Public Assessment Report
Decentralised Procedure

Apercap 0.2ml Gastro-Resistant Capsules

Peppermint Oil

UK/H/3268/001/DC

UK licence no: PL 17507/0067

Auden Mckenzie (Pharma Division)Ltd
LAY SUMMARY

On 23rd March 2011, the MHRA granted Auden Mckenzie (Pharma Division) Ltd Marketing Authorisation for the medicinal product Apercap 0.2 ml Gastro-Resistant Capsules (PL 17507/0067). This is a General Sale Licence (GSL).

Apercap Gastro-Resistant Capsules contain peppermint oil as an active substance. Peppermint oil helps to restore normal bowel action by relaxing the muscle spasm in the bowel wall. This reduces symptoms such as bloating, trapped wind, bowel discomfort and pain.

Apercap Capsules are used to relieve the symptoms of irritable bowel syndrome (IBS).

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Apercap 0.2 ml Gastro-Resistant Capsules outweigh the risks, hence a Marketing Authorisation has been granted.
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## Module 1

<table>
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<tr>
<th><strong>Product Name</strong></th>
<th>Apercap 0.2ml Gastro-Resistant Capsules</th>
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<td>Generic, Article 10.3</td>
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<td><strong>Active Substance</strong></td>
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<td>Gastro-Resistant Capsules</td>
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<td><strong>Strength</strong></td>
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<tr>
<td><strong>MA Holder</strong></td>
<td>Auden Mckenzie (Pharma Division) Ltd</td>
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<td></td>
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<td>UK/H/3268/001/DC</td>
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<td><strong>Timetable</strong></td>
<td>Day 210 – 14th February 2011</td>
</tr>
</tbody>
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Module 2
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Apercap 0.2 ml Gastro-Resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 0.2ml peppermint oil (\textit{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

\textit{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.

\textit{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.

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.

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 menthofuran" (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 bilirubin 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
24 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
Auden Mckenzie (Pharma Division) Ltd
McKenzie House
Bury Street
Ruislip
Middlesex
HA4 7TL
UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 17507/0067

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
23/03/2011

10 DATE OF REVISION OF THE TEXT
23/03/2011
Module 3

PACKAGE LEAFLET

PATIENT INFORMATION LEAFLET

APERCAP 0.2 ml GASTRO-RESISTANT CAPSULES

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without a prescription. However you still need to take Apercap 0.2 ml Gastro-Resistant Capsules carefully to get the best results from it.

• Keep this leaflet. You may need to read it again.
• Ask your pharmacist if you need more information or advice.
• You must contact your doctor if your symptoms worsen or do not improve after 14 days.
• If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What is APERCAP and what is it used for?
2. Before you take APERCAP
3. How to use APERCAP
4. Possible side effects
5. Storing APERCAP
6. Further information

1. What is APERCAP and what is it used for?

Apercap Capsules are used to relieve the symptoms of irritable bowel syndrome (IBS).

These capsules are specially coated to allow them to pass intact through the stomach and the first part of the bowel. This allows the capsules to reach the part of the gut where they are needed. It is only then that the peppermint oil is released from the capsule to do its work.

Peppermint oil helps to restore normal bowel action by relaxing the muscle spasm in the bowel wall. This reduces symptoms such as bloating, trapped wind, bowel discomfort and pain.

2. Before you take APERCAP

Do not take the capsules if:

• you are allergic to the peppermint oil, menthol or any of the other ingredients in the capsules (see section 6 ‘Further Information’).
• you suffer from inflammation of the bile duct, gallstones or any other bile disorders.
• you suffer from a condition called ‘achlorhydria’ that prevents normal digestion of food.
Talk to your doctor first if any of the following apply to you and follow the advice given:

- this is the first time you have suffered from any of the symptoms such as bloating, trapped wind or bowel discomfort and pain.
- you are over 40 years of age and you have not had this problem recently or if your symptoms appear to be different from before.
- you are feeling sick, or have been sick.
- you have a temperature or feel feverish.
- you have severe constipation.
- you suffer from heartburn.
- you have pain or difficulty when passing urine.
- you are pale and tired.
- you have lost your appetite or lost weight.
- you have passed blood from your bowel.
- you have unusual vaginal bleeding or discharge.
- you have travelled abroad recently.

Are you pregnant or breast-feeding?

Tell your doctor if you are pregnant, think you might be pregnant or are trying to become pregnant.

Tell your doctor if you are breast-feeding.

Taking other medicines

You should not take Apercap Capsules at the same time as:

- medicines used for indigestion (antacids).
- medicines used for stomach or intestinal ulcers and acid reflux (histamine-2 blockers and proton pump inhibitors).

It is unlikely Apercap Capsules will interfere with the action of any other medicines you may be taking. However, it may sometimes affect the clearance of some medicines from the body. It is always sensible to tell your doctor and/or pharmacist what these medicines are — mention prescription medicines, or medicines, including vitamins and herbal preparations, that you have purchased yourself.

Driving and using machines

Apercap should not affect your ability to drive or use machines.

3. How to take APERCAP

Take the capsules by mouth with a drink of water. Swallow the capsules whole; do not chew or break them because this will damage the special coating that enables them to get to the correct part of your bowel.

Do not take the capsules immediately after food.
The usual dose is:

**Adults** (including elderly people)
One capsule three times a day, before meals.

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

**Children:**
Aercap Capsules are not recommended for children.

Aercap Capsules are usually only needed for a short period to relieve symptoms. However, if your condition does not improve after two weeks, you should consult your doctor who may decide to continue the treatment for up to three months.

If you take more capsules than you should:

If you have taken more Aercap Capsules than you should, contact your doctor, pharmacist, or hospital casualty department immediately.

Symptoms of overdose include severe stomach upset, diarrhoea, rectal ulcers, fits, loss of consciousness, difficulty in breathing, feeling of sickness and abnormal beating of the heart.

If you miss a dose of Aercap Capsules:
Wait and take the next dose at the normal time.

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### 4. Possible side effects

In some people, the following side effects have occurred:

- allergic reactions (rash, itchiness or shortness of breath)
- headache
- slow heartbeat
- trembling
- unsteadiness
- skin rash
- heartburn
- itching around the back passage
- blurred vision
- feelings of sickness (nausea)
- vomiting
- urine and stools with an odour to menthol
- pain or difficulty when passing urine
- inflammation of part of the penis

If you notice any side effects or you are worried about other symptoms tell your doctor or pharmacist.
5. Storing APERCAP

Keep Apercap Capsules out of the reach and sight of children. Do not store above 25°C.

There is an expiry date (Month/Year) on the pack. The capsules should not be used after the end of the month shown.

6. Further Information

The name of your medicine is Apercap 0.2 ml Gastro-Resistant Capsules. As well as containing 0.2 ml of peppermint oil, each capsule contains gelatin, glycerol, purified water, titanium dioxide powder (E171), chlorophyllin copper complex sodium (E141), aqua polish and propylene glycol.

Apercap 0.2 ml Gastro-Resistant Capsules are opaque, green and white, oval shaped, soft gelatino capsules containing a clear liquid.

Apercap 0.2 ml Gastro-Resistant Capsules are available in blister packs of 20, 28, 30 or 84 capsules. Not all pack sizes may be marketed.

Marketing Authorisation Holder:
Auden Mckenzie (Pharma Division) Ltd.
Mckenzie House,
Bury Street,
Ruislip,
Middlesex,
HA4 7TL,
UK.

Manufacturer:
Swiss Caps AG,
Husenstrasse.35,
CH-9533,
Kirchberg,
Switzerland.

Date of preparation of this leaflet: February 2011
Module 4
Labelling
PAR Apercap 0.2ml Gastro-Resistant Capsules

Use of the product: For the effective relief of:
- Stomach Cramps
- Wind & Bloating
- Symptoms of Irritable Bowel Syndrome

For children under 5 years, use on advice from a healthcare professional.

Keep out of reach of children.

Store in a cool, dry place.

Do not use if the seal is broken or damaged.

For medical advice, consult a healthcare professional.

Active ingredient:
- Peppermint Oil

Packaging:
- 30 Gastro-Resistant Capsules

Manufactured by:
[Manufacturer's Details]
Module 5
Scientific discussion during initial procedure

I INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) considers that the application for Apercap 0.2ml Gastro-Resistant Capsules in the treatment of symptomatic relief of minor spasms of the gastrointestinal tract, flatulence and abdominal pain, especially in patients with irritable bowel syndrome, could be approved.

This application was submitted under Article 10(3) of the Directive 2001/83/EC, cross-refering to Mintec 0.2ml Capsules, which was first licensed to Monmouth Pharmaceuticals Ltd, UK, on 21st July 1995.

With the UK as the RMS in this Decentralised Procedure (UK/H/3268/01/DC), Auden Mckenzie Limited applied for the Marketing Authorisation for Apercap 0.2ml Gastro-Resistant Capsules.

Peppermint oil is an aromatic carminative that relaxes gastrointestinal smooth muscle and relieves flatulence and colic. Peppermint oil enteric coated capsules have been available in the UK market for the treatment of irritable bowel syndrome for over 20 years. Enteric coated capsules are used for delivery of peppermint oil into the lower digestive tract and colon which is the target organ. Non-EC coated capsules are not therapeutically as effective and may also have increased adverse events. The therapeutic effects of peppermint oil are due to its local action on intestinal smooth muscle.

No new preclinical and clinical studies were conducted, which is acceptable given that the application was based on being essentially similar to an originator product that has been licensed for over 10 years. A bioequivalence study was carried out in accordance with Good Clinical Practice (GCP).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these product types at all sites responsible for the manufacture and assembly of this product. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

The RMS considers that the Pharmacovigilance System as described by the applicant fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country. A suitable justification has been provided for non-submission of a Risk Management Plan.

The Reference Member State (UK) has agreed to grant respective licence for the above product at the end of procedure (Day 210 – 14th February 2011). After a subsequent national phase, the UK granted a licence for this product on 23rd March 2011 (PL 17507/0067).
## II. ABOUT THE PRODUCT

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<th>Name of the product in the Reference Member State</th>
<th>Apercap 0.2ml Gastro-Resistant Capsules</th>
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<tr>
<td>Name and address of the authorisation holder</td>
<td>Auden Mckenzie (Pharma Division) Ltd McKenzie House Bury Street Ruislip Middlesex HA4 7TL UK</td>
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</table>
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

Nomenclature
- rINN peppermint oil
- CAS Registry No. 8006-90-4

General properties
Peppermint oil is obtained by steam distillation from the fresh aerial parts of the flowering plant *Mentha x piperita* L. The oil is a colourless, pale yellow or pale greenish-yellow liquid with a characteristic odour and taste follows by a cold sensation. It is miscible with alcohol, ether and methylene chloride. It has a boiling point of 215°C, relative density 0.900 – 0.916 g/ml at 20°C and refractive index of 1.46 at 20°C.

The drug substance, peppermint oil is described in the Ph Eur. It complies and is controlled in line with the Ph Eur. The active substance is also confirmed to be manufactured according to Good Manufacturing Practice. It is controlled by a suitable drug substance specification.

DRUG PRODUCT

Other Ingredients
Other ingredients consist of the pharmaceutical excipients gelatin, glycerol, titanium dioxide (E171), chlorophyllin copper complex sodium (E141), water purified, aqua polish and propylene glycol.

All excipients comply with their respective European Pharmacopoeia monographs with the exception of chlorophyllin copper complex sodium (E141) which complies with an in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

The gelatin used in the manufacture of the product is derived from animal origin. The supplier has provided TSE certificates from the European Directorate for the Quality of Medicines (EDQM). None of the other excipients are sourced from animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of this product.

Pharmaceutical Development
The objective of the development programme was to formulate robust, stable capsules that contain the same active ingredient as Mintec 0.2ml Capsules.

Suitable pharmaceutical development data have been provided for this application.

Manufacture
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results. Process validation data has been provided for three consecutive commercial scale batches. The results are satisfactory.

Finished Product Specification
The finished product specification is satisfactory. Test methods have been described and adequately validated. Batch data have been provided and comply with the specification. Certificates of Analysis have been provided for any working standards used.
Container-Closure System
The finished product is packed in 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.

Specifications and Certificates of Analysis for all packaging materials have been provided. These are satisfactory. All primary packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 24 months with a storage condition of “Do not store above 25°C” is set. This is satisfactory.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling
The SmPC, PIL and labels are pharmaceutically acceptable.

A package leaflet has been submitted to the MHRA together with results of consultations with target patient groups (“user testing”), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

The proposed artwork complies with the relevant statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

Marketing Authorisation Application (MAA) Forms
The MAA form is pharmaceutically satisfactory.

Expert report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
There are no objections to the approval of this product from a pharmaceutical point of view.

III.2 PRE-CLINICAL ASPECTS
The pharmacological, pharmacokinetic and toxicological properties of peppermint oil are well-known.

No new preclinical data have been supplied with this application and none are required for applications of this type. The pre-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the pre-clinical aspects of the dossier.

A suitable justification has been provided for non-submission of environmental risk assessment.
There are no objections to the approval of this product from a preclinical point of view.

III.3 CLINICAL ASPECTS

Clinical Pharmacology

Pharmacokinetics

In support of this application, the marketing authorisation holder has submitted the following bioequivalence study:

Study 1

This is a randomized, open label, balanced, two-treatment, two-period, two-sequence, single-dose, crossover bioequivalence study of Peppermint oil 0.2 ml in enteric coated soft gelatin capsules (test) and Mintec 0.2ml capsules (reference) in 12 healthy male volunteers under fasting conditions.

Standard meals were provided at 4, 8 and 12 hours respectively after drug administration in each period. The two periods were separated by a wash-out phase of 5 days. Urine samples (10mls each) were collected from the subjects as per the following time points in each period: Pre-dose (-1.5 to -1.0 hr), 0.25, 0.25–1.0, 1.0–2.0, 2.0–3.0, 3.0–4.0, 4.0–6.0, 6.0–8.0, 8.0–12.0 and 12.0–24.0 hours post-dose (10 samples per subject in each period).

ANOVA 90% CI (Log transformed) and CV% for primary parameters of Peppermint oil 0.2ml (test vs. reference) (Fasting, n=12).

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<th>Variable</th>
<th>Geometric mean</th>
<th>Confidence limits</th>
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<td>R_{max} (ratio test/reference)</td>
<td>101.58</td>
<td>94.25 – 109.48</td>
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<tr>
<td>A{e20.1} (ratio test/reference)</td>
<td>99.46</td>
<td>92.36 – 107.12</td>
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The 90% confidence intervals calculated for the primary parameters all fall within the acceptance range (80 – 125%) after single dose administration. Bioequivalence has been shown between the Test and Reference formulations.

Pharmacodynamics

No new data have been submitted and none are required for this generic application.

Clinical Efficacy

No new data have been submitted and none are required.

Clinical Safety

No new data have been submitted and none are required.

Expert Report

A clinical overall summary, written by an appropriately qualified physician, has been provided. This is a satisfactory, non-critical summary of Module 5.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling

The SmPC, PIL and labelling are medically satisfactory and consistent with those for the reference product.
Clinical Expert Report
The clinical expert report is written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Marketing Authorisation Application (MAA) Forms
The MAA form is medically satisfactory.

Clinical Conclusion
There are no objections to the approval of this product from a clinical point of view.
IV. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT
QUALITY
The important quality characteristics of Apercap 0.2ml Gastro-Resistant Capsules are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
Bioequivalence have been demonstrated between the applicant’s Peppermint oil 0.2 ml in enteric coated soft gelatin capsules and the reference product, Mintec 0.2ml Capsules.

No new or unexpected safety concerns arise from this application.

The SmPC and PIL are satisfactory and consistent with that of the reference product. Satisfactory labelling has also been submitted.

RISK-BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with peppermint oil is considered to have demonstrated the therapeutic value of the compound. The risk-benefit is, therefore, considered to be positive.
Module 6

**STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY**

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