Part VI: Summary of the risk management plan

Summary of risk management plan for Colpermin® (peppermint oil)

This is a summary of the risk management plan (RMP) for Colpermin®. The RMP details important risks of Colpermin®, how these risks can be minimised, and how more information will be obtained about Colpermin®'s risks and uncertainties (missing information).

Colpermin®'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Colpermin® should be used.

Important new concerns or changes to the current ones will be included in updates of Colpermin®'s RMP.

I. The medicine and what it is used for

Colpermin® is authorised for the symptomatic relief of minor spasms of the gastrointestinal tract, flatulence and abdominal pain, especially in patients with irritable bowel syndrome (see SmPC for the full indication). It contains peppermint oil as the active substance and it is given by mouth.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Colpermin®, together with measures to minimise such risks and the proposed studies for learning more about Colpermin®'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 (e.g. 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, including PSUR assessment - 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 Colpermin® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Colpermin® 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 Colpermin®. 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 (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	– Use in patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders – Hypersensitivity reactions incl. anaphylactic shock
Important potential risks	– Use in children under 8 years of age due to the presence of pulegone and menthofuran in peppermint oil
Missing information	– Exposure during pregnancy and lactation

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Important identified risk: Use in patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders	
Evidence for linking the risk to the medicine	According to the 'Public Statement on the Use of Herbal Medicinal Products containing Pulegone and Menthofuran' (Rev 1), (EMA, 2016), rodent subchronic chronic studies showed that the liver is one of the main target organs for pulegone and menthofuran. A plausible mechanism for toxicity is the formation of reactive metabolites, which is also supported by in-vitro experimental data. There is however no confirmed cases of liver damage caused by peppermint oil, mint oil or herbal preparations of peppermint leaves reported [1, 2].
Risk factors and risk groups	Unknown
Risk minimisation measures	**Routine risk minimisation measures** SmPC – Section 4.3 PIL – Section 2

Important identified risk: Use in patients with liver disease, cholangitis, achlorhydria, gallstones and any other biliary disorders	
	Additional risk minimisation measures None.
Additional pharmacovigilance activities	None.

Important identified risk: Hypersensitivity reactions incl. anaphylactic shock	
Evidence for linking the risk to the medicine	Colpermin capsules contain arachis oil (peanut oil), and should not be taken by patients known to be allergic to peanut. The estimated prevalence of peanut allergy in developed countries is between 0.6% and 1.0% [3]. In the 'Assessment Report on Mentha X Piperita L., Aetheroleum' (EMA, 2008), reference is made to one case report of anaphylactic shock (Germany). No further information is provided [2].
Risk factors and risk groups	Unknown
Risk minimisation measures	<u>SmPC</u> – Section 4.3 – Section 4.8 <u>PIL</u> – Section 2 – Section 4 **Additional risk minimisation measures** None.
Additional pharmacovigilance activities	None.

Important potential risk: Use in children under 8 years of age due to the presence of pulegone and menthofuran in peppermint oil	
Evidence for linking the risk to the medicine	In the 'Public Statement on the Use of Herbal Medicinal Products containing Pulegone and Menthofuran' (Rev 1) (EMA, 2016) [1], the following is stated about use in children: <u>*Sensitive groups: Children*</u> *If children are included in the usage of certain products the daily amount of pulegone + menthofuran has to be adjusted to the body weight of the age group: e.g. body weight of 20*

Important potential risk: Use in children under 8 years of age due to the presence of pulegone and menthofuran in peppermint oil	
	kg would lead to an acceptable daily intake of 15 mg/day (life–long exposure) or 30 mg/day for a short-term exposure (less than 1 year).
Risk factors and risk groups	Unknown
Risk minimisation measures	**Routine risk minimisation measures** SmPC – Section 4.1 – Section 4.2 – Section 4.3 PIL – Section 2 – Section 3 **Additional risk minimisation measures** None.
Additional pharmacovigilance activities	None.

Missing information: Exposure during pregnancy and lactation	
Risk minimisation measures	**Routine risk minimisation measures** SmPC – Section 4.6 PIL – Section 2 **Additional risk minimisation measures** None.
Additional pharmacovigilance activities	None.

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 Colpermin®.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Colpermin®.