregnancy

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

Lactation

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

Fertility

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

**4.7 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.

**4.8 Undesirable effects**

Many of the listed undesirable effects can be assigned to the anticholinergic properties of HYOSPAN SYRUP.

Adverse events have been ranked under headings of frequency using the following convention:

Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to <1/100); rare (≥ 1/10000 to <1/1000); very rare (<1/10000); not known (cannot be estimated from the available data).

<u>Immune system disorders</u>

Not known*: anaphylactic shock, anaphylactic reactions, dyspnea, and other hypersensitivity

<u>Cardiac disorders</u>

Uncommon: tachycardia

<u>Gastrointestinal disorders:</u>

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

* This adverse reaction has been observed in post-marketing experience. With 95% certainty, the frequency category is not greater than uncommon (3/1,368) but might be lower. A precise frequency estimation is not possible as the adverse drug reaction did not occur in a clinical trial database of 1,368 patients.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorization 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 https://pvims.rwandafda.gov.rw/security/landing

**4.9 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 the skin, 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 Hyospan Syrup 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. Catheterization may be required for urinary retention.

In addition, appropriate supportive measures should be administered as required.

**5. Pharmacological properties**

**5.1 Pharmacodynamic properties**

Hyospan Syrup exerts a spasmolytic action on the smooth muscle of the gastrointestinal, biliary and genito-urinary tracts. As a quaternary ammonium derivative, hyoscine butyl bromide 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.

**5.2 Pharmacokinetic properties**

Absorption

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 bio availabilities 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 is 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.

**5.3 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.

**6. Pharmaceutical particulars**

**6.1 List of excipients**

Cello Cell 100H

Sorbitol 70% Solution B.P

Sodium Benzoate

Potassium Sorbate

Sodium Saccharin

Tween 80

Peppermint Oil

Green Colour

De-ionized water to make up to volume

**6.2 Incompatibilities**

None stated.

**6.3 Shelf life**

Three years.

**6.4 Special precautions for storage**

Hyospan should be protected from direct sunlight and stored in a dry cool place below 30°C.

**6.5 Nature and contents of container**

60 ml amber coloured (Glass/PET) bottles, 25 mm Aluminium caps, Hyospan Syrup 60ml unit boxes

Hyospan Syrup Literatures, Hyospan Syrup 60ml labels, 150 x 60ml Shippers, Brown Bopp tape

**6.6 Special precautions for disposal and other handling**

Any unused medicinal product or waste material should be disposed off in accordance with local requirements

**7. Marketing authorization holder**

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**8. Marketing authorization number(s)**

PPB- 11743

**9. Date of first authorization/renewal of the authorization**

07/06/1999

**10. Date of revision of the text**

01/10/2022

**LEGAL CATEGORY**