Approved Professional Information for BUSCOPAN® 10 mg tablets

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

BUSCOPAN® 10 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains hyoscine butylbromide 10 mg.

Contains sugar: 41,2 mg sucrose per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

White sugar-coated biconvex tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BUSCOPAN is used in the treatment of conditions associated with gastrointestinal spasm.

4.2 Posology and method of administration

Posology

Adults:

1 tablet 3 times daily. The dose can be increased at the discretion of the medical practitioner up to 2 tablets 4 times daily if necessary.

Children 6 – 12 years:

1 tablet 3 times daily.

The tablets should be swallowed whole with adequate liquid and not be chewed.

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

Special populations

Paediatric population:

For infants and children under 6 years BUSCOPAN 0,1 % syrup (containing 5 mg hyoscine butylbromide per 5 mL) is available.

4.3 Contraindications

BUSCOPAN is contraindicated in:

- patients who have demonstrated prior hypersensitivity to hyoscine butylbromide or any other component of the product (see section 6.1)
- myasthenia gravis
- mechanical stenosis in the gastrointestinal tract
- paralytic or obstructive ileus
- megacolon
- narrow angle glaucoma
- porphyria
- enlarged prostate
- fever
- tachycardia.

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.

Because of the potential risk of anticholinergic complications, caution should be used in patients prone to narrow angle glaucoma as well as in patients susceptible to intestinal or urinary outlet obstructions and in those inclined to tachyarrhythmia.

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

Elevation of intraocular pressure may be produced by the administration of anticholinergic medicines such as BUSCOPAN 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 Buscopan.

Caution is advised in patients with impaired metabolic, liver or kidney function, as adverse central nervous system effects may be more likely in these patients.

Cases of anaphylaxis including episodes of shock have been observed.

As the tablet coat contains sucrose (41,2 mg), patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take BUSCOPAN.

4.5 Interaction with other medicines and other forms of interaction

The anticholinergic effect of medicines 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 BUSCOPAN.

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

The tachycardic effects of beta-adrenergic medicines may be enhanced by BUSCOPAN.

BUSCOPAN should be used with caution in patients receiving other central depressants concomitantly as central nervous system depression may be enhanced.

4.6 Fertility, 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. As a precautionary measure BUSCOPAN is not recommended during pregnancy.

Breastfeeding

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 of BUSCOPAN 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 BUSCOPAN.

Adverse events have been ranked under headings of frequency using the following convention: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

Immune system disorders:

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

Cardiac disorders:

Uncommon: tachycardia

Not known: bradycardia followed by tachycardia with palpitations and arrhythmias

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.

* 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 authorisation of BUSCOPAN is important. It allows continued monitoring of the benefit/risk balance of BUSCOPAN. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

- https://www.sahpra.org.za/Publications/Index/8, or to the
- Pharmacovigilance Unit at Sanofi at za.drugsafety@sanofi.com (email) or 011 256 3700 (tel).

4.9 Overdose

Symptoms:

In case of overdose, anticholinergic effects may be observed.

Toxic doses cause tachycardia, rapid or stertorous respiration, hyperpyrexia, restlessness, confusion and excitement, and hallucinations passing into delirium. A rash may appear on the face and upper trunk. In severe intoxication depression of the central nervous system may occur with hypertension or circulatory failure and respiratory depression. Quaternary ammonium anticholinergic medicines such as BUSCOPAN usually have some ganglion-blocking activity so that high doses may cause postural hypotension; in toxic doses non-depolarising neuro-muscular block may be produced.

Therapy:

Treatment is symptomatic and supportive. If required, parasympathomimetic medicines should be administered. Ophthalmological advice should be sought urgently in cases of glaucoma. 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. In addition, appropriate supportive measures should be used as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Hyoscine butylbromide belongs to the medicine class A 11.2 Gastro-intestinal antispasmodics and cholinolytics (anticholinergics).

Hyoscine butylbromide is a quaternary ammonium anticholinergic medicine that acts at the parasympathetic ganglia in the walls of the viscera where it exerts a specific antispasmodic action on the smooth muscle of the gastrointestinal, biliary and urinary tracts.
As a quaternary ammonium derivative, hyoscine butylbromide does not readily pass the blood-brain barrier to enter the central nervous system.

5.2 Pharmacokinetic properties

Absorption:

As a quaternary ammonium compound, hyoscine butylbromide is highly polar and hence only partially absorbed following oral (8 %) or rectal (3 %) administration. After oral administration of single doses of hyoscine butylbromide 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 butylbromide each were found to be less than 1 %.

Distribution:

Because of its high affinity for muscarinic receptors and nicotinic receptors, hyoscine butylbromide 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 butylbromide is approximately 4,4 %. Animal studies demonstrate that hyoscine butylbromide does not pass the blood-brain barrier, but no clinical data to this effect is available. Hyoscine butylbromide (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 butylbromide 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 butylbromide 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 1 420 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 butylbromide.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Dibasic calcium phosphate

Maize starch, starch soluble

colloidal silica

Tartaric acid

Stearic acid.

Tablet coating:

Polyvidone

Sucrose

Talc

Acacia

Titanium dioxide

Polyethylene glycol 6000

Carnauba wax

Beeswax white.

6.2 Incompatibilities

None stated.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 °C.

6.5 Nature and contents of container

PVC/Aluminium blister strips of 10 or 20 tablets packed into cartons of 10, 20 or 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

2 Bond Street

1685 Midrand

South Africa

8. REGISTRATION NUMBER

E 501 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Old medicine

10. DATE OF REVISION OF THE TEXT

19 April 2022