

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SPASMOMEN 40 mg – film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 40 mg of otilonium bromide.

Excipient(s) with known effect: approximately 28 mg of lactose monohydrate per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

White to almost-white round shaped, biconvex film-coated tablets of 5.4 mm diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Irritable Bowel Syndrome (IBS); relief of abdominal pain, distension and motility disorders characterised by smooth muscle spasm.

Spasmomen is indicated in adults.

4.2 Posology and method of administration

Posology

1 Tablet 2-3 times a day, according to the physician's judgement.

Special populations

Patients with hepatic or renal impairment

Dose adjustment is not necessary (see section 5.2).

Elderly

Dose adjustment is not necessary.

Paediatric population

Clinical data on the use of otilonium bromide 40 mg coated tablets in paediatric patients below 18 years is limited, therefore this medicinal product is not recommended for use in this population.

Method of administration

Oral administration.

Tablets should be swallowed whole, with a glass of water, preferably 20 minutes before meal.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

To be used with caution in subjects with glaucoma, prostatic hypertrophy and pyloric stenosis.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interactions with other medicinal products and other forms of interaction

No interaction studies of otilonium bromide with other products were performed.

At the recommended dose of 40 mg 2 or 3 times daily, the effect of Otilonium bromide on total time of gastrointestinal transit seems to be not significant.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of Otilonium Bromide in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Spasmomen during pregnancy, unless absolutely necessary and under close medical supervision.

Breast-feeding

It is unknown whether Otilonium Bromide is excreted in human milk.

A risk to the newborns/infants cannot be excluded.

Spasmomen should only be recommended to breast-feeding mothers if absolutely necessary and under close medical supervision.

Fertility

There are no data on the effect of Otilonium Bromide on human fertility. No effects on fertility have been observed in animal studies with female and male rats (see section 5.3).

4.7 Effects on ability to drive and use machines

Spasmomen has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects are described in accordance with their system organ class and based on their estimated frequency from post-authorisation studies and spontaneous reporting.

Frequencies are defined as follows: very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$); not known (frequency cannot be estimated from the available data).

System organ classification	Frequency	Undesirable effects
Skin and subcutaneous tissue disorders	Not known	Angioedema* Urticaria*
Gastrointestinal disorders	Not known	Dry mouth Nausea

*Undesirable effects coming from post-marketing experience

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

ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

In the animal, otilonium bromide was proven practically devoid of toxicity, used in doses that exceeded many times the usual pharmacological dose (please see section 5.3). Consequently also in the human, no particular overdosage-related problems should appear. In case of overdose a possible symptomatic and support therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: synthetic anticholinergics, quaternary ammonium compounds. ATC code: A03AB06.

Otilonium bromide is the prototype of a class of 2-aminoethyl-N-benzoylamino-benzoate quaternary salts.

Mechanism of action

Otilonium bromide is endowed with a marked spasmolytic action on the smooth muscle of the digestive tract.

Otilonium Bromide acts predominantly by modifying Ca^{2+} ion fluxes from cellular and extracellular sites and therefore reduces the trigger of contractile activity and visceral pain, most likely through the inhibition of L- and T-type Ca-channels into intestinal smooth muscle cells and peripheral sensory neurons, respectively. Additionally pharmacological effects could be exerted through the interaction with NK1 and NK2 tachykinin receptors.

Pharmacodynamic effects

Otilonium bromide possesses an antispastic action on the smooth muscle of the distal part of the intestine (colon and rectum). It has this effect at doses that do not affect gastric secretion or produce typical atropine-like adverse effects.

Clinical efficacy and safety

An extended analysis of a double-blind, placebo-controlled, 15-week study with otilonium bromide, conducted in 378 IBS patients (SpC1M study) showed that the rate of response to treatment within 2–4 months was significantly higher in the otilonium bromide group (36.9%) than in the placebo group (22.5%; $P=0.007$). In each month of treatment, the rate of monthly response was higher in the otilonium bromide group as compared to the placebo group ($P < 0.05$). The total monthly and weekly shares of population that responded to the treatment regarding single endpoints (intensity and frequency of pain and discomfort, meteorism/abdominal distension, severity of diarrhoea or constipation and mucus in the stool) were significantly bigger in the group treated with otilonium bromide than in the placebo-treated group, with differences of shares ranging from 10% to 20%. The subgroup analysis of the outcome of frequency of defecation and stool consistency indicates that patients with diarrhoea have an additional benefit. Safety findings about use of otilonium bromide were superimposable to those of placebo.

Otilonium bromide has been confirmed effective in a double-blind, placebo-controlled large ($n=356$ IBS patients) clinical trial (OBIS study) confirming its superiority to placebo in reducing the frequency of abdominal pain, severity of abdominal bloating and prevention from symptom relapse.

5.2 Pharmacokinetic properties

Absorption

Otilonium bromide comes to the site of pharmacological effect probably directly through the intestinal wall, because the systemic absorption of the drug after oral administration is very low (3%). Therefore, its plasma concentration is low.

Distribution

After oral use, high distribution of the drug in the smooth muscle of the colon and rectum has been described. Drug used shortly before the meal ensures pharmacologically effective local

bioavailability of the product, on the site of therapeutic action and in time of the expected most prominent symptoms of the disease.

Renal and hepatic impairment

Otilonium bromide is not studied in patients with impaired renal and hepatic function. Since orally used otilonium bromide is very scarcely absorbed in systemic circulation, the effect of reduced hepatic and renal function on its local exposition is not expected.

5.3 Preclinical safety data

Acute toxicity: otilonium bromide displayed low oral toxicity, as the lowest lethal oral doses were 900 and 1250 mg/kg in rats and mice, respectively, whereas no mortalities were observed in dogs up to 1000 mg/kg.

Chronic toxicity: no signs of toxicity, including alterations of hematochemical and histological exams, were observed in dogs orally dosed up to 80 mg/kg/day for 26 weeks.

Genotoxicity: no mutagenic or clastogenic effects have been observed in standard in vitro or in vivo tests performed.

Carcinogenicity: no effects have been observed in long-term studies carried out in mice (87 weeks) and rats (104 weeks) up to doses of 300 mg/kg/day.

Reproductive and developmental toxicity: no effects on fertility, and no embryotoxic, fetotoxic, teratogenic or developmental effects have been observed in rats up to 60 mg/kg/day. Likewise, no teratogenic, embryotoxic or fetotoxic effects have been detected at this dose in rabbits (see Section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each tablet contains:

Tablet core

Lactose
rice starch
sodium starch glycolate
magnesium stearate

Tablet coat

hydroxypropylmethyl cellulose
titanium dioxide
polyethylene glycol
talc

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

36 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

PVC/PVDC//Al blister packs with 30 film-coated tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

A. Menarini Industrie Farmaceutiche Riunite Srl
Via Sette Santi 3, 50131 Florence, Italy

8. MARKETING AUTHORIZATION NUMBER(S)

MA 205/00401

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 30 May 2006
Date of latest renewal: 30 September 2012

10. DATE OF REVISION OF THE TEST

01 February 2021