VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Chemotherapy induced nausea and vomiting (CINV) continues to be one of the most undesirable side effects in subjects receiving chemotherapy. In addition to lowering the quality of life for subjects, CINV can potentially delay or reduce the dosage of planned chemotherapy regimens for subsequent cycles and may result in a reduction in the number of planned cycles.
In adults, aprepitant administered concomitantly with a 5-HT3 antagonist and a corticosteroid regimen is considered the standard of care and recommended by the Multinational Association of Supportive Cancer Care (MASCC)/ European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) for the prevention of nausea and vomiting associated with HEC and selected MEC regimens.

Aprepitant (EMEND) is a selective, high-affinity antagonist of human substance P/neurokinin 1 (NK1) receptors.
The mechanism of emesis is believed to be similar in adults and children, that is a complex process between neurotransmitters and receptors in both the central and peripheral nervous systems initiated

by the stimulation of dopamine, opiate, histamine, acetylcholine, neurokinin (NK1) and/or serotonin type-3 (5-HT3) receptors. Neurokinin-1 (NK1) receptor antagonists have been identified as a novel class of anti-emetics. Substance P is the preferred agonist for NK1 receptors and belongs to a family of neuropeptides known as tachykinins. In experimental models, NK1 receptor antagonists have been shown to have potent and usually long-lasting, anti-emetic activity against a broad spectrum of both central and peripheral emetogens whereas 5-HT3 antagonists show a more limited spectrum of activity with efficacy mostly against peripheral emetogens.

VI.2.2 Summary of treatment benefits

In adults, aprepitant administered concomitantly with a 5-HT3 antagonist and a corticosteroid regimen is considered the standard of care and recommended by the Multinational Association of Supportive Cancer Care (MASCC)/ European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN) for the prevention of nausea and vomiting associated with HEC and selected MEC regimens.
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VI.2.3 Unknowns relating to treatment benefits

For aprepitant no clinical data on exposed pregnancies are available. The potential for reproductive toxicity of aprepitant has not been fully characterised, since exposure levels above the therapeutic exposure in humans at the 125 mg/80 mg dose could not be attained in animal studies.

There are limited data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment. [Invented name] should be used with caution in these patients

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability

Safety concern in lay language *(medical term)*	**Brief summary in lay language**	**Whether risk can be minimised or mitigated, and how**
Hypersensitivity	Overall, the adverse events observed during clinical trials were comparable to the types of adverse events expected in patients with cancer receiving emetogenic chemotherapy. Listings of subjects with hypersensitivity Adverse Events have been provided. This includes a variety of AEs (eg "dermatitis allergic", "rash", "urticaria") where only a single event is termed "anaphylactic shock".	You should be warned to contact your doctor if hypersensitivity develops, and healthcare professionals should advise patients on appropriate treatment and whether aprepitant needs to be stopped.
Drug interaction: reduction of efficacy hormonal contraceptives	The efficacy of hormonal contraceptives may be reduced during and for 28 days after administration of [invented name]. Alternative non-hormonal back-up methods of contraception should be used during treatment with aprepitant] and for 2 months following the last dose of aprepitant	You should discuss with your doctor possibilities of alternative methods of contraception during therapy with aprepitant.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Potential for medication error	The safety and efficacy of [Invented name] 40 mg in children and adolescents below 18 years of age have not yet been established. The safety and efficacy of the 80 mg and 125 mg capsules have not been demonstrated in children less than 12 years of age. No data are available. Refer to the powder for oral suspension SmPC for appropriate dosing in infants, toddlers and children aged 6 months to less than 12 years. <u>*General*</u> Efficacy data in combination with other corticosteroids and 5-HT_3 antagonists are limited. For additional information on the co-administration with corticosteroids. Please refer to the SmPC of co-administered 5-HT_3 antagonist medicinal products.

Missing information

Risk	What is known
Use in pregnancy	For aprepitant no clinical data on exposed pregnancies are available. The potential for reproductive toxicity of aprepitant has not been fully characterised, since exposure levels above the therapeutic exposure in humans at the 125 mg/80 mg dose could not be attained in animal studies.
Use in patients with moderate or severe hepatic impairment	There are limited data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment. [Invented name] should be used with caution in these patients

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 (PIL). 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

Not applicable

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

Version	Date	Safety concerns	Change
1.0	18.05.2017	**Important identified risks** • Hypersensitivity • Drug interaction:reduction of efficacy hormonal contraceptives **Important potential risks** • Potential for medication error **Missing information** • Use in pregnancy • Use in patients with moderate or severe hepatic impairment	Initial version
1.0	18.04.2018		SmPC/PIL updated