# PRESCRIBING INFORMATION AND PATIENT MEDICATION INFORMATION

**ACCEL-HYOSCINE**

Hyoscine Butylbromide Tablets
Mfr. Std.

10 mg

Antispasmodic

Accel Pharma Inc.
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## PART I: HEALTH PROFESSIONAL INFORMATION

### SUMMARY PRODUCT INFORMATION

| Route of Administration | Dosage Form / Strength | All Nonmedicinal Ingredients |
|---|---|---|
| Oral | Tablets, 10 mg | lactose monohydrate, lecithin (soya), macrogol, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, povidone, talc, titanium dioxide |

### INDICATIONS AND CLINICAL USE

ACCEL-HYOSCINE (hyoscine butylbromide) tablets are indicated for:

- The relief of smooth muscle spasm/cramping of the gastrointestinal system and its associated pain and discomfort.

**Geriatrics:**
*No data is available.*

**Pediatrics:**
*No data is available.*

### CONTRAINDICATIONS

- Hypersensitivity to hyoscine butylbromide, atropinics (see WARNINGS AND PRECAUTIONS) or to any of the product excipients (See DOSAGE FORMS, COMPOSITION AND PACKAGING).

- ACCEL-HYOSCINE (hyoscine butylbromide) tablets are contraindicated in patients with myasthenia gravis, megacolon, mechanical stenosis in the gastrointestinal tract, glaucoma, obstructive prostatic hypertrophy, paralytic or obstructive ileus.

## WARNINGS AND PRECAUTIONS

### General

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

Patients intolerant of one belladonna alkaloid or derivative may also be intolerant of other belladonna alkaloids or derivatives such as hyoscine butylbromide.

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.

After administration of hyoscine butylbromide, cases of anaphylaxis, including episodes of shock have been observed. As with all drugs causing such reactions, patients receiving ACCEL-HYOSCINE should be kept under observation.

### Cardiovascular

ACCEL-HYOSCINE can cause adverse reactions of tachycardia and hypotension, which may be more serious or more severe in patients with cardiac conditions such as coronary heart disease, cardiac arrhythmias, hypertension, and mitral stenosis, and in cardiac surgery. Monitoring of these patients is advised until conditions return to normal. Emergency equipment and personnel trained in its use must be readily available.

The increase in heart rate may also be undesirable in patients with unstable cardiovascular status in an acute hemorrhage situation.

Because of the potential risk of anticholinergic complications, exercise caution in patients inclined to tachyarrhythmia for ACCEL-HYOSCINE tablet.

### Gastrointestinal

Because of the potential risk of anticholinergic complications, caution should be used in patients susceptible to intestinal outlet obstructions for ACCEL-HYOSCINE tablet.

Exercise caution in patients with reflux esophagitis or gastrointestinal tract obstructive disease (i.e., achalasia and pyloroduodenal stenosis) due to the ability of anticholinergics/systemic antispasmodics to decrease smooth muscle motility and tone resulting in gastric retention.

Anticholinergics may aggravate hiatal hernia associated with reflux esophagitis, myasthenia gravis or pyloric obstruction.

In patients with ulcerative colitis, large anticholinergic doses may suppress intestinal motility, possibly causing paralytic ileus or resulting in obstruction; also, use may precipitate or aggravate toxic megacolon.

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.

**Genitourinary**

Because of the potential risk of anticholinergic complications, caution should be used in patients susceptible to urinary outlet obstructions for ACCEL-HYOSCINE tablets.

ACCEL-HYOSCINE (hyoscine butylbromide) should be used with caution in patients with prostatic enlargement. Hyoscine butylbromide may precipitate or aggravate urinary retention in patients with the following conditions: non-obstructive prostatic hypertrophy, urinary retention (or the predisposition to) or obstructive uropathy such as a bladder neck obstruction due to prostatic hypertrophy (see CONTRAINDICATIONS).

**Ophthalmologic**

Because of the potential risk of anticholinergic complications, caution should be used in patients prone to narrow angle glaucoma for ACCEL-HYOSCINE tablets

The administration of hyoscine butylbromide, particularly of higher doses, has been reported to cause transient disturbances of accommodation which recede spontaneously. Therefore, patients should be cautioned about potential visual problems and the need to exercise care while driving or operating machinery after receiving ACCEL-HYOSCINE.

Therapy should be discontinued if the patient reports any unusual visual disturbances or pressure pain within the eyes.

Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as ACCEL-HYOSCINE 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 ACCEL-HYOSCINE.

**Special Populations**

**Fertility, pregnancy and nursing:**

There is limited data from the use of hyoscine butylbromide in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

There is insufficient information on the excretion of hyoscine butylbromide and its metabolites in human milk.

As a precautionary measure, it is preferable to avoid the use of ACCEL-HYOSCINE (hyoscine butylbromide) during pregnancy and nursing.

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

**Pediatrics:**
ACCEL-HYOSCINE is not currently recommended for use in children.

**Geriatrics:**
Geriatric patients are especially susceptible to the anticholinergic side effects of constipation, dryness of mouth and urinary retention (especially in males). If these side effects continue or are severe, discontinuation of medication should be considered.

Due care is necessary when anticholinergics are administered to geriatric patients due to the danger of precipitating undiagnosed acute angle-closure glaucoma.

Administration of anticholinergics/systemic antispasmodics to elderly patients with intestinal atony or in debilitated patients may result in intestinal obstruction.

**Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed.

However, patients should be advised that they may experience undesirable effects such as accommodation disorder or dizziness during treatment with ACCEL-HYOSCINE. Therefore, caution should be recommended when driving a car or operating machinery. If patients experience accommodation disorder or dizziness, they should avoid potentially hazardous tasks such as driving or operating machinery.

## ADVERSE REACTIONS

**Adverse Drug Reaction Overview**

Many of the listed undesirable effects can be assigned to the anticholinergic properties of hyoscine butylbromide. Anticholinergic side effects of hyoscine butylbromide are generally mild and self-limited.

Accumulated clinical and postmarketing experience indicates that the following adverse reactions can be expected with the use of ACCEL-HYOSCINE (hyoscine butylbromide):

**Tablets**

**Cardiac disorders**
Tachycardia

**Eye disorders**
Visual accommodation disorders, mydriasis, increased intraocular pressure.

**Gastrointestinal disorders**
Xerostomia (dry mouth), diarrhea, nausea.

**Immune system disorders**
There have been very rare reports of anaphylactic reactions and anaphylactic shock.

Skin reactions (e.g. urticaria, rash, erythema, pruritus), and other hypersensitivity, angioedema and fixed drug eruptions have been reported rarely.

Dyspnea

**Renal and urinary disorders**
Urinary retention

**Skin and subcutaneous tissue disorders**
Hypohidrosis, heat sensation/transpiration.

**Vascular disorders**
Adverse events reported during therapy with hyoscine butylbromide include increased pulse rate.

## DRUG INTERACTIONS

### Overview

As hyoscine butylbromide can reduce the motility and secretory activity of the gastrointestinal system, the systemic absorption and pharmacologic effects of other oral medications may be delayed.

### Drug-Drug Interactions

**Table 1 - Established or Potential Drug-Drug Interactions**

| Hyoscine Butylbromide | Effect | Clinical comment |
|---|---|---|
| Tri-and tetracyclic antidepressants<br><br>Antipsychotics<br><br>Atropine-like compounds | Can potentiate the anticholinergic effect. | |
| Antihistamines | Can potentiate the anticholinergic effect. | |
| Quinidine | Can potentiate the anticholinergic effect. | |

| Hyoscine Butylbromide | Effect | Clinical comment |
|---|---|---|
| Disopyramide | Can potentiate the anticholinergic effect. | |
| Amantadine | Can potentiate the anticholinergic effect. | |
| MAO inhibitors | May result in intensified anticholinergic side effects.<br><br>Also, may block detoxification of anticholinergics thus potentiating their action. | |
| Anticholinergics | May intensify anticholinergic effects. | |
| Potassium chloride | May increase the severity of potassium chloride induced gastrointestinal lesions. | |
| Dopamine antagonists such as metoclopramide. | May result in diminution of the effects of both drugs on the gastrointestinal tract. | |
| Beta-adrenergic agents | May enhanced tachycardic effects. | |
| Antacids or adsorbent antidiarrheals | May reduce the absorption of anticholinergics, resulting in decreased therapeutic effectiveness. | Anticholinergics such as hyoscine butylbromide should be given at least one hour before these medications. |

**Drug-Food Interactions**
*Interactions with food have not been established.*

**Drug-Herb Interactions**
*Interactions with herbs have not been established.*

**Drug-Laboratory Interactions**
*Interactions with laboratory tests have not been established.*

## DOSAGE AND ADMINISTRATION

**Dosing Considerations**
Individual response to ACCEL-HYOSCINE (hyoscine butylbromide) may vary and doses should be adjusted accordingly.

**Recommended Dose and Dosage Adjustment**
One to two 10 mg tablets per day up to a maximum of 6 tablets per day. In prolonged illness which requires repeated dosing, 1 tablet 3 to 5 times a day is recommended.

**Missed Dose**
In case a dose has been missed, take the next dose as scheduled. Do not double the dose.

**Administration**
Tablets should be swallowed whole with a glass of water.

## OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

**Symptoms**
In the case of overdose, anticholinergic effects may be observed.

Single oral doses of up to 590 mg and quantities of active drug up to 1090 mg within 5 hours have produced dry mouth, tachycardia, slight drowsiness and transient visual disorders. Other symptoms include urinary retention, reddening of the skin, and inhibition of gastrointestinal motility.

Other symptoms which occurred in animals and which may be encountered in humans include: shock, Cheyne-Stokes respiration, respiratory paralysis, clonic spasms, paresis of the striated muscle, coma, paralytic ileus and cystoparalysis.

**Treatment**
In the case of an oral overdose, perform gastric lavage with activated charcoal followed by magnesium sulfate (15%). Hyoscine butylbromide overdose symptoms respond to parasympathomimetics.

For patients with glaucoma, administer pilocarpine locally. If necessary, parasypathomimetics should be administered, e.g. neostigmine 0.5-2.5 mg i.m. or i.v.. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis: intubation, artificial respiration.

Catheterisation may be required for urinary retention.

Other overdosage symptoms should be treated with standard supportive therapy.

## ACTION AND CLINICAL PHARMACOLOGY

**Mechanism of Action**
ACCEL-HYOSCINE (hyoscine butylbromide) is an antispasmodic agent which relaxes the smooth muscle of the gastrointestinal, biliary and urinary (parenteral formulation) tracts. It is believed to act predominantly at the parasympathetic ganglia in the walls of the viscera of these organs. Structurally, hyoscine butylbromide exists as a quaternary ammonium compound and as a single positively charged cation throughout the entire pH range.

**Pharmacokinetics**

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 $AUC_{0-tz}$-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 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 butylbromide.

## STORAGE AND STABILITY

ACCEL-HYOSCINE tablets should be stored at 15 – 30°C and are stable up to the expiration date indicated on the label.

## DOSAGE FORMS, COMPOSITION AND PACKAGING

**Dosage Form**
Round, white to off-white, biconvex film-coated tablets with '10' debossed on one side and plain on the other side, each containing 10 mg of hyoscine butylbromide.

**Composition**

Tablets: Hyoscine butylbromide

Non-medicinal ingredients include: lactose monohydrate, lecithin (soya), macrogol, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, povidone, talc and titanium dioxide.

**Packaging**

Blister packages of 10 tablets in cartons of 20 tablets.
Bottles of 100 tablets.

## PART II: SCIENTIFIC INFORMATION

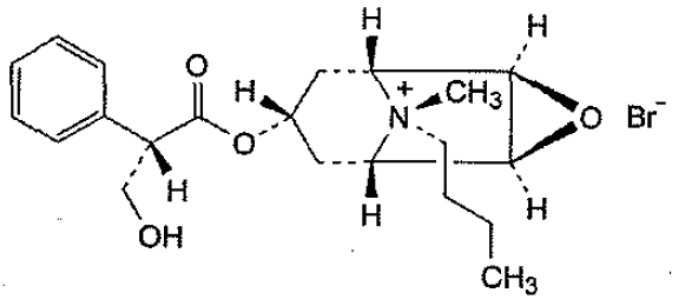
## PHARMACEUTICAL INFORMATION

### Drug Substance

Proper name: hyoscine butylbromide

Chemical name: (1R,2R,4S,5S,7s,9r)-9-Butyl-7-[[(2S)-3-hydroxy-2 phenylpropanoyl]oxy]-9-methyl-3-oxa-9-azatricyclo[3.3.1.02,4]nonan-9-ium bromide

Chemical structure:




Molecular formula and molecular mass: $C_{21}H_{30}BrNO_4$, 440.4 g/mol

Physicochemical properties: A white or almost white, crystalline powder. Freely soluble in water and in methylene chloride, sparingly soluble in anhydrous ethanol.
Melting point: 139°C to 141°C
Partition coefficient: Log P (octanol/water) = 1.1
pH: 5.5 to 6.5 (5.0% w/v solution in $CO_2$ free water)

## CLINICAL TRIALS

### Comparative Bioavailability Studies

A randomized, single-dose, two-treatment, four-way, fully replicated crossover comparative bioavailability study of ACCEL-HYOSCINE 10 mg tablets (Accel Pharma Inc.) with Buscopan® 10 mg tablets (sanofi-aventis Canada Inc.) was conducted in healthy, adult, male subjects under fasting conditions. Comparative bioavailability data from the 42 subjects that received at least one dose of both the test and reference product are presented in the following table:

**Table 2: Summary Table of the Comparative Bioavailability Data**

| Butyl Hyoscine (2 x 10 mg) Geometric Mean Arithmetic Mean (CV %) | | | | |
|---|---|---|---|---|
| Parameter | Test[1] | Reference[2] | % Ratio of Geometric Means | 90% Confidence Interval |
| $AUC_T$ (pg·hr/mL) | 1297.9<br>1767.7 (75.0) | 1181.8<br>1644.2 (78.2) | 109.8 | 101.7 – 118.6 |
| $AUC_I$ (pg·hr/mL) | 1343.9<br>1801.8 (73.9) | 1226.8<br>1680.0 (76.8) | 109.5 | 101.8 – 117.9 |
| $C_{max}$ (pg/mL) | 162.5<br>214.6 (69.0) | 155.4<br>209.5 (74.7) | 104.6 | 95.3 – 114.8 |
| $T_{max}$[3] (hr) | 3.5 (1.0 - 6.0) | 4.3 (1.0 - 6.0) | | |
| $T_{1/2}$[4] (hr) | 6.9 (23.3) | 6.8 (26.1) | | |

[1]Accel-Hyoscine (hyoscine butylbromide) tablets, 10 mg (Accel Pharma Inc.)
[2]Buscopan® (hyoscine butylbromide) tablets, 10 mg (sanofi-aventis Canada Inc.)
[3]Expressed as the median (range) only
[4]Expressed as arithmetic mean (CV%) only.

### Study demographics and trials design

The study 218.202 was designed as a 3-week oral, multi-center, randomized, placebo controlled, double-blind, parallel-group comparison in outpatients who were confirmed to be eligible in terms of pain intensity and compliance after a 1-week, single-blind placebo run-in phase.

The aim of the study was to demonstrate statistical superiority of the fixed oral combination product, HBB + APAP [hyoscine butylbromide (10 mg) + acetaminophen (500 mg); t.i.d] against individual constituents Hyoscine butylbromide (HBB); 10 mg t.i.d. & Paracetamol (acetaminophen (APAP); 500 mg t.i.d.), and Placebo in patients with recurrent painful gastric or intestinal spasms.

A total of 1,637 patients with functional gastrointestinal disorders in which painful spasm was the principal symptom were entered into a four-arm double-blind study (Table 3). After a 1 week placebo run-in, they were randomized to 3 weeks of treatment with one of the four therapies with assessments after 1, 2 and 3 weeks. Pain intensity (Visual Analogue Scale) and pain frequency (Verbal Rating Scale) were self-assessed daily

**Table 3 - Summary of baseline demographic characteristics (ITT population)**

| Study # | Trial design | Dosage, route of administration and duration | Study subjects (n=number) | Mean age (range) | Gender (M/F) |
|---|---|---|---|---|---|
| 218.202 | Multicenter double-blind randomized placebo-controlled parallel-group comparison, after single-blind placebo run-in phase for eligibility. | | Total: 1637 | | |
| | | **HBB**<br>10 mg p.o 3 times daily | 400 | 44<br>(17-76) | 34%/66% |
| | | **APAP**<br>500 mg p.o 3 times daily | 390 | 45<br>(17-74) | 35%/65% |
| | | **HBB + APAP**<br>10 mg + 500 mg paracetamol p.o<br>3 times daily | 387 | 44<br>(18-73) | 36%/64% |
| | | **Placebo**<br>3 times daily | 394 | 45<br>(17-76) | 37%/63% |
| | | Duration: 21 days | | | |

The primary endpoint was the mean decrease in pain intensity, measured by VAS(PI) visual analogue scale, over a treatment period of 3 weeks in the treatment phase of the study (study day 8-28) recorded daily by patients in the evening in their patient dairies. The mean decrease was calculated as the absolute difference between the mean of the VAS(PI) entries over the first 21 days of the treatment phase and the entry on the last day of the placebo run-in phase (baseline value).

The mean decrease in the frequency of the pain, measured on the VRS verbal rating scale, the global assessment of efficacy and tolerability by the patient at the end of the study, the global assessment of efficacy and tolerability by the investigator at the end of the study and the reporting of adverse events were evaluated as secondary criteria.

**Study results**

Pain intensity on the Visual Analogue Scale (VAS) decreased in all treatment groups. The mean decreases of the VAS (PI) from baseline of 2.37, 2.28 and 2.35 cm (adjusted means, ITT) for the treatments with HBB + APAP, Hyoscine butylbromide (HBB) and Paracetamol (APAP) were significantly larger (p= 0.0001) than that for Placebo (1.85); the mean decrease of the VAS (PI) for HBB + APAP, was not significantly different from that for Hyoscine butylbromide (p= 0.176) and Paracetamol (p=0.415).

**Table 4: Descriptive statistics (Mean ± SD) of the VAS (PI, cm): baseline, mean on treatment and mean change from baseline (ITT population)**

| Vas (PI, cm) | HBB + APAP | Hyoscine butylbromide | Paracetamol | Placebo |
|---|---|---|---|---|
| Baseline | 5.12 ± 1.76 | 5.08 ± 1.70 | 5.06 ± 1.68 | 5.09 ± 1.74 |
| Mean value on treatment | 2.50 ± 1.64 | 2.64 ± 1.62 | 2.55 ± 1.49 | 3.05 ± 1.73 |
| Mean change from baseline | 2.62 ± 2.11 | 2.45 ± 2.07 | 2.51 ± 1.97 | 2.04 ± 1.95 |

**Table 5: p-value and 95 % CI for the estimated-treatment differences of the mean changes of VAS (PI) from baseline (ITT population)**

| Treatment contrast | Mean difference | 95 % CI | p-value |
|---|---|---|---|
| HBB + APAP vs. Hyoscine butylbromide | 0.096 | -0.106 to 0.298 | 0.1759 |
| HBB + APAP vs. Paracetamol | 0.022 | -0.181 to 0.225 | 0.4149 |
| HBB + APAP vs. Placebo | 0.522 | 0.319 to 0.725 | 0.0001 |
| Hyoscine butylbromide vs. Placebo | 0.426 | 0.225 to 0.627 | 0.0001 |
| Paracetamol vs. Placebo | 0.499 | 0.297 to 0.702 | 0.0001 |

After 21 days of treatment, the mean VRS (pain frequency) [maximum score of 3] decreased from 1.68 ± 0.76 to 0.62 ± 0.71, from 1.68 ± 0.75 to 0.69 ±0.75, from 1.67 ± 0.71 to 0.73 ± 0.76 and from 1.67 ± 0.71 to 0.93 ± 0.85 under treatment with HBB + APAP, Hyoscine butylbromide, Paracetamol and Placebo, respectively (ITT). The mean decreases of the VRS (pain frequency) from baseline of 0.71, 0.68 and 0.68 (ls_adjusted means, ITT) for the treatments with HBB + APAP, Hyoscine butylbromide and Paracetamol were statistically significantly larger (p= 0.0001) than that for placebo (p= 0.53); the mean decrease of the VRS (pain frequency) for HBB + APAP was not significantly different from that for Hyoscine butylbromide (p= 0.158) and Paracetamol (p= 0.201).

**Table 6: Descriptive statistics (Mean ± SD) of the VRS (frequency) at baseline and after 1, 7, 14 and 21 days of the treatment phase (ITT population)**

| ITT | HBB + APAP | Hyoscine butylbromide | Paracetamol | Placebo |
|---|---|---|---|---|
| Baseline | 1.68 ± 0.76 | 1.68 ± 0.75 | 1.67 ± 0.71 | 1.67 ± 0.71 |
| Day 1 | 1.43 ± 0.72 | 1.40 ± 0.68 | 1.49 ± 0.71 | 1.50 ± 0.75 |
| Day 7 | 0.96 ± 0.83 | 1.03 ± 0.77 | 0.96 ± 0.76 | 1.10 ± 0.80 |
| Day 14 | 0.79 ± 0.80 | 0.86 ± 0.78 | 0.79 ± 0.78 | 1.04 ± 0.83 |
| Day 21 | 0.62 ± 0.71 | 0.69 ± 0.75 | 0.73 ± 0.76 | 0.93 ± 0.85 |
| Mean value on treatment | 0.91 ± 0.56 | 0.95 ± 0.55 | 0.95 ± 0.53 | 1.11 ± 0.60 |
| Mean change from baseline | 0.77 ± 0.82 | 0.73 ± 0.78 | 0.72 ± 0.75 | 0.56 ± 0.71 |

**Table 7: p-values and 95 % CI for the estimated-treatment differences of the mean changes of VRS (pain frequency) from baseline (ITT population)**

| Treatment contrast | Mean difference | 95 % CI | p-value |
|---|---|---|---|
| HBB + APAP vs. Hyoscine butylbromide | 0.034 | -0.034 to 0.104 | 0.1578 |
| HBB + APAP vs. Paracetamol | 0.030 | -0.039 to 0.098 | 0.2005 |
| HBB + APAP vs. Placebo | 0.188 | 0.118 to 0.257 | 0.0001 |
| Hyoscine butylbromide vs. Placebo | 0.153 | 0.084 to 0.221 | 0.0001 |
| Paracetamol vs. Placebo | 0.158 | 0.089 to 0.227 | 0.0001 |

All treatments were well tolerated: 16%, 14%, 17% and 11% of patients on HBB, APAP, combination and placebo groups reported at least one adverse event.

There were no treatment effects in baseline and all active treatments were statistically significantly superior to Placebo from visit 2 to 4 in patients with recurrent painful gastric or intestinal spasms.

## REFERENCES


1. Mueller-Lissner S, Tytgat GN, Paulo LG, Quigley EMM, Bubeck J, Peil H, Schaefer E. Placebo-and paracetamol-controlled study on the efficacy and tolerability of hyoscine butylbromide in the treatment of patients with recurrent crampy abdominal pain. Aliment Pharmacol Ther 2006;23:1741 1748.

2. Buscopan® tablets, 10 mg, submission control no: 245198, Prescribing Information, Sanofi-Consumer Health Inc. Mar. 31, 2021

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE**

**PATIENT MEDICATION INFORMATION**

**ACCEL-HYOSCINE**
**Hyoscine Butylbromide Tablets**
**Mfr. Std.**

Read this carefully before you start taking **ACCEL-HYOSCINE.** This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ACCEL-HYOSCINE.**

**What are ACCEL-HYOSCINE tablets used for?**

- For the relief of abdominal spasms (cramps), pain and discomfort in the:
  - stomach,
  - gut (intestines / bowel),
  - biliary tract.

**How do ACCEL-HYOSCINE tablets work?**

- Abdominal cramps (spasms) are caused by sudden, strong tightening of muscles.
- Relieves cramps (spasms), pain, discomfort by relaxing tight muscles of the:
  - stomach,
  - gut (intestines / bowel),
  - biliary tract.

**What are the ingredients in ACCEL-HYOSCINE tablets?**
Medicinal Ingredient: Hyoscine butylbromide.
Non-medicinal Ingredients: lactose monohydrate, lecithin (soya), macrogol, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, povidone, talc and titanium dioxide.

**ACCEL-HYOSCINE comes in the following dosage form:**
Tablets, 10 mg.

**Do not use ACCEL-HYOSCINE tablets if you:**
- are allergic to:
  - hyoscine butylbromide.
  - atropinics.
  - any of the ingredients in the product (see list in **What are the ingredients in ACCEL-HYOSCINE tablets**).
- have any of the below conditions:
  - muscle wasting disease (myasthenia gravis).
  - untreated high pressure inside of your eye (closed-angle glaucoma).

- narrowing parts of the gastrointestinal tract (stenosis).
- problems with urination due to prostate issues.
- your intestine stopped working or may be blocked;
    - Symptoms include:
        - severe abdominal pain with absence of stools,
        - nausea,
        - vomiting
- enlarged bowel (megacolon).

- are pregnant, likely to get pregnant, or are breast-feeding.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ACCEL-HYOSCINE. Talk about any health conditions or problems you may have, including if you:**

- are a man and have prostate problems
- are at risk of narrow angle glaucoma (high pressure in the eyes)
- are at risk of having problems with urinating due to a blockage
- are at a risk of tachyarrhythmia (high heart rate)
- have stomach acid backing up in your throat (reflux-esophagitis)
- have or at a risk of any blockage in your gastrointestinal tract. This includes your esophagus, stomach, intestines and anus.
- have inflamed bowels (e.g. ulcerative colitis).

**Other warnings you should know about**:
You should not be taking ACCEL-HYOSCINE daily for a long period of time. Your healthcare professional should investigate the cause of your stomach pain. Talk to your healthcare professional about how long you should be taking ACCEL-HYOSCINE.

If the following occurs after you take ACCEL-HYOSCINE, get medical help immediately:

- if you have severe and unexplained stomach pain that does not go away or gets worse
- if you have severe and unexplained stomach pain that occurs with other symptoms such as:
    - fever
    - nausea
    - vomiting
    - changes in bowel movements
    - abdominal tenderness
    - decreased blood pressure
    - fainting
    - blood in stool

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines. The following may interact with ACCEL-HYOSCINE:**

- Amantadine, medicine used to prevent or treat certain flu infections (type A)
- Anticholinergics (e.g. ipratropium, atropine).
- Antihistamines, medicines used to treat allergies (e.g. diphenhydramine, hydroxyzine).
- Beta-adrenergic agents, medicines used to treat the symptoms of asthma, bronchitis, emphysema, and other lung diseases (e.g. salbutamol).
- Dopamine antagonists, medicines used for the prevention of vomiting (e.g. metoclopramide).
- Heart medications (e.g. disopyramide, quinidine).
- MAO inhibitors, medicines used to treat depression and mood disorders (e.g. moclobemide, selegiline, tranylcypromine, phenelzine).
- Tricyclic antidepressants, medicines used to treat anxiety or depression (e.g. amitriptyline, doxepin).

If you are taking antacids or adsorbent anti-diarrheals, your healthcare professional may tell you to take them at least 1 hour before taking ACCEL-HYOSCINE.

**How to take ACCEL-HYOSCINE tablets:**

**Usual dose (Adults):**

- Take 1 to 2 tablets per day. Do not take more than 6 tablets per day.
- In prolonged illness, your doctor may recommend taking one tablet 3 to 5 times a day. Do not take more than directed.
- Swallow tablets whole with a glass of water.

**Overdose:**

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|---|
| If you think you, or a person you are caring for, have taken too much ACCEL-HYOSCINE, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms. |

**Missed Dose:**
In case a dose has been missed, take the next dose as scheduled. Do not double the dose.

**What are the possible side effects from using ACCEL-HYOSCINE tablets?**

This drug may sometimes cause:

- dry mouth.
- diarrhea.
- nausea.
- feeling hot and decreased sweating.
- increased heart rate.

- not being able to pass urine.
- increase fluid pressure inside of the eye.
- other rare side effects such as:
    - allergic reactions (skin rash and itching).
    - skin reactions (e.g. hives, rash, skin redness, itching).
    - rapid swelling of the skin and skin tissue (angioedema).
    - difficulty in breathing (usually in patients who suffer with asthma or allergy).

There have been very rare reports of severe, allergic reactions and severe allergic shock.

If you experience any of these effects which persist or become troublesome or any side effects not listed here, talk to your healthcare professional.

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or

- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Storage:**
Store at room temperature (15 - 30°C). Product is stable up to the labelled expiry.

Keep out of reach and sight of children.

**If you want more information about ACCEL-HYOSCINE:**
- Talk to your healthcare professional.
- Find the full Prescribing Information that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by contacting the sponsor, Accel Pharma Inc, by visiting **www.accelpharma.com**, or by calling **1-877-822-2235**.

This leaflet was prepared by Accel Pharma Inc.

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