

Public Assessment Report

Gaviscon Cool Mint Liquid

**Calcium carbonate
Sodium hydrogen carbonate
Sodium alginate**

PL 00063/0158

Reckitt Benckiser Healthcare (UK) Ltd

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Lay Summary

The MHRA granted Reckitt Benckiser (UK) Ltd a marketing authorisation (licence) for the medicinal product Gaviscon Cool Mint Liquid on 13/11/2008. This product is available without a prescription.

The product is indicated for gastric reflux, reflux oesophagitis, heartburn, hiatus hernia, flatulence associated with gastric reflux, heartburn of pregnancy, all cases of epigastric and retrosternal distress where the underlying cause is gastric reflux and is available without prescription.

The drug product was demonstrated to be similar to the reference product Gaviscon Tablets PL 00063/0134, also held by Reckitt Benckiser (UK) Ltd.

Scientific Discussion

INTRODUCTION

The MHRA granted a market authorisation for the medicinal product Gaviscon Cool Mint Liquid to Reckitt Benckiser (UK) Ltd on 13/11/2008.

The product is indicated for gastric reflux, reflux oesophagitis, heartburn, hiatus hernia, flatulence associated with gastric reflux, heartburn of pregnancy, all cases of epigastric and retrosternal distress where the underlying cause is gastric reflux and is available without prescription.

The application has been made under Article 10a of Directive 2001/83/EC, so called bibliographic application. The cross-reference product is stated as being PL 00063/0134, Gaviscon Tablets which was itself granted under Article 10a of Directive 2001/83/EC also held by Reckitt Benckiser (UK) Ltd

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Sodium Alginate

A satisfactory specification for Sodium alginate has been provided. The drug substance complies with the requirements of the Ph Eur monograph. Consideration has been given to the potential impurities arising from the natural origins of sodium alginate (sodium alginate is a sodium salt of alginic acid obtained from the brown seaweed *Laminaria hyperborea*) and the extraction and blending process involved in its production and appropriate control measures and specification requirements have been put in place. Batch analysis data are provided and comply with the proposed specification.

Sodium Bicarbonate

Sodium bicarbonate is the subject of a Ph Eur Monograph. Sodium bicarbonate is adequately controlled by the Ph Eur monograph. No additional controls on solid state properties are considered necessary since sodium bicarbonate is readily soluble. Representative Certificates of Analysis have been provided for three batches of sodium bicarbonate confirming compliance with the proposed specification.

Calcium Carbonate

Calcium carbonate is the subject of a Ph Eur Monograph. A satisfactory specification for calcium carbonate has been provided. The drug substance complies with the requirements of the Ph Eur monograph, in addition the specification includes additional tests for bulk density, soluble alkali and particle size. Representative Certificates of Analysis have been provided for three batches of calcium carbonate confirming compliance with the proposed specification.

Stability studies have not been carried out on calcium carbonate and sodium bicarbonate since they are simple inorganic salts with long-established use as a pharmaceutical ingredient, defined by pharmacopoeial standards and the stability profile of these salts is well established.

Stability studies on sodium alginate have not been performed since it is a well established pharmaceutical ingredient with long established use and its stability profile well recognised. Sodium alginate is normally used within 3 months of shipping, if it is not used within this time, it will be re-tested for critical parameters (viscosity, gel strength, pH and volatile matter) before use to ensure compliance with the specification.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, Carbomer 974P, methyl (E218) and propyl (E216) parahydroxybenzoate, saccharin sodium, mint flavour no. 4, mint flavour no. 5, sodium hydroxide and purified water.

All excipients with the exception of the mint flavours 4 & 5 are adequately controlled by the Ph Eur monograph. Mint flavours 4 & 5 are satisfactorily controlled by in-house specifications and statements from the suppliers stating that they conform to the requirements of EC Directive 88/388 relating to flavourings in foodstuffs has been provided. Representative certificate of analysis has been provided for the mint flavourings. No excipients of human/animal origin are used

Manufacture

The product is declared to be manufactured by the same manufacturer and by the same method as the reference product.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Essential Similarity

As this application is submitted as a bibliographic application, this is not applicable.

Container Closure System

The drug product is stored in glass amber bottles with a polypropylene cap which meet current requirements.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years has been set, which is satisfactory. Storage conditions are "Avoid freezing" "Do not store above 30°".

ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY AND ADVICE

A Marketing Authorisation was granted.

PRE-CLINICAL ASSESSMENT

No pre-clinical data were presented and none were required for this application.

MEDICAL ASSESSMENT

INTRODUCTION

This cool mint flavoured suspension contains;

Sodium alginate 500 mg / 10 ml
Sodium bicarbonate 267 mg / 10 ml
Calcium carbonate, 160 mg / 10 ml

and is intended for the treatment of gastric reflux. Treatment of symptoms of gastro-oesophageal reflux such as acid regurgitation, heartburn and indigestion, for example, following meals or during pregnancy.

CLINICAL PHARMACOLOGY

On ingestion, the liquid reacts rapidly with gastric acid to form a raft of alginic acid gel which has a pH very close to neutral. This floats on the stomach contents, thus impeding gastro=oesophageal reflux. In severe cases of reflux, the raft itself may enter the oesophagus, having a demulcent effect.

The mode of action of Gaviscon Cool Mint Liquid is physical and does not depend on absorption into the systemic circulation.

The mode of action of Gaviscon products is to impede reflux by the formation of an alginate raft which floats on the surface of the stomach contents. The other ingredient vital for formation of the raft is sodium bicarbonate, which acts as a source of carbon dioxide to provide buoyancy. Calcium carbonate provides a source of calcium ions which cross-link the alginate molecules and increase the raft strength. In addition, calcium carbonate and sodium bicarbonate have a neutralising effect on gastric acid.

The action of alginate in preventing reflux, or in severe cases being itself refluxed into the oesophagus and exerting a demulcent effect, results in relief of symptoms of gastric reflux and additionally may prevent further attack of the oesophageal mucosa, allowing healing to take place. Efficacy of alginate treatment has been shown both in clinical trials and long-term experience of every day use.

As the clinical expert states, the aim of the development of this suspension was to provide a liquid format for delivery of sodium alginate, which would have similar raft-forming capabilities as other variations of Gaviscon. Only one flavour variant (cool mint) has been developed, the aim of this formulation being to provide a formula with a cooling flavour.

EFFICACY

Five studies have been performed to evaluate the efficacy of Liquid Gaviscon in the treatment of symptoms of gastro-oesophageal reflux (GOR).

Overall, as the clinical expert states, the efficacy of both 10 ml and 20 ml doses of Liquid Gaviscon have been demonstrated in the relief of symptoms of gastro-oesophageal reflux (GOR). 10 ml of Gaviscon Advance has been shown to have equivalent raft-forming capabilities as 20 ml Liquid Gaviscon. There have been no placebo – controlled studies of the efficacy of either 10 ml or 20 ml q.i.d. dosing with Liquid Gaviscon. However it has been shown that 5 ml and 10 ml doses of Gaviscon Advance taken q.i.d are superior to placebo in the treatment of symptoms of reflux. The same can be expected to be true for 10 and 20 ml doses of Liquid Gaviscon.

Also, 5 – 10 ml doses of Gaviscon Advance taken as required up to a maximum of 40 ml / day have been shown to relieve heartburn and regurgitation during pregnancy. The same level of efficacy would be expected for 10 – 20 ml doses of Liquid Gaviscon taken on the same basis.

SAFETY

In all the studies for Gaviscon Advance, Gaviscon peppermint Tablets and Liquid Gaviscon, the numbers of events considered to be possibly or probably related to treatment were low and of mild, or at most moderate, severity. Post-marketing experience has produced a very low incidence of adverse events. Liquid Gaviscon has been widely used during pregnancy and lactation for the past 25+ years. Gaviscon Cool Mint Liquid differs from Liquid Gaviscon only in terms of flavouring systems used, the lack of a colourant and consequential changes in excipients.

EXPERT REPORT

There is a satisfactory clinical expert report written by a suitably qualified person.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

This is satisfactory.

PATIENT INFORMATION AND LABEL, COMBINED

This is satisfactory.

CONCLUSION

A market authorisation may be granted.

Overall Conclusion and Risk/Benefit Analysis

Quality

The applicant has provided satisfactory evidence that the product is of the same quality as the reference product.

Pre-Clinical

No pre-clinical data were submitted and none were required for this application.

Clinical

The clinical benefits have been demonstrated to be the same as the reference product.

Risk/Benefit Analysis

The product has been shown to be identical to the reference product and, therefore, has the same positive risk/benefit.

Steps Taken During Assessment

1	The MHRA received the application on 23/03/2005.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 06/04/2005.
3	Following assessment of the application the MHRA requested further information from the applicant regarding the quality assessment on 16/02/2006, 11/10/2007 and 06/06/2008 and on the medical assessment on 22/07/2005.
4	The applicant provided further information in regard to the quality assessment on 21/10/2006, 06/06/2008 and 01/09/2008 and on the medical assessment on 30/10/2005.
5	The application was determined on 13/11/2008.

Steps Taken after Assessment

No non-confidential changes have been made to the market authorisation.

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Gaviscon Cool Mint Liquid

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml dose contains sodium alginate 500 mg, sodium hydrogen carbonate 267 mg and calcium carbonate 160 mg.

Excipients: methyl parahydroxybenzoate (E218) and propylparahydroxybenzoate (E216).

For full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of symptoms of gastro-oesophageal reflux such as acid regurgitation, heartburn and indigestion, for example, following meals or during pregnancy.

4.2 Posology and method of administration

For oral administration.

Adults and children 12 years and over: 10-20 ml after meals and at bedtime.

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

Elderly: No dose modifications necessary for this age group.

4.3 Contraindications

Hypersensitivity to any of the ingredients, including the esters of hydroxybenzoates (parabens)

4.4 Special warnings and precautions for use

Each 10 ml dose has a sodium content of 141 mg (6.2 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.

Each 10 ml dose contains 160 mg (1.6 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.

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

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

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Pregnancy and lactation

Open controlled studies in 281 pregnant women did not demonstrate any significant adverse effects of Gaviscon on the course of pregnancy or on the health of the foetus/new-born child. Based on this and previous experience, this product may be used during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Very rarely ($\leq 1/10,000$) patients may develop allergic manifestations such as urticaria or bronchospasm, anaphylactic or anaphylactoid reactions.

4.9 Overdose

In the event of overdosage symptomatic treatment should be given. The patient may notice abdominal distension.

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic classification: A02BX. Other drugs for peptic ulcer and gastro-oesophageal reflux disease.

5.1 Pharmacodynamic properties

On ingestion the medicinal product reacts rapidly 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 mode of action of the medicinal product is physical and does not depend on absorption into the systemic circulation.

5.3 Preclinical safety data

No pre-clinical findings of any relevance to the prescriber have been reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carbomer 974P, methyl (E218) and propyl (E216) parahydroxybenzoate, saccharin sodium, mint flavour no. 4, mint flavour no. 5, sodium hydroxide and purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

Amber glass bottles with a polypropylene cap with a polyethylene tamper-evident band lined with expanded polyethylene wad and containing 100, 150, 200, 300, 500 or 600 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None required.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Limited, Dansom Lane, Hull, HU8 7DS, United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0158.

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

13/11/2008

10 DATE OF REVISION OF THE TEXT

13/11/2008

Labels and Leaflets



GAVISCON COOL MINT LIQUID
Sodium alginate
Sodium hydrogen carbonate
Calcium carbonate

PATIENT INFORMATION LEAFLET
PLEASE READ THIS LEAFLET
CAREFULLY BEFORE
YOU TAKE THIS MEDICINE.

**IF YOU ARE NOT SURE ABOUT
ANYTHING ASK YOUR
PHARMACIST OR DOCTOR**

What is Gaviscon Cool Mint Liquid?
This product belongs to a group of medicines called "reflux suppressants". Reflux is a process in which the acid (stomach juices) flow back up into the food pipe. Unlike the stomach the lining of the food pipe is not resistant to acid so that when reflux occurs, it causes the pain and discomfort commonly known as heartburn. This product forms 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.

What is Gaviscon Cool Mint Liquid used for?
This product is used for the relief of heartburn and acid indigestion (also known as dyspepsia). Heartburn and acid indigestion are common and experienced by most people at some time. They may be felt as a burning sensation across the lower part of the chest, a pain spreading from the stomach towards the throat or regurgitation of a sour tasting liquid. Heartburn and acid indigestion often occur during pregnancy. Heartburn and acid indigestion can be made worse if you eat fatty or very spicy foods, drink too much alcohol, smoke, wear very tight clothing, are over weight or when you bend forward or lie down.

Before taking Gaviscon Cool Mint Liquid:
Do not take if you know that you are allergic to any of the ingredients. (see further information for a full list) You can take this product if you are pregnant or breast feeding. Each 10ml dose contains 4.6mmol of sodium. If you have been advised to follow a low sodium (salt) diet please consult your doctor before taking this product. This product contains methyl (E218) and propyl (E216) parahydroxybenzoates which may cause allergic reactions (possibly delayed).

This treatment maybe less effective if you have decreased amounts of gastric acid produced in your stomach.

How to take Gaviscon Cool Mint Liquid:
Adults, including the elderly and children 12 years and over: 10-20ml (two to four 5ml spoonfuls) after meals and at bedtime, or as directed.
Children under 12 years: Should only be taken on medical advice. Shake well before use.

After taking Gaviscon Cool Mint Liquid:
If you forget a dose it is not necessary to double the dose next time, just carry on taking as before. 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.

Possible side effects:
Less than 1 in 10,000 chance of skin rash or difficulty in breathing due to an allergic reaction from the ingredients. Consult your doctor if you experience these or any other side-effects.

Storing your medicine:
Do not use this product after the expiry date (EXP: month/year) shown
• Keep out of the reach and sight of children
• Do not refrigerate or freeze
• Check that the cap seal is unbroken before first using this product.

Further information:
Each 10 ml of oral suspension contains sodium alginate 500mg, sodium hydrogen carbonate 267mg and calcium carbonate 160mg as the active ingredients. The other ingredients are calcium carbonate, carbomer, methyl (E218) and propyl (E216) parahydroxybenzoates, sodium saccharin, sodium hydroxide, mint flavour and purified water. This product does not contain sugar or gluten. Gaviscon Cool Mint Liquid is available in bottles of 150ml and 300ml.

Manufacturer and Product Licence Holder in UK:
Reckitt Benckiser Healthcare (UK) Ltd,
Hu, HUB 7DS,
Export Distributors:
Reckitt & Colman (Overseas) Ltd,
Hu, HUB 7DS,
Gaviscon and the sword & circle are trade marks.
Text Revised: August 2008.

GAVISCON Cool Mint Liquid

ORAL SUSPENSION
Sodium alginate
Sodium hydrogen carbonate
Calcium carbonate

Cool Mint Flavour
Heartburn & Indigestion

e 300ml

After using this product: Symptoms persist: consult your doctor or pharmacist. If you take too much of this product you may feel bloated. It is unlikely to cause you any harm, but please consult your doctor or pharmacist. If you forget to take a dose, it is not necessary to double the dose next time, just carry on taking as before. Do not use this medicine after the expiry date (EXP - month/year) shown. Keep all medicines out of the sight and reach of children. Do not store above 30°C. Do not refrigerate or freeze. Check that the cap seal is unbroken before first taking this product.

What is this product?
Each 10ml of oral suspension contains 500mg sodium alginate, 287 sodium hydrogen carbonate and 160mg calcium carbonate as the active ingredients. It also contains carboxymethyl (E218) and propyl (E216) parahydroxybenzoates, sodium saccharin, mint flavourings, sodium hydroxide and water. This product is sugar free and gluten free. You can take this product if you are pregnant or breast feeding.

How to use this product?
Adults: When symptoms occur take 10-20ml (two to four 5ml spoonfuls) after meals and at bedtime, or as directed.
Children 12 years and over & the elderly: follow adult dosage instructions. Children under 12 years: Should only be taken on medical advice. Before taking this product: Each 10ml contains 6.2mmol of sodium. If you have been advised to follow a low sodium (salt) diet ask your doctor before taking this product. Do not take if you know you are allergic to any of the ingredients as very rarely difficulty in breathing and skin rashes have occurred (possibly delayed). Consult your doctor if you experience these or any other side-effects.

BN **EXP**