European Union Risk Management Plan (EU-RMP)
Guaifenesin and Guaifenesin/Menthol

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

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Summary of Risk Management Plan for Guaifenesin

This is a summary of the risk management plan (RMP) for guaifenesin and guaifenesin/menthol. The RMP details important risks of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol, how these risks can be minimised, and how more information will be obtained about Benylin Mucus Cough Honey & Lemon Flavour's and Benylin Mucus Cough Menthol's risks and uncertainties (missing information).

Benylin Mucus Cough Honey & Lemon Flavour's and Benylin Mucus Cough Menthol's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol should be used.

Important new concerns or changes to the current ones will be included in the RMP updates for Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol.

I. The Medicine and What it is Used For

Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol is authorised for the symptomatic relief of cough (see SmPC for the full indication). It contains guaifenesin and guaifenesin/menthol as the active substances and are given orally.

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol, together with measures to minimise such risks and the proposed studies for learning more about Benylin Mucus Cough Honey & Lemon Flavour's and Benylin Mucus Cough Menthol's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine);

List of Important Risks and Missing Information	
Important identified risks	Hypersensitivity reactions to the active substances (guaifenesin, menthol) or to any of the formulation excipients
Important potential risks	Use in conditions with persistent or chronic cough, or where cough is accompanied by excessive secretions
Missing information	Use during pregnancy and breastfeeding; and effect on fertility

II.B. Summary of Important Risks

Important Identified Risk: Hypersensitivity reactions to the active substances (guaifenesin, menthol) or to any of the formulation excipients	
Evidence for linking the risk to the medicine	Hypersensitivity reactions to guaifenesin range from mild and pruritic to severe and life-threatening systemic anaphylactic responses (Ray et al, 2009). Hypersensitivity reactions due to menthol ranges from urticaria, rhinitis, to asthma (Arikan-Ayyildiz et al, 2013). Also, 2 cases of anaphylaxis due to menthol have been reported in literature (Hennessey, 2002; Arikan-Ayyildiz et al, 2013). Evidence supporting hypersensitivity to guaifenesin and menthol was limited to case reports.

Important Identified Risk: Hypersensitivity reactions to the active substances (guaifenesin, menthol) or to any of the formulation excipients	
	Based on a review done by the MAH in the Guaifenesin and Guaifenesin/Menthol PBRER (06 April 2017 to 05 October 2017), guaifenesin and guaifenesin/menthol continue to have a favourable benefit-risk profile.
Risk factors and risk groups	In general, people with known hypersensitivity to the product or to any of the excipients are at risk.
Risk minimisation measures	Please refer to Section 4.3 (Contraindications) and Section 4.8 (Undesirable Effects) of the Guaifenesin CCDS and Guaifenesin/Menthol CCDS. Please refer to Section 4.3 (Contraindications) and Section 4.8 (Undesirable Effects) of the SmPC.
Important Potential Risk: Use in conditions with persistent or chronic cough, or where cough is accompanied by excessive secretions	
Evidence for linking the risk to the medicine	There is paucity of literature pertaining to guaifenesin use in conditions with persistent or chronic cough, or where cough is accompanied by excessive secretions. In patients with increased mucus secretion, guaifenesin further increases airway water or volume of secretions which may lead to excessive secretions, mucus retention and ultimately, inflammation and airway damage. The seriousness, outcomes, and severity of airway damage associated with guaifenesin use would depend on the airway inflammation response of each of the conditions with increased mucus secretion. Based on a review done by the MAH in the Guaifenesin and Guaifenesin/Menthol PBRER (06 April 2017 to 05 October 2017), guaifenesin and guaifenesin/menthol continue to have a favourable benefit-risk profile.
Risk factors and risk groups	Patients at risk include those with increased mucus secretion such as those with middle lobe syndrome, cough-dominant (cough-variant) asthma, severe asthma, forms of lung cancer associated with bronchorrhoea, chronic obstructive pulmonary disease, and cystic fibrosis (Rogers, 2007; Rubin et al, 2014).
Risk minimisation measures	Please refer to Section 4.4 (Special Warnings and Special Precautions for Use) of the Guaifenesin CCDS and Guaifenesin/Menthol CCDS. Please refer to Section 4.4 (Special Warnings and Precautions for Use) of the SmPC.
Missing Information: Use during pregnancy and breastfeeding; and effect on fertility	
Risk minimisation measures	Please refer to Section 4.6 (Fertility, Pregnancy and Lactation) and Section 5.3 (Preclinical Safety Data) of the Guaifenesin CCDS and Guaifenesin/Menthol CCDS. Please refer to Section 4.6 (Fertility, Pregnancy and Lactation) and Section 5.3 (Preclinical Safety Data) of the SmPC.
Key: CCDS=Company Core Data Sheet; MAH=Marketing Authorisation Holder; PBRER=Periodic Benefit-Risk Evaluation Report; SmPC=Summary of Product Characteristics	

II.C. Post-Authorisation Development Plan

II.C.1. Studies Which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol.

II.C.2. Other Studies in Post-Authorisation Development Plan

There are no studies required for Benylin Mucus Cough Honey & Lemon Flavour and Benylin Mucus Cough Menthol.