# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Bysimin 20mg/ml solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml ampoule contains 20 mg hyoscine butylbromide.

Excipient with known effect: Contains less than 1 mmol of sodium (23 mg) per dose.
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection
Clear, colourless or almost colourless solution free from visible particles.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Acute spasm of the gastrointestinal tract, biliary tract, pancreas and urogenital tract.
As antispasmodic agent in radiology in different diagnostic procedures where spasm may be a problem.

### 4.2 Posology and method of administration

Posology

*Adults*
1-2 ampoules (20-40 mg) intramuscularly, subcutaneously or intravenously slowly.

Maximum daily dose: 100mg (5 vials).

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

*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.

Method of administration
For intramuscular, subcutaneous or slow intravenous injection.

### 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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

## 4.4 Special warnings and precautions for use

Hyoscine butylbromide injection should not be given by intramuscular injection to patients being treated with anticoagulant drugs since intramuscular haematoma may occur. These patients can receive slow subcutaneous or intravenous injection.

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 etiology of the symptoms.

Hyoscine butylbromide should be used with caution in conditions characterized by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure and in cardiac surgery where it may further accelerate the heart rate.

Because of the possibility that anticholinergics may reduce sweating, hyoscine butylbromide 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 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.

After parenteral administration of hyoscine butylbromide, cases of anaphylaxis including episodes of shock have been observed. Patients receiving hyoscine butylbromide should be kept under observation.

**Bysimin contains sodium chloride.**
This medicinal product contains less than 1 mmol sodium (23 mg) per 5 vials (the maximum daily dose) and therefore is essentially sodium free.

## 4.5 Interaction with other medicinal products and other forms of interaction

The anticholinergic effect of drugs such as tri- and tetracyclic antidepressants, antihistamines, antipsychotics, quinidine, amantadine, disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by hyoscine butylbromide.

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

The tachycardic effects of beta-adrenergic agents may be enhanced by hyoscine butylbromide.

## 4.6 Fertility, pregnancy and lactation

<u>Pregnancy</u>

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.

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

Many of the listed undesirable effects can be assigned to the anticholinergic properties of hyoscine butylbromide. Anticholinergic side effects of hyoscine butylbromide are usually mild and transient.

Adverse events have been ranked under headings of frequency using the following convention: very common ≥1/10; common ≥1/100, <1/10; uncommon ≥1/1,000, <1/100; rare ≥1/10,000, <1/1,000, very rare <1/10,000; not known: cannot be estimated from the available data.

Immune system disorders
Not known*: anaphylactic shock including cases with fatal outcome, anaphylactic reactions, hypersensitivity reactions.

Nervous system disorders
Common: dizziness.

Eye disorders
Common: accommodation disorders.
Not known*: mydriasis, increased intraocular pressure.

Cardiac disorders
Common: tachycardia.

Vascular disorders
Not known*: blood pressure decreased, flushing.

Respiratory, thoracic and mediastinal disorders
Not known*: dyspnoea.

Gastrointestinal disorders
Common: dry mouth, constipation.
Skin and subcutaneous tissue disorders
Not known*: skin reactions (e.g. urticaria, rash, erythema, pruritus), dyshidrosis.

Renal and urinary disorders
Not known*: urinary retention.

Injection site pain, particularly after intramuscular use, occurs.

*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. Precise frequency estimation is not possible as the adverse drug reaction did not occur in a clinical trial database of 185 patients.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

## 4.9 Overdose

Symptoms
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.

Treatment
Symptoms of hyoscine butylbromide overdosage respond to parasympathomimetics. For patients with glaucoma, an ophthalmologist should promptly be consulted, pilocarpine should be given locally. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis, intubation and artificial respiration.
Catheterisation may be required for urinary retention.
In addition, appropriate supportive measures should be used as required.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Belladonna alkaloids, semisynthetic, quaternary ammonium compounds, 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.

Hyoscine butylbromide, due to its chemical structure as a quaternary ammonium derivate, is not expected to enter the central nervous system. Hyoscine butylbromide does not readily pass the blood-brain barrier. However, it cannot totally be ruled out that under certain circumstances psychiatric disorders (e.g. confusion) may also occur after administration of hyoscine butylbromide.

## 5.2 Pharmacokinetic properties

Absorption and distribution

After intravenous administration hyoscine butylbromide is rapidly distributed (t½α =4 min, t½β=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.

Metabolism and elimination
The main metabolic pathway is the hydrolytic cleavage of the ester bond. The half-life of the terminal elimination phase (t½γ) 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.

Paediatric population
No particular pharmacokinetic studies concerning hyoscine butylbromide have been performed in children.

### 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 chloride
Sodium hydroxide (for pH adjustment)
Hydrochloric acid, concentrated (for pH adjustment)
Water for injection

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

3 years

### 6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

### 6.5 Nature and contents of container and special equipment for use, administration or implantation

Box containing 5 x 1 ml or 10 x 1 ml or 50 x 1 ml type I clear glass ampoules in PVC trays sealed with PE transparent foil.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

No special requirements for disposal.

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

## 7. MARKETING AUTHORISATION HOLDER

Medochemie Ltd, 1-10 Constantinoupoleos Street, 3011 Limassol, Cyprus.

## 8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

## 10. DATE OF REVISION OF THE TEXT

2025-05-09