IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the IMB has granted a marketing authorisation for Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup, from McNeil Healthcare (Ireland) Ltd on 9th September 2011 for the symptomatic relief of productive cough.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Benylin Non-Drowsy for Chesty Coughs, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for guaifenesin/levomenthol. Guaifenesin has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Benylin Non-Drowsy for Chesty Coughs.

The current prescription status of the products is 'Product Not Subject to Medical Prescription', 'Supply through pharmacies only'.

The Summary of Product Characteristics for (SPC) for this medicinal product is available on the IMB's website at www.imb.ie

Name of the product

Benylin Phlegm Cough Syrup Guaifenesin 100 mg/5ml Levomenthol 1.1 mg/ 5 ml Syrup

Name(s) of the active substance(s) (INN)	GUAIFENESIN
Pharmacotherapeutic classification (ATC code)	R05CA Expectorants
Pharmaceutical form and strength(s)	100mg/5ml + 1.1mg/5ml Syrup
Marketing Authorisation Number(s) in Ireland (PA)	PA23490/031/001
Marketing Authorisation Holder	JNTL Consumer Health I (Ireland) Limited

II. QUALITY ASPECTS

II.1. Introduction

This application is for a duplicate licence to an already licenced product. As all Quality aspects are identical to the authorised "Benylin non-drowsy for Chesty Coughs Syrup, guaifenesin 100mg/5ml & levomenthol 1.1mg/5ml" product, Module 3 data has not been submitted and therefore not assessed. The name of the product is Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup.

II.2 Drug substance

The active substances are guaifenesin and levomenthol. Both are established active substances described in the European Pharmacopoeia, and are manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

II.3 Medicinal product

P.1 Composition

A clear red syrup with a characteristic odour.

The syrup contains the active substances guaifenesin 100mg / 5ml and levomenthol 1.1 mg /5ml. It also the following excipients:
Sodium benzoate (E211)
Sucrose
Liquid Glucose
Glycerol
Citric acid monohydrate
Sodium citrate

Saccharin sodium
Ethanol 96%
Caramel T12 (E150)
Ponceau 4R (E124)
Concentrated raspberry essence double strength
Natural sweetness enhancer
Carbomer
Purified water

P.2 Pharmaceutical Development

The product is an established pharmaceutical form.
The satisfactory P.3 (Manufacture of the Product), P.4 (Control of Other Substances) and P.5 (Control of Finished Product) sections of the reference product are applied to the proposed product.

P.6 Packaging material

As for the reference product, the product is presented as either:

Amber glass bottles (pharmacopoeial grade III) with an aluminium ROPP cap with melinex-faced pulpboard wad or with a 3 piece plastic child resistant, tamper evident closure fitted with a PE-Alu-PET or polyethylene/ expanded polyethylene laminated wad or with a plastic HDPE cap fitted with a PE-Alu-PET wad.

The authorised pack sizes are 30 ml, 125 ml or 300 ml.

P.7 Stability of the Finished Product

Using data provided in supporting the reference product, the products are considered stable for 3 years when kept in the original container and not above 30°C.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are as those accepted for the reference product marketed by McNeil Healthcare (Ireland) Ltd. Based on this the consistent quality of Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup is assured.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is the same as that present in Benylin Non-drowsy For Chesty Coughs Syrup (PA 823/20/1) on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

IV. CLINICAL ASPECTS

IV.1 Introduction

Guaifenesin and levomenthol are well known active substances with established efficacy and tolerability.
The content of the SPC approved during the national procedure is in accordance with that accepted for the reference product Benylin Non-Drowsy for Chesty Coughs marketed by MAH McNeil Healthcare (Ireland) Ltd/Johnson & Johnson.
This type of application is known as an 'informed consent' application, therefore no new data were submitted and this is in accordance with Article 10c of Directive 2001/83/EC.

IV.2 Pharmacokinetics

The following information has already been established for this active substance and is consistent with the information contained in the SPC for the reference product. In this context, no new data were submitted with this application which is in accordance with Article 10c of Directive 2001/83/EC.

Guaifenesin is well absorbed from the gastro-intestinal tract following oral administration, although limited information is available on its pharmacokinetics. After the administration of 600 mg guaifenesin to healthy adult volunteers, the C_{max} was approximately 1.4 ug/ml, with t_{max} occurring approximately 15 minutes after drug administration.

Distribution

No information is available on the distribution of guaifenesin or menthol in humans.

Metabolism and elimination

Guaifenesin appears to undergo both oxidation and demethylation. Following an oral dose of 600 mg guaifenesin to 3 healthy male volunteers, the $t_{½}$ was approximately 1 hour and the drug was not detectable in the blood after approximately 8 hours.

Menthol is hydroxylated in the liver by microsomal enzymes to p-menthane -3, 8 diol. This is then conjugated with glucuronide and excreted both in urine and bile as the glucuronide.

Pharmacokinetics in Renal/Hepatic Impairment

There have been no specific studies of Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup, menthol or guaifenesin in hepatic or renal impairment.

Pharmacokinetics in the Elderly

There have been no specific studies in the use of Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup, menthol or guaifenesin in the elderly.

IV.3 Pharmacodynamics

The following information has already been established for the active substances and is consistent with the information contained in the SPC for the reference product. In this context, no new data were submitted with this application which is in accordance with Article 10c of Directive 2001/83/EC.
Guaifenesin is thought to exert its pharmacological action by stimulating receptors in the gastric mucosa. This increases the output from secretory glands of the gastrointestinal system and reflexly increases the flow of fluids from glands lining the respiratory tract. The result is an increase in volume and decrease in viscosity of bronchial secretions. Other actions may include stimulating vagal nerve endings in bronchial secretory glands and stimulating certain centres in the brain which in turn enhance respiratory fluid flow. Guaifenesin produces its expectorant action within 24 hours.

Menthol has mild local anaesthetic and decongestant properties.

IV.4 Clinical Efficacy

This active substance is the same as that present in Benylin Non-drowsy For Chesty Coughs Syrup (PA 823/20/1) on the European market. No new data concerning clinical efficacy have been submitted. This is acceptable for this type of application (informed consent) and is in accordance with Article 10c of Directive 2001/83/EC.

IV.5 Clinical Safety

Given that this is an informed consent application (Article 10c of Directive 2001/83/EC), no new clinical trials were conducted in respect of this submission which is acceptable for this type of application.

A Risk Management Plan has not been proposed and this is considered acceptable given the established safety profile for the active substances.

The schedule for Periodic Safety Update Reports (PSUR) submission should be in line with that of the reference product. A three yearly cycle is proposed at this time.

The Marketing Authorisation Holder submitted a set of documents describing the Pharmacovigilance System, including information on the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

IV.6 Discussion on the clinical aspects

Guaifenesin /levomenthol are well known active substances with established efficacy and tolerability.
The content of the SPC approved during the national procedure is in accordance with that accepted for the reference product Benylin Non-Drowsy for Chesty Coughs marketed by MAH McNeil Healthcare (Ireland) Ltd/Johnson & Johnson.
This type of application is known as an 'informed consent' application, therefore no new data were submitted and this is in accordance with Article 10c of Directive 2001/83/EC.

V. OVERALL CONCLUSIONS

BENEFIT/RISK ASSESSMENT AND RECOMENDATION

Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup is the same as Benylin Non-Drowsy for Chesty Coughs syrup. Benylin Non-Drowsy for Chesty Coughs syrup is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established efficacy and safety profile.

This type of application is known as an 'informed consent' application, therefore no new data were submitted and this is in accordance with Article 10c of Directive 2001/83/EC.
The content of the SPC approved during the national procedure is in accordance with that accepted for the reference product Benylin Non-Drowsy for Chesty Coughs marketed by MAH McNeil Healthcare (Ireland) Ltd/Johnson & Johnson.

The IMB, on the basis of the data submitted considered that Guaifenesin / Levomenthol McNeil 100mg/5ml + 1.1mg/5ml Syrup was the same as the reference product Benylin Non-Drowsy for Chesty Coughs syrup and therefore granted a marketing authorisation.

VI. REVISION DATE

March 2024

VII. UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
MA Transfer	CRN00DHHF	SmPC section 7, 8, 10 Package Leaflet New MA Holder: JNTL Consumer Health I (Ireland) Limited New PA number: PA23490/031/001	N/A	28/03/2024