GAVISCON ADVANCE PEPPERMINT FLAVOUR ORAL SUSPENSION

PL 00063/0612

UKPAR

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GAVISCON ADVANCE PEPPERMINT FLAVOUR ORAL SUSPENSION

PL 00063/0612

LAY SUMMARY

On 11th October 2010, the MHRA granted Reckitt Benckiser Healthcare (UK) Limited a Marketing Authorisation (licence) for the medicinal product Gaviscon Advance Peppermint Flavour Oral Suspension (PL 00063/0612). This product is available through Pharmacies (P).

Gaviscon Advance Peppermint Flavour Oral Suspension provides fast, soothing and long lasting relief from the pain and discomfort of heartburn and acid indigestion, which can occur after meals or during pregnancy. The product belongs to a group of medicines called ‘reflux suppressants’, which form a protective layer on top of the stomach contents to prevent acid escaping from the stomach where it works into the food pipe where it hurts.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Gaviscon Advance Peppermint Flavour Oral Suspension outweigh the risks; hence a Marketing Authorisation has been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted a Marketing Authorisation for the medicinal product Gaviscon Advance Peppermint Flavour Oral Suspension (PL 00063/0612) to Reckitt Benckiser Healthcare (UK) Limited on the 11th October 2010. This medicine is available in Pharmacies and it is used in the treatment of symptoms of gastro-oesophageal reflux such as acid regurgitation, heartburn and indigestion (related to reflux), for example, following meals, or during pregnancy, or in patients with symptoms related to reflux oesophagitis.

This application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, cross-referring to Gaviscon Advance Peppermint Flavour (PL 00063/0103) also held by Reckitt Benckiser Healthcare (UK) Limited, which was granted a marketing authorisation on 7th October 2003 as a line extension to the Gaviscon Advance Oral Suspension (PL 00063/0097).

No new data were submitted nor were they necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated.

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 not submitting a risk management plan for this product. The applicant’s justification for absence of RMP is satisfactory.

No environmental risk assessment has been undertaken, as this is not considered necessary.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 00063/0612
PROPRIETARY NAME: Gaviscon Advance Peppermint Flavour Oral Suspension
COMPANY NAME: Reckitt Benckiser Healthcare (UK) Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: P

1 INTRODUCTION
This is a simple, informed consent application for Gaviscon Advance Peppermint Flavour Oral Suspension, submitted under Article 10c of Directive 2001/83/EC. The application cross-refers to Gaviscon Advance Peppermint Flavour (PL 00063/0103), approved on 7th October 2003 as a line extension to the Gaviscon Advance Oral Suspension (PL 00063/0097) to the marketing authorisation holder Reckitt Benckiser Healthcare (UK) Limited. The current application is considered valid.

2 MARKETING AUTHORISATION APPLICATION (MAA)
2.1 Name(s)
The proposed name of the product is Gaviscon Advance Peppermint Flavour Oral Suspension. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
The product contains the active ingredients sodium alginate and potassium hydrogen carbonate.

The product is packaged in an amber glass bottles with moulded polypropylene cap having a tamper evident strip and lined with an expanded polyethylene wad. The pack sizes are 80, 100, 125, 140, 150, 180, 200, 250, 300, 400, 500, 560 or 600 ml suspension.

Specification and Certificate of Analysis for all packaging components used have been provided and are satisfactory. The packaging and pack sizes are the same as those for the reference product.

The proposed shelf life is 2 years before opening and 6 months after opening with a storage condition ‘Do not refrigerate’. The shelf-life and storage condition are identical to those for the reference product and are satisfactory.

2.3 Legal status
The product is available in Pharmacies (P).

2.4 Marketing authorisation holder/Contact Persons/Company
The proposed Marketing Authorisation holder is Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull, HU8 7DS, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a Curriculum Vitae (CV) is included.
2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the reference product and evidence of Good Manufacturing Practice compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specifications
The proposed finished product and shelf-life specification are in line with the details registered for the reference product.

2.9 Drug substance specification
The proposed drug substance specifications conform to the current European Pharmacopoeia monograph for sodium alginate and potassium hydrogen carbonate, and are in-line with those for the reference product.

2.10 TSE Compliance
No materials of human or animal origin have been used in the manufacture of this product. This is consistent with the reference product.

2.11 Bioequivalence
No bioequivalence data are required to support this informed consent application, as the proposed product is manufactured to the same formula utilising the same process as the reference product Gaviscon Advance Peppermint Flavour (PL 00063/0103).

3 EXPERT REPORT
The applicant has included detailed expert reports of the application. Signed declarations and copies of the experts’ CVs are enclosed for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4 PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to that of the reference product.

5 SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the reference product.
6. **PATIENT INFORMATION LEAFLET (PIL)/LABELLING**
A combined Patient Information Leaflet and Labelling has been prepared in line with the details registered for the reference product.

The applicant has submitted results of PIL user testing of Gaviscon Double Action Liquid (PL 00063/0156). The results indicate that the PIL is well-structured and organised, easy to understand and written in a comprehensive manner. Therefore, the bridging report is acceptable.

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.

7. **CONCLUSIONS**
The data submitted with the application is acceptable. The grant of a marketing authorisation is recommended.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.
CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.
OVERALL CONCLUSION AND BENEFIT RISK ASSESSMENT

QUALITY
The data for this application are consistent with those previously assessed for the reference product and, as such, have been judged to be satisfactory.

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

EFFICACY
This application is identical to the previously granted application for Gaviscon Advance Peppermint Flavour (PL 00063/0103), granted to Reckitt Benckiser Healthcare (UK) Limited on 7th October 2003.

Pharmaceutical preclinical and clinical expert statements have been provided, together with CVs showing the experts are appropriately qualified. The experts confirm that the product is identical in composition, manufacture and pharmaceutical characteristics to the respective reference product and that there are no toxicological or clinical issues.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the reference product. Extensive clinical experience with sodium alginate and potassium hydrogen carbonate is considered to have demonstrated the therapeutic values of the compounds. The risk benefit is, therefore, considered to be positive.
**GAVISCON ADVANCE PEPPERMINT FLAVOUR ORAL SUSPENSION**

**PL 00063/0612**

## STEPS TAKEN FOR ASSESSMENT

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<th>Details</th>
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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 28th August 2010</td>
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<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 20th November 2010</td>
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<td>3</td>
<td>Following assessment of the application the MHRA requested further information on 2nd January 2009</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s request, providing further information on 13th January 2010</td>
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<td>5</td>
<td>The application was determined on 11th October 2010</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Gaviscon Advance Peppermint Flavour
Oral Suspension.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 10 ml dose contains sodium alginate 1000 mg and potassium hydrogen carbonate 200 mg. 1 ml contains sodium alginate 100 mg and potassium hydrogen carbonate 20.0 mg.

Each 10 ml dose is equivalent to two 5 ml measuring spoons.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral suspension.
Off-white viscous suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Treatment of symptoms of gastro-oesophageal reflux such as acid regurgitation, heartburn and indigestion (related to reflux), for example, following meals, or during pregnancy, or in patients with symptoms related to reflux oesophagitis.

4.2 Posology and method of administration
Adults and children 12 years and over: 5-10 ml after meals and at bedtime (one to two 5 ml measuring spoons).

Children under 12 years: Should be given only on medical advice.

Elderly: No dose modification is required for this age group.

4.3 Contraindications
The medicinal product is contraindicated in patients with known or suspected hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings and precautions for use
Each 10 ml dose has a sodium content of 106 mg (4.6 mmol) and a potassium content of 78 mg (2.0 mmol). This should be taken into account when a highly restricted salt diet is recommended, e.g. in some cases of congestive cardiac failure and renal impairment or when taking drugs which can increase plasma potassium levels.

Each 10 ml contains 200 mg (2.0 mmol) of calcium carbonate. Care needs to be taken in treating patients with hypercalcaemia, nephrocalcinosis and recurrent calcium containing renal calculi.

There is a possibility of reduced efficacy in patients with very low levels of gastric acid.

Treatment of children younger than 12 years of age is not generally recommended, except on medical advice.

If symptoms do not improve after seven days, the clinical situation should be reviewed.

This medicinal product contains Methyl hydroxybenzoate and Propyl hydroxybenzoate, which may cause allergic reactions (possibly delayed).
4.5 Interaction with other medicinal products and other forms of interaction
None known.

4.6 Pregnancy and lactation
An open, uncontrolled study in 146 pregnant women did not demonstrate any significant undesirable effects of Gaviscon Advance on the course of the pregnancy or on the health of the foetus/new-born child. Based on this and previous experience, Gaviscon Advance - Peppermint Flavour may be used during pregnancy and lactation. Nevertheless, taking into account the presence of calcium carbonate it is recommended to limit the treatment duration as much as possible.

4.7 Effects on ability to drive and use machines
Not relevant.

4.8 Unwanted effects
Very rarely (<1/10,000) patients may develop allergic manifestations such as urticaria or bronchospasm, anaphylactic or anaphylactoid reactions.

4.9 Overdose
In the event of overdose, symptomatic treatment should be given. The patient may notice abdominal distension.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD).

ATC code: A02BX.

On ingestion the suspension reacts with gastric acid to form a raft of alginic acid gel having a near-neutral pH and which floats on the stomach contents effectively impeding gastro-oesophageal reflux. In severe cases the raft itself may be refluxed into the oesophagus in preference to the stomach contents and exert a demulcent effect.

5.2 Pharmacokinetic properties
The mechanism of action of the medicinal product is physical and does not depend on absorption into the systemic circulation.

5.3 Preclinical safety data
No preclinical findings of relevance to the prescriber have been reported.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Calcium carbonate
Carbomer 974P
Methyl parahydroxybenzoate E218
Propyl parahydroxybenzoate E216
Saccharin sodium
Peppermint flavour
Sodium hydroxide for pH adjustment
Purified water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
Shelf life: 2 years.
Shelf-life after opening: 6 months.
6.4 Special precautions for storage
Do not refrigerate.

6.5 Nature and contents of container
Amber glass bottles with moulded polypropylene cap having a tamper evident strip and lined with an expanded polyethylene wad. The bottles are enclosed in a cardboard outer containing either a measuring device (natural polypropylene) containing 5, 10, 15 and 20 ml graduations or a clear injection moulded crystal polystyrene measuring spoon with one bowl containing 2.5 ml and 5 ml measure. The pack sizes are 80, 100, 125, 140, 150, 180, 200, 250, 300, 400, 500, 560 or 600 ml suspension. Not all pack sizes may be marketed. The carton and measuring device or spoon may not be made available in all markets/pack sizes.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Reckitt Benekiser Healthcare (UK) Limited,
Dansom Lane,
Hull,
HU8 7DS,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)
PL 00063/0612

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATON
11/10/2010

10 DATE OF REVISION OF THE TEXT
11/10/2010
PATIENT INFORMATION LEAFLET AND LABELLING
Gaviscon Advance Peppermint Flavour Oral Suspension provides fast, soothing and long lasting relief from the pain and discomfort of heartburn and acid indigestion, which, for example, can occur after meals or during pregnancy. This product belongs to a group of medicines called ‘buffering agents’, which form a protective layer on top of the stomach contents to prevent acid escaping from the stomach where it works into the food pipe where it hurts.

What is this product? Each 15ml dose of oral suspension contains sodium alginate 100mg and potassium hydrogen carbonate 200mg as the active ingredients. It also contains calcium carbonate, carboner, methyl (2E) and propyl (2E) para-hydroxybenzoates, sodium lauryl sulphate, sodium hydroxide, peppermint flavour and pure water.

This product is sugar-free and gluten-free. You can take Gaviscon Advance if you are pregnant or breast feeding. As with all medicines, the treatment duration should be limited as much as possible.

Storage: Shake well before use. Adults, including the elderly and children 12 years and over: 5-10ml (one to two 5ml spoonfuls) after meals and at bedtime, or as directed. Children under 12 years: Should only be taken on medical advice.

When taking this product: Each 15ml dose contains 4.8 mmol of sodium, 2.0 mmol of potassium and 2.8 mmol of calcium. If you have been advised to follow a diet restricted in any of these please consult your doctor before taking this product. This product contains methyl and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed). This treatment may be less effective if you have decreased amounts of gastric acid produced in your stomach. If you forget to dose it is not necessary to double the dose next time, just carry on taking as before.

Keep all medicines safely away from children.

If symptoms persist after 7 days consult your doctor. If you take too much of this product it is unlikely to cause you any harm. However, you may feel bloated. Consult your doctor or pharmacist if this does not go away. Do not take if you know you are allergic to any of the ingredients or also rash and difficulty in breathing have been reported. Consult your doctor if you experience these or any other side-effects. Do not refrigerate. Check that the cap seal is unbroken before first using this product. Do not use this product after the expiry date (EXP: month/year) shown.

Manufacturer and PL Holder in UK: Reckitt Benckiser Healthcare (UK) Ltd, Hull, HU8 7DS.
UK Distributor: Britannia Pharmaceuticals Limited.
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