1 NAME OF THE MEDICINAL PRODUCT

Apercap 0.2 ml Gastro-Resistant Capsules
Peppermint Oil 0.2 ml Gastro-Resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 0.2ml peppermint oil (*Mentha x piperita* L.aetheroleum)

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gastro-resistant capsule, soft

Opaque green and white, size 3, oval shaped, soft gelatin capsules containing a clear liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic relief of minor spasms of the gastrointestinal tract, flatulence and abdominal pain, especially in patients with irritable bowel syndrome.

4.2 Posology and method of administration

Route of administration: Oral use

Adults and elderly:

One capsule to be taken three times a day, preferably before meals with a small quantity of water. The capsules must not be taken immediately after food. The capsules should be swallowed whole, i.e. not broken or chewed, because this would release the peppermint oil prematurely, possibly causing local irritation of the mouth and oesophagus.

When symptoms are more severe, the dose may be increased to two capsules three times a day.

Apercap capsules should be taken until the symptoms resolve, usually within one or two weeks. At times when the symptoms are more persistent, the intake of the gastro-resistant capsules can be continued for periods of no longer than 3 months per course.

Children under 12 years

Not recommended for children.

4.3 Contraindications

Hypersensitivity to peppermint oil or menthol. Patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders.

4.4 Special warnings and precautions for use

If this is the first occurrence of these symptoms, a doctor should be consulted before self medication begins, to confirm the suitability of the treatment.

Before beginning self medication, a doctor should be consulted if:

- the patient is over 40 years old and it is some time since their last attack, or the symptoms have changed;
- blood has been passed from the bowel;
- the patient has experienced nausea or vomiting, loss of appetite or loss of weight, paleness and tiredness, severe constipation, fever, abnormal vaginal bleeding or discharge, difficulty or pain in passing urine.
- the patient has recently travelled abroad.
- the patient is pregnant or possibly pregnant; they should consult their doctor prior to self medication.

If there are new symptoms or a deterioration of the condition or failure to improve over two weeks of treatment, the patient should consult their doctor.

Patients, who already suffer from heartburn or hiatal hernia have sometimes an exacerbation of this symptom after taking peppermint oil. Treatment should be discontinued in these patients.
Excipients

Sodium
This medicinal product 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

Use of food or antacids administered at the same time could cause early release of capsule content. Other medicinal products used to decrease stomach acid, like histamine-2-blockers and proton pump inhibitors may cause premature dissolution of the enteric coating and should be avoided.

There is some evidence that peppermint oil can inhibit the cytochrome P450 isoenzyme CYP3A4 and may affect the clearance of medicines whose metabolism is controlled by this enzyme.

4.6 Pregnancy and lactation

There are no adequate data from the use of peppermint oil in pregnant women. Animal studies are insufficient with respect to effects on pregnancy and embryonic foetal development.

It is unknown whether peppermint oil is excreted in human breast milk.

In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Urine and stools with an odour to menthol were observed; dysuria and inflammation of the glans of the penis have been reported. The frequency is not known.

Allergic reactions to menthol were reported, with headache, bradycardia, muscle tremor, ataxia, anaphylactic shock and erythematous skin rash. The frequency is not known.

Heartburn, perianal burning, blurred vision, nausea and vomiting were reported. The frequency is not known.

If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.

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 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

Overdose may cause severe gastro-intestinal symptoms, diarrhoea, rectal ulceration, epileptic convulsions, loss of consciousness, apnoea, nausea, disturbances in cardiac rhythms, ataxia and other CNS problems, probably due to the presence of menthol.

In the event of overdose, the stomach should be emptied by gastric lavage. Observation should be carried out with symptomatic treatment if necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: *Other drugs for functional bowel disorders*

ATC code: *AO3AX*

In vitro studies

The principal pharmacodynamic effect of peppermint oil relevant to the gastrointestinal tract is a dose-related antispasmodic effect on the smooth musculature, due to the interference of menthol with the movement of calcium across the cell membrane.

Peppermint oil showed antifoaming and carminative activity *in vitro*. Reductions in gastric and intestinal foam volume were observed *in vitro* studies with peppermint oil.

In vivo studies

In several studies in healthy subjects or patients, who underwent exposure to peppermint oil either by topical intraluminal (stomach or colon) or oral administration by single doses, result

in effects, indicating a substantial spasmolytic action of peppermint oil on the smooth muscles of the gastrointestinal tract.

The enteric coating delays the release of the product until it reaches the distal small bowel, exerting local effects of colonic relaxation.

Peppermint appears to enhance production of bile. The choleretic and antifoaming effects of peppermint oil play an additional role to the antispasmodic action, decreasing the abdominal distension, as the discomfort and abdominal pain.

5.2 Pharmacokinetic properties

Menthol and other terpene constituents of peppermint oil are fat soluble and rapidly absorbed at the proximal small intestinal tract.

To some extent, they are excreted in the form of glucoronide. The peak menthol urinary excretion levels were lower and secretion delayed with the modified-release preparations, than with the immediate release preparations.

In one clinical study with peppermint oil and one clinical study with menthol, some inhibition of CYP3A4 activity has been described. Further investigations are necessary.

5.3 Preclinical safety data

Peppermint oil was negative in two validated tests of genotoxicity, the Ames test and the mouse lymphoma assay. There is more evidence for genotoxicity potential of menthol and there seems to be a discrepancy between peppermint oil and its most important constituent menthol. However, the present evidence points to a very weak or totally absent genotoxicity of peppermint oil.

The highest recommended daily dose in EU is 1.2 ml peppermint oil i.e. 1,080 mg peppermint oil, which contains maximum 140 mg pulegone + menthofuran (Ph Eur). For a 60 kg person this would correspond to a daily intake of 2.3 mg/kg bw. No cases of liver damage caused by peppermint oil or mint oil were reported under that posology (see SCF report referred to in the HMPC ‘Public statement on the use of herbal medicinal products containing pulegone and menthofurane’ (EMEA/HMPC/138386/2005)).

The oral toxicity of menthone was evaluated in an animal model. The decrease in plasma creatinine and the increase in phosphatase alkaline and bilirrubin were dose dependent, after levels of 0, 200, 400 and 800 mg/kg bw/day. The nonobservable- effect-level (NOEL) for menthone in this study was lower than 200 mg/kg bw/day. A NOEL of 400 mg/kg bw/day was reported in a 28 day toxicity study in rats.

In 2000, the FAO/WHO Joint Expert Committee on Foods Additives established an acceptable daily intake (ADI) of 0 - 4 mg/kg bw/day for menthol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule shell
Gelatin
Glycerol
Purified Water
Titanium Dioxide (E171)
Chlorophyllin Copper Complex Sodium (E141)

Gastro resistant coating
Aqua Polish
Propylene Glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/PVdC blister pack with an aluminium foil lidding in a cardboard carton containing 20, 28, 30 or 84 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited
Ridings Point,
Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom

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