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APPROVED
By Jacques Viljoen at 3:27 pm, Mar 17, 2025
Bhavik Hira
Digitally signed by Bhavik Hira
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PROFESSIONAL INFORMATION

SCHEDULING STATUS S4

1 NAME OF THE MEDICINE

EASAN powder for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 245,3 mg of fosaprepitant dimeglumine equivalent to 150 mg of fosaprepitant free acid.
Contains sugar: lactose monohydrate 395 mg per vial.
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder for solution for infusion.
White or off-white block-shaped solid or powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

EASAN, in combination with other anti-emetic medicines, is indicated for the prevention of acute (0 to 24 hours) and delayed (> 24 to 120 hours) nausea and vomiting associated with initial and repeat courses of:

- highly emetogenic cancer chemotherapy (see Section 4.2).
- moderately emetogenic cancer chemotherapy (see Section 4.2).

4.2 Posology and method of administration

Posology

EASAN powder for solution for infusion is a lyophilised pro-drug of aprepitant. EASAN is administered on Day 1 as an infusion over 20 to 30 minutes initiated approximately 30 minutes prior to chemotherapy. EASAN should be administered in conjunction with a corticosteroid and a 5-HT_3 antagonist as specified in the tables below. The professional information for the co-administered 5-HT_3 antagonist must be consulted prior to initiation of treatment with EASAN.
Recommended dosing for the prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy.

Highly Emetogenic Chemotherapy Regimen				
	Day 1	Day 2	Day 3	Day 4
EASAN	150 mg IV	None	None	None
Dexamethasone**	12 mg orally	8 mg orally	8 mg orally twice daily	8 mg orally twice daily
5-HT_3 antagonist	See the professional information for the selected 5-HT_3 antagonist for the 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. Dexamethasone should also be administered in the evenings on Days 3 and 4. The dose of dexamethasone accounts for interactions.

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

Moderately Emetogenic Chemotherapy Regimen	
	Day 1
EASAN	150 mg IV
Dexamethasone**	12 mg orally
5-HT_3 antagonist	See the professional information for the selected 5-HT_3 antagonist for the appropriate dosing information.

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

General information

See section 4.5 for additional information on the administration of EASAN with corticosteroids. Refer to the full prescribing information for co-administered anti-emetic medicines. No dosage adjustment is necessary for the elderly. 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 > 9) (see Section 4.4).

Method of administration

EASAN is for intravenous administration. **For single use only.** Discard any unused portion.

Preparation of EASAN for Infusion

1. Inject 5 ml saline into the vial. Assure that saline is added to the vial along the vial wall in order to prevent foaming. Swirl the vial gently. Avoid shaking and jetting saline into the vial. After reconstitution, use only if the solution is a clear colourless or pale yellow to yellow solution, free from visible particles.
2. Prepare an infusion bag filled with 145 ml of saline.
3. Withdraw the entire volume from the vial and transfer it into an infusion bag containing 145 ml of saline to yield a total volume of 150 ml. Gently invert the bag 2 to 3 times. EASAN should be inspected visually for particulate matter and discolouration before administration whenever solution and container permit. See section 6.2 for incompatibilities and section 6.4 for storage conditions after reconstitution and dilution.

4.3 Contraindications

- Hypersensitivity to aprepitant, polysorbate 80, or to any of the excipients (see section 6.1).
- Co-administration with pimozide, terfenadine, astemizole or cisapride. Inhibition of cytochrome P450 isoenzyme 3A4 (CYP3A4) by aprepitant could result in elevated plasma concentrations of these medicines potentially causing serious or life-threatening reactions. (see Section 4.5).
- Pregnancy and breastfeeding (see Section 4.6).
- Paediatric patients, as the safety and efficacy have not been established.

4.4 Special warnings and precautions for use

Patients with moderate to severe hepatic impairment

There are limited data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment. EASAN should be used with caution in these patients (see Section 5.2).

Severe hepatic insufficiency

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 EASAN is administered in these patients. Since EASAN is rapidly converted to aprepitant (a weak to moderate inhibitor of CYP3A4), EASAN should be used with caution in patients receiving concomitant medicines that are primarily metabolised through CYP3A4; some chemotherapy medicines are metabolised by CYP3A4 (see section 4.5).Weak inhibition of CYP3A4 by EASAN could result in elevated plasma concentrations of these concomitant medicines (see section 4.5). Concomitant administration of EASAN with strong CYP3A4 inhibitors {e.g. ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir) should be approached with caution. The effect of oral aprepitant on the pharmacokinetics of orally administered CYP3A4 substrates is greater than the effect of oral aprepitant on the pharmacokinetics of intravenously administered CYP3A4 substrates (see section 4.5).

CYP3A4 interactions

EASAN should be used with caution in patients receiving concomitant active substances that are metabolised primarily through CYP3A4 and with a narrow therapeutic range, such as ciclosporin, tacrolimus, sirolimus, everolimus, alfentanil, ergot alkaloid derivatives, fentanyl, and quinidine (see Section 4.5). Additionally, concomitant administration with irinotecan should be approached with particular caution as the combination might result in increased toxicity.

Co-administration with warfarin (a CYP2C9 substrate)

In patients on chronic warfarin therapy, the International Normalised Ratio (INR) should be monitored closely for 14 days, particularly at 7 to 10 days following the use of EASAN with each chemotherapy cycle (see section 4.5).

Co-administration with hormonal contraceptives

The efficacy of hormonal contraceptives may be reduced during and for 28 days after administration of EASAN. Alternative non-hormonal back-up methods of contraception should be used during treatment with EASAN and for 2 months following the use of EASAN (see section 4.5).

Hypersensitivity reactions

Immediate hypersensitivity reactions including flushing, erythema, dyspnoea, and anaphylaxis/anaphylactic shock have occurred during or soon after infusion of fosaprepitant (as in EASAN). These hypersensitivity reactions have generally responded to discontinuation of the infusion and administration of appropriate therapy. It is not recommended to reinitiate the infusion in patients who experience hypersensitivity reactions.

Administration and infusion site reactions

Infusion site reactions (ISRs) have been reported with the use of EASAN (see section 4.8). The majority of severe ISRs, including thrombophlebitis and vasculitis, were reported with concomitant vesicant (e.g., anthracycline-based) chemotherapy administration, particularly when associated with extravasation. Necrosis was also reported in some patients with concomitant vesicant chemotherapy. Mild injection site thrombosis has been observed at higher doses without concomitant vesicant chemotherapy. EASAN should not be given as a bolus injection, but should always be diluted and given as a slow intravenous infusion. EASAN should not be administered intramuscularly or subcutaneously. If signs or symptoms of local irritation occur, the injection or infusion should be terminated and restarted in another vein.

Excipient warning

Contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not receive EASAN.

4.5 Interaction with other medicines and other forms of interaction

When administered intravenously fosaprepitant is rapidly converted to aprepitant. EASAN, given as a single dose, is a weak inhibitor of CYP3A4. Fosaprepitant (as in EASAN) does not seem to interact with the P-glycoprotein transporter, as demonstrated by the lack of interaction of oral aprepitant with digoxin. It is anticipated that fosaprepitant would cause less or no greater induction of CYP2C9, CYP3A4 and glucuronidation than that caused by the administration of oral aprepitant. Data are lacking regarding effects on CYP2C8 and CYP2C19. Interactions with other medicines following administration of intravenous fosaprepitant as in EASAN) are likely to occur with active substances that interact with oral aprepitant. The following information was derived from studies conducted with oral aprepitant and studies conducted with intravenous single-dose fosaprepitant co-administered with dexamethasone, midazolam, or diltiazem.

Effect of fosaprepitant on the pharmacokinetics of other active substances

CYP3A4 inhibition

As a weak inhibitor of CYP3A4, the fosaprepitant (as in EASAN) 150 mg single dose can cause a transient increase in plasma concentrations of co-administered active substances that are metabolised through CYP3A4. The total exposure of CYP3A4 substrates may increase up to 2-fold on Days 1 and 2 after co-administration with a single 150 mg fosaprepitant dose. EASAN must not be used concurrently with pimozide, terfenadine, astemizole, or cisapride. Inhibition of CYP3A4 by fosaprepitant could result in elevated plasma concentrations of these active substances, potentially causing serious or life-threatening reactions. (see Section 4.3). Caution is advised during concomitant administration of EASAN and active substances that are metabolised primarily through CYP3A4 and with a narrow therapeutic range, such as ciclosporin, tacrolimus, sirolimus, everolimus, alfentanil, diergotamine, ergotamine, fentanyl, and quinidine (see Section 4.4).

Corticosteroids

Dexamethasone: The oral dexamethasone dose should be reduced by approximately 50 % when co-administered with fosaprepitant (see section 4.2). Fosaprepitant 150 mg administered as a single intravenous dose on Day 1 increased the $AUC_{0\text{-}24hr}$ of dexamethasone, a CYP3A4 substrate, by 100 % on Day 1,86 % on Day 2 and 18 % on Day 3 when dexamethasone was co-administered as a single 8 mg oral dose on Days 1, 2, and 3.
Methylprednisolone: Oral aprepitant, 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.

Chemotherapeutic medicines

Interaction studies with fosaprepitant 150 mg and chemotherapeutic medicines have not been conducted; however, based on studies with oral aprepitant and docetaxel and vinorelbine, EASAN is not expected to have a clinically relevant interaction with intravenously administered docetaxel and vinorelbine. An interaction with orally administered chemotherapeutic medicines metabolised primarily or partly by CYP3A4 (e.g., etoposide, vinorelbine) cannot be excluded. Caution is advised and additional monitoring may be appropriate in patients receiving medicines metabolised primarily or partly by CYP3A4 (see section 4.4). Post-marketing events of neurotoxicity, a potential adverse reaction of ifosfamide, have been reported after aprepitant and ifosfamide co-administration.

Immunosuppressants

Following a single 150 mg fosaprepitant dose, a transient moderate increase for two days possibly followed by a mild decrease in exposure of immunosuppressants metabolised by CYP3A4 (e.g. ciclosporin, tacrolimus, everolimus and sirolimus) is expected. Given the short duration of increased exposure, dose reduction of the immunosuppressant based on Therapeutic Dose Monitoring is not recommended on the day of and the day after administration of EASAN.

Midazolam

Fosaprepitant 150 mg administered as a single intravenous dose on Day 1 increased the AUC0-∞ of midazolam by 77 % on Day 1 and had no effect on Day 4 when midazolam was co-administered as a single oral dose of 2 mg on Days 1 and 4. Fosaprepitant 150 mg is a weak CYP3A4 inhibitor as a single dose on Day 1 with no evidence of inhibition or induction of CYP3A4 observed on Day 4. The potential effects of increased plasma concentrations of midazolam or other benzodiazepines metabolised via CYP3A4 (alprazolam, triazolam) should be considered when co-administering these medicines with EASAN.

Diltiazem

Interaction studies with fosaprepitant 150 mg and diltiazem have not been conducted; however, the following study with 100 mg of fosaprepitant should be considered when using EASAN with diltiazem. In patients with mild to moderate hypertension, infusion of 100 mg of fosaprepitant over 15 minutes with diltiazem 120 mg 3 times daily, resulted in a 1,4-fold increase in diltiazem AUC and a small but clinically meaningful decrease in blood pressure, but did not result in a clinically meaningful change in heart rate, or PR interval.

Induction

The fosaprepitant 150 mg single dose did not induce CYP3A4 on Days 1 and 4 in the midazolam interaction study. It is anticipated that EASAN would cause less or no greater induction of CYP2C9, CYP3A4, and glucuronidation than that caused by the administration of the 3-day oral aprepitant regimen, for which a transient induction with its maximum effect 6-8 days after first aprepitant dose has been observed. The 3-day oral aprepitant regimen resulted in an about 30-35 % reduction in AUC of CYP2C9 substrates and up to a 64 % decrease in ethinyl estradiol trough concentrations. Data are lacking regarding effects on CYP2C8 and CYP2C19. Caution is advised when warfarin, acenocoumarol, tolbutamide, phenytoin or other active substances that are known to be metabolised by CYP2C9 are administered with EASAN.

Warfarin

In patients on chronic warfarin therapy, the prothrombin time (INR) should be monitored closely during treatment with and for 14 days following the use of EASAN for the prevention of chemotherapy induced nausea and vomiting (see section 4.4).

Hormonal contraceptives

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 use of fosaprepitant.

5-HT_3 antagonists

Interaction studies with fosaprepitant 150 mg and 5-HT_3 antagonists have not been conducted; however, in clinical interaction studies, the oral aprepitant regimen did not have clinically important effects on the pharmacokinetics of ondansetron, granisetron, or hydrodolasetron (the active metabolite of dolasetron). Therefore, there is no evidence of interaction with the use of EASAN and 5-HT_3 antagonists.

Effect of other medicines on the pharmacokinetics of aprepitant

Concomitant administration of fosaprepitant with active substances that inhibit CYP3A4 activity (e.g., ketoconazole, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin, nefazodone, and protease inhibitors) should be approached cautiously, as the combination is expected to result in several-fold increased plasma concentrations of aprepitant (see Section 4.4). Ketoconazole increased the terminal half-life of oral aprepitant about 3-fold. Concomitant administration of fosaprepitant with active substances that strongly induce CYP3A4 activity (e.g., rifampicin, phenytoin, carbamazepine, phenobarbital) should be avoided as the combination could result in reductions of the plasma concentrations of aprepitant that may result in decreased efficacy. Concomitant administration of fosaprepitant with herbal preparations containing St. John's Wort (*Hypericum perforatum*) is not recommended. Rifampicin decreased the mean terminal half-life of oral aprepitant by 68 %.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Contraception in males and females

The efficacy of hormonal contraceptives may be reduced during and for 28 days after administration of EASAN. Alternative non-hormonal back-up methods of contraception should be used during treatment with EASAN and for 2 months following the last dose of EASAN (see Sections 4.4 and 4.5).

Pregnancy

Safety in pregnancy has not been established.
EASAN should not be used during pregnancy.

Breastfeeding

Aprepitant is excreted in the milk of lactating rats after intravenous administration of fosaprepitant as well as after oral administration of aprepitant. It is not known whether aprepitant is excreted in human milk. Therefore, breastfeeding is not recommended during treatment with EASAN.

Fertility

The potential for effects of fosaprepitant and aprepitant on fertility has not been fully characterised because exposure levels above the therapeutic exposure in humans could not be attained in animal studies. These fertility studies did not indicate direct or indirect harmful effects with respect to mating performance, fertility, embryonic/foetal development, or sperm count and motility.

4.7 Effects on ability to drive and use machines

EASAN may affect the patient's ability to drive and use machines. Dizziness and fatigue may occur following administration of EASAN (see section 4.8).

4.8 Undesirable effects

a. Summary of the safety profile

Since fosaprepitant is converted to aprepitant, those adverse experiences associated with aprepitant are also expected to occur with EASAN.
The overall safety of fosaprepitant was evaluated in 1 143 individuals, and the overall safety of oral aprepitant was evaluated in approximately 6 500 individuals.

Oral aprepitant

The most frequent adverse reactions reported at a greater incidence in adults treated with the aprepitant regimen than with standard therapy in patients receiving HEC were: hiccups (4,6 % versus 2,9 %), alanine aminotransferase (ALT) increased (2,8 % versus 1,1 %), dyspepsia (2,6 % versus 2,0 %), constipation (2,4 % versus 2,0 %), headache (2,0 % versus 1,8 %), and decreased appetite (2,0 % versus 0,5 %). The most frequent adverse reaction reported at a greater incidence in patients treated with the aprepitant regimen than with standard therapy in patients receiving MEC was fatigue (1,4 % versus 0,9 %).

b. Tabulated summary of adverse reactions - aprepitant

The following adverse reactions were observed in a pooled analysis of the HEC and MEC studies at a greater incidence with oral aprepitant than with standard therapy in patients or in post-marketing use. The frequency categories given in the table are based on the studies in adults; the observed frequencies in the paediatric studies were similar or lower, unless shown in the table. Some less frequent ADRs in the adult population were not observed in the paediatric studies. Frequencies are defined as: frequent; less frequent and frequency unknown (cannot be estimated from the available data).

MedDRA system organ class	Frequency	Adverse reactions
Infections and infestations	Less frequent	Candidiasis, staphylococcal infection
Blood and lymphatic system disorders	Less frequent	Febrile neutropenia, anaemia
Immune system disorders	Frequency unknown	Hypersensitivity reactions including anaphylactic reactions
Metabolism and nutrition disorders	Frequent	Decreased appetite
	Less frequent	Polydipsia
Psychiatric disorders	Less frequent	Anxiety, disorientation, euphoric mood
Nervous system disorders	Frequent	Headache
	Less frequent	Dizziness, somnolence, cognitive disorder, lethargy, dysgeusia
Eye disorders	Less frequent	Conjunctivitis
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Less frequent	Palpitations, bradycardia, cardiovascular disorder
Vascular disorders	Less frequent	Hot flush/flushing
Respiratory, thoracic and mediastinal disorders	Frequent	Hiccups
	Less frequent	Oropharyngeal pain, sneezing, cough, postnasal drip, throat irritation
Gastrointestinal disorders	Frequent	Constipation, dyspepsia
	Less frequent	Eructation, nausea*, vomiting*, gastroesophageal reflux disease, abdominal pain, dry mouth, flatulence, duodenal ulcer perforation, stomatitis, abdominal distension, faeces hard, neutropenic colitis
Skin and subcutaneous tissue disorders	Less frequent	Rash, acne, photosensitivity reaction, hyperhidrosis, seborrhoea, skin lesion, rash pruritic, Stevens-Johnson syndrome/toxic epidermal necrolysis
	Frequency unknown	Pruritus, urticaria
Musculoskeletal and connective tissue disorders	Less frequent	Muscular weakness, muscle spasms
Renal and urinary disorders	Less frequent	Dysuria, pollakiuria
General disorders and administration site conditions	Frequent	Fatigue
	Less frequent	Asthenia, malaise, oedema, chest discomfort, gait disturbance
Investigations	Frequent	Increased ALT
	Less frequent	Increased AST, increased blood alkaline phosphatase, red blood cells urine positive, decreased blood sodium, decreased weight, decreased neutrophil count, glucose urine present, increased urine output

*Nausea and vomiting were efficacy parameters in the first 5-days of post-chemotherapy treatment and were reported as adverse reactions only thereafter.

c. Description of selected adverse reactions

The adverse reactions profiles in the Multiple-Cycle extension of HEC and MEC studies in adults for up to 6 additional cycles of chemotherapy were generally similar to those observed in Cycle 1.
In an additional active-controlled clinical study in 1,169 adult patients receiving aprepitant and HEC, the adverse reactions profile was generally similar to that seen in the other HEC studies with aprepitant.
Additional adverse reactions were observed in adult patients treated with aprepitant for post-operative nausea and vomiting (PONV) and a greater incidence than with ondansetron: abdominal pain upper, bowel sounds abnormal, constipation*, dysarthria, dyspnoea, hypoaesthesia, insomnia, miosis, nausea, sensory disturbance, stomach discomfort, sub-ileus*, visual acuity reduced, wheezing.
*Reported in patients taking a higher dose of aprepitant.

Fosaprepitant

In an active-controlled clinical study in adult patients receiving HEC, safety was evaluated for 1 143 patients receiving the 1-day regimen of fosaprepitant 150 mg compared to 1 169 patients receiving the 3-day regimen of aprepitant. Additionally, in a placebo-controlled clinical trial in adult patients receiving MEC, safety was evaluated for 504 patients receiving a single dose of fosaprepitant 150 mg compared to 497 patients receiving the control regimen.
In a pooled analysis of 3 active-controlled clinical studies in paediatric patients (aged 6 months to 17 years) receiving either HEC or MEC and a single dose of fosaprepitant at or above the recommended 1-day regimen dose, safety was evaluated for 139 patients receiving the 1-day regimen of fosaprepitant. In the same analysis, safety was evaluated for 199 patients receiving either HEC or MEC and a single dose of fosaprepitant at or above the recommended 3-day regimen of fosaprepitant. Safety data following the administration of the 3-day IV/oral/oral regimen were also included.
No data are available following the administration of a 3-day IV fosaprepitant regimen in paediatric patients. The safety profile of the 3-day IV fosaprepitant regimen in paediatric patients is expected to be similar to that of the 1-day fosaprepitant regimen as the low daily trough levels do not significantly increase the exposures on subsequent days.
The safety profile of fosaprepitant in adult and paediatric patients was generally similar to that observed with aprepitant.

Tabulated list of adverse reactions – fosaprepitant

The following are adverse reactions reported in adult patients receiving fosaprepitant in clinical studies or post-marketing that have not been reported with aprepitant as described above. The frequency categories in the table are based on studies in adults; the observed frequencies in the paediatric studies were similar or lower. Some adverse reactions that are frequently observed in the adult population were not observed in the paediatric studies. Infusion site reactions (ISRs) have been reported with the use of fosaprepitant (see section 4.4).

MedDRA system organ class	Frequency	Adverse reactions
Immune system disorders	Frequency unknown	Hypersensitivity reactions including anaphylactic reactions/ anaphylactic shock
Vascular disorders	Less frequent	Flushing, thrombophlebitis (predominantly, infusion-site thrombophlebitis)
Skin and subcutaneous tissue disorders	Less frequent	Erythema, pruritus, rash, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis
General disorders and administration site conditions	Less frequent	Infusion site erythema, infusion site pain, infusion site pruritus, infusion site induration
	Frequency unknown	Immediate hypersensitivity reactions including flushing, erythema, dyspnoea, anaphylactic reactions/ anaphylactic shock
Investigations	Less frequent	Increased blood pressure

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

In the event of overdose, EASAN should be discontinued and general supportive treatment and monitoring should be provided.
Aprepitant cannot be removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiemetics and antinauseants, ATC code: A04AD12
Pharmacological classification: A.5.7.2 Anti-emetics and antivertigo preparations

Fosaprepitant dimeglumine is a pro-drug of aprepitant. When administered intravenously it is rapidly converted to aprepitant, a substance P neurokinin 1 (NK_1) receptor antagonist. Its anti-emetic effects are attributable to aprepitant. NK_1-receptor antagonists inhibit emesis induced by cytotoxic chemotherapeutic medicines, such as cisplatin, via central actions. Human Positron Emission Tomography (PET) studies with aprepitant have shown that it penetrates the brain and occupies brain NK_1 receptors.

5.2 Pharmacokinetic properties

Fosaprepitant, a pro-drug of aprepitant, when administered intravenously is rapidly converted to aprepitant. Plasma concentrations of fosaprepitant are below quantifiable levels within 30 minutes of the completion of infusion.

Aprepitant after fosaprepitant administration

Following a single intravenous 150 mg dose of fosaprepitant administered as a 20-minute infusion to healthy adult volunteers, the mean $AUC_{0\text{-}\infty}$ of aprepitant was 35,0 µg·hr/ml and the mean maximal aprepitant concentration was 4,01 µg/ml.

Distribution

Aprepitant is highly protein bound, with a mean of 97 %. The geometric mean volume of distribution at steady state (Vd_{ss}) of aprepitant estimated from a single 150 mg intravenous dose of fosaprepitant is approximately 82 L in humans.
Aprepitant crosses the placenta and blood brain barrier.

Biotransformation

Fosaprepitant was rapidly converted to aprepitant in *in vitro* incubations with liver preparations from humans. Furthermore, fosaprepitant underwent rapid and nearly complete conversion to aprepitant in S9 preparations from other human tissues including kidney, lung and ileum. Thus, it appears that the conversion of fosaprepitant to aprepitant can occur in multiple tissues. In humans, fosaprepitant administered intravenously was rapidly converted to aprepitant within 30 minutes following the end of infusion.

Aprepitant undergoes extensive metabolism. In healthy young adults, aprepitant accounts for approximately 19 % of the radioactivity in plasma over 72 hours following a single intravenous administration 100 mg dose of [14C]- fosaprepitant, a pro-drug for aprepitant, indicating a substantial presence of metabolites in the plasma. Twelve metabolites of aprepitant have been identified in human plasma. The metabolism of aprepitant occurs largely via oxidation at the morpholine ring and its side chains and the resultant metabolites were only weakly active. In vitro studies using human liver microsomes indicate that aprepitant is metabolised primarily by CYP3A4 and potentially with minor contribution by CYP1A2 and CYP2C19.

All metabolites observed in urine, faeces and plasma following an intravenous 100 mg [14C]-fosaprepitant dose were also observed following an oral dose of [14C]-aprepitant. Upon conversion of 245,3 mg of fosaprepitant dimeglumine (equivalent to 150 mg fosaprepitant) to aprepitant, 23,9 mg of phosphoric acid and 95,3 mg of meglumine are liberated.

Elimination

Aprepitant is not excreted unchanged in urine. Metabolites are excreted in urine and via biliary excretion in faeces. Following a single intravenously administered 100 mg dose of [^{14}C]- fosaprepitant to healthy subjects, 57 % of the radioactivity was recovered in urine and 45 % in faeces.

The pharmacokinetics of aprepitant is non-linear across the clinical dose range. The terminal half-life of aprepitant following a 150 mg intravenous dose of fosaprepitant was approximately 11 hours. The geometric mean plasma clearance of aprepitant following a 150 mg intravenous dose of fosaprepitant was approximately 73 ml/min.

Pharmacokinetics in special populations

Hepatic impairment: Fosaprepitant is metabolised in various extrahepatic tissues; therefore hepatic impairment is not expected to alter the conversion of fosaprepitant to aprepitant. Mild hepatic impairment (Child-Pugh class A) does not affect the pharmacokinetics of aprepitant to a clinically relevant extent. No dose adjustment is necessary for patients with mild hepatic impairment. Conclusions regarding the influence of moderate hepatic impairment (Child-Pugh class B) on aprepitant pharmacokinetics cannot be drawn from available data. There are no clinical or pharmacokinetic data in patients with severe hepatic impairment (Child-Pugh class C).
Renal impairment: A single 240 mg dose of oral aprepitant was administered to patients with severe renal impairment (CrCl < 30 ml/min) and to patients with end stage renal disease (ESRD) requiring haemodialysis.
In patients with severe renal impairment, 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 aprepitant was not significantly affected in patients with renal impairment compared with healthy subjects. Haemodialysis conducted 4 or 48 hours after dosing had no significant effect on the pharmacokinetics of aprepitant; less than 0,2 % of the dose was recovered in the dialysate.
No dose adjustment is necessary for patients with renal impairment or for patients with ESRD undergoing haemodialysis.

Paediatric population

Fosaprepitant has not been evaluated in patients below 18 years of age (see Section 4.3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Edetate disodium (E386)
Lactose monohydrate
Polysorbate 80 (E433)
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injection

6.2 Incompatibilities

EASAN is incompatible with any solutions containing divalent cations (e.g. Ca^{2+}, Mg^{2+}), including Hartman's and Lactated Ringer's Solution. EASAN must not be reconstituted or mixed with solutions for which physical and chemical compatibility have not been established.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a refrigerator (2 – 8 ˚C). The reconstituted final medicine solution is stable for 24 hours at ambient room temperature (at or below 25 °C) and should be used within 24 hours after reconstitution. If not used immediately, in-use storage times should not be longer than 24 hours at 2 to 8 °C.

6.5 Nature and contents of container

10 ml colourless transparent injection vials made of neutral borosilicate glass tubing, with grey rubber closure and aluminium cap.
Pack size: one vial per cardboard carton.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Juno Pharma SA (Pty) Ltd
3 Gwen Lane, 4th Floor,
Sandton, 2031.
Email: pv@trinitypharma.co.za
Contact number: +27 (0)10 594 5610

8 REGISTRATION NUMBER

55/5.7.2/0659

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

7 March 2023

10 DATE OF REVISION OF THE TEXT

N.A

L12305 C/23

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

EASAN 150 mg powder for solution for infusion
Fosaprepitant
Contains sugar: lactose monohydrate 395 mg per vial

Read all of this leaflet carefully before you are given EASAN
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What EASAN is and what it is used for
2. What you need to know before you receive EASAN
3. How to use EASAN
4. Possible side effects
5. How to store EASAN
6. Contents of the pack and other information

1. What EASAN is and what it is used for
EASAN contains the active substance fosaprepitant which is converted to aprepitant in your body. It belongs to a group of medicines called "neurokinin 1 (NK_1) receptor antagonists". The brain has a specific area that controls nausea and vomiting. EASAN works by blocking signals to that area, thereby reducing nausea and vomiting.

EASAN is used in adults in combination with other medicines to prevent nausea and vomiting caused by chemotherapy (cancer treatment) that is a strong or moderate trigger of nausea and vomiting.

2. What you need to know before you receive EASAN
EASAN should not be administered to you:
- If you are hypersensitive (allergic) to fosaprepitant, or any of the other ingredients of EASAN (listed in section 6).
- With medicines containing pimozide (used to treat psychiatric illnesses), terfenadine and astemizole (used for hay fever and other allergic conditions), cisapride (used for treating digestive problems). Using these medicines with EASAN can cause serious or life-threatening reactions. Tell your doctor if you are taking these medicines since the treatment must be modified before you start using EASAN.
- If you are pregnant or breastfeeding.
- If you are under 18 years of age.

Warnings and precautions
Take special care with EASAN:
- If you have liver disease because the liver is important in breaking down the medicine in the body. Your doctor may therefore have to monitor the condition of your liver.
- If you are taking or using birth control medicines (see 'Other medicines and EASAN').
- If you are taking warfarin or other medicines to thin your blood (see 'Other medicines and EASAN').
- If you experience skin reactions or irritation at the injection site (see 'Possible side effects').

Children and adolescents
EASAN should not be administered to children under 18 years of age.

Other medicines and EASAN
Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

EASAN can affect other medicines both during and after treatment with EASAN. There are some medicines that should not be taken with EASAN (such as pimozide, terfenadine, astemizole, and cisapride) or that require a dose adjustment (see also 'EASAN should not be administered to you').

The effects of EASAN or other medicines might be influenced if you take EASAN together with other medicines including those listed below. Please talk to your doctor or pharmacist if you are taking any of the following medicines:
- 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 EASAN. Another or additional non-hormonal form of birth control should be used during treatment with EASAN and for up to 2 months after using EASAN.
- ciclosporin, tacrolimus, sirolimus, everolimus (immunosuppressants).
- alfentanil, fentanyl (used to treat pain).
- irinotecan, etoposide, vinorelbine, ifosfamide (medicines used to treat cancer).
- quinidine (used to treat an irregular heartbeat).
- medicines containing ergot alkaloid derivatives such as ergotamine and diergotamine (used for treating migraines).
- warfarin, acenocoumarol (blood thinners; blood tests may be required).
- rifampicin, clarithromycin, telithromycin (antibiotics used to treat infections).
- phenytoin (a medicine used to treat seizures).
- carbamazepine (used to treat depression and epilepsy).
- midazolam, triazolam, phenobarbital (medicines used to produce calmness or help you sleep).
- St. John's Wort (an herbal preparation used to treat depression).
- protease inhibitors (used to treat HIV infections).
- itraconazole, voriconazole, posaconazole (antifungals).
- nefazodone (used to treat depression).
- diltiazem (a medicine used to treat high blood pressure).
- corticosteroids (such as dexamethasone or methylprednisolone).
- anti-anxiety medicines (such as alprazolam).
- tolbutamide (a medicine used to treat diabetes).

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before receiving this medicine.

EASAN should not be administered during pregnancy and breastfeeding.
For information regarding birth control, see 'Other medicines and EASAN.

It is not known whether EASAN is excreted in human milk; therefore, breast-feeding is not recommended during treatment with EASAN.

Driving and using machines
It should be taken into account that some people get dizzy and get sleepy after receiving EASAN. If you get dizzy or get sleepy, avoid driving or using machines after receiving EASAN (see 'Possible side effects').

EASAN contains lactose monohydrate
EASAN contains lactose monohydrate. If you have been told that you have an intolerance to some sugars, you should not use EASAN.

3. How to use EASAN
Do not share medicines prescribed for you with any other person.

You will not be expected to give yourself EASAN. It will be given to you by a person who is qualified to do so.

The usual dose in adults (18 years of age and older) is EASAN 150 mg on Day 1 (day of chemotherapy).

Your doctor may ask you to take other medicines including a corticosteroid (such as dexamethasone) and a '5HT3 antagonist' (such as ondansetron) for preventing nausea and vomiting. Check with your doctor or pharmacist if you are not sure.

The powder is reconstituted and diluted before use. The solution for infusion is given to you by a healthcare professional, such as a doctor or nurse, via an intravenous infusion (a drip) approximately 30 minutes before you start the chemotherapy treatment in adults. Your doctor will tell you how long your treatment with EASAN will last. If you have the impression that the effect of EASAN is too strong or too weak, tell your doctor or pharmacist.

If you receive more EASAN than you should
Since a healthcare provider will administer EASAN, he/ she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of EASAN
Since a healthcare provider will administer EASAN, it is unlikely that the dose will be missed.

4. Possible side effects
EASAN can have side effects.
Not all side effects reported for EASAN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving EASAN, please consult your healthcare provider for advice.

If any of the following happens, stop receiving EASAN and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, tongue and mouth or throat, which may cause difficulty in swallowing or breathing,
- Stevens-Johnson syndrome/toxic epidermal necrolysis (rare severe skin reaction)
- rash or itching,
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to EASAN. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- Infusion site reactions (ISR) at or near the infusion site. Most severe ISR have happened with a certain type of chemotherapy medicine that can burn or blister your skin (vesicant) with side effects, including pain, swelling and redness. Death of skin tissue (necrosis) has happened in some people getting this type of chemotherapy medicine.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent
- constipation, indigestion,
- headache,
- tiredness,
- loss of appetite,
- hiccups,
- increased amount of liver enzymes in your blood.

Less frequent
- dizziness, sleepiness,
- acne, rash, hives
- anxiousness,
- burping, nausea, vomiting, heartburn, stomach pain, dry mouth, passing wind,
- increased painful or burning urination,
- weakness, generally feeling unwell,
- reddening of the face/skin, hot flush,
- fast or irregular heartbeats, blood pressure increased,
- fever with increased risk of infection, lowering of red blood cells,
- infusion site pain, infusion site redness, infusion-site itching, infusion site vein inflammation, infusion site duration (pain at the injection site),
- difficulty thinking, lack of energy, taste disturbance,
- sensitivity of the skin to sun, excessive sweating, oily skin, sores on skin,
- euphoria (feeling of extreme happiness), disorientation,
- bacterial infection, fungal infection,
- severe constipation, stomach ulcer, inflammation of the small intestine and colon, sores in mouth, bloating,
- frequent urination, passing more urine than normal, presence of sugar or blood in urine,
- chest discomfort, swelling, change in the manner of walking,
- cough, mucus in back of throat, throat irritation, sneezing, sore throat,
- eye discharge and itching,
- ringing in the ear,
- muscle spasms, muscle weakness,
- excessive thirst,
- slow heartbeat, heart and blood vessel disease,
- lowering of white blood cells, low sodium levels in the blood, weight loss,
- hardening of site of infusion.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8
By reporting side effects, you can help provide more information on the safety of EASAN.

5. How to store EASAN
Store all medicines out of reach of children.
- Store in a refrigerator at 2 – 8 ˚C.
- The reconstituted and diluted solution is stable for 24 hours at 25 °C.
- Do not use after the expiry date stated on the label / carton.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What EASAN contains
- Each EASAN vial contains 245,3 mg of fosaprepitant dimeglumine equivalent to 150 mg of fosaprepitant free acid.
- Contains sugar: lactose monohydrate 395 mg per vial.
- The other ingredients are edetate disodium (E386), lactose monohydrate, polysorbate 80 (E433), hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and water for injection.

What EASAN looks like and contents of the pack
EASAN is a white or off-white block-shaped solid or powder.
EASAN is packed 10 ml colourless transparent injection vials made of neutral borosilicate glass tubing, with grey rubber closure and aluminium cap.
Pack size: one vial per cardboard carton.

Holder of Certificate of Registration
Juno Pharma SA (Pty) Ltd
3 Gwen Lane, 4th Floor,
Sandton, 2031.
Email: pv@trinitypharma.co.za
Contact number: +27 (0)10 594 5610

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Access to the corresponding Professional Information
www.trinitypharma.co.za

PASIËNTINLIGTINGSTUK

SKEDULERINGSTATUS

S4

EASAN 150 mg poeier vir oplossing vir infusie
Fosaprepitant
Bevat suiker: laktose monohidraat 395 mg per flessie

Lees hierdie inligtingstuk sorgvuldig voordat EASAN vir jou gegee word
- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorg verskaffer indien jy verdere vrae het

Wat in hierdie inligtingstuk is

1. Wat EASAN is en waarvoor dit gebruik word
2. Wat jy behoort te weet voordat jy EASAN ontvang
3. Hoe om EASAN te gebruik
4. Moontlike newe-effekte
5. Hoe om EASAN te bewaar
6. Inhoud van die pak en ander inligting

1. Wat EASAN is en waarvoor dit gebruik word
EASAN bevat die aktiewe bestanddeel fosaprepitant wat in jou lyf na aprepitant omgeskakel word. Dit behoort aan 'n groep medisyne wat "neurokinien 1 (NK_1) reseptor antagoniste" genoem word. Die brein het 'n spesifieke area wat naarheid en braking beheer. EASAN werk deur seine na daardie area toe te blok, en sodoende naarheid en braking te verminder.

EASAN word in volwassenes gebruik in kombinasie met ander medisyne om naarheid en braking te voorkom wat deur chemoterapie (kanker behandeling), wat 'n sterk of matige sneller van naarheid en braking is, veroorsaak word.

2. Wat jy behoort te weet voordat jy EASAN ontvang
EASAN behoort nie aan jou toegedien te word:
- Indien jy hipersensitief (allergies) vir fosaprepitant of enige van die ander bestanddele van EASAN is nie (gelys in afdeling 6).
- Met medisyne wat pimosied (gebruik om psigiatriese siektes te behandel), terfenadien en astemisool (gebruik vir hooikoors en ander allergiese toestande), sisapried (gebruik vir die behandeling van spysverteringsprobleme) bevat nie. Die gebruik van hierdie medisyne saam met EASAN kan ernstige of lewensgevaarlike reaksies veroorsaak. Vertel jou dokter indien jy hierdie medisyne gebruik, aangesien die behandeling aangepas moet word voordat jy EASAN begin gebruik.
- Indien jy swanger is of borsvoed nie.
- Indien jy onder die ouderdom van 18 jaar is nie.

Waarskuwings en voorsorgmaatreëls
Spesiale sorg moet geneem word met EASAN:
- indien jy lewersiekte het omdat die lewer belangrik is om die medisyne in die liggaam af te breek. Jou dokter sal daarom moontlik die toestand van jou lewer moet monitor.
- indien jy voorbehoedmiddels neem of gebruik (sien 'Ander medisyne en EASAN').
- indien jy warfarien of ander medisyne neem om jou bloed te verdun (sien 'Ander medisyne en EASAN').
- indien jy velreaksies of irritasie by die plek van inspuiting ervaar (sien 'Moontlike newe-effekte').

Kinders en adolessente
EASAN moet nie aan kinders onder die ouderdom van 18 jaar toegedien word nie.

Ander medisyne en EASAN
Vertel altyd vir jou gesondheidsorg verskaffer indien jy enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in.)

EASAN kan ander medisyne beïnvloed beide tydens en na behandeling met EASAN.

Daar is sommige medisyne wat nie saam met EASAN geneem moet word nie (soos pimosied, terfenadien, astemisool, en sisapried) of wat 'n dosisaanpassing benodig (sien ook 'EASAN behoort nie aan jou toegedien te word').

Die effekte van EASAN of ander medisyne kan beïnvloed word indien jy EASAN saam met ander medisyne gebruik, insluitend die wat hieronder gelys word. Praat asseblief met jou dokter of apteker indien jy enige van die volgende medisyne neem:
- voorbehoedmiddels, wat hormone vrystel, wat voorbehoedpille, velplakkers, inplantings, en sekere Intra-uteriene toestelle (IUT) kan insluit, werk moontlik nie voldoende indien dit saam met EASAN geneem word nie. 'n Ander en addisionele nie-hormonale vorm van voorbehoeding moet gebruik word tydens behandeling met EASAN en vir tot 2 maande nadat EASAN gebruik is.
- siklosporien, takrolimus, sirolimus, everolimus (immuunonderdrukkers).
- alfentaniel, fentaniel (gebruik vir die behandeling van pyn).
- irinotekan, etoposied, vinorelbien, ifosfamied (medisyne gebruik vir die behandeling van kanker).
- kinidien (gebruik om 'n onreëlmatige hartklop te behandel).
- medisyne wat ergot alkaloïed derivate soos ergotamien en diërgotamien (gebruik vir behandeling van skeelhoofpyn) bevat.
- warfarien, asenokumarol (bloedverdunners; bloedtoetse mag benodig word).
- rifampisien, klaritromisien, telitromisien (antibiotika gebruik om infeksies te behandel).
- fenitoïen ('n medisyne gebruik om aanvalle se behandel).
- karbamasepien (gebruik om depressie en epilepsie te behandel).
- midasolam, triasolam, fenobarbital (medisyne wat gebruik word om jou kalm te maak of om te help slaap).
- Johanneskruid ('n kruie medisyne wat gebruik word om depressie te behandel).
- protease inhibeerders (gebruik om MIV infeksies te behandel).
- itrakonasool, vorikonasool, posakonasool (swamteenmiddels).
- nefasodoon (gebruik om depressie te behandel).
- diltiasem ('n medisyne wat gebruik word om hoë bloeddruk te behandel).
- kortikosteroïede (soos deksametasoon of metielprednisoloon).
- medisyne teen angs (soos alprasolam).
- tolbutamied ('n medisyne gebruik vir die behandel van diabetes).

Swangerskap, borsvoeding en fertiliteit
Indien jy swanger is of jou baba borsvoed, dink dat jy moontlik swanger kan wees of beplan om 'n baba te hê, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorg verskaffer vir advies voordat jy hierdie medisyne ontvang.

EASAN moet nie tydens swangerskap en borsvoeding toegedien word nie.

Vir inligting rakende voorbehoeding, sien 'Ander medisyne en EASAN'.
Dit is nie bekend of EASAN in menslike melk uitgeskei word nie, daarom word borsvoeding nie tydens behandeling met EASAN aanbeveel nie.

Bestuur en gebruik van masjinerie
Dit moet in ag geneem word dat party mense duiselig en slaperig kan word nadat hulle EASAN ontvang het. Indien jy duiselig of slaperig word, vermy om te bestuur of masjinerie te gebruik nadat jy EASAN ontvang het (sien 'Moontlike newe-effekte').

EASAN bevat laktose monohidraat:
EASAN bevat laktose monohidraat. Indien daar vir jou gesê is dat jy 'n onverdraagsaamheid teenoor sommige suikers het, moet jy nie EASAN gebruik nie.

3. Hoe om EASAN te neem
Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.

Daar sal nie van jou verwag word om EASAN vir jouself te gee nie. Dit sal aan jou gegee word deur iemand wat gekwalifiseerd is om dit te doen.

Die gewone dosis in volwassenes (18 jaar en ouer) is EASAN 150 mg op Dag 1 (dag van chemoterapie).

Jou dokter kan jou vra om ander medisyne te neem, insluitend 'n kortikosteroïed (soos deksametason) en 'n '5HT3-antagonis' (soos ondansetron) om naarheid en braking te voorkom. Raadpleeg jou dokter of apteker indien jy onseker is.

Die poeier word hersaamgestel en verdun voor gebruik. Die oplossing vir infusie word aan jou gegee deur 'n gesondheidsorg verskaffer, soos 'n dokter of verpleegster, via 'n intraveneuse infusie ('n drup) ongeveer 30 minute voordat jy met die chemoterapie behandeling in volwassenes begin.

Jou dokter sal vir jou sê hoe lank jou behandeling met EASAN sal duur. Indien jy onder die indruk is dat die effek van EASAN te sterk of te swak is, sê vir jou dokter of apteker.

Indien jy meer EASAN ontvang as wat jy behoort te ontvang
Aangesien 'n gesondheidsorg verskaffer EASAN vir jou gaan toedien, sal hy/sy die dosering kontrolleer. In die geval van oordosering, sal jou dokter egter die oordosis bestuur.

Indien jy 'n dosis EASAN oorgeslaan het
Aangesien 'n gesondheidsorg verskaffer EASAN sal toedien, is dit onwaarskynlik dat die dosis oorgeslaan sal word.

4. Moontlike newe-effekte
EASAN kan newe-effekte hê.
Nie alle newe-effkte wat vir EASAN gerapporteer is, is in hierdie inligtingstuk ingesluit nie. Sou jou algemene gesondheid versleg of jy enige onaangename gevolge ondervind terwyl jy EASAN ontvang, kontak jou gesondheidsorg verskaffer vir advies.

Indien enige van die volgende gebeur, hou op om EASAN te ontvang en sê vir jou dokter onmiddelik of gaan na die ongevalle afdeling van jou naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe, tong en mond of keel, wat dit moeilik kan maak om asem te haal of te sluk;
- Stevens-Johnson-sindroom/toksiese epidermale nekrolise (seldsame ernstige velreaksie)
- uitslag of gejeuk,
- floute.

Hierdie is almal baie ernstige newe-effkte. Indien jy dit het, mag jy 'n ernstige allergiese reaksie teen EASAN gehad het. Jy mag dringende mediese aandag of hospitalisering nodig hê.

Vertel jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy een van die volgende opmerk:
- Infusie plek reaksies (IPRs) by of naby die infusie plek. Die ernstigste IPR het gebeur met 'n sekere soort chemoterapie medisyne wat jou vel kan verbrand of blase maak (vesikant) met newe-effekte, insluitend pyn, swelling en rooiheid. Die afsterwe van velweefsel (nekrose) het gebeur by sommige mense wat hierdie tipe chemoterapie medisyne gekry het.

Hierdie is almal ernstige newe-effekte. Jy mag dringende mediese aandag nodig hê.

Sê vir jou dokter indien jy enige van die volgende waarneem:
Gereeld
- konstipasie, slegte spysvertering,
- hoofpyn,
- moegheid,
- verlies van eetlus,
- hik,
- verhoogde hoeveelheid lewerensieme in jou bloed.

Minder gereeld
- duiseligheid, slaperigheid,
- aknee, uitslag, netelroos
- angstigheid,
- winde opbring, naarheid, braking, sooibrand, maagpyn, droë mond, winde laat,
- verhoogde pynlike of brandende urinering,
- swakheid, voel oor die algemeen sleg,
- rooiheid van die gesig/vel, warm gloed,
- vinnige of onreëlmatige hartkloppings, verhoogde bloeddruk,
- koors met verhoogde risiko van infeksie, verlaging van rooibloedselle,
- pyn by die plek van infusie, rooiheid by die plek van infusie, gejeuk by die plek van infusie, inflammasie van die aar by die plek van infusie, verharding by die plek van infusie (pyn by die plek van inspuiting),
- sukkel om te dink, verlies van energie, smaakversteurings,
- sensitiwiteit van die vel vir son, oormatige sweet, olierige vel, sere op vel,
- euforie (gevoel van uiterste geluk), disoriëntasie,
- bakteriële infeksie, swaminfeksie,
- ernstige konstipasie, maag ulkus, inflammasie van die dunderm en dikderm, sere in die mond, opgeblasenheid,
- gereelde urinering, skei meer uriene uit as gewoonlik, teenwoordigheid van suiker of bloed in urine.
- borskas ongemak, swelling, verander in die manier van loop,
- hoes, slym agter in die keel, keel irritasie, nies, seer keel,
- oog afskeiding en gejeuk,
- lui geluid in die oor,
- spierspasmas, spierswakheid,
- oormatige dors,
- stadige hartklop, hart- en bloedvatsiekte,
- verlaging van witbloedselle, lae natriumvlakke in die bloed, gewigsverlies,
- verharding van plek van infusie.

Lig asseblief jou dokter of apteker in indien jy enige newe-effek ervaar wat nie in hierdie inligtingstuk genoem word nie.

Aanmelding van newe-effekte
Indien jy newe-effekte kry praat met jou dokter, apteker of verpleegkundige. Jy kan ook newe-effekte aan SAHPRA rapporteer via die **"6.04 Adverse Drug Reaction Reporting Form"**, wat aanlyn gevind kan word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8.
Deur newe-effekte aan te meld kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van EASAN.

5. Hoe om EASAN te bewaar
Bewaar alle medisyne buite bereik van kinders
- Bewaar in 'n yskas by 2 – 8 °C.
- Die hersaamgestelde en verdunde oplossing is stabiel vir 24 ure by 25 °C.
- Moet nie na die vervaldatum op die etiket/karton gebruik nie.

Neem alle ongebruikte medisyne terug na jou apteker.
Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) gooi nie.

6. Inhoud van die pak en ander inligting
Wat EASAN bevat
- Elke EASAN flessie bevat 245,3 mg van fosaprepitant dimeglumien gelykstaande aan 150 mg fosaprepitant vrye suur.
- Bevat suiker: laktose monohidraat 395 mg per flessie.
- Die ander bestanddele is dinatriumedetaat (E386), laktose monohidraat, polisorbaat 80 (E433), soutsuur (om die pH aan te pas), natriumhidroksied (om die pH aan te pas) en water vir inspuiting.

Hoe EASAN lyk en inhoud van die pak
EASAN is 'n wit of naaswit blokvormige vaste stof of poeier.
EASAN is verpak in 10 ml kleulose deursigte inspuitingsflessies wat van neutrale borosilikaat glasbuis gemaak word, met grys rubberstopper en aliminium proppie.
Pakgrootte: een flessie per kartonhouer.

Houer van die Registrasiesertifikaat
Juno Pharma SA (Edms) Bpk
3 Gwen Laan, 4de vloer
Sandton, 2031.
E-pos: pv@trinitypharma.co.za
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