HYOSCINE BUTYLBROMIDE INJECTION

Solution for Injection
20 mg/mL

Sterile

Sandoz Standard

Antispasmodic
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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

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<th>Route of Administration</th>
<th>Dosage Form / Strength</th>
<th>Clinically Relevant Nonmedicinal Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td>Vial / 20 mg/mL</td>
<td>Sodium chloride and water for injection</td>
</tr>
</tbody>
</table>

INDICATIONS AND CLINICAL USE

Hyoscine Butylbromide Injection (hyoscine butylbromide) is indicated for the relief of acute genitourinary or gastrointestinal spasm (e.g. renal or biliary colic), or to produce smooth muscle relaxation prior to radiological procedures such as pyelography or other diagnostic procedures where spasm may be a problem (e.g. gastroduodenal endoscopy).

Geriatrics:
No data is available

Pediatrics:
No data is available

CONTRAINDICATIONS

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

- Parenteral administration is contraindicated in patients with myasthenia gravis, untreated narrow angle glaucoma, prostatic hypertrophy with urinary retention, stenotic lesions of the gastrointestinal tract, tachycardia, angina, cardiac failure and megacolon.

- Hyoscine butylbromide should not be given by intramuscular injection to patients being treated with anticoagulant drugs since intramuscular haematoma may occur. In these patients, the subcutaneous or intravenous routes may be used.
WARNINGS AND PRECAUTIONS

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

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.

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

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

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

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: nonobstructive prostatic hypertrophy, urinary retention (or the predisposition to) or obstructive uropathy such as a bladder neck obstruction due to prostatic hypertrophy (see CONTRAINDICATIONS). In addition, exercise caution in patients inclined to tachyarrhythmia.

Cardiovascular
As large doses of anticholinergics/systemic antispasmodics may cause an increase in heart rate, due care is necessary in patients with cardiac disease, especially cardiac arrhythmias, congestive heart failure, coronary artery disease and mitral stenosis. The increase in heart rate may also be undesirable in patients with unstable cardiovascular status in an acute hemorrhage situation.

Gastrointestinal
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.
**Ophthalmologic**
The parenteral 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 hyoscine butylbromide.

The mydriatic effect of anticholinergics/systemic antispasmodics may result in increased intraocular pressure. Hyoscine butylbromide should be used with caution in patients with angle-closure glaucoma or with this predisposition, as anticholinergics/systemic antispasmodics may precipitate an acute angle-closure glaucoma attack (see CONTRAINDICATIONS).

Patients should seek urgent ophthalmological advice in case they should develop a painful eye with loss of vision after injection of hyoscine butylbromide.

**Special Populations**

**Fertility, pregnancy and lactation**

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 hyoscine butylbromide during pregnancy and lactation.

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

**Pediatrics:**
Hyoscine Butylbromide Injection 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 glaucoma.

Administration of anticholinergics/systemic antispasmodics to elderly patients with intestinal atony or in debilitated patients may result in 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 Hyoscine Butylbromide Injection. 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 hyoscine butylbromide: xerostomia (dry mouth), dyshidrosis, visual accommodation disorders, mydriasis, increased intraocular pressure, tachycardia, dyspnea, and urinary retention.

There have been rare reports of dizziness, blood pressure decreased and flushing.

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

There have been very rare reports of anaphylactic reactions and anaphylactic shock including fatal outcome.

Adverse events reported during therapy with hyoscine butylbromide include increased pulse rate, diarrhea, nausea, retinal pigmentation, and glaucoma.

**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

<table>
<thead>
<tr>
<th>Hyoscine Butylbromide</th>
<th>Effect</th>
<th>Clinical comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tri- and tetracyclic antidepressants</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>Atropine-like compounds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>Quinidine</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>Amantadine</td>
<td>Can potentiate the anticholinergic effect.</td>
<td></td>
</tr>
<tr>
<td>MAO inhibitors</td>
<td>May result in intensified anticholinergic side effects of hyoscine butylbromide.</td>
<td>Also, may block detoxification of anticholinergics thus potentiating their action.</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>May intensify anticholinergic effects.</td>
<td>May increase the severity of potassium chloride induced gastrointestinal lesions.</td>
</tr>
<tr>
<td>Dopamine antagonists such as metoclopramide.</td>
<td>May result in diminution of the effects of both drugs on the gastrointestinal tract.</td>
<td></td>
</tr>
<tr>
<td>Beta-adrenergic agents</td>
<td>May enhance tachycardic effects.</td>
<td></td>
</tr>
<tr>
<td>Antacids or adsorbent antidiarrheals</td>
<td>May reduce the absorption of anticholinergics, resulting in decreased therapeutic effectiveness.</td>
<td>Anticholinergics such as hyoscine butylbromide should be given at least one hour before these medications.</td>
</tr>
</tbody>
</table>

**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 hyoscine butylbromide may vary and doses should be adjusted accordingly.

**Recommended Dose and Dosage Adjustment**
One-half (10 mg/0.5 mL) to one vial (20 mg/1 mL) administered parenterally by intramuscular, subcutaneous or intravenous routes, at an injection rate of 1 mL/min. No dilution of the vial contents is necessary prior to administration. The maximum dose should not exceed 100 mg/day (5 vials).

**Administration**
The rapid action of injected hyoscine butylbromide is advantageous in acutely ill patients and in those situations where prompt spasmolytic activity facilitates diagnostic procedures such as radiological examinations. Hyoscine Butylbromide Injection may also be used intramuscularly 10 to 15 minutes before radiological examinations of the stomach to slow peristaltic movements.

**Dilution and Stability of Parenteral Hyoscine Butylbromide Injection:**
Although dilution prior to administration is not required, Hyoscine Butylbromide Injection solution is compatible with the following solutions, should dilution be desirable:

- Ringers Solution
- Ringers Lactate
- NaCl 0.9%
- Laevulose 5%
- Glucose 10%

Solutions must be mixed under sterile conditions and are stable for 8 hours.

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

**OVERDOSAGE**
For management of a suspected drug overdose, contact your regional Poison Control Centre.
**Symptoms**

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, parasympathomimetics should be administered, e.g. neostigmine 0.5-2.5 mg IM or IV. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis: intubation, artificial respiration.

Catherisation may be required for urinary retention.

Other overdosage symptoms should be treated with standard supportive therapy.

**ACTION AND CLINICAL PHARMACOLOGY**

**Mechanism of Action**

Hyoscine butylbromide is an antispasmodic agent which relaxes the smooth muscle of the gastrointestinal, biliary and urinary 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 and distribution:**

After intravenous administration hyoscine butylbromide is rapidly distributed ($t_{1/2\alpha} = 4$ min, $t_{1/2\beta} = 29$ min) into the tissues. The volume of distribution ($V_{ss}$) is 128 L (corresponding to approx. 1.7 L/kg). 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:
The main metabolic pathway is the hydrolytic cleavage of the ester bond. The half-life of the terminal elimination phase ($t_{1/2\gamma}$) is approximately 5 hours. The total clearance is 1.2 L/min. Clinical studies with radiolabeled hyoscine butylbromide show that after intravenous injection 42 to 61% of the radioactive dose is excreted renally and 28.3 to 37% faecally.

The portion of unchanged active ingredient excreted in the urine is approximately 50%. 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

Store between 15 and 30°C. Protect from light. Protect from freezing.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms
Hyoscine Butylbromide Injection is available as a 20 mg/mL solution of hyoscine butylbromide in 1 mL preservative free, single use, amber glass vials. Discard any unused portion.

Composition
Each mL contains: hyoscine butylbromide 20 mg, sodium chloride 6.6 mg, hydrochloric acid and/or sodium hydroxide to adjust pH, and water for injection.

Packaging
1 mL vials, boxes of 10.
PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

Proper Name: Hyoscine butylbromide

Chemical Name: (1S,3S,5R,6R,7S,8R)-6,7-epoxy-8-butyl-3-[(S)-tropoyloxy] tropanium bromide

Structural Formula:

![Structural Formula Image]

Molecular Formula: C_{21}H_{30}BrNO_{4}

Molecular Weight: 440.4 g/mol

Description: A white or almost white, odourless or almost odourless, crystalline powder, soluble 1 to 1 in water, 1 in 50 of alcohol, and 1 in 5 of chloroform. A 10% solution in water has a pH of 5.5 to 6.5. The melting point is approximately 139-141°C.
REFERENCES

1. Boehringer Ingelheim (Canada) Ltd., Buscopan®, Product Monograph, Control no.161305, Date of Revision: June 4, 2013
PART III: CONSUMER INFORMATION

Hyoscine Butylbromide Injection

This leaflet is part III of a three-part "Product Monograph" published when Hyoscine Butylbromide Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Hyoscine Butylbromide Injection. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Hyoscine Butylbromide Injection is used for relief of acute genitourinary or gastrointestinal spasm, or to produce smooth muscle relaxation prior to radiological procedures where spasm may be a problem.

What it does:
Stomach cramps are caused by sudden, irregular tightening up of muscles in the wall of the intestine. Hyoscine Butylbromide Injection works by relaxing the tight muscles, so relieving the cramps.

When it should not be used:
Do not use Hyoscine Butylbromide if:

- You are hypersensitive (allergic) to hyoscine butylbromide or atropinics or to any of the nonmedicinal ingredients (See What the important nonmedicinal ingredients are).

- You have myasthenia gravis, untreated narrow angle glaucoma, difficulty in urination due to inflammation of the prostate, stenotic lesions (narrowing of a duct/canal) of the gastrointestinal tract, tachycardia (fast heartbeat), angina, heart failure and megacolon (enlarged colon).

- You are taking Hyoscine Butylbromide Injection by the intramuscular route and you are currently being administered anticoagulant drugs (blood thinners) as intramuscular bleeding may occur with this combination.

What the medicinal ingredient is:

Hyoscine butylbromide

What the important nonmedicinal ingredients are:
sodium chloride and water for injection

What dosage forms it comes in:
Vials, 20 mg/mL

WARNINGS AND PRECAUTIONS

BEFORE you use Hyoscine Butylbromide Injection talk to your doctor or pharmacist if:

- you are pregnant, likely to become pregnant or if you are breast feeding as it is recommended that you do not use Hyoscine Butylbromide Injection in these conditions
- you are a man who suffers from prostate problems
- you have narrow angle glaucoma, megacolon or myasthenia gravis
- you have a very fast heart rate or other heart problems
- you have reflux esophagitis or ulcerative colitis
- you are hypersensitive or “allergic” to hyoscine-N-butylbromide or any of the other ingredients
- you have previously been treated by a doctor for a severe sweating disorder
- you are taking antidepressants, major tranquilizers, antihistamines, antivirals, dopamine antagonists (e.g. metoclopramide) or medicines to treat heart problems
- you have sudden or severe abdominal pain along with symptoms such as fever, nausea, vomiting, blood in the stool, or low blood pressure (e.g., lightheadedness), contact your doctor immediately
- you have a rare hereditary condition of fructose (a sugar) intolerance you should not take this medication as it contains lactose.

If in doubt, ask your doctor or pharmacist.

Exercise care in driving or operating machinery until you know how Hyoscine Butylbromide Injection may affect your vision.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with Hyoscine Butylbromide Injection include: tricyclic antidepressants, antihistamines, quinidine, disopyramide, amantadine, MAO inhibitors, anticholinergics, dopamine antagonists such as metoclopramide, beta-adrenergic agents, antacids or adsorbent anti diarrheals.
**PROPER USE OF THIS MEDICATION**

**Usual adult dose:**
One half (10 mg/0.5 mL) to one vial (20 mg/mL) administered parenterally by intramuscular, subcutaneous, or intravenous routes, at an injection rate of 1 mL/min. No dilutions of the vial is necessary prior to administration. The maximum dose should not exceed 100 mg/day (5 vials).

**Overdose:**
In case of drug overdose, contact a health care practitioner (or doctor), hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

When using the product, the patient should not take more doses than directed. Particularly in the case of overdose, the side effects listed below may be observed.

Your doctor will advise you that certain antacids or adsorbent antidiarrheals should be taken at least one hour before Hyoscine Butylbromide Injection.

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

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

All medicines sometimes cause side-effects. Hyoscine Butylbromide Injection may occasionally cause a dry mouth, blurred vision, mydriasis (pupil dilation), increased eye pressure, diarrhea, nausea, reduced ability to sweat, an increase in heart rate and the inability to pass urine.

Other possible rare side-effects include, dizziness, flushing, allergic reactions (particularly skin rash and itching), skin reactions (e.g., hives, rash, skin redness, itching), angioedema (swelling of the lips), decreased blood pressure, and difficulty in breathing (usually in patients who suffer with asthma or allergy).

There have been very rare reports of anaphylactic (severe, allergic) reactions and anaphylactic shock including death.

If you experience any of these effects and they persist or become troublesome, consult your doctor.

Should you suffer from a painful red eye with loss of vision, seek urgent medical advice.

If you experience any other effects not mentioned above, consult your doctor or pharmacist.

*This is not a complete list of side effects. For any unexpected effects while taking Hyoscine Butylbromide Injection, contact your doctor or pharmacist.*

**HOW TO STORE IT**

Hyoscine Butylbromide Injection vials should be protected from light and freezing. Products should be stored between 15 and 30°C.

Keep out of reach of children.

**REPORTING SUSPECTED SIDE EFFECTS**

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)
Call toll-free at 1-866-234-2345
Complete a Canada Vigilance Reporting Form and:
- Fax toll-free to 1-866-678-6789, or
- Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect).

**NOTE:** Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

**MORE INFORMATION**
This document, plus the full Product Monograph prepared for health professionals, can be obtained by contacting the sponsor, Sandoz Canada Inc., at:
1-800-361-3062

or
by written request at:
145, Jules-Léger
Boucherville, (QC), Canada
J4B 7K8

or by email at:
medinfo@sandoz.com

This leaflet was prepared by Sandoz Canada Inc.

Last revised: March 24, 2016