1. NAME OF THE MEDICINAL PRODUCT

HYOSCINE BUTYLBROMIDE INJECTION BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Each ml contains:

Hyoscine Butylbromide	BP	20 mg
Water for Injections	BP	q.s.

3. PHARMACEUTICAL FORM

Liquid Injection

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Hyoscine Butylbromide Injections are indicated in acute spasm, as in renal or biliary colic, in radiology for differential diagnosis of obstruction and to reduce spasm and pain in pyelography, and in other diagnostic procedures where spasm may be a problem, e.g. gastro-duodenal endoscopy.

4.2 Posology and Method of Administration

Adults:

One ampoule (20 mg) intramuscularly or intravenously, repeated after half an hour if necessary.

Intravenous injection should be performed 'slowly' (in rare cases a marked drop in blood pressure and even shock may be produced by Hyoscine). When used in endoscopy this dose may need to be repeated more frequently.

Maximum daily dose of 100mg.

Special populations:

Elderly: 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.

Paediatric population:

Not recommended for children.

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

Dosage:

For IM/IV use only.

4.3 Contraindications

Hyoscine Butylbromide injections are contraindicated in patients with:

- Hypersensitivity to the active substance or to any of the excipients
- Narrow angle glaucoma
- Hypertrophy of the prostate with urinary retention
- Mechanical stenosis in the gastrointestinal tract
- Paralytical or obstructive ileus
- Megacolon
- Tachycardia
- Myasthenia gravis

Hyoscine Butylbromide injections should not be given by intramuscular injection to patients being treated with anticoagulant drugs since intramuscular haematoma may occur.

4.4 Special Warning 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, appropriate diagnostic measures are needed to investigate the aetiology of the symptoms.

Hyoscine Butylbromide injections can cause tachycardia, hypotension and anaphylaxis, therefore use with caution in patients with cardiac conditions such as cardiac failure, coronary heart disease, cardiac arrhythmia or hypertension, and in cardiac surgery. Monitoring of these patients is advised.

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

Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as Hyoscine Butylbromide injection 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 after the injection of Hyoscine Butylbromide injections.

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. phenothiazines, butyrophenones), disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by Hyoscine Butylbromide injections.

The tachycardic effects of beta-adrenergic agents may be enhanced by Hyoscine Butylbromide injections.

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

4.6 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 Hyoscine Butylbromide is not recommended during pregnancy.

Lactation

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 hyoscine butylbromide 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. However, patients should be advised that they may experience undesirable effects such as accommodation disorder or dizziness during treatment with hyoscine Butylbromide ampoules. 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.

4.8 Undesirable Effecsts

Many of the listed undesirable effects can be assigned to the anticholinergic properties of hyoscine butylbromide.

Immune system disorders

Not known*: anaphylactic shock including cases with fatal outcome, anaphylactic reactions, dyspnoea, skin reactions (e.g. urticaria, rash, erythema, pruritus) and other hypersensitivity.

Cardiac disorders

Common: tachycardia

Vascular disorders

Common: dizziness

Not known*: blood pressure decreased, flushing

Gastrointestinal disorders

Common: dry mouth

Constipation

Skin and subcutaneous tissue disorders

Not known*: dyshidrosis

Renal and urinary disorders

Not known*: urinary retention

*This adverse reaction has been observed in post-marketing experience. With 95% certainty, the frequency category is not greater than common, 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 185 patients.

4.9 Overdose

Symptoms

Serious signs of poisoning following acute overdosage have not been observed in man. In the case of overdosage, anticholinergic symptoms 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.

Symptoms of Hyoscine Butylbromide injection 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, artificial respiration should be considered. Catheterisation may be required for urinary retention.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Belladonna alkaloids, semisynthetic, quaternary.S

ATC code: A03BB01

Hyoscine butylbromide is an antispasmodic agent which relaxes smooth muscle of the organs of the abdominal and pelvic cavities. It is believed to act predominantly on the intramural parasympathetic ganglia of these organs.

5.2 Pharmacokinetic Properties

Absorption and distribution: After intravenous administration hyoscine butylbromide is rapidly distributed ($t_{½\alpha}$= 4 min, $t_{½\beta}$= 29 min) into the tissues. The volume of distribution (Vss) 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 ($t_{½\gamma}$) 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.

5.3 Preclinical Safety Data

In limited reproductive toxicity studies hyoscine butylbromide 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

- Sodium Metabisulphite BP
- Trisodium Citrate BP
- Chlorobutanol Hemihydrate BP
- Disodium Edetate BP
- Water for Injections BP

6.2 Incompatibilities

None known.

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store at a temperature not exceeding 30°C. Protect from light.

Keep all medicines out of reach of children.

6.5 Nature and Contents of Container and Special Equipment for use, Administration or Implantation

10 x 1ml amber coloured ampoules packed in a unit carton along with pack insert.

6.6 Special Precautions for Disposal and Other Handling

For single use only. Any unused solution should be discarded.

7.0 APPLICANT/SOLE AGENT

Embassy Pharmaceutical & Chemical Ltd.

41, Ademola Street, South West Ikoyi, Lagos, Nigeria.

Manufacturer

LABORATE PHARMACEUTICALS INDIA LIMITED

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