SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Mebeverine Hydrochloride IBS 135mg Film-coated Tablets

Boots IBS Symptom Relief 135mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 135mg mebeverine hydrochloride.

Excipient with known effect:
Each film-coated tablet contains 97 mg lactose monohydrate equivalent to 92.15 mg of lactose (see section 4.4).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated Tablet.
(Tablet)

White to off-white, round film-coated tablets debossed with M135 on one side and plain on other side with 10mm diameter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of Irritable Bowel Syndrome.

4.2 Posology and method of administration

Posology

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.

Adults (including the elderly):
One tablet three times a day, preferably 20 minutes before meals. If symptoms persist for more than 2 weeks, consult your doctor.
Warning: Do not exceed the stated dose.

Paediatric population:
Mebeverine hydrochloride 135 mg film-coated tablets are not recommended for use in children and adolescents below 18 years, 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 film-coated tablets should be swallowed with a sufficient amount of water (at least 100 ml water). Tablets should not be chewed because of the unpleasant taste.

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

If this is the first time you have had these symptoms, consult your doctor before using any treatment.

If any of the following apply, do not use mebeverine. It may not be the right treatment for you. See your doctor as soon as possible if:

- you are aged 40 years or over
- you have passed blood form the bowel

- you are feeling sick or vomiting
- you are looking pale and feeling tired
- you are suffering from severe constipation
- you have a fever
- you have recently travelled abroad
- you are or may be pregnant
- you have abnormal vaginal bleeding or discharge
- you have difficulty or pain passing urine

Talk to your doctor if you have developed new symptoms, or if your symptoms worsen, or if they do not improve after 2 weeks treatment.

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

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

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.

Breast-feeding

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 reported.

Immune system disorders:
Hypersensitivity (anaphylactic reactions)

Skin and subcutaneous tissue disorders:
Urticaria, angioedema, face oedema and 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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

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: A03A A04.

Mechanism of action

Mebeverine is a musculotropic antispasmodic drug 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 anaesthetic 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 anticholinergics 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 C_{max} of DMAC for the flim-coated tablets with 135 mg is 1670 ng/ml and t_{max} 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/m2) 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,
Silicified microcrystalline cellulose,
Sodium starch glycolate (Type A),
Povidone,
Talc (E553b),
Magnesium stearate.

Film-coating:
Poly (vinyl alcohol) - part hydrolyzed (E1203), talc (E553b), titanium dioxide (E171), glycerol monocaprylocaprate (type I) and sodium laurilsulfate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25^{o}C. Store in the original package.

6.5 Nature and contents of container

PVC/PVdC-Alu blister containing packs of 7, 10, 12, 14, 15, 18, 20, 21, 28, 30, 56, 60, 84, 90 and 100 tablets are available.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Morningside Healthcare Ltd.
Unit C, Harcourt Way
Leicester, LE19 1WP, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 20117/0322

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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