SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

EMEND® 80 mg Capsules

EMEND® 125 mg Capsules

EMEND® Combi Pack Capsules

COMPOSITION

Each capsule contains 80 mg or 125 mg Aprepitant.

EMEND capsules contain sucrose.

Inactive ingredients: Hydroxypropyl cellulose, sodium lauryl sulphate, sucrose, microcrystalline cellulose, gelatin capsule and black ink.

PHARMACOLOGICAL CLASSIFICATION

A.5.7.2 Anti-emetics and antivertigo preparations

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

EMEND (aprepitant MSD) is a substance P neurokinin 1 (NK_1) receptor antagonist.

Aprepitant is a selective high affinity antagonist at human substance P neurokinin 1 (NK_1) receptors. Counter-screening assays showed that aprepitant was at least 3 000-fold selective for the NK_1 receptor over other enzyme, transporter, ion channel and receptor sites including the dopamine and serotonin receptors that are targets for existing Chemotherapy Induced Nausea and Vomiting (CINV) therapies.

NK_1-receptor antagonists have been shown pre-clinically to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. Pre-clinical and human Positron Emission Tomography (PET) studies with aprepitant have shown that it is brain penetrant and occupies brain NK_1 receptors. Pre-clinical studies show that aprepitant has a long duration of central activity, inhibits both the acute and delayed phases of cisplatin-induced emesis, and augments the anti-emetic activity of the 5-HT_3-receptor antagonist ondansetron and the corticosteroid dexamethasone against cisplatin-induced emesis.

Pharmacokinetic properties

Absorption

The mean absolute oral bioavailability of aprepitant is approximately 60 to 65 % and the mean peak plasma concentration (C_{max}) of aprepitant occurred at approximately 4 hours (T_{max}). Oral administration of the capsule with a standard breakfast had no clinically meaningful effect on the bioavailability of aprepitant.

The pharmacokinetics of aprepitant are non-linear across the clinical dose range. In healthy young adults, the increase in $AUC_{0-\infty}$ was 26 % greater than dose proportional between 80 mg and 125 mg single doses administered in the fed state.

Following oral administration of a single 125 mg dose of EMEND on Day 1 and 80 mg once daily on Days 2 and 3, the $AUC_{0\text{-}24hr}$ was approximately 19,5 mcg•hr/ml and 20,1 mcg•hr/ml on Day 1 and Day 3, respectively. The C_{max} of 1,5 mcg/ml and 1,4 mcg/ml were reached in approximately 4 hours (T_{max}) on Day 1 and Day 3, respectively.

Distribution

Aprepitant is > 95 % bound to plasma proteins. The geometric mean apparent volume of distribution at steady state (Vd_{ss}) is approximately 66 litres in humans.

Aprepitant crosses the placenta in rats, and crosses the blood brain barrier in rats and ferrets. PET studies in humans indicate that aprepitant crosses the blood brain barrier (see **"PHARMACOLOGICAL ACTION, Pharmacodynamic properties"**).

Metabolism

Aprepitant undergoes extensive metabolism. In healthy young adults, aprepitant accounts for approximately 24 % of the radioactivity in plasma over 72 hours following a single oral 300 mg dose of [^{14}C]-aprepitant, indicating a substantial presence of metabolites in the plasma. Seven metabolites of aprepitant, which are only weakly active, have been identified in human plasma. The metabolism of aprepitant occurs largely via oxidation at the morpholine ring and its side chains. *In vitro* studies using human liver microsomes indicate that aprepitant is metabolised primarily by CYP3A4 with minor metabolism by CYP1A2 and CYP2C19, and no metabolism by CYP2D6, CYP2C9 or CYP2E1.

Elimination

Aprepitant is eliminated primarily by metabolism; aprepitant is not renally excreted. Following administration of a single oral 300 mg dose of [^{14}C]-aprepitant to healthy subjects, 5 % of the radioactivity was recovered in urine and 86 % in faeces.

The apparent plasma clearance of aprepitant ranged from approximately 60 to 84 ml/min. The apparent terminal half-life ranged from approximately 9 to 13 hours.

Gender

Following oral administration of a single 125 mg dose of EMEND, the $AUC_{0\text{-}24hr}$ and C_{max} for aprepitant are 9 % and 17 % higher, respectively, in females as compared with males. The half-life of aprepitant is approximately 25 % lower in females as compared with males and its T_{max} occurs at approximately the same time. These differences are not considered clinically meaningful. No dosage adjustment is necessary based on gender.

Elderly

Following oral administration of a single 125 mg dose of EMEND on Day 1 and 80 mg once daily on Days 2 through 5, the $AUC_{0\text{-}24hr}$ of aprepitant was 21 % higher on Day 1 and 36 % higher on Day 5 in elderly (65 years and older) relative to younger adults. The C_{max} was 10 % higher on Day 1 and 24 % higher on Day 5 in elderly relative to younger adults. These differences are not considered clinically meaningful. No dosage adjustment for EMEND is necessary in elderly patients.

Paediatric

The pharmacokinetics of EMEND have not been evaluated in patients below 18 years of age.

Hepatic insufficiency

EMEND was well tolerated in patients with mild to moderate hepatic insufficiency. Following administration of a single 125 mg dose of EMEND on Day 1 and 80 mg once daily on Days 2 and 3 to patients with mild hepatic insufficiency (Child-Pugh score 5 to 6), the $AUC_{0\text{-}24hr}$ of aprepitant was 11 % lower on Day 1 and 36 % lower on Day 3, as compared with healthy subjects given the same regimen. In patients with moderate hepatic insufficiency (Child-Pugh score 7 to 9), the $AUC_{0\text{-}24hr}$ of aprepitant was 10 % higher on Day 1 and 18 % higher on Day 3, as compared with healthy subjects given the same regimen. These differences in $AUC_{0\text{-}24hr}$ are not considered clinically meaningful; therefore, no dosage adjustment for EMEND is necessary in patients with mild to moderate hepatic insufficiency.

There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh score > 9).

Renal insufficiency

A single 240 mg dose of EMEND was administered to patients with severe renal insufficiency (CrCl < 30 ml/min) and to patients with end stage renal disease (ESRD) requiring haemodialysis.

In patients with severe renal insufficiency, the $AUC_{0\text{-}\infty}$ of total aprepitant (unbound and protein bound) decreased by 21 % and C_{max} decreased by 32 %, relative to healthy subjects. In patients with ESRD undergoing haemodialysis, the $AUC_{0\text{-}\infty}$ of total aprepitant decreased by 42 % and

C_{max} decreased by 32 %. Due to modest decreases in protein binding of aprepitant in patients with renal disease, the AUC of pharmacologically active unbound medicine was not significantly affected in patients with renal insufficiency compared with healthy subjects. Haemodialysis conducted 4 or 48 hours after dosing had no significant effect on the pharmacokinetics of aprepitant; < 0,2 % of the dose was recovered in the dialysate.

No dosage adjustment for EMEND is necessary for patients with severe renal insufficiency or for patients with ESRD undergoing haemodialysis.

INDICATIONS

EMEND in combination with other anti-emetic agents, is indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of:

- highly emetogenic cancer chemotherapy (see **"DOSAGE AND DIRECTIONS FOR USE"**).
- moderately emetogenic cancer chemotherapy (see **"DOSAGE AND DIRECTIONS FOR USE"**).

CONTRAINDICATIONS

EMEND is contraindicated in patients who are hypersensitive to any component of the product.

EMEND should not be used concurrently with pimozide, astemizole or cisapride. Inhibition of cytochrome P450 isoenzyme 3A4 (CYP3A4) by aprepitant could result in elevated plasma concentrations of these agents, potentially causing serious or life-threatening reactions, (see **"INTERACTIONS"**).

Paediatric use

Safety and effectiveness in paediatric patients have not been established.

WARNINGS AND SPECIAL PRECAUTIONS

EMEND should be used with caution in patients receiving concomitant medicinal products that are primarily metabolised through CYP3A4; some chemotherapy agents are metabolised by CYP3A4 (see **"INTERACTIONS"**). Inhibition of CYP3A4 by aprepitant could result in elevated plasma concentrations of these concomitant medicinal products (see **"INTERACTIONS"**). Consequently, concomitant administration of EMEND with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir) should be approached with caution.

Co-administration of EMEND with warfarin may result in a clinically significant decrease in International Normalised Ratio (INR) or prothrombin time. In patients on chronic warfarin therapy, the INR should be closely monitored in the 2 week period, particularly at 7 to 10 days following initiation of the 3-day regimen of EMEND with each chemotherapy cycle (see **"INTERACTIONS"**).

The efficacy of hormonal contraceptives during and for 28 days after administration of EMEND may be reduced. Alternative or back-up methods of contraception should be used during treatment with EMEND and for 1 month following the last dose of EMEND (see **"INTERACTIONS"**).

Contains sucrose. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take EMEND. Contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Severe hepatic insufficiency (Child-Pugh score > 9)

There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency. Caution should be exercised when EMEND is administered in these patients.

Use in the elderly

In clinical studies, the efficacy and safety of EMEND in the elderly (65 years and older) were comparable to those seen in younger patients (younger than 65 years). No dosage adjustment is necessary in elderly patients.

Effects on ability to drive and use machines

EMEND may have minor influence on the ability to drive and use machines. Dizziness and fatigue may occur following administration of EMEND (see **"SIDE EFFECTS"**).

INTERACTIONS

Aprepitant is a substrate, a moderate inhibitor, and an inducer of CYP3A4. Aprepitant is also an inducer of CYP2C9.

Effect of EMEND capsules on the pharmacokinetics of other medicines

As a moderate inhibitor of CYP3A4, aprepitant can increase plasma concentrations of co-administered medicinal products that are metabolised through CYP3A4.

EMEND should not be used concurrently with pimozide, astemizole or cisapride. Inhibition of CYP3A4 by EMEND could result in elevated plasma concentrations of these medicines, potentially causing serious or life-threatening reactions (see **"CONTRAINDICATIONS"**).

EMEND has been shown to induce the metabolism of S(-) warfarin and tolbutamide, which are metabolised through CYP2C9. Co-administration of EMEND with these medicines or other medicines that are known to be metabolised by CYP2C9, such as phenytoin, may result in lower plasma concentrations of these medicines.

EMEND is unlikely to interact with medicines that are substrates for the P-glycoprotein transporter, as demonstrated by the lack of interaction of EMEND with digoxin in a clinical medicine interaction study.

5-HT_3 antagonists

In clinical medicine interaction studies, EMEND did not have clinically important effects on the pharmacokinetics of ondansetron, granisetron or hydrodolasetron (the active metabolite of dolasetron).

Corticosteroids

Dexamethasone: EMEND when given as a regimen of 125 mg with dexamethasone co-administered orally as 20 mg on Day 1, and EMEND when given as 80 mg/day with

dexamethasone co-administered orally as 8 mg on Days 2 through 5, increased the AUC of dexamethasone, a CYP3A4 substrate by 2,2-fold, on Days 1 and 5. The usual oral dexamethasone doses should be reduced by approximately 50 % when co-administered with EMEND, to achieve exposures of dexamethasone similar to those obtained when it is given without EMEND. The daily dose of dexamethasone administered in clinical studies with EMEND reflects an approximate 50 % reduction of the dose of dexamethasone (see **"DOSAGE AND DIRECTIONS FOR USE"**).

Methylprednisolone: EMEND, when given as a regimen of 125 mg on Day 1 and 80 mg/day on Days 2 and 3, increased the AUC of methylprednisolone, a CYP3A4 substrate, by 1,3-fold on Day 1 and by 2,5-fold on Day 3, when methylprednisolone was co-administered intravenously as 125 mg on Day 1 and orally as 40 mg on Days 2 and 3. The usual IV methylprednisolone dose should be reduced by approximately 25 %, and the usual oral methylprednisolone dose should be reduced by approximately 50 % when co-administered with EMEND, to achieve exposures of methylprednisolone similar to those obtained when it is given without EMEND.

Chemotherapeutic agents

In clinical studies, EMEND was administered with the following chemotherapeutic agents metabolised primarily or in part by CYP3A4: Etoposide, vinorelbine, docetaxel, ifosfamide, cyclophosphamide, irinotecan and paclitaxel. The doses of these agents were not adjusted to account for potential medicine interactions. Caution and careful monitoring are advised in patients receiving these agents or other chemotherapy agents metabolised primarily by CYP3A4. Post-marketing events of neurotoxicity, a potential adverse reaction of ifosfamide,

have been reported after EMEND and ifosfamide co-administration (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Docetaxel

In a clinical study, EMEND did not influence the pharmacokinetics of docetaxel.

Warfarin

A single 125 mg dose of EMEND was administered on Day 1 and 80 mg/day on Days 2 and 3 to healthy subjects who were stabilised on chronic warfarin therapy. Although there was no effect of EMEND on the plasma AUC of R(+) or S(-) warfarin determined on Day 3, there was a 34 % decrease in S(-) warfarin (a CYP2C9 substrate) trough concentration accompanied by a 14 % decrease in the prothrombin time (reported as International Normalised Ratio or INR) 5 days after completion of dosing with EMEND. In patients on chronic warfarin therapy, the prothrombin time (INR) should be closely monitored in the 2-week period, particularly at 7 to 10 days following initiation of the 3-day regimen of EMEND with each chemotherapy cycle.

Tolbutamide

EMEND, when given as 125 mg on Day 1 and 80 mg/day on Days 2 and 3, decreased the AUC of tolbutamide (a CYP2C9 substrate) by 23 % on Day 4, 28 % on Day 8, and 15 % on Day 15, when a single dose of tolbutamide 500 mg was administered orally prior to the administration of the 3-day regimen of EMEND and on Days 4, 8 and 15.

Oral contraceptives

EMEND, when given once daily for 14 days as a 100 mg capsule with an oral contraceptive containing 35 mcg of ethinylestradiol and 1 mg of norethindrone, decreased the AUC of ethinylestradiol by 43 %, and decreased the AUC of norethindrone by 8 %.

In another study, a single dose of an oral contraceptive containing ethinylestradiol and norethindrone was administered on Days 1 through 21 with EMEND, given as a regimen of 125 mg on Day 8 and 80 mg/day on Days 9 and 10 with ondansetron 32 mg IV on Day 8 and oral dexamethasone given as 12 mg on Day 8 and 8 mg/day on Days 9, 10 and 11. In the study, the AUC of ethinylestradiol decreased by 19 % on Day 10 and there was as much as a 64 % decrease in ethinylestradiol trough concentrations during Days 9 through 21. While there was no effect of EMEND on the AUC of norethindrone on Day 10, there was as much as a 60 % decrease in norethindrone trough concentrations during Days 9 through 21.

The efficacy of hormonal contraceptives during and for 28 days after administration of EMEND may be reduced. Alternative or back-up methods of contraception should be used during treatment with EMEND and for 1 month following the last dose of EMEND.

Midazolam

EMEND increased the AUC of midazolam, a sensitive CYP3A4 substrate, by 2,3-fold on Day 1 and 3,3-fold on Day 5, when a single oral dose of midazolam 2 mg was co-administered on Day 1 and Day 5 of a regimen of EMEND 125 mg on Day 1 and 80 mg/day on Days 2 through 5. The potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolised via CYP3A4 (alprazolam, triazolam) should be considered when co-administering these agents with EMEND.

In another study with intravenous administration of midazolam, EMEND was given as 125 mg on Day 1 and 80 mg/day on Days 2 and 3, and midazolam 2 mg IV was given prior to the administration of the 3-day regimen of EMEND and on Days 4, 8 and 15. EMEND increased the AUC of midazolam by 25 % on Day 4 and decreased the AUC of midazolam by 19 % on Day 8 relative to the dosing of EMEND on Days 1 through 3. These effects were not considered clinically important. The AUC of midazolam on Day 15 was similar to that observed at baseline.

Effect of other medicines on the pharmacokinetics of EMEND capsules

EMEND should be used with caution in patients receiving concomitant medicinal products, including chemotherapy agents that are primarily metabolised through CYP3A4.

EMEND is a substrate for CYP3A4; therefore, co-administration of EMEND with medicines that inhibit CYP3A4 activity may result in increased plasma concentrations of aprepitant. Consequently, concomitant administration of EMEND with strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir) should be approached with caution. Because moderate CYP3A4 inhibitors (e.g. diltiazem) result in a 2-fold increase in plasma concentrations of aprepitant, concomitant administration should also be approached with caution.

EMEND is a substrate for CYP3A4; therefore, co-administration of EMEND with medicines that strongly induce CYP3A4 activity (e.g. rifampin, carbamazepine, phenytoin) may result in reduced plasma concentrations of EMEND that may result in decreased efficacy of EMEND.

Ketoconazole

When a single 125 mg dose of EMEND was administered on Day 5 of a 10-day regimen of 400 mg/day of ketoconazole, a strong CYP3A4 inhibitor, the AUC of EMEND increased approximately 5-fold and the mean terminal half-life of EMEND increased approximately 3-fold. Concomitant administration of EMEND with strong CYP3A4 inhibitors should be approached cautiously.

Rifampicin

When a single 375 mg dose of EMEND was administered on Day 9 of a 14-day regimen of 600 mg/day of rifampicin, a strong CYP3A4 inducer, the AUC of EMEND decreased approximately 11-fold and the mean terminal half-life decreased approximately 3-fold. Co-administration of EMEND with medicines that induce CYP3A4 activity may result in reduced plasma concentrations and decreased efficacy of EMEND.

Additional interactions

Diltiazem: In patients with mild to moderate hypertension, administration of EMEND once daily, as a tablet formulation comparable to 230 mg of the capsule formulation, with diltiazem 120 mg 3 times daily for 5 days, resulted in a 2-fold increase of EMEND AUC and a simultaneous 1,7-fold increase of diltiazem AUC. These pharmacokinetic effects did not result in clinically meaningful changes in ECG, heart rate, or blood pressure beyond those changes induced by diltiazem alone.

Paroxetine

Co-administration of once daily doses of EMEND, as a tablet formulation comparable to 85 mg or 170 mg of the capsule formulation, with paroxetine 20 mg once daily, resulted in a decrease in AUC by approximately 25 % and C_{max} by approximately 20 % of both EMEND and paroxetine.

PREGNANCY AND LACTATION

Pregnancy

The safety and efficacy of EMEND in pregnancy and lactation has not been established, as there are no adequate and well-controlled studies in pregnant women.

Lactation

Women breastfeeding their infants should not use EMEND. Aprepitant is excreted in the milk of lactating rats. It is not known whether EMEND is excreted in human milk. Mothers on EMEND should not breastfeed their babies.

DOSAGE AND DIRECTIONS FOR USE

EMEND is given for 3 days as part of a regimen that includes a corticosteroid for 4 days and a 5-HT_3 antagonist on day one. The package insert for the co-administered 5-HT_3 antagonist must be consulted prior to initiation of treatment with EMEND. The recommended dose of EMEND is 125 mg orally 1 hour prior to chemotherapy treatment (Day 1) and 80 mg once daily in the morning on Days 2 and 3.

Recommended dosing for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy:

	Day 1	Day 2	Day 3	Day 4
EMEND	125 mg	80 mg	80 mg	None
Dexamethasone**	12 mg orally	8 mg orally	8 mg orally	8 mg orally
5-HT_3 antagonist	See the package insert for the selected 5-HT_3 antagonist for appropriate dosing information	None	None	None

**Dexamethasone should be administered 30 minutes prior to chemotherapy treatment on Day 1 and in the morning on Days 2 through 4. The dose of dexamethasone was chosen to account for drug interactions.

Recommended dosing for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy:

	Day 1	Day 2	Day 3
EMEND	125 mg	80 mg	80 mg
Dexamethasone**	12 mg orally	8 mg orally	8 mg orally
5-HT_3 antagonist	See the package insert for the selected 5-HT_3 antagonist for appropriate dosing	None	None

	information		

**Dexamethasone should be administered 30 minutes prior to chemotherapy treatment on Day 1. The dose of dexamethasone accounts for interactions.

See **"INTERACTIONS"** for additional information on the administration of EMEND with corticosteroids.

Refer to the full prescribing information for co-administered anti-emetic agents.

EMEND may be taken with or without food.

No dosage adjustment is necessary based on age, gender, race or Body Mass Index (BMI).

No dosage adjustment is necessary for patients with severe renal insufficiency (creatinine clearance < 30 ml/min) or for patients with end stage renal disease undergoing haemodialysis.

No dosage adjustment is necessary for patients with mild to moderate hepatic insufficiency (Child-Pugh score 5 to 9). There are no clinical data in patients with severe hepatic insufficiency (Child-Pugh score > 9).

SIDE EFFECTS

The overall safety of EMEND was evaluated in approximately 6 500 individuals.

Highly Emetogenic Chemotherapy

In 2 clinical trials in patients receiving highly emetogenic cancer chemotherapy (HEC), EMEND was given in combination with ondansetron and dexamethasone (aprepitant regimen) and compared with ondansetron and dexamethasone alone.

The most common aprepitant-related adverse experiences reported in patients treated with the aprepitant regimen and greater than the comparator therapy were: Hiccups (4,6 %), increased ALT (2,8 %), dyspepsia (2,6 %), constipation (2,4 %), headache (2,0 %) and decreased appetite (2,0 %).

Moderately Emetogenic Chemotherapy

In 2 clinical trials in patients receiving moderately emetogenic cancer chemotherapy (MEC) EMEND was given in combination with ondansetron and dexamethasone (aprepitant regimen).

In Cycle 1, aprepitant-related adverse experiences were reported in approximately 14 % of patients treated with the EMEND regimen. EMEND was discontinued due to aprepitant-related adverse experiences in 0,7 % of patients treated with the EMEND regimen.

The most common aprepitant-related adverse experience reported at a greater incidence with the EMEND regimen than with standard therapy was fatigue (1,4 %).

Highly and Moderately Emetogenic Chemotherapy

The following medicine-related adverse experiences were observed in patients treated with the EMEND regimen and at a greater incidence than treatment with ondansetron and dexamethasone therapy:

Very common (≥ 1/10), Common (≥ 1/100, < 1/10), Uncommon (≥ 1/1 000, < 1/100), Rare (≥ 1/10 000, < 1/1 000), Very rare (< 1/10 000)

Infection and infestations

Rare: Candidiasis, staphylococcal infection

Blood and the lymphatic system disorders

Uncommon: Anaemia, febrile neutropenia

Metabolism and nutrition disorders

Common: Decreased appetite

Rare: Polydipsia

Psychiatric disorders

Uncommon: Anxiety

Rare: Disorientation, euphoria

Nervous system disorders

Uncommon: Dizziness, somnolence

Rare: Cognitive disorder, lethargy, dysgeusia

Eye disorders

Rare: Conjunctivitis

Ear and labyrinth disorders

Rare: Tinnitus

Cardiac disorders

Uncommon: Palpitations

Rare: Bradycardia, cardiovascular disorder

Vascular disorders

Uncommon: Hot flushes

Respiratory, thoracic and mediastinal disorders

Common: Hiccups

Rare: Oropharyngeal pain, sneezing, cough, post-nasal drip, throat irritation

Gastrointestinal disorders

Common: Dyspepsia

Uncommon: Eructation, nausea, gastroesophageal reflux disease, vomiting, abdominal pain, dry mouth, flatulence

Rare: Hard faeces, duodenal ulcer perforation, neutropenic colitis, stomatitis, abdominal distension

Skin and subcutaneous tissue disorders

Uncommon: Rash, acne

Rare: Photosensitivity reaction, hyperhidrosis, seborrhoea, skin lesion (patch of skin that does not resemble the area surrounding it), pruritic rash

Musculoskeletal and connective tissue disorders

Rare: Muscle spasms, muscle weakness

Renal and urinary disorders

Uncommon: Dysuria

Rare: Pollakiuria (abnormally frequent urination)

General disorders and administration site conditions

Common: Fatigue

Uncommon: Asthenia, malaise

Rare: Oedema, chest discomfort, gait disturbance

Investigations

Common: Increased ALT

Uncommon: Increased AST, increased blood alkaline phosphatase

Rare: Increased urine output, positive red blood cells urine, decreased blood sodium, decreased weight, glucose urine present, decreased neutrophil count

The adverse experience profiles in the Multiple-Cycle extensions for up to 6 cycles of chemotherapy were generally similar to those observed in Cycle 1.

In other clinical studies, isolated cases of serious adverse experiences were reported. Stevens-Johnson syndrome was reported in a patient receiving EMEND with cancer chemotherapy in another chemotherapy induced nausea and vomiting (CINV) study. Angioedema and urticaria were reported in a patient receiving EMEND in a non-CINV study.

Post-Marketing Experience

The following adverse reactions have been identified during post-marketing use of EMEND. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to the medicine.

Skin and subcutaneous tissue disorders: Pruritus, rash, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Immune system disorders: Hypersensitivity reactions including anaphylactic reactions.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

No specific information is available on the treatment of overdosage with EMEND.

Drowsiness and headache were reported in one patient who ingested 1 440 mg of EMEND.

In the event of overdose, EMEND should be discontinued and general supportive treatment and monitoring should be provided.

EMEND cannot be removed by haemodialysis.

IDENTIFICATION

EMEND 80 mg capsule: White, opaque hard gelatin capsule with 461 and 80 mg printed radially in black ink.

EMEND 125 mg capsule: Opaque, hard gelatin capsule with white body and pink cap with 462 and 125 mg printed radially in black ink.

PRESENTATION

EMEND 80 and 125 mg Capsules are supplied in a carton containing 5 capsules individually packaged in single aluminium foil blisters. Each carton contains 5 blisters.

EMEND Combi Pack Capsules are supplied as individually packaged single aluminium foil blister packs as a combination containing one 125 mg capsule and two 80 mg capsules in a carton.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Keep out of reach of children.

REGISTRATION NUMBERS

EMEND 80 Capsules: A38/5.7.2/0626

EMEND 125 Capsules: A38/5.7.2/0627

EMEND Combi Pack Capsules: A38/5.7.2/0625

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

MSD (Pty) Ltd

117 16th Road

Halfway House

1685

South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT

Date on the registration certificate: 23 September 2005

Date of the most recently revision as approved: 10 June 2016

Namibia Only: Emend 80 mg 5's	
Registration Number	10/5.7.2/0111
Scheduling Status	NS2

Namibia Only: Emend 125 mg 5's	
Registration Number	10/5.7.2/0112
Scheduling Status	NS2

Namibia Only: Emend Combi Pack	
Registration Number	10/5.7.2/0113
Scheduling Status	NS2

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