Creon 10 000, 25 000 and 40 000 gastro-resistant capsule, hard

15 SEP 2014, version 4.0

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of Disease Epidemiology

Pancreatin is used by children and adults with "pancreatic exocrine insufficiency" (PEI). People with PEI do not have enough pancreatic enzymes, so their body does not digest important nutrients such as fat, carbohydrates and protein to get the nutrients it needs. PEI is often found in people who suffer from a rare genetic disorder called cystic fibrosis, long-lasting inflammation of the pancreas, or who had a part or the whole of their pancreas removed, as well as in other conditions.

People with PEI may experience loss of appetite, loose, oily stools, stomach pain, and flatulence (gas). If PEI is not treated, serious problems such as weight loss or malnourishment may develop. Children with PEI may fail to thrive. Maintaining normal nutrition is a key element of treatment of people with PEI.

VI.2.2 Summary of Treatment Benefits

Pancreatin does not cure exocrine pancreatic insufficiency. It contains a mixture of digestive enzymes including lipase, protease, and amylase from pig pancreas that help break down fats, carbohydrates, and proteins. Taken as prescribed, pancreatin replaces the enzymes that the pancreas is no longer producing, helping to digest nutrients. Pancreatin may thereby reduce the symptoms of PEI and helps to prevent serious problems such as weight loss, malnourishment, or failure to thrive.

The treatment benefits of pancreatin have been shown in studies involving people who were suffering from PEI due to cystic fibrosis, chronic inflammation of the pancreas, or because a part or the whole of their pancreas had been removed.

VI.2.3 Unknowns Relating to Treatment Benefits

Children and adults of both sexes and different ethnic backgrounds participated in the studies conducted with pancreatin. Over the years, pancreatin has been used by millions of patients worldwide. In rare instances, people felt that the medicine did not work as good as expected. It seems that in many of these instances, pancreatin was not taken exactly as recommended in the patient information leaflet. There has been no suspicion to date that pancreatin might not work in certain people.

VI.2.4 Summary of Safety Concerns

Important Identified Risks

Risk	What Is Known	Preventability
Not applicable – no important risks are known that are most likely caused by pancreatin.		

Important Potential Risks

Risk	What is Known (Including Reason Why It Is Considered a Potential risk)
Possibility that pancreatic enzyme products might increase the chance of having a serious bowel condition called fibrosing colonopathy	Fibrosing colonopathy (FC) is a rare condition where the bowel is narrowed or blocked. This condition is serious and may require bowel surgery. FC is seen almost exclusively in children with cystic fibrosis and treated with pancreatic enzyme products. There is a possibility that FC is more likely to develop if pancreatic enzyme products are taken at high doses. However, the cause of FC is unknown, and it is uncertain whether pancreatin may cause FC at all. Some researchers believe that FC might be caused by a type of tablet coating that is not used for this reviewed medicine, or that FC is caused by the underlying cystic fibrosis itself.

Missing information

Risk	What Is Known
Limited information on use of pancreatin in women who want to become pregnant, are pregnant or who are breastfeeding	As with most medicines, pregnant and breastfeeding women were excluded from the studies conducted with pancreatin. There is however no evidence from animal studies or any other information source that pancreatin may be harmful to the unborn fetus or breastfed baby, when taken by the mother.

VI.2.5 Summary of Risk Minimization 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 minimizing them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimization measures.

The Summary of Product Characteristics and the Package Leaflet for pancreatin can be found in the pancreatin's EPAR.

This medicine has no additional risk minimization measures.

VI.2.6 Planned Post-Authorization Development Plan

List of Studies in Post-Authorization Development Plan

Study/Activity (Including Study Number)	**Objectives**	**Safety Concerns / Efficacy Issue Addressed**	**Status**	**Planned Date for Submission of (Interim and) Final Results**
Fibrosing colonopathy observational study in patients with CF (CFFC- OB-11) (Non- interventional, 2)	Monitor and evaluate whether the risk of FC in CF patients receiving PERT varies from what is known, including assessment of possible dose effects.	Fibrosing colonopathy (Important potential risk) Long-term overdose as a potential risk factor for the occurrence of FC (Important potential risk)	Study started in July 2012	Final study report planned for 2022.

VI.2.6.1 Studies which are a Condition of the Marketing Authorization

The above study has been requested by a regulatory authority from all companies that are marketing pancreatic enzyme products.

VI.2.7 Summary of Changes to the Risk Management Plan over Time

List of Major Changes to the Risk Management Plan

Version	Date	Safety Concerns	Comment
1.0	June 2010	Identified Risks: • None Potential Risks: • Fibrosing colonopathy • Viral exposure from the product source Missing information: • Fertility; pregnant/ lactating women	Inclusion of a warning on the theoretical risk of viral transmission to the SmPC and PIL
2.0	January 2012	"Long-term overdose as a potential risk factor for occurrence of FC" added as a potential risk	Addition pursuant to an MHRA request, to address this aspect of FC as a separate potential risk. Not a new safety concern per se.
3.0	March 2013	No safety concerns added or removed	Routine update.
4.0	September 2014	"Viral exposure from the product source" was removed as important potential risk	Removal pursuant to an EMA position paper concluding that – based on a CHMP / BWP assessment – a harmonized warning statement in the SmPCs of all products across the EU was not required because the viral risk is not empirically proven. Additionally, routine update according to the current RMP template as published by the EMA