PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN BY PRODUCT

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Important identified risks	• Local tolerability • Hypersensitivity • Drug interaction with CYP3A4 enzyme, warfarin and hormonal contraceptives
Important potential risks	• None
Missing information	• Use in pregnancy and lactation • Use in patients < 18 years of age • Use in patients with moderate or severe hepatic impairment

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable.

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable.

VI.1.4 Summary table of risk minimisation measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Important identified risk:	Sections 4.2, 4.4, 4.8, 4.9 and 5.3 of fosaprepitant SmPC and corresponding	None proposed

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Local tolerability	section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	
Important identified risk: Hypersensitivity	Sections 4.3, 4.4 and 4.8 of fosaprepitant SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	None proposed
Important identified risk: Drug interaction with CYP3A4 enzyme, warfarin and hormonal contraceptives	Sections 4.3, 4.4, 4.5 and 4.6 of fosaprepitant SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	None proposed
Missing Information: Use in pregnancy and lactation	Sections 4.6 and 5.3 of fosaprepitant SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	None proposed

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
Missing Information: Use in patients < 18 years of age	Sections 4.2 of fosaprepitant SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	None proposed
Missing Information: Use in patients with moderate or severe hepatic impairment	Sections 4.2, 4.4 and 5.2 of fosaprepitant SmPC and corresponding section of PIL has information on this safety concern. Other routine risk minimisation measure includes the status of the product as "prescription only".	None proposed

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Nausea and vomiting caused by chemotherapy

Two of the most common side effects with medicines given to kill cancer cells are nausea and vomiting. These side effects have a significant impact on quality of life and can interfere with the cancer treatment. The frequency of nausea and vomiting is related to the drug or combination of drugs being administered for cancer treatment. 99% of the patients on cisplatin cancer therapy experienced nausea if used without any nausea preventing drugs. Nausea and vomiting are mainly observed in child patients with cancer. Although both male and female are affected by vomiting and nausea with anti-cancer drugs however in some studies female patients experienced in more extent than male. Cancer drug-induced nausea and vomiting affects children of all ages;

however, children younger than 6 years have been shown to have a lower occurrence than older children when receiving similar drugs.

VI.2.2 Summary of treatment benefits

Fosaprepitant has been studied in one main study comparing a single 150-mg infusion of fosaprepitant with a three-day course of Emend capsules, both in combination with ondansetron and dexamethasone. The study involved over 2,000 adults with cancer who were receiving their first course of chemotherapy including cisplatin. The main measure of effectiveness was the number of patients who did not have any nausea or vomiting over the five days after receiving chemotherapy. The study showed that a single 150-mg infusion of fosaprepitant was as effective as a three-day course of Emend in preventing nausea and vomiting. Around 72% of both groups did not have any nausea or vomiting over the five days after receiving chemotherapy.

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of fosaprepitant Accord in children and adolescents below 18 years of age has not yet been established. No data are available for use in patients with severe hepatic impairment.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
How well a patient can stand a particular medicine or treatment (Local tolerability)	Fosaprepitant should be administered intravenously and should not be given by the intramuscular or subcutaneous route. Intravenous administration	If you get any side effects, talk to doctor, pharmacist, or nurse.

	occurs preferably through a running intravenous infusion over 20-30 minutes. Fosaprepitant should not be administered as a bolus injection or undiluted solution. Uncommon side effects (may affect up to 1 in 100 people) are infusion site pain, infusion-site redness, infusion-site itching and infusion site vein inflammation. Hardening of site of infusion are rare side effects (may affect up to 1 in 1,000 people) of fosaprepitant.	
Allergy (Hypersensitivity)	Possible side effects like hives, rash, itching and difficulty breathing or swallowing.	Patients are advised not to take fosaprepitant if they are allergic (hypersensitive) to fosaprepitant, aprepitant, or to polysorbate 80 or any of the other ingredients of this medicine. Stop taking fosaprepitant and see a doctor immediately if you notice these side-effects which may be serious, and

		for which you may need urgent medical treatment.
Drug interaction: decrease effectiveness of hormonal birth control medicines (Drug interaction with CYP3A4 enzyme, warfarin and hormonal contraceptives)	Birth control medicines which can include birth control pills, skin patches, implants and certain intrauterine devices (IUDs) that release hormones may not work adequately when taken together with fosaprepitant Accord.	Talk to doctor or pharmacist if you are taking these medicines. Do not take fosaprepitant with hormonal birth control medicines. Another or additional non-hormonal form of birth control should be used during treatment with fosaprepitant Accord and for up to 2 months after using fosaprepitant Accord.

Missing Information

Risk	**What is known**
Use in pregnancy and lactation	*Pregnancy* The efficacy of hormonal contraceptives may be reduced during and for 28 days after administration of fosaprepitant. Alternative non-hormonal back-up methods of contraception should be used during treatment with fosaprepitant and for 2 months following the last dose of fosaprepitant. *Lactation* Aprepitant is excreted in the milk of lactating rats after intravenous administration of fosaprepitant as well as after oral

	administration of aprepitant. Therefore, breast-feeding is not recommended during treatment with Fosaprepitant Accord.
Use in patients < 18 years of age	Do not give fosaprepitant Accord to children and adolescents under 18 years of age, because it has not been studied in this population.
Use in patients with moderate or severe abnormal liver function (Use in patients with moderate or severe hepatic impairment)	There are limited data in patients with moderate abnormal liver function and no data in patients with severe abnormal liver function. Talk to doctor, pharmacist, or nurse before using fosaprepitant Accord. Before treatment with this medicine, tell doctor if you have liver disease because your liver is important in breaking down the medicine in your body. Your doctor may therefore have to monitor the condition of your liver.

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. 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 minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

No studies planned.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety Concern	Comment
3.0	30 October 2017	No change	RMP has been updated as per RMS Day 120 comments of Fosaprepitant Accord (PT/H/1783/001/DC).
2.0	16 May 2017	No change	RMP has been updated as per RMS Day 70 and Day 100 Preliminary Assessment Report of Fosaprepitant (PT/H/1783/001/ DC)

.