Hyoscine-N-Butylbromide

Hyos®

20 mg/mL Solution for Injection
(I.M./I.V./S.C.)

ANTICHOLINERGIC / ANTISPASMODIC

FORMULATION
Each mL solution for injection contains:
Hyoscine-N-butylbromide ……..…….…….…… 20 mg

PRODUCT DESCRIPTION
Hyoscine-N-butylbromide (Hyos®) 20 mg/mL Solution for Injection is a clear, colorless, sterile aqueous solution free from extraneous matter packed in a 2 mL clear glass ampule.

PHARMACODYNAMICS
Hyoscine-N-butylbromide is a quaternary ammonium derivative of hyoscine. It relaxes the smooth muscles of the gastrointestinal, biliary and urinary tracts by blocking the action of acetylcholine. Hyoscine-N-butylbromide reduces the tone and peristalsis of smooth muscles in hollow organs with parasympathetic innervation. It has peripheral anticholinergic effects that are less pronounced and of shorter duration than those of atropine. It does not penetrate the blood-brain barrier contributing to its minimal central effects.

PHARMACOKINETICS
Hyoscine-N-butylbromide is rapidly distributed into the tissues after intravenous administration. It is partially metabolized in the liver to inactive compounds. The terminal elimination half-life is approximately 5 hours.

Its main route of excretion is through the kidneys; total body clearance is 1.2 L/minute. The main metabolites found in the urine are poorly bound to muscarinic receptors. It is not known whether hyoscine-N-butylbromide is removed by peritoneal dialysis or hemodialysis.

INDICATIONS
- For the symptomatic relief of :
  - Gastrointestinal and genitourinary disorders characterized by smooth muscle spasm
  - Spasm and dyskinesia of the biliary system
  - Irritable bowel syndrome (IBS)
- As an aid to produce smooth muscle relaxation prior to radiological or other diagnostic procedures where spasm may be a problem (e.g., gastroduodenal endoscopy)

DOSAGE AND ADMINISTRATION
Hyoscine-N-butylbromide injection may be administered by slow intravenous (IV), intramuscular (IM) or subcutaneous (SC) injection.

- IM injections should be administered 10-15 minutes prior to radiological/diagnostic procedures

Age Group	Recommended IV, IM or SC Dose
Adults and adolescents over 12 years	20 – 40 mg (1 – 2 ampules) several times a day • 5 mg/hour as a continuous infusion has been used for up to 4 days • Maximum Dose: 100 mg per day
Infants and children up to 12 years	Severe cases: 0.3 – 0.6 mg per kg body weight several times a day. • Maximum Dose: 1.2 mg/kg body weight per day
	Or, as prescribed by a physician.

CONTRAINDICATIONS
- Hypersensitivity to hyoscine-N-butylbromide, belladonna alkaloids or derivatives, or any ingredient of the product.
- Patients with porphyria, untreated angle-closure glaucoma, prostatic enlargement, myasthenia gravis, and severe ulcerative colitis or toxic megacolon.
- Patients with tachycardia
- Patients with acute hemorrhage whose cardiovascular status is unstable.
- Patients with stomach or bowel obstruction or in conditions where there is reduced bowel activity (e.g., pyloroduodenal stenosis, achalasia), paralytic ileus, or intestinal atony.
- Should not be given intramuscularly (IM) in patients being treated with anticoagulant therapy. Subcutaneous or intravenous routes may be used in these patients.

WARNINGS and PRECAUTIONS
Anticholinergics such as hyoscine-N-butylbromide should be used with caution in the following conditions:
- Patients with Down's syndrome, hepatic or renal disease and hyperthyroidism.
- Conditions characterized by tachycardia (including thyrotoxicosis, hyperthyroidism, cardiac insufficiency, cardiac surgery) since hyoscine-N-butylbromide may further increase the heart rate.
- Patients with gastric ulcer, gastroesophageal reflux disease or hiatal hernia associated with reflux esophagitis.
- Patients with autonomic neuropathy, partial obstructive uropathy and diarrhea.
- Those with known or suspected GI infections such as *Clostridium difficile*-associated diarrhea and colitis, shigellosis and dysentery since the drug may decrease GI motility causing retention of the pathogenic organism or toxin.
- Patients with mild to moderate ulcerative colitis to prevent paralytic ileus that may lead to toxic megacolon.
- Patients with pyrexia since the drug may reduce sweating.

Patients should immediately consult their ophthalmologist if they experience a painful, red eye with loss of vision. This may be due to increased intraocular pressure produced by the anticholinergic effect of hyoscine-N-butylbromide.

Cases of anaphylaxis including episodes of shock have been reported after parenteral administration of hyoscine-N-butylbromide.

DRUG INTERACTIONS
- Alcohol, other CNS depressants (e.g., barbiturates and benzodiazepines), other anticholinergic drugs (e.g., antidepressants, neuroleptics, H1 antihistamines, antiparkinsons, etc.), antiarrhythmic agents with anticholinergic effects (e.g., quinidine, disopyramide, procainamide) increase the sedative effect of hyoscine-N-butylbromide.
- Concomitant use of hyoscine with propantheline and slow-dissolving tablets of digoxin may increase serum digoxin concentrations.
- Tachycardic effects of beta-adrenergic agents may be enhanced by hyoscine-N-butylbromide.
- Concomitant use of anticholinergics with levodopa may decrease the extent of absorption of levodopa in the small intestine. Discontinuation of the anticholinergics should have a concomitant reduction in the levodopa dose to prevent toxicity resulting from increased absorption of levodopa.
- Anticholinergics may decrease GI absorption of ketoconazole. Anticholinergic drugs should be given 2 hours after ketoconazole administration.
- Anticholinergic drugs potentiate the local GI mucosal effects of potassium chloride.

HIGH RISK GROUPS
Use in Pregnancy

Pregnancy Category C
Reproduction studies have not been performed in humans. Experience in a limited number of pregnant women has shown no evidence of ill effects during human pregnancy. There is also no evidence of teratogenic or embryotoxic effects in rat and rabbit studies. However, the usual precautions regarding the use of drugs during pregnancy should be observed especially during the first trimester.

Use in Breastfeeding Mothers
There are no reports of any clinical effects of hyoscine-N-butylbromide on the breastfed infant. The American Academy of Pediatrics states that the drug may be considered compatible with breastfeeding. However, as with any drug, consult a doctor before using this product if the patient is breastfeeding.

Use in Children
Hyoscine-N-butylbromide should be used with caution in children. Infants and children with spastic paralysis or brain damage, and patients with Down's syndrome may be hypersensitive to the anticholinergic effects (e.g., mydriasis, positive chronotropic effect) of hyoscine-N-butylbromide.

Use in the Elderly
Elderly or debilitated patients should use anticholinergics with caution since they are more susceptible to the adverse effects of such drugs. Mental confusion and/or excitement may also occur in geriatric patients using such drugs.

Use in Patient with Renal or Hepatic Function
Patients with impaired metabolic, liver and kidney function should use hyoscine-N-butylbromide with caution to avoid exacerbation of CNS effects.

Effects on Ability to Drive or Operate Machines
Patients who need to perform activities requiring mental alertness or physical coordination should avoid hyoscine-N-butylbromide since it may cause drowsiness and blurred vision.

UNDESIRABLE / ADVERSE EFFECTS
- Frequent adverse reactions associated with the use of anticholinergic drugs include xerostomia, dry skin, accommodation disorders, blurred vision, cycloplegia, mydriasis, photophobia, anhidrosis, urinary hesitancy and retention, transient bradycardia (followed by tachycardia, hypotension, palpitations and arrhythmia), reduced bronchial secretions, xerophthalmia, and constipation.
- Rarely, anaphylactic shock including fatal outcome, anaphylactoidic reactions, dyspnea, skin reactions, and other hypersensitivity
- Other adverse events include increased ocular tension (especially in patients with angle-closure glaucoma), sedation, drowsiness, irritability, disorientation, hallucinations, decreased blood pressure, loss of taste, headache, nervousness, weakness, flushing, insomnia, urinary retention, dry mouth, nausea, vomiting, and bloated feeling.

OVERDOSAGE AND TREATMENT
Serious signs of acute overdosage have not been observed in man. Symptoms of acute overdoses are usually transitory parasympatholytic effects on salivary secretion, heart rate and accommodation. These may include dryness of mouth, tachycardia and blurring of vision owing to loss of accommodation, all of which are transitory.

Hyoscine-N-butylbromide may produce a curariform neuromuscular block and ganglionic blockade manifested as respiratory paralysis.

Acute anticholinergic overdosage can be managed by symptomatic and supportive therapy. Symptoms of overdosage respond to parasympathomimetics (e.g., neostigmine 0.5-2.5 mg IM or IV). Urgent ophthalmological advice should be sought and pilocarpine should be given locally in patients with glaucoma. Cardiovascular complications should be treated according to usual therapeutic principles. Intubation and artificial respiration should be considered in case of respiratory paralysis. Patients who experience urinary retention may require catheterization.

STORAGE CONDITION
Store at temperatures not exceeding 30°C.

CAUTION
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
Hyoscine-N-butylbromide (Hyos®) 20 mg/mL Solution for Injection in box of 10 ampules

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Manufactured by
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