Summary of Product Characteristics (SPC)

1. NAME OF FINISHED PHARMACEUTICAL PRODUCT:

HYOCE (Hyoscine Butylbromide Injection BP)

1.1 Strength

20mg/ml

1.2 Pharmaceutical form

A clear, colourless to slightly yellow liquid Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Sr. No.	Ingredients	Specification	Quantity per ml	Activity
1.	Hyoscine butylbromide	BP	20mg	Antispasmodic
2.	Water for Injections	BP	q.s.	Vehicle

3. PHARMACEUTICAL FORM:

A clear, colourless to slightly yellow liquid Injection.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

Hyoce injection is 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

The usual dose is 20 mg by intramuscular or intravenous 2 to 3 times a day.

For infants and children upto 3 years: 5 mg by intramuscular or intravenous 2 to 3 times a day. For children upto 6 years: 10 mg by intramuscular or intravenous 2 to 3 times a day.

4.3 Method of administration

Intramuscular/ Intravenous route

4.4 Contraindications

Hyoce should not be administered to patients with myasthenia gravis, megacolon, narrow angle glaucoma, tachycardia, prostatic enlargement with urinary retention, mechanical stenosis in the region of the gastrointestinal tract or paralytic ileus.

Hyoce injection should not be used in patients who have demonstrated prior hypersensitivity to hyoscine butylbromide or any other component of the product. Hyoce injection should not be given by intramuscular injection to patients being treated with anticoagulant drugs since intramuscular haematoma may occur.

4.5 Special warning and Precautions for use.

The safe use of hyoscine butylbromide contentious in patients with porphyria.

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 alkaloid 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 injection 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. In addition, exercise caution in patients inclined to tachyarrhythmia.

Special Precautions:

Hyoce should be used with caution in patients with pyloric stenosis, those who have bladder outflow obstruction or in patients with intestinal obstruction.

Patients should not consume alcohol whilst using Hyoce.

Hyoce should also be used with caution in elderly patients, and in patients with impaired hepatic or renal function.

In rare cases, confusion state and visual hallucinations may occur. In such cases, Hyoce should be removed immediately. If severe symptoms persist, appropriate therapeutic measures should be taken.

Idiosyncratic reactions may occur with ordinary therapeutic doses of hyoscine.

In isolated cases an increase in seizure frequency in epileptic patients has been reported.

Care should be taken after removal of the system as side – effects may persist for upto 24 hours or longer.

4.6 Paediatric population

Not applicable.

4.7 Interactions with other FPPs and other forms of interactions

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.

Table 1: Established or potential Drug- Drug interactions.

Hyoscine Butylbromide	**Effect**	**Clinical comment**
Tricyclic antidepressants, Antihistamines, Quinidine, Disopyramide, Amantidine	Can potential the anticholinergic effects of parenterally administered hyoscine butylbromide	--
MOA inhibitors	May result in intensified anticholinergic side effects of hyoscine butylbromide. Also, may block detoxification of anticholinergic thus potentiating their action.	--
Anticholinergics	May intensify anticholinergic effect. May increase the severity of potassium chloride induced gastrointestinal lesion.	--

Dopamine antagonists such as metoclopramide	May result in diminution of the effect of both drugs on the gastrointestinal tract.	--
Beta-adrenergic agents	May result tachycardic effects	--
Antacids or adsorbent antidiarrheals	May reduce the absorption of anticholinergics, resulting in decrease therapeutic effectiveness	Anticholinergics such as hyoscine butylbromide should be given at least one hour before these medications.

4.8 Additional information on special populations

Not available.

4.9 Paediatric population

Not available.

4.10 Fertility, Pregnancy and Lactation

Fertility

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

Pregnancy

Use of Hyoce during pregnancy may cause respiratory depression in the neonate, and should only be given during pregnancy when the potential benefits clearly outweighs the foetal hazard.

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 Hyoce Injection during breast feeding is not recommended

4.11 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 Hyoce 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.

4.12 Undesirable effects

Adverse reactions that may be caused by using the drug are usually minor or mild. On the other hand, it may also give rise to many serious adverse reactions. Common side effects caused by it are bloated feeling; constipation; blurred vision, decrease sweating, dilation of pupils, difficulty in sleeping; dizziness; dry mouth; drowsiness, headache; nausea, loss of taste; nervousness; urinary retention. If any severe adverse reactions occur, consult the doctor right away. A few such effects are diarrhea; changes in heartbeat; difficulty in focusing your eyes; pounding in the chest; difficulty in urination; rapid heart rate; vomiting and unusual weakness.

4.13 Overdose

Symptoms

Over dosage cause tachycardia, rapid respiration, hyperpyrexia and central nervous system stimulation marked by restlessness, confusion, excitement, paranoid and psychotic reactions, hallucinations and delirium, and occasionally seizures or convulsions. A rash may appear on the face or upper trunk. In severe intoxication central stimulation may give way to central nervous system depression, coma, circulatory and respiratory failure and death. Quaternary ammonium antimuscarinic agents usually have some ganglionic- blocking activity so that high dose may cause postural hypotension and impotence, in toxic doses non –depolarizing neuromuscular block may be produced. There is considerable variation in susceptibility to the belladonna alkaloids; recovery has occurred after 1g, whereas deaths have been reported from doses of 100 mg or less for adults 10 mg for children.

Therapy

Treatment is to empty the stomach by aspiration and lavage or by induction of emesis. The giving of activated charcoal to reduce absorption prior to lavage, has been suggested. Supportive therapy should be given as required.

5. PHARMACOLOGICAL PROPERTIES:

5.1. Pharmacodynamic properties

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

Following Excipients used in HYOCE:

Water for Injections BP

6.2 Incompatibilities

NA

6.3 Shelf life

24 Months from the date of manufacture.

6.4 Special precautions for storage

Store below 30^0C, protected from light.

6.5 Nature and contents of container

Hyoscine butylbromide BP 20 mg/ ml is filled in 1 ml amber colored glass ampoules with white ring at constriction. 10 such labelled ampoules are placed in a plastic tray. One such plastic tray is packed in a carton along with leaflet.

6.6 Special precaution for disposal and other handling

Keep out of reach of children.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS:

Manufactured By:

KILITCH DRUGS (INDIA) LIMITED.

Plot no- C-301/2, M.I.D.C T.T.C, Industrial Area, Pawane Village, Navi Mumbai - 400 705, Maharashtra, INDIA.

8. MARKETING AUTHORIZATION NUMBERS:

Not applicable.

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION:

Date of first authorization: 03.07.2012

10. DATE OF REVISION OF THE TEXT:

Not Applicable.

11. DOSIMETRY (IF APPLICABLE)

Not Applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not Applicable.

The Summary of Product Characteristics (SPC) is satisfactory.