Abbott Laboratories South Africa (Pty) Ltd	**Submission date: 25 November 2022**	**Type: Post-registration variations (format update, editorial changes and clinical safety update)**
Colofac 135 mg tablets	**Approval Date: 26 January 2023**	**Category: IA_{IN}, IB**
135 mg mebeverine hydrochloride	**Implemented: 26 January 2023**	**Code: C.I.0.1, C.I.0.2a, C.I.0.3**
Country code: ZA	**Reg no.: Q/11.2/165**	**Sequence no.: 0000 (eSub)**

PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

COLOFAC 135 mg coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 135 mg mebeverine hydrochloride.

COLOFAC 135 mg contains sugar (79 mg sucrose and 97 mg lactose monohydrate per tablet).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablets.

White, round sugar-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Primary irritable colon characterised by persistent diarrhoea, alternating constipation and diarrhoea, abdominal pain and postprandial distension.

Secondary irritable colon due to organic lesions such as regional enteritis, diverticulitis, specific and non-specific inflammatory conditions of the gastro-intestinal tract.

4.2 Posology and method of administration

Posology

Take one (1) tablet three (3) times daily, preferably before meals. After a period of a few weeks when the desired effect has been obtained, the dosage may be gradually reduced.

As atropine-like effects are absent, COLOFAC 135 mg is not contraindicated in patients with glaucoma or prostatic hypertrophy.

Method of administration

For oral use.

The coated tablets should be swallowed with a sufficient amount of water (at least 100 mL water).

The coated tablets should not be chewed because of the unpleasant taste.

4.3 Contraindications

Hypersensitivity to mebeverine hydrochloride or any excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The safety of COLOFAC 135 mg in pregnancy has not been established (see section 4.6).

Excipients

COLOFAC 135 mg contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take COLOFAC 135 mg.

COLOFAC 135 mg contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take COLOFAC 135 mg.

4.5 Interaction with other medicines 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

The safety of COLOFAC 135 mg in pregnancy has not been established.

COLOFAC 135 mg is not recommended during pregnancy.

Breastfeeding

It is unknown whether mebeverine or its metabolites are excreted in breast milk. The excretion of mebeverine in milk has not been studied in animals. COLOFAC 135 mg should not be used during breastfeeding.

Fertility

There are no clinical data on male or female fertility, however animal studies do not indicate harmful effects of mebeverine.

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.

COLOFAC 135 mg may cause dizziness, which should be taken into account before patients drive or use machines.

4.8 Undesirable effects

After the administration of COLOFAC 135 mg cases of depression, headache, dizziness, diarrhoea and constipation (most probably not attributable to the medicine) were reported.

The following adverse reactions have been reported spontaneously during post-marketing 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 medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A. 11.2 Gastro-intestinal anti-spasmodics and cholinolytics.

Pharmacotherapeutic group: Synthetic anticholinergics, esters with tertiary amino group

ATC code: A03AA04

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 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 anti-cholinergics are absent.

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 metabolised 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 hours. During multiple dosing C_{max} of DMAC for the coated tablets with 135 mg is 1 670 ng/mL and t_{max} is 1 hour.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose monohydrate

Magnesium stearate

Povidone

Starch (potato)

Talc

Tablet coating

Acacia

Carnauba wax

Gelatin

Sucrose

Talc

6.2 Incompatibilities

None known.

6.3 Shelf life

60 months.

6.4 Special precautions for storage

Store in a dry, dark place, at temperatures not exceeding 30 °C.

6.5 Nature and contents of container

PVC/aluminium blister strips in an outer carton.

Pack sizes: 10, 20, 100 and 500 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Abbott Laboratories S.A. (Pty) Ltd

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Johannesburg, South Africa

8. REGISTRATION NUMBER

Q/11.2/165

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 March 1983

10. DATE OF REVISION OF THE TEXT

26 January 2023

Namibia reg. no. 90/11.10/0009 NS2