PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Mylan's pancreatin products

This is a summary of the risk management plan (RMP) for Mylan's pancreatin products. The RMP details important risks of Mylan's pancreatin products risks and uncertainties (missing information).

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

I. The medicine and what it is used for

Mylan's pancreatin products is authorised for the treatment of pancreatic exocrine insufficiency in the EEA. It contains pancreatin as the active substance and it is given orally.

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

Important risks of Mylan's pancreatin products, together with measures to minimise such risks and the proposed studies for learning more about Mylan's pancreatin products 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute *routine risk minimisation* measures.

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

II.A List of important risks and missing information

Important risks of Mylan's pancreatin products are those risks that need special risk management activities to further investigate or minimise them, so that the medicinal product can be safely administered to/taken by patients. 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 Mylan's pancreatin products Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but the definite causal 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/use in special patient populations etc.);

Table 42 Part VI: Summary of safety concerns

List of important risks and missing information	
Important identified risks	None
Important potential risks	• Fibrosing colonopathy • Contamination of pancreatin with zoonotic viruses
Missing information	None

II.B Summary of important risks

As outlined in the preceding sections, there is no important identified risk for pancreatin that qualifies for inclusion in this RMP version.

Important Potential Risk Fibrosing colonopathy (FC)	
Evidence for linking the risk to the medicine	Based on pancreatin clinical trials, post-marketing data and literature data, this safety concern has been classified as an important potential risk.
Risk factors and risk groups	strong association with the long-term (months or years) use of high doses of both high strength and standard strength pancreatic enzymes; intake of enteric coated drug products, e.g., pancreatic enzymes or mesalazine containing the methacrylic acid copolymer Eudragit®. Mylan's pancreatin does not contain coating material Eudragit®. Additional possible risk factors seen in CF patients

Important Potential Risk Fibrosing colonopathy (FC)	
	include previous intestinal surgery and DIOS. higher rates of gastrointestinal complications and more long-term use of histamine H2-receptor blockers, corticosteroids, and dornase alfa No specific further risk groups or risk factors have been identified among the subgroup of CF patients treated with high doses of PERT.
Risk minimisation measures	Routine risk communication: SmPC section 4.8. Routine risk minimisation activities recommending specific clinical measures to address the risk: Fibrosing colonopathy together with symptoms the medic should assess in order to exclude the possibility of occurrence is mentioned in SmPC section 4.4 Other risk minimisation measures beyond the Product Information: Medicine's legal status: Prescription only medicine in most countries, in particular for high dose preparations

Important Potential Risk Contamination of pancreatin with zoonotic viruses	
Evidence for linking the risk to the medicine	Based on the fact that pancreatin is manufactured from porcine pancreatic tissue from animals that have been declared suitable for human consumption, there is a theorectical potential risk of transmission of infectious agents, which may be present in the raw material. The zoonotic viruses, may be transmissible to humans by the oral route. The risk that contaminated pancreas glands are entering the manufacturing process cannot be completely excluded.
Risk factors and risk groups	Proximity to pig populations (farms, slaughter houses) and consumption of raw or under-cooked pork products. The risk in patients treated with CREON® is unknown, since this is only a

Important Potential Risk Contamination of pancreatin with zoonotic viruses	
	theoretical concern.
Risk minimisation measures	To determine the potential risk of viral contamination Mylan has performed a risk analysis and has implemented measures to control and reduce potential contamination at all steps of production, including careful selection of animal materials, a controlled and validated manufacturing process, testing and release of the final product (please refer to section 2.3.A of the dossier).

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

Evaluation of swHEV and pRotaV A qPCR assays on Pancreatin: in compliance with the condition pursuant to Article 21a or 22 of Directive 2001/83/EC, the MAH will complete, within 6 months after marketing authorization further evaluation of swHEV and pRotaV A qPCR assays on Pancreatin.

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

There are no required additional post-authorisation studies for pancreatin in EU.