VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

MOVIPREP® is licensed in many Member States of the European Union (EU) for bowel cleansing prior to any clinical procedures requiring a clean bowel e.g. bowel endoscopy or radiology.

In Europe, about 15 million colonoscopies are performed every year. This means approximately 5% of the overall European population goes through the procedure of colonoscopy at some stage in life. Some specific inter-country variations are expected, because of the setup of large intestine cancer screening programmes. Germany is one of these countries with screening programme using colonoscopy as a first line test. Repeat colonoscopies are rare and are conducted only in special circumstances in certain patients. Overall, colonoscopy is a safe procedure with rare chance of complications (only in 1-5% cases) and rate of death in this procedure is calculated to be less than 0.1%. Although all segments of population could need a large intestine procedure, the majority is expected to be in the population over 50 years of age. It has been calculated that approximately 80% colon procedures take place in the patient population between 50 to 90 years of age while the remaining 20% are carried in patients between 18-49 years of age.

VI.2.2 Summary of treatment benefits

MOVIPREP® is indicated "for bowel cleansing prior to any clinical procedures requiring a clean bowel, e.g., bowel endoscopy or radiology, or digestive tract surgery" in adults over the age of 18 years.

Colonoscopy is the current standard method for evaluation of the colon (the large intestine). Successful colonoscopy requires complete bowel emptying so that the doctor could see the inner lining of the intestine clearly. Many choices are available to clean the bowel before colonoscopy. These include low volume preparations which may contain magnesium citrate or sodium phosphate. However, such preparations can lead to body fluid and mineral disturbances and so are usually avoided in people with heart failure, kidney problems, liver damage, elderly population or patients with mineral deficiencies. Macrogols (Polyethylene Glycol, PEG) are commonly used as bowel cleansers because of their favourable safety profile. However, an unpleasant taste and large volume of PEG in older preparations leads to poor tolerability and may result in patient dissatisfaction in 5% to 15% of patients.

MOVIPREP® is a lower volume PEG based bowel product where 2 litres are required rather than 4 litres with other higher volume PEG preparations. MOVIPREP® can be taken in one dose or split dose (split over two days). This means one dose can be taken on the night before and the other in the morning of colonoscopy. The advantage of split-dose preparation over full–dose has been demonstrated in multiple clinical trials, and collective analysis of observational studies. In general, the use of a split dose has been demonstrated to improve cleansing and has also been shown to also increase the chances of adenoma detection.

VI.2.3 Unknowns relating to treatment benefits

There is no data available on efficacy or safety of MOVIPREP® in pregnant and breast-feeding women. Similarly no data are available for efficacy and safety in children under 18 years of age.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Excessive loss of fluids from the body and abnormalities of minerals in the body	Due to profound diarrhoea that MOVIPREP® is to produce for cleaning the bowel and since it may cause vomiting in some patients, there are reports of excessive loss of fluids and minerals from the body especially in some patients with generally poor health, poor nutritional status or with a serious medical condition. In the severe cases, patients can develop very high sodium levels, or even very low potassium levels. All of these levels have the potential to be very dangerous and can affect blood pressure, heart, brain and so on.	It is recommended to drink a further one litre of clear liquid (in addition to MOVIPREP®) to prevent you feeling very thirsty and becoming dehydrated. Water, clear soup, fruit juice (without pulp), soft drinks, tea or coffee (without milk) are all suitable. These drinks can be taken at any time.
Severe allergic reactions	Contents of MOVIPREP® has produced allergic reaction in some patients. This can range from a simple rash or itching to severe reactions for example, swelling of eyes and face, ankles or other part of the body, very rapid heart rate, extreme fatigue and shortness of breath. Some patients may even develop low blood pressure and collapse.	In case of known allergies to any factors or medicines, the patient should discuss with the doctor and use MOVIPREP® with caution only. If there is known hypersensitivity/allergy to any of its contents, the product should not be used.
Temporary increase in blood pressure	Since MOVIPREP® produces profound diarrhoea (also vomiting in some patients), excessive loss of fluid from the body may produce a temporary salt retention in the body and may increase blood pressure temporarily. Temporary rise in blood pressure has been reported in some patients, patients with known hypertension could be more at risk.	Using the product as advised by your doctor, taking plenty of fluids can help reduce this risk. Patients with high blood pressure should discuss the precautions with the doctor in advance.
Seizure or sudden, jerky, irregular movements of	Since MOVIPREP® produces profound diarrhoea (also vomiting in some patients),	Using the product as advised by your doctor, taking plenty of fluids can help reduce this

Risk	What is known	Preventability
the body due to decreased salt in the body	excessive loss of fluid from the body may produce a temporary salt depletion in the body. In some patients, especially elderly and with poor general health, this may cause sudden jerky movements of the body like a seizure.	risk. In case of this risk happening, doctor should be contacted immediately and patient should be taken to a hospital.

Important potential risks

Risk	What is known (including reason why it is considered a potential risk)
Perforation/aggravation of the condition in patients with toxic megacolon as a result of severe IBD (Inflammatory bowel disease)	Toxic megacolon is a rare, life-threatening widening of the large intestine that develops within a few days. It's usually a complication of IBD (such as Ulcerative colitis or Crohn's disease). Toxic megacolon occurs when IBDs cause the colon to expand, dilate, and distend. When this happens, the colon is unable to remove gas or faeces from the body. If gas and faeces build up in the colon, large intestine may eventually rupture. Since MOVIPREP® produces profound diarrhoea with strong propelling movement of the intestinal wall, the possibility of rupture increases many folds. Use of MOVIPREP® is not recommended in such patients.
Aspiration in unconscious patients especially if prepared with a nasogastric tube	Since MOVIPREP® is prepared as a solution and taken orally, in unconscious patients stomach movements are quite slow and sometimes may even be absent. When a litre of the product solution is given to such patients, in some patients due to slow movements of the stomach, fluid may remain in the stomach and with persistent regurgitation such patients can inhale the solution in to the lungs and get pneumonia. In the unconscious patients therefore use of MOVIPREP® is not recommended. Extreme caution must be exercised if absolutely necessary to use the product in such cases.
Heart failure	MOVIPREP® is an osmotic laxative (product to produce profound diarrhoea by exchanging water and salts with the blood in the large intestine wall) and is used as 2 litres of solution with another litre or so of clear fluids, patients with risk factors for heart failure may go into fluid overload and hence their heart may not be able to handle/pump enough fluid entering the blood vessels. Such patients may develop a condition called heart failure. Patients with known risks of heart disease must discuss with their doctors before using this product.
Kidney failure	MOVIPREP® is an osmotic laxative (product to produce profound diarrhoea by exchanging water and salts with the blood in the large intestine wall). Patients with known kidney disease or with risk factors of kidney disease may develop kidney

Risk	What is known (including reason why it is considered a potential risk)
	failure due to excessive loss of fluids and minerals due to the profound diarrhoea caused by MOVIPREP®.
Atrial Fibrillation (an Irregular and very fast heart rate)	Irregular and very fast heart rate, often called atrial fibrillation, is a condition that is common in elderly population. A potential imbalance of fluids and minerals in the body owing to the profound diarrhoea caused by MOVIPREP® may cause this condition in some patients, especially the elderly ones and the ones with poor general health.

Missing information

Risk	What is known
Hereditary abnormality of not having enough of the enzyme glucose-6-phosphate dehydrogenase, or G6PD in the body which helps red blood cells (RBCs) function normally and may produce anaemia.	This hereditary condition is rare and people are often not aware that they have it. If known, MOVIPREP® should not be used. This is because MOVIPREP® contains ascorbic acid (Vitamin C) high doses of which may damage red blood cells in such patients and may cause severe anaemia.
Use in children under 18 years of age	Use of MOVIPREP® has not been studied in children under the age of 18 years. It should not be prescribed to children unless considered necessary by the physician.
Use in pregnant or breast-feeding women	Use of MOVIPREP® has not been studied in pregnant or breast-feeding women. It should not be prescribed to pregnant or breast feeding women unless considered necessary by the physician.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. A shortened version of this in layman language is provided in the form of the package leaflet (PL)/patient information leaflet (PIL) for the patients. The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for MOVIPREP® can be found in the MOVIPRP®'s EPAR page. MOVIPREP® has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
3.0	02 Jul 2009	**Identified Risks:** • Dehydration and electrolyte abnormalities • Anaphylaxis/ significant allergic reactions **Potential Risks** • Perforation/aggravation of the condition in patients with toxic megacolon as a result of severe IBD • Aspiration in unconscious patients especially if prepared with a nasogastric tube • Cardiac failure • Renal failure • Atrial fibrillation **Missing information** • Patients with G6PD deficiency	
3.1	02 Nov 2009	Following risk were added as identified risks: • Transient increase in blood pressure • Convulsions in association with severe hyponatremia	Based on post-authorisation reports and upon the request of the RMS
4.0	10-Feb-2016	• RMP prepared in the latest GVP-template • Safety specifications were updated • Risk characterisation updated with cumulative analysis of post authorisation reports in the MAH's safety database • Following text added to the missing information: Use in paediatric population Use in pregnant and lactating women	Up to date risk characterisation ensured.