Public Assessment Report

Gaviscon Advance Aniseed flavour Oral Suspension

(Sodium alginate and potassium hydrogen carbonate)

UK Licence No.: PL 00063/0749

Reckitt Benckiser Healthcare (UK) Limited
Lay Summary
Gaviscon Advance Aniseed flavour Oral Suspension
(Sodium alginate and potassium hydrogen carbonate)

This is a summary of the Public Assessment Report (PAR) for Gaviscon Advance Aniseed flavour Oral Suspension (PL 00063/0749). This medicinal product will be referred to as Gaviscon Oral Suspension in this lay summary for ease of reading.

This summary explains how Gaviscon Oral Suspension was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Gaviscon Oral Suspension.

For practical information about using Gaviscon Oral Suspension, patients should read the package leaflet or contact their doctor or pharmacist.

What is Gaviscon Oral Suspension and what is it used for?
This product is identical to the previously authorised product, Gaviscon Advance Aniseed Suspension (PL 00063/0108; Reckitt Benckiser Healthcare (UK) Limited).

Gaviscon Oral Suspension is used to prevent and relieve the symptoms of heartburn and acid indigestion and relieve the symptoms of conditions such as hiatus hernia (protrusion of muscle though a muscle wall), reflux oesophagitis (inflamed foodpipe) and symptoms of hoarseness and other voice disorders, sore throat and cough associated with reflux. It can also be used to control heartburn symptoms which may occur when taking, or following withdrawal of medication to reduce stomach acid such as proton pump inhibitors (PPIs) or H₂ antagonists.

How does Gaviscon Oral Suspension work?
Gaviscon Oral Suspension contains the active ingredients sodium alginate and potassium hydrogen carbonate, which belong to a group of medicines called ‘reflux suppressants’. This product works by forming a protective layer that floats on top of the stomach contents. This layer prevents reflux and keeps the stomach contents away from the lining of the food pipe to relieve the symptoms of heartburn and acid indigestion.

How is Gaviscon Oral Suspension used?
Gaviscon Oral Suspension is taken by mouth. The bottle must be shaken well before use.

The recommended dose for adults, the elderly and children over 12 years is 5-10 ml (one to two 5 ml spoonfuls) after meals and at bedtime.

Gaviscon Oral Suspension should only be used in children under 12 years under medical supervision.

This medicine can be obtained without a prescription and is available on the General Sales List (GSL).

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

What benefits of Gaviscon Oral Suspension have been shown in studies?
No additional studies were needed as Gaviscon Oral Suspension acts in a physical way forming a raft on the stomach contents and is pharmaceutically equivalent to the reference product Gaviscon Advance Aniseed Suspension (PL 00063/0108).
What are the possible side effects of Gaviscon Oral Suspension?
Like all medicines, Gaviscon Oral Suspension can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Gaviscon Oral Suspension, see section 4 of the package leaflet available on the MHRA website.

For the full list of restrictions, see the package leaflet.

Why was Gaviscon Oral Suspension approved?
The MHRA decided that the benefits of Gaviscon Oral Suspension outweigh the identified risks and it was recommended that it be approved for use.

What measures are being taken to ensure the safe and effective use of Gaviscon Oral Suspension?
A risk management plan (RMP) has been developed to ensure that Gaviscon Oral Suspension is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Gaviscon Oral Suspension including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Gaviscon Oral Suspension
A Marketing Authorisation was granted in the UK on 26 April 2017.

This summary was last updated in June 2017.
Table of Contents

I Introduction .................................................... Page 5
II Quality aspects ................................................. Page 6
III Non-clinical aspects ........................................... Page 7
IV Clinical aspects ................................................ Page 7
V User consultation .............................................. Page 13
VI Overall conclusion, benefit/risk assessment and recommendation ........................................ Page 13

Table of content of the PAR update ................................ Page 15
I  INTRODUCTION

This product is available on the General Sales List (GSL) and is indicated for the treatment of symptoms resulting from the reflux of acid, bile and pepsin into the oesophagus such as acid regurgitation, heartburn, indigestion (occurring due to the reflux of stomach contents), for instance, after gastric surgery, as a result of hiatus hernia, during pregnancy, accompanying reflux oesophagitis, including symptoms of laryngopharyngeal reflux such as hoarseness and other voice disorders, sore throats and cough. It can also be used to treat the symptoms of gastro-oesophageal reflux during concomitant treatment with or following withdrawal of acid suppressing therapy.

This application was submitted as an abridged simple application, according to Article 10c of Directive 2001/83/EC, as amended. The applicant has cross-referred to Gaviscon Advance Aniseed Suspension, which was first authorised to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0108) on 29 April 2002.

This medicinal product contains active substances sodium alginate and potassium hydrogen carbonate. On ingestion the suspension reacts with gastric acid to rapidly form a raft of alginic acid gel having a near-neutral pH which floats on the stomach contents effectively impeding gastro-oesophageal reflux for up to 4 hours, and protecting the oesophagus from acid, pepsin and bile. In severe cases the raft itself may be refluxed into the oesophagus in preference to the stomach contents and exert a demulcent effect. In addition in vitro evidence has shown that the raft has a secondary action and is able to entrap bile and pepsin within its structure, further protecting the oesophagus from these gastric components.

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.

A summary of the pharmacovigilance system and a detailed risk management plan have been provided with this application and these are satisfactory.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of this product.
II  QUALITY ASPECTS

II.1  Introduction
This is a simple, informed consent application for Gaviscon Advance Aniseed flavour Oral Suspension (PL 00063/0749) submitted under Article 10c of Directive 2001/83/EC, as amended. The applicant has cross-referred to Gaviscon Advance Aniseed Suspension, which was first authorised to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0108) on 29 April 2002. The application is considered valid.

II.2.  Drug Substances
Drug substance specifications
The proposed drug substance specifications are consistent with the details registered for the cross-reference product.

II.3.  Medicinal Product
Name
The proposed product name for this application is Gaviscon Advance Aniseed flavour Oral Suspension. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack size
Each 10 ml solution contains 1000 mg sodium alginate and 200 mg potassium hydrogen carbonate, as active ingredients. The route of administration is oral.

The finished product is packed 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 or 300ml suspension.

The proposed shelf-life is 2 years with a storage condition ‘Do not refrigerate’.

The proposed packaging, shelf-life and storage condition are consistent with the details registered for the cross-reference product.

Legal status
This product is available on the General Sales List (GSL).

Marketing Authorisation Holder/Contact Persons/Company
Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull, HU8 7DS, East Yorkshire, UK.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory Curriculum Vitae (CV) has been provided.

Manufacturer
The proposed manufacturing site is consistent with that registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

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

Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.
Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference product.

TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference product.

Bioequivalence
No bioequivalence data are required to support this simple abridged application as the proposed product is manufactured to the same formula utilising the same process as the cross-reference product, Gaviscon Advance Aniseed Suspension, which was first authorised to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0108).

Expert Report
The applicant cross-refers to the data for Gaviscon Advance Aniseed Suspension, which was first authorised to Reckitt Benckiser Healthcare (UK) Limited (PL 00063/0108) to which this application is claimed to be identical. This is acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.

III NON-CLINICAL ASPECTS
Introduction
As this is an abridged simple application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Environmental Risk Assessment (ERA)
A suitable justification has been provided for not submitting an environmental risk assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS
Introduction
As this is an abridged simple application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)
The Marketing Authorisation Holder (MAH) has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Gaviscon Advance Aniseed flavour Oral Suspension.
A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, is listed below:

<table>
<thead>
<tr>
<th>SAFETY CONCERN</th>
<th>ROUTINE RISK MINIMISATION MEASURES</th>
<th>ADDITIONAL RISK MINIMISATION MEASURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPERSENSITIVITY</td>
<td>4.3 Contraindications: This medicinal product is contraindicated in patients with known or suspected hypersensitivity to the active substances or to any of the excipients listed in section 6.1, including methyl parahydroxybenzoate (E216) and propyl parahydroxybenzoate (E216) (see section 4.4).</td>
<td>None required</td>
</tr>
<tr>
<td>INCLUDING RASH, URTICARIA, PRURITUS, BRONCHOSPASM, AND ANAPHYLAXIS</td>
<td>4.4 Special warnings and precautions for use: Contains methyl parahydroxybenzoate (E216) and propyl parahydroxybenzoate (E216): May cause allergic reactions (possibly delayed).</td>
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<tr>
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<td><strong>RISK OF HYPERKALAEMIA</strong></td>
<td><em>(Proposed) text in SmPC:</em> 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 73 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. <em>(Proposed) text on the PIL:</em> 2. What you need to know before you take Gaviscon Advance (aniseed flavour): This medicine contains sodium (4.6 mmol per 10 ml), potassium (2.0 mmol per 10 ml) and calcium. -If you have been advised to follow a diet restricted in any of these please consult your doctor before taking this product. -Please also talk to your doctor regarding these salt contents if you suffer or have suffered from significant kidney or heart disease, as certain salts could interfere with these diseases.</td>
<td>None required</td>
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<tr>
<td>(Proposed) text on the label: 2 Before taking this medicine: This medicine contains sodium (4.6 mmol per 10 ml), potassium (2.0 mmol per 10 ml) and calcium.  -If you have been advised to follow a diet restricted in any of these please consult your doctor before taking this product.  -Please also talk to your doctor regarding these salt contents if you suffer or have suffered from significant kidney or heart disease, as certain salts could interfere with these diseases.</td>
<td>None required</td>
<td></td>
</tr>
<tr>
<td>RISK OF HYPOCHLORAEMIA</td>
<td>(Proposed) text in SmPC: 4.4 Special warnings and precautions for use: 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.</td>
<td></td>
</tr>
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<td>(Proposed) text on the PIL: 2 What you need to know before you take Gaviscon Advance (aniseed flavour): This medicine contains sodium (4.6 mmol per 10 ml), potassium (2.0 mmol per 10 ml) and calcium.  -If you have been advised to follow a diet restricted in any of these please consult your doctor before taking this product.  -Please also talk to your doctor regarding these salt contents if you suffer or have suffered from significant kidney or heart disease.</td>
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<td>Disease, as certain salts could interfere with these diseases.</td>
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<td>None required</td>
</tr>
<tr>
<td>Potential of worsening of existing cardiac failure or renal impairment in patients on a highly restricted salt diet</td>
<td>(Proposed) text in SmPC: 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.</td>
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<tr>
<td></td>
<td>Please also talk to your doctor regarding these salt contents if you suffer or have suffered from significant kidney or heart disease, as certain salts could interfere with these diseases.</td>
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<tr>
<td>5.2 Before taking this medicine:</td>
<td>This medicine contains sodium (4.6 mmol per 10 ml), potassium (2.0 mmol per 10 ml) and calcium.</td>
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<td>If you have been advised to follow a diet restricted in any of these please consult your doctor before taking this product.</td>
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<td>Please also talk to your doctor regarding these salt contents if you suffer or have suffered from significant kidney or heart disease, as certain salts could interfere with these diseases.</td>
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<tr>
<td>RISK IN PATIENTS WITH RENAL DISORDERS (INCLUDING HYPERCALCAEMIA, NEPHROCALCINOSIS AND RECURRENT CALCIUM CONTAINING RENAL CALCULI</td>
<td>(Proposed) text in SmPC: 4.4 Special warnings and precautions for use: Each 10ml dose contains 200mg (2.0mmol) of calcium carbonate. Care needs to be taken in treating patients with hypercalcaemia, nephrocalcinosis and recurrent calcium containing renal calculi.</td>
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Routine risk minimisation is provided through the SmPC and the patient information leaflet. No additional risk minimisation measures are planned for this product.

**Discussion on the clinical aspects**
The grant of a Marketing Authorisation is recommended.

**V User consultation**
User-testing of the patient information leaflet (PIL) for Gaviscon Advance Aniseed flavour Oral Suspension has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Gaviscon Advance Oral suspension (PL 00063/0097) as the ‘parent PIL’.

**VI Overall conclusion, benefit/risk assessment and recommendation**
The quality of the product is acceptable, and no new non-clinical or clinical 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 value of the compounds. The benefit-risk assessment is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The Summary of Product Characteristics and Patient Information Leaflet (PIL) are consistent with the details registered for the cross-reference product.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Gaviscon Advance Aniseed flavour Oral Suspension is presented below:
Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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