SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Mebeverine hydrochloride 135 mg coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains 135 mg of mebeverine hydrochloride.

Excipient with known effect: Also contains 121.50 mg of lactose monohydrate and 60.00 mg of sucrose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Coated tablet

Round, white to off-white, sugar coated tablets, plain on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic treatment of irritable bowel syndrome and other conditions usually included in this grouping, such as: chronic irritable colon, spastic constipation, mucous colitis, spastic colitis. Mebeverine is effectively used to treat the symptoms of these conditions, such as: colicky abdominal pain and cramps, persistent, non-specific diarrhoea (with or without alternating constipation) and flatulence.

4.2 Posology and method of administration

Posology

Adults (including the elderly):

One tablet three times a day, preferably 20 minutes before meals. After a period of several weeks, when the desired effect has been obtained, the dosage may be gradually reduced.

Paediatric Population

This medicine is not recommended for use in children and adolescents below 18, due to insufficient data on safety and efficacy.

Special Population

No posology studies in elderly, renal and/or hepatic impaired patients have been performed. No specific risk for elderly, renal and/or hepatic impaired patients could be identified from available post-marketing data. No dosage adjustment is deemed necessary in elderly, renal and/or hepatic impaired patients.

Method of administration

For oral use.

The coated tablets should be swallowed with a sufficient amount of water (at least 100 ml water). They should not be chewed because of the unpleasant taste.

Duration of use is not limited.

If one or more doses are missed, the patient should continue with the next dose as prescribed; the missed dose(s) should not be taken in addition to the regular dose.

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

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

The coated tablets contain sucrose and should not be used by patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed, except with alcohol. *In vitro* and *in vivo* studies in animals have demonstrated the absence of any interaction between mebeverine hydrochloride and ethanol.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amounts of data from the use of mebeverine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Mebeverine is not recommended during pregnancy.

Lactation

It is unknown whether mebeverine or its metabolites are excreted in human milk. The excretion of mebeverine in milk has not been studied in animals. Mebeverine should not be used during breast-feeding.

Fertility

There are no clinical data on male or female fertility; however, animal studies do not indicate harmful effects of mebeverine (see section 5.3).

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. The pharmacodynamic and pharmacokinetic profiles as well as postmarketing experience do not indicate any harmful effect of mebeverine on the ability to drive or to use machines.

4.8 Undesirable effects

The following adverse reactions have been reported spontaneously during postmarketing use. A precise frequency cannot be estimated from available data.

Allergic reactions mainly but not exclusively limited to the skin have been observed.

Immune system disorders:

Hypersensitivity (anaphylactic reactions)

Skin and subcutaneous tissue disorders:

Urticaria, angioedema, face oedema, exanthema

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Theoretically CNS excitability may occur in cases of overdose. In cases where mebeverine was taken in overdose, symptoms were either absent or mild and usually rapidly reversible. Observed symptoms of overdose were of a neurological and cardiovascular nature.

No specific antidote is known and symptomatic treatment is recommended.

Gastric lavage should only be considered in case of multiple intoxication or if discovered within about one hour. Absorption reducing measures are not necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Synthetic anticholinergics, esters with tertiary amino group, ATC code: A03AA04

Mechanism of action

Mebeverine is a musculotropic antispasmodic with a direct action on the smooth muscle of the gastrointestinal tract, without affecting normal gut motility. The exact mechanism of action is not known, but multiple mechanisms, such as a decrease in ion channel permeabilities, blockade of noradrenaline reuptake, a local anesthetic effect, changes in water absorption as well as weak anti-muscarinergic and phosphodiesterase inhibitory effect might contribute to the local effect of mebeverine on the gastrointestinal tract. Systemic side-effects as seen with typical anti-cholinergics are absent.

Clinical efficacy and safety

All formulations of mebeverine were generally safe and well tolerated in the recommended dose regimen.

Paediatric population

The safety and efficacy of the product has only been evaluated in adults.

5.2 Pharmacokinetic properties

Absorption

Mebeverine is rapidly and completely absorbed after oral administration of tablets.

Distribution

No significant accumulation occurs after multiple doses.

Biotransformation

Mebeverine hydrochloride is mainly metabolized by esterases, which split the ester bonds into veratric acid and mebeverine alcohol firstly.

The main metabolite in plasma is DMAC (demethylated carboxylic acid).

The steady state elimination half-life of DMAC is 2.45 h. During multiple dosing Cmax of DMAC for the coated tablets with 135 mg is 1670 ng/ml and tmax is 1 h.

Elimination

Mebeverine is not excreted as such, but metabolised completely; the metabolites are excreted nearly completely. Veratric acid is excreted into the urine, mebeverine alcohol is also excreted into the urine, partly as the corresponding carboxylic acid (MAC) and partly as the demethylated carboxylic acid (DMAC).

Paediatric population

The safety and efficacy of the product has only been evaluated in adults.

5.3 Preclinical safety data

Effects in repeat-dose toxicity studies, after oral and parenteral doses, were indicative of central nervous involvement with behavioural excitation, mainly tremor and convulsions. In the dog, the most sensitive species, these effects were seen at oral doses equivalent to 3 times the maximum recommended clinical dose of 400mg/day based on body surface area (mg/m^2) comparisons.

The reproductive toxicity of mebeverine was not sufficiently investigated in animal studies.

There was no indication of teratogenic potential in rats and rabbits. However, embryotoxic effects (reduction in litter size, increased incidence of resorption) were noticed in rats at doses equivalent to twice the maximum daily clinical

dose. This effect was not observed in rabbits. No effects on male or female fertility were noted in rats at doses equivalent to the maximum clinical dose.

In conventional in vitro and in vivo genotoxicity tests mebeverine was devoid of genotoxic effects. No carcinogenicity studies have been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose monohydrate

Maize starch

Povidone K 30

Purified talc

Isopropyl alcohol

Magnesium stearate (E470b)

Tablet coat

Sucrose

Gelatin

Purified talc

Ethanol

Shellac (E904)

Carnauba wax yellow (E903)

Beeswax white (E901)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Clear PVC/PVDC and Aluminium blister packs of 10, 15, 84 or 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd
Unit 3, Canalside,
Northbridge Road,
Berkhamsted,
Hertfordshire HP4 1EG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0430

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/01/2025

10 DATE OF REVISION OF THE TEXT

23/01/2025