Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Mebecon 135 mg Coated tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains Mebeverine hydrochloride 135 mg.

Excipients: also includes Lactose monohydrate 97.0 mg per tablet and sucrose 79.0 mg per tablet.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Coated Tablet.

White, circular, sugar coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the management of irritable bowel syndrome (particularly gastrointestinal spasm).

4.2 Posology and method of administration

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

Adults and children over 10 years:
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.

Duration of use is not limited. However, after a period of several weeks when the desired effect has been obtained, the dosage may be gradually reduced.
In case of missed dose(s), the patient should continue with the next dose as prescribed; do not take the missed dose(s) in addition to the regular dose.

Children under 10 years:
Mebecon should not be used in children aged 3 years and younger as no clinical data is available for this age group. For children from 3 – 10 years mebeverine 135mg tablets should not be used due to the high content of the active substance.

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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Prior to treating patients with mebeverine, care should be taken to exclude organic disease of the bowel, particularly malignancy.

Since Mebecon coated tablets contain lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

Since Mebecon coated tablets contain sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Only interaction studies with alcohol have been performed*in vitro* and *in-vivo* studies in animals have demonstrated the absence of any interaction between Mebecon and ethanol.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of mebeverine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Mebecon 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. Mebecon 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 Mebecon (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 profile as well as post-marketing 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 events have been reported spontaneously during post-marketing use. A precise frequency can not 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 disordes:
Urticaria, angioedema, face edema, exanthema

4.9 Overdose

Theoretically, CNS excitability may occur in cases of overdosage. In cases where mebeverine was taken in overdose, symptoms were either absent or mild and usually rapidly reversible. Observed symptoms of overdose were of 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 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 and pharmacodynamic effects
Mebeverine is a musculotropic antispasmodic with a direct effect on the smooth muscle of the gastrointestinal tract, relieving spasm without affecting normal gut motility. Since this effect is not mediated by the autonomic nervous system, the typical anti-cholinergic side-effects are absent.

Clinical efficacy and safety
The clinical efficacy and safety of different formulations of mebeverine was evaluated in more than 1500 patients. Considerable improvements in the predominant syptomatology of ittitable bowel syndrome (e.g. abdominal pain, stool characteristics) were generally observed in reference or baseline-controlled clinical studies.

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

Paediatric population
Clinical trials with the tablet or capsule formulations have been performed in adults only. Clinical efficacy and safety data from clinical trials as well as from post-marketing experience with a suspension formulation of mebeverine pamoate > 3 years of age have shown that mebeverine is efficacious, safe and well tolerated.

Clinical studies with mebeverine suspension showed that mebeverine was efficacious in ameliorating the symptoms of irritable bowel syndrome in childhood. Further open, baseline-controlled studies with mebeverine suspension confirmed the efficacy of the drug.

The dosing schedule for the tablet or capsule formulation was calculated based on the consistent safety and favourable tolerability of mebeverine.

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 coated tablets with 135mg 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 in the urine, mebeverine alcohol is also excreted in the urine, partly as the corresponding carboxylic acid (MAC) and partly as the demethylated carboxylic acid (DMAC).

Paediatric population
No pharmacokinetic studies have been conducted in children with any formulation of mebeverine.

5.3 Preclinical safety data

During its development phase the entity mebeverine was tested in several animal species in acute, (sub) chronic and reproduction investigations.

In single and repeat dose oral toxicity studies effects on the central nervous system with behavioural excitation (mainly tremor and convulsions) were observed in rats, rabbits and dogs. In dogs convulsions were seen at doses equivalent to 2 fold the maximal clinical dose in humans of 400mg/day. In rats and rabbits these effects were only observed at doses considerably higher than the clinical dose in humans (e.g. for rats at doses 15 fold the maximal human dose).

The reproductive toxicity of mebeverine was not sufficiently investigated in animal studies. Yet there was no indication of teratogenic potential in rats and rabbits up to doses of 100 mg/kg/day, given as a single dose. However, embryotoxic effects (reduced growth, embryo lethality) were noticed in rats administered 50 mg/kg twice a day, which is equivalent to 2 fold the maximal clinical dose in humans. This effect was not observed in rabbits.

In oral fertility study in female and male rats, no effects were noticed in the F0 and three F1 generations up to and including the dose level of 1 fold the human dose.

No teratogenic effects were seen in both species.

In the standard in vitro and in vivo genotoxicity tests mebeverine was devoid of genotoxic effects. No carcinogenic studies have been performed given that there is no suspicion of carcinogenic potential.

In a study investigating the potential effect of mebeverine and mebeverine acid on the ethanol-metabolizing Cytochrome P-system 2E1 employing human liver microsomes neither mebeverine nor mebeverine acid inhibited the CYP2E1.

Effects of mebeverine and ethanol on motor co-ordination were investigated in rats. Results of the study showed that neither mebeverine dosage affected motor co-ordination, either in presence or absence of ethanol. Mebeverine did not potentiate the ethanol effect.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Potato starch
Povidone (K25)
Talc
Magnesium stearate

Coating:
Talc
Sucrose
Gelatin
Acacia
Carnauba wax.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Boxes containing 100 tablets in PVC/Al blister strips.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

7 MARKETING AUTHORISATION HOLDER

Abbott Heathcare Products Limited
Mansbridge Road
West End
Southampton
SO18 3JD
England

8 MARKETING AUTHORISATION NUMBER

PA0108/033/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 September 2000

Date of last renewal: 29 September 2010

10 DATE OF REVISION OF THE TEXT

March 2013