FOSAPREPITANT- fosaprepitant injection, powder, lyophilized, for solution
NorthStar RxLLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FOSAPREPITANT FOR INJECTION safely and effectively. See full prescribing information for FOSAPREPITANT FOR INJECTION.
FOSAPREPITANT for injection, for intravenous use

Initial U.S. Approval: 2008

INDICATIONS AND USAGE

Fosaprepitant for injection is a substance P/neurokinin-1 (NK_1) receptor antagonist, indicated in adults, in combination with other antiemetic agents, for the prevention of (1):

- acute and delayed nausea and vomiting associated with initial and repeat coursesof highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC).

Limitations of Use (1)

- Fosaprepitant for injection has not been studied for treatment of established nausea and vomiting.

DOSAGE AND ADMINISTRATION

- Recommended Dosage (2.1)
- Administer fosaprepitant for injection as an intravenous infusion; complete the infusion approximately 30 minutes prior to chemotherapy.
- Adults: 150 mg on Day 1.
- Administer fosaprepitant for injection on Day 1 as an intravenous infusion over 20 to 30 minutes (adults).
- See Full Prescribing Information for dosages of concomitantantiemetic(s). (2.1)

DOSAGE FORMS AND STRENGTHS

Fosaprepitant for injection: 150 mg fosaprepitant, lyophilized cake or powder in single-dose vial for reconstitution (3)

CONTRAINDICATIONS

- Known hypersensitivity to any component of this drug. (4, 5.2)
- Concurrent use with pimozide. (4)

WARNINGS AND PRECAUTIONS

- CYP3A4 Interactions: Fosaprepitant is a weak inhibitor of CYP3A4, and aprepitant, the active moiety, is a substrate, inhibitor, and inducer of CYP3A4; see Full Prescribing Information for recommendations regarding contraindications, risk of adverse reactions, and dosage adjustment of fosaprepitant and concomitant drugs. (4, 5.1, 7.1, 7.2)
- Hypersensitivity Reactions (including anaphylaxis and anaphylactic shock): May occur during or soon after infusion; if symptoms occur, discontinue the drug. Do not reinitiate fosaprepitant if symptoms occur with previous use. (4, 5.2)
- Infusion Site Reactions (including thrombophlebitis, necrosis, and vasculitis): Majority of reactions reported in patients receiving vesicant chemotherapy. Avoid infusion into small veins. Discontinue infusion and administer treatment if a severe reaction develops. (5.3)
- Warfarin (a CYP2C9 substrate): Risk of decreased INR of prothrombin time; monitor INR in 2–week period, particularly at 7 to 10 days, following initiation of fosaprepitant. (5.4, 7.1)
- Hormonal Contraceptives: Efficacy of contraceptives may be reduced during and for 28 days following administration of fosaprepitant. Use effective alternative or back-up methods of contraception. (5.5, 7.1, 8.3)

ADVERSE REACTIONS

Most common adverse reactions in adults (≥2%) are: fatigue, diarrhea, neutropenia, asthenia, anemia, peripheral neuropathy, leukopenia, dyspepsia, urinary tract infection, pain in extremity. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact NorthStar RxLLC at 1-844-375-6847or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

See Full Prescribing Information for a list of clinicallysignificant drug interactions. (4, 5.1, 5.4, 5.5, 7.1, 7.2)
Pediatric use information is approved for Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s Emend (fosaprepitant) for injection. However, due to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2020

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Fosaprepitant for injection, in combination with other antiemetic agents, is indicated in adults for the prevention of:

- acute and delayed nauseaand vomiting associated with initial and repeat coursesof highly emetogenic cancer chemotherapy (HEC) including high-dose cisplatin.
- delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC)

Limitations of Use

- Fosaprepitant for injection has not been studied for the treatment of established nausea and vomiting. *Pediatric use information is approved for Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s Emend (fosaprepitant) for injection. However, due to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information.*

2 DOSAGE AND ADMINISTRATION

2.1 Prevention of Nausea and Vomiting Associated with HEC and MEC in Adult Patients

The recommended dosage of fosaprepitant for injection, dexamethasone, and a 5-HT_3antagonist for the prevention of nausea and vomiting associated with administration of HEC or MEC in adults is shown in Table 1 or Table 2, respectively. Administer fosaprepitant for injectionas an intravenous infusion on Day 1 over 20 to 30 minutes, completing the infusion approximately 30 minutes priorto chemotherapy.

Table 1Recommended Adult Dosing for the Prevention of Nausea and Vomiting Associated with HEC

	Day 1	Day 2	Day 3	Day 4
Fosaprepitant for injection	150 mg intravenously over 20 to 30 minutes	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 selected 5-HT_3 antagonist prescribing information for the recommended dosage	none	none	none

*Administer dexamethasone 30 minutes prior to chemotherapy treatment on Day 1 and in the morning on Days 2 through 4. Also administer dexamethasone in the evenings on Days 3 and 4. A 50% dosage reduction of dexamethasone on Days 1 and 2 is recommended to account for a drug interaction with fosaprepitant for injection [see ClinicalPharmacology (12.3)].

Table 2 Recommended Adult Dosing for the Prevention of Nausea and Vomiting Associated with MEC

	Day 1
Fosaprepitant for injection	150 mg intravenously over 20 to 30 minutes
Dexamethasone*	12 mg orally
5-HT_3 antagonist	See selected 5-HT_3 antagonist prescribing information for the recommended dosage

*Administer dexamethasone 30 minutes prior to chemotherapy treatment on Day 1. A 50% dosage reduction of dexamethasone is recommended to account for a drug interaction with fosaprepitant dimeglumine [see Clinical Pharmacology (12.3)].

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2.3 Preparation of Fosaprepitant for Injection

Table 5 Preparation Instructions for Fosaprepitant for Injection (150 mg)

Step 1	Aseptically inject 5 mL 0.9% Sodium Chloride Injection, USP into the vial. Assure that 0.9% Sodium Chloride Injection, USP is added to the vial along the vial wall in order to prevent foaming. Swirl the vial gently. Avoid shaking and jetting 0.9% Sodium Chloride Injection, USP into the vial.
Step 2	Aseptically prepare an infusion bag filled with 145 mL of 0.9% Sodium Chloride Injection, USP.
Step 3	Aseptically withdraw the entire volume from the vial and transfer it into the infusion bag containing 145 mL of 0.9% Sodium Chloride Injection, USP to yield a **total** volume of 150 mL and a final concentration of 1 mg/mL.
Step 4	Gently invert the bag 2 to 3 times.
Step 5	AdultsThe entire volume of the prepared infusion bag (150 mL) should be administered.
Step 6	Before administration, inspect the bag for particulate matter and discoloration. Discard the bag if particulate and/or discoloration are observed.

Caution: Do not mix or reconstitute fosaprepitant for injection with solutions for which physicaland chemical compatibility have not been established. Fosaprepitant for injection is incompatible with any solutions containing divalent cations (e.g., Ca^{2+}, Mg^{2+}), including Lactated Ringer's Solution and Hartmann's Solution.

Storage

The reconstituted final drug solution is stable for 24 hours at ambient room temperature [at or below 25°C (77°F)].

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3 DOSAGE FORMS AND STRENGTHS

Fosaprepitant for injection: 150 mg fosaprepitant, white to off white cake or powder in single-dose glass vial for reconstitution.

4 CONTRAINDICATIONS

Fosaprepitant is contraindicated in patients:

- who are hypersensitive to any component of the product Hypersensitivity reactions includinganaphylactic reactions, flushing, erythema, and dyspnea have been reported [see Warnings and Precautions (5.2), Adverse Reactions (6.2)].
- taking pimozide. Inhibition of CYP3A4 by aprepitant, the active moiety,could result in elevated plasma concentrations of this drug, which is a CYP3A4 substrate, potentially causing serious or life- threatening reactions, such as QT prolongation, a known adverse reaction of pimozide [see Warnings and Precautions(5.1)].

5 WARNINGS AND PRECAUTIONS

5.1 Clinically Significant CYP3A4 Drug Interactions

Fosaprepitant, a prodrug of aprepitant, is a weak inhibitor of CYP3A4, and aprepitant is a substrate, inhibitor, and inducer of CYP3A4.

- Use of fosaprepitant with other drugs that are CYP3A4 substrates, may result in increased plasma concentration of the concomitant drug.
  o Use of pimozidewith fosaprepitant is contraindicated due to the risk of significantly increased plasma concentrations of pimozide, potentially resulting in prolongation of the QT interval, a known adverse reactionof pimozide [see Contraindications (4)].
- Use of Fosaprepitant with strong or moderate CYP3A4 inhibitors (e.g., ketoconazole, diltiazem) may increase plasma concentrations of aprepitant and result in an increased risk of adversereactions related to fosaprepitant.
- Use of fosaprepitant with strong CYP3A4 inducers(e.g., rifampin) may result in a reductionin aprepitant plasma concentrations and decreased efficacy of fosaprepitant.
  See Table 7 and Table 8 for a listing of potentially significant drug interactions [see Drug Interactions (7.1, 7.2)].

5.2 Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis and anaphylactic shock, during or soon after infusionof fosaprepitant have occurred. Symptoms including flushing, erythema,dyspnea, hypotension and syncope have been reported [see Adverse Reactions (6.2)].

Monitor patients during and after infusion. If hypersensitivity reactions occur, discontinue the infusion and administer appropriate medicaltherapy. Do not reinitiate fosaprepitant in patients who experience thesesymptoms with previous use [see contraindications (4)].

5.3 Infusion Site Reactions

Infusion site reactions (ISRs) have been reported with the use of fosaprepitant for injection *[see Adverse Reactions (6.1)]*. The majority of severe ISRs, including thrombophlebitis and vasculitis, were reported with concomitant vesicant (anthracycline-based) chemotherapy administration, particularly when associated with extravasation. Necrosis was also reported in some patients with concomitant vesicant chemotherapy. Most ISRs occurred with the first, second or third exposure to single doses of fosaprepitant for injection and in some cases, reactions persisted for two weeks or longer. Treatment of severe ISRs consisted of medical, and in some cases surgical, intervention.

Avoid infusion of fosaprepitant for injection into small veins or through a butterfly catheter. If a severe ISR develops during infusion, discontinue the infusion and administer appropriate medical treatment.

5.4 Decrease in INR with Concomitant Warfarin

Coadministration of fosaprepitant with warfarin, a CYP2C9 substrate, may result in a clinically significant decrease in the International Normalized Ratio (INR) of prothrombin time *[see Clinical Pharmacology (12.3)]*. Monitor the INR in patients on chronic warfarin therapy in the 2-week period, particularly at 7 to 10 days, following initiation of fosaprepitant with each chemotherapy cycle *[see Drug Interactions (7.1)]*.

5.5 Risk of Reduced Efficacy of Hormonal Contraceptives

Upon coadministration with fosaprepitant, the efficacy of hormonal contraceptives may be reduced during administration of and for 28 days followingthe last dose of fosaprepitant *[see ClinicalPharmacology (12.3)]*. Advise patients to use effective alternative or back-up methods of contraception during treatment with fosaprepitant and for 1 month following administration of fosaprepitant *[see Drug Interactions (7.1), Use in Specific Populations (8.3)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions *[see Warnings and Precautions (5.2)]*
- Infusion Site Reactions *[see Warnings and Precautions (5.3)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug

and may not reflect the rates observed in clinical practice.

The overall safety of fosaprepitant for injection was evaluated in approximately 1600 adult patients.

Adverse Reactions in Adults for the Prevention of Nausea and Vomiting Associated with MEC

In an active-controlled clinical trial in patients receiving MEC, safety was evaluated in 504 patients receiving a single dose of fosaprepitant for injection in combination with ondansetron and dexamethasone (fosaprepitant dimeglumine regimen) compared to 497 patients receiving ondansetron and dexamethasone alone (standard therapy). The most common adverse reactions are listed in Table 6.

Table 6 Most Common Adverse Reactions in Patients Receiving MEC*

	Fosaprepitant for injection, ondansetron, and dexamethasone†(N=504)	**Ondansetron and dexamethasone‡(N=497)**
fatigue	15%	13%
diarrhea	13%	11%
neutropenia	8%	7%
asthenia	4%	3%
anemia	3%	2%
peripheral neuropathy	3%	2%
leukopenia	2%	1%
dyspepsia	2%	1%
urinary tract infection	2%	1%
pain in extremity	2%	1%

*Reported in ≥2% of patients treated with the fosaprepitant dimeglumine regimen and at a greater incidence than standard therapy.

† fosaprepitant dimeglumine regimen

‡Standard therapy

Infusion-site reactions were reported in 2.2% of patients treated with the fosaprepitant dimeglumine regimen compared to 0.6% of patients treated with standard therapy. The infusion-site reactions included: infusion-site pain (1.2%, 0.4%), injection-site irritation (0.2%, 0.0%), vessel puncture-site pain (0.2%, 0.0%), and infusion-site thrombophlebitis (0.6%, 0.0%), reported in the fosaprepitant dimeglumine regimen compared to standard therapy, respectively.

Adverse Reactions in Adults for the Prevention of Nausea and Vomiting Associated with HEC

In an active-controlled clinical study in patients receiving HEC, safety was evaluated for 1143 patients receiving a single dose of fosaprepitant for injection compared to 1169 patients receiving the 3-day regimen of oral aprepitant [see Clinical Studies (14.1)]. The safety profile was generallysimilar to that seen in the MEC study with fosaprepitant and prior HEC studies with aprepitant. However,infusion-site reactionsoccurred at a higher incidence in patients in the fosaprepitant group (3.0%) comparedto those in the aprepitant group (0.5%). The following additional infusion-site reactions occurredin the HEC study and were not reported in the MEC study described above: infusion-site erythema(0.5%, 0.1%), infusion-site pruritus (0.3%, 0.0%), and infusion-site induration (0.2%, 0.1%), reported in the fosaprepitant group compared to the aprepitant group, respectively.

Because fosaprepitant is converted to aprepitant, those adverse reactions associated with aprepitant might also be expected to occur with fosaprepitant for injection. See the full prescribing information for aprepitant capsules for complete safety information regarding studies performed with oral aprepitant.

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6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of fosaprepitant. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possibleto reliably estimatetheir frequency or establish a causal relationship to drug exposure.

Skin and subcutaneous tissue disorders: pruritus, rash, urticaria, Stevens-Johnson syndrome/toxic epidermalnecrolysis. *[see Warnings and Precautions (5.2)].*

Immune system disorders: hypersensitivity reactions including anaphylaxis and anaphylactic shock *[see Contraindications (4), Warnings and Precautions (5.2)].*

Nervous system disorders: ifosfamide-induced neurotoxicity reported after fosaprepitant and ifosfamide coadministration.

7 DRUG INTERACTIONS

7.1 Effect of Fosaprepitant/Aprepitant on the Pharmacokinetics of Other Drugs

When administered intravenously, fosaprepitant, a prodrug of aprepitant, is converted to aprepitant within 30 minutes.Therefore, drug interactions following administration of fosaprepitant for injection are likely to occur with drugs that interact with oral aprepitant.

Fosaprepitant, given as a single 150-mg dose, is a weak inhibitor of CYP3A4, and the weak inhibition of CYP3A4 continues for 2 days after single dose administration. Single dose fosaprepitant does not induce CYP3A4. Aprepitant is a substrate, an inhibitor, and an inducer of CYP3A4. Aprepitant is also an inducerof CYP2C9 *[seeClinical Pharmacology (12.3)].*

Some substrates of CYP3A4 are contraindicated with fosaprepitant *[see Contraindications (4)].*

Dosage adjustment of some CYP3A4 and CYP2C9 substrates may be warranted, as shown in Table 7.

Table 7 Effects of Fosaprepitant/Aprepitant on the Pharmacokinetics of Other Drugs

CYP3A4 Substrates	
Pimozide	
Clinical Impact	Increased pimozide exposure
Intervention	Fosaprepitant is contraindicated *[see Contraindications (4)].*
Benzodiazepines	
Clinical Impact	Increased exposure to midazolam or other benzodiazepines metabolized via CYP3A4(alprazolam, triazolam) may increase the risk of adverse reactions *[see Clinical Pharmacology (12.3)].*
Intervention	Monitor for benzodiazepine-related adverse reactions.
Dexamethasone	
Clinical Impact	Increased dexamethasone exposure *[see Clinical Pharmacology (12.3)].*
Intervention	Reducethe dose of oral dexamethasone by approximately 50% *[see Dosageand Administration (2.1)].*
Methylprednisolone	
Clinical Impact	Increased methylprednisolone exposure *[see Clinical Pharmacology (12.3)].*
Intervention	Reduce the dose of oral methylprednisolone by approximately 50% on Days 1 and 2 for patients receiving HEC and on Day 1 for patients receiving MEC.Reduce the dose of intravenous methylprednisolone by 25% on Days 1 and 2 for patients receiving HEC and on Day 1 for patients receiving MEC.
Chemotherapeutic agents that are metabolized by CYP3A4	
Clinical Impact	Increased exposure of the chemotherapeutic agentmay increase the risk of adverse reactions *[see Clinical Pharmacology (12.3)].*
Intervention	Vinblastine, vincristine, or ifosfamide or other chemotherapeutic agentsMonitor for chemotherapeutic-related adverse reactions.Etoposide, vinorelbine, paclitaxel, and docetaxelNo dosage adjustment needed.
Hormonal Contraceptives	
Clinical Impact	Decreased hormonal exposure duringadministration of and for 28 days after administration of the last dose of fosaprepitant *[see Warnings and Precautions (5.5), Use in Specific Populations (8.3), and Clinical Pharmacology (12.3)].*
Intervention	Effective alternative or back-up methods of contraception (such as condoms and spermicides) should be used during treatment with fosaprepitant and for 1 month following administration of fosaprepitant.
Examples	birth control pills, skin patches, implants, and certain IUDs
CYP2C9 Substrates	
Warfarin	
Clinical Impact	Decreased warfarin exposure and decreased prothrombin time (INR) *[see Warnings and Precautions (5.4), Clinical Pharmacology (12.3)].*
Intervention	In patients on chronic warfarin therapy, monitor the prothrombin time(INR) in the2-week period, particularly at 7 to 10 days, following administration of fosaprepitant with each chemotherapy cycle.
Other	
5-HT_3 Antagonists	
Clinical Impact	No change in the exposure of the 5-HT_3 antagonist *[see Clinical Pharmacology (12.3)].*
Intervention	No dosage adjustment needed
Examples	ondansetron, granisetron, dolasetron

7.2 Effect of Other Drugs on the Pharmacokinetics of Fosaprepitant/Aprepitant

Aprepitant is a CYP3A4 substrate *[see Clinical Pharmacology (12.3)].* Co-administration of fosaprepitant with drugs that are inhibitors or inducers of CYP3A4 may result in increased or decreased plasma concentrations of aprepitant, respectively, as shown in Table 8.

Table 8 Effects of Other Drugs on Pharmacokinetics of Fosaprepitant/Aprepitant

Moderate to Strong CYP3A4 Inhibitors	
Clinical Impact	Significantly increased exposure of aprepitant may increase the risk of adverse reactions associated with fosaprepitant *[see Adverse Reactions (6.1) and Clinical Pharmacology (12.3)].*
Intervention	Avoid concomitant use of fosaprepitant
Examples	Moderate inhibitor: diltiazemStrong inhibitors:ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir, nelfinavir
Strong CYP3A4Inducers	
Clinical Impact	Substantially decreased exposure of aprepitant in patients chronically taking a strong CYP3A4 inducer may decrease the efficacy of fosaprepitant *[see Clinical Pharmacology (12.3)].*
Intervention	Avoid concomitant use of fosaprepitant.
Examples	rifampin, carbamazepine, phenytoin

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are insufficient data on use of fosaprepitant in pregnant women to inform a drug associated risk. In animal reproduction studies, no adverse developmental effects were observed in rats or rabbits exposed during the period of organogenesis to systemic drug levels (AUC) approximately equivalent to the exposure at the recommended human dose (RHD) of 150 mg *[seeData].*

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. In the U.S. general population, the estimated background risk of majorbirth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

In embryofetal development studies in rats and rabbits, aprepitant was administered during the period of organogenesis at oral dosesup to 1,000 mg/kg twicedaily (rats) and up to the maximum tolerated dose of 25 mg/kg/day (rabbits). No embryofetal lethality or malformations were observed at any dose level in eitherspecies. The exposures(AUC) in pregnantrats at 1,000 mg/kg twice daily and in pregnant rabbits at 25 mg/kg/day were approximately equivalent to the exposure at the RHD of 150 mg. Aprepitant crosses the placenta in rats and rabbits.

8.2 Lactation

Risk Summary

Lactation studies have not been conducted to assess the presence of aprepitant in human milk, the effects on the breastfed infant,or the effects on milk production. Aprepitant is present in rat milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for fosaprepitant and any potential adverse effects on the breastfed infant from fosaprepitant or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Contraception

Upon administration of fosaprepitant, the efficacy of hormonal contraceptives may be reduced. Advise females of reproductive potential using hormonal contraceptives to use an effective alternative or back-up non-hormonal contraceptive (such as condoms and spermicides) during treatment with fosaprepitant and for 1 month following the last dose *[see Drug Interactions (7.1),Clinical Pharmacology (12.3)].*

8.4 Pediatric Use

The safety and effectiveness of fosaprepitant dimeglumine for the prevention of nausea and vomiting associated with HEC or MEC have not been established in patients less than 6 months of age.

Juvenile Animal Toxicity Data

In juvenile dogs treated with fosaprepitant, changes in reproductive organs were observed. In juvenile rats treated with aprepitant, slight changes in sexual maturation were observed without an effect on reproduction. No effects on neurobehavior, sensory and motor function, or learning and memory were observed in rats.

In a toxicity study in juvenile dogs treated with fosaprepitant from postnatal day 14 (equivalent to a newborn human) to day 42 (approximately equivalent to a 2 year old human), decreased testicular weight and Leydig cell size were seen in the males at 6 mg/kg/day and increased uterine weight, hypertrophy of the uterus and cervix, and edema of vaginal tissues were seen in females from 4 mg/kg/day. A study was also conducted in young rats to evaluate the effects of aprepitant on growth and on neurobehavioral and sexual development. Rats were treated at oral doses up to the maximum feasible dose of 1000 mg/kg twice daily from the early postnatal period (Postnatal Day 10 (equivalent to a newborn human) through Postnatal Day 58 (approximately equivalent to a 15 year old human)). Slight changes in the onset of sexual maturation were observed in female and male rats; however, there were no effects on mating, fertility, embryonic-fetal survival, or histomorphology of the reproductive organs. There were no effects in neurobehavioral tests of sensory function, motor function, and learning and memory.

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8.5 Geriatric Use

Of the 1649 adult cancer patients treated with intravenous fosaprepitant in HEC and MEC clinical studies, 27% were aged 65 and over, while 5% were aged 75 and over. Other reported clinical experience with fosaprepitant has not identified differences in responses between elderly and younger patients. In general, use caution when dosing elderly patients as they have a greater frequency of decreased hepatic, renal or cardiac function and concomitant disease or other drug therapy *[see Clinical Pharmacology (12.3)].*

8.6 Patients with Hepatic Impairment

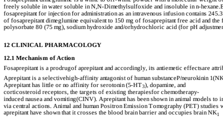
The pharmacokinetics of aprepitant in patients with mild and moderate hepatic impairment were similar to those of healthy subjects with normal hepatic function.No dosage adjustment is necessary for patients with mild to moderatehepatic impairment (Child-Pugh score 5 to 9). Thereare no clinical or pharmacokinetic data in patientswith severe hepaticimpairment (Child-Pugh score greater than 9). Therefore, additional monitoring for adverse reactions in these patients may be warranted when fosaprepitant is administered *[see Clinical Pharmacology (12.3)].*

10 OVERDOSAGE

There is no specificinformation on the treatment of overdosage with fosaprepitant or aprepitant.In the event of overdose, fosaprepitant should be discontinued and general supportive treatment and monitoring should be provided. Because of the antiemetic activity of fosaprepitant, drug-induced emesis may not be effective in cases of fosaprepitant overdosage.Aprepitant is not removedby hemodialysis.

11 DESCRIPTION

Fosaprepitant for injection is a sterile, lyophilized formulation containing fosaprepitant dimeglumine,a prodrug of aprepitant a substance P/neurokinin-1 (NK_1) receptor antagonist, an antiemetic agent, chemically described as 1 Deoxy-1-(methylamino)-D-glucito[3-[[(2R,3S)-2-[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]-3-(4 fluorophenyl)-4-morpholinyl]methyl]-2,5-dihydro-5-oxo-1H-1,2,4-triazol-1-yl]phosphonate(2:1) (salt).Its empirical formula is $C_{23} H_{22} F_7 N_4 O_6 P \bullet 2(C_7 H_{17} NO_5)$ and its structural formula is:



Fosaprepitant dimeglumine is a white to off-white powder with a molecular weight of 1004.83. It is freely soluble in water soluble in N,N-Dimethylsulfoxide and insoluble in n-hexane.Each vial of fosaprepitant for injection for administration as an intravenous infusion contains 245.3 mg of fosaprepitant dimeglumine equivalent to 150 mg of fosaprepitant free acid and the following inactive ingredients: edetatedisodium (5.4 mg), lactose anhydrous(375 mg), polysorbate 80 (75 mg), sodium hydroxide and/orhydrochloric acid (for pH adjustment).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Fosaprepitant is a prodrugof aprepitant and accordingly, its antiemetic effectsare attributable to aprepitant.

Aprepitant is a selectivehigh-affinity antagonist of human substanceP/neurokinin 1(NK1) receptors. Aprepitant has little or no affinity for serotonin (5-HT_3), dopamine, and corticosteroid receptors, the targets of existing therapiesfor chemotherapy-induced nausea and vomiting(CINV). Aprepitant has been shown in animal models to inhibit emesis induced by cytotoxicchemotherapeutic agents, such as cisplatin, via central actions. Animal and human Positron Emission Tomography (PET) studies with aprepitant have shown that it crosses the blood brain barrier and occupies brain NK_1

receptors. Animal and humanstudies have shown that aprepitant augmentsthe antiemetic activityof the 5-
HT_3 -
receptor antagonist ondansetron and the corticosteroid dexamethasone and inhibitsboth the acuteand delayed phasesof cisplatin-
induced emesis.

12.2 Pharmacodynamics

Cardiac Electrophysiology

In a randomized, double-blind, positive-controlled, thorough QTc study, a single 200-
mgdose of fosaprepitant (approximately 1.3 times the recommended dose) had no effect on the QTc interval.

12.3 Pharmacokinetics

Aprepitant after Fosaprepitant Administration

Following administration of a single intravenous 150-mg dose of fosaprepitant, a prodrug of aprepitant administered as a 20-minute infusion to healthy subjects, the mean $AUC_{0-\infty}$ of aprepitant was 37.4 (±14.8) mcg•hr/mL and the mean maximal aprepitant concentration (C_{max}) was 4.2 (±1.2) mcg/mL. Plasma concentrations of fosaprepitant are below the limits of quantification (10 ng/mL) within 30 minutes of the completion of infusion.

Distribution

Aprepitant is greater than 95% bound to plasma proteins. The mean apparent volume
of distribution at steady state(Vd_{ss}
) was approximately 70 L in humans.Aprepitant crossesthe blood brainbarrier in humans[see Clinical Pharmacology (12.1)].

Elimination

Metabolism

Fosaprepitant is converted to aprepitant in in vitro incubations with human liver preparations and in S9 preparations from multiple other human tissues including kidney, lung and ileum. Thus, it appears that the conversion of fosaprepitant to aprepitant can occur in multiple extrahepatic tissues in addition to the liver.Aprepitant undergoes extensive metabolism. In vitro studies using human liver microsomes indicate that aprepitant is metabolized primarily by CYP3A4 with minor metabolism by CYP1A2 and CYP2C19. Metabolism is largely via oxidation at the morpholine ring and its side chains. No metabolism by CYP2D6, CYP2C9, or CYP2E1 was detected.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, havebeen identified in human plasma.

Excretion

Following administration of a singleintravenous 100-mg dose of [^{14}C]-
fosaprepitant to healthy subjects, 57% of the radioactivity was recovered in urine and 45% in feces.Aprepitant is eliminated primarilyby metabolism; aprepitant is not renally excreted. The apparent terminal half-liferanged from approximately 9 to 13 hours.

Specific Populations

Age:Geriatric Population

Following oral administration of a single 125-mg dose of aprepitant on Day 1 and 80 mg once daily on Days 2 through 5, the AUC_{0-24hr} of aprepitant was 21% higher on Day 1 and 36% higher on Day 5 in elderly (65 years and older) relativeto 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 [see Use in Specific Populations (8.5)].

Sex

Following oral administration of a single dose of aprepitant, ranging from 40 mg to 375 mg, the AUC_{0-24hr} and C_{max} are 9% and 17% higher in females as compared with males. The half-life of aprepitantis approximately 25% lower in femalesas compared with males and T_{max} occursat approximately the same time. These differences are not considered clinically meaningful.

Race/Ethnicity

Following oral administration of a single dose of aprepitant, ranging from 40 mg to 375 mg, the AUC_{0-24hr} and C_{max} are approximately 27% and 19% higher in Hispanicsas compared with Caucasians. The AUC_{0-24hr} and C_{max} were 74% and 47% higher in Asians as compared to Caucasians. There was no difference in AUC_{0-24hr} or C_{max} between Caucasians and Blacks.These differences are not considered clinicallymeaningful.

Renal Impairment

A single 240-mg oral dose of aprepitant was administered to patients with severe renal impairment (creatinine clearance less than 30 mL/min/1.73 m^2 as measured by 24-hour urinary creatinine clearance) and to patients with end stage renal disease(ESRD) requiring hemodialysis.

In patients with severe renal impairment, the $AUC_{0-\infty}$ of total aprepitant (unbound and protein bound) decreased by 21% and Cmax decreased by 32%, relative to healthy subjects (creatinine clearance greater than 80 mL/min estimated by Cockcroft-Gault method). In patients with ESRD undergoing hemodialysis, the $AUC_{0-\infty}$ of total aprepitant decreased by 42% and C_{max} decreased by 32%. Due to
Hemodialysis conducted4 or 48 hours after dosing had no significant effect on the pharmacokineticsof aprepitant; less than 0.2% of the dose was recovered in the dialysate.

Hepatic Impairment

Fosaprepitant is metabolized in various extrahepatic tissues; therefore hepaticimpairment is not expected to alter the conversion of fosaprepitant to aprepitant.Following administration of a single 125-mg oral dose of aprepitant on Day 1 and 80 mg once daily on Days 2 and 3 to patients with mild hepatic impairment (Child-Pugh score 5 to 6), the AUC_{0-24hr} of aprepitant was 11% loweron Day 1 and 36% lower on Day 3, as comparedwith healthy subjectsgiven the same regimen. In patientswith moderate hepatic impairment (Child-Pugh score 7 to 9), the AUC_{0-24hr} 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_{0-24hr} are not considered clinically meaningful. There
are no clinical or pharmacokinetic data in patientswith severe hepaticimpairment (Child-Pugh scoregreater than 9) [see Use in Specific Populations (8.6)]

Body Mass Index (BMI)

For every 5 kg/m^2 increase in BMI, AUC_{0-24hr} and C_{max} of aprepitant decrease by 9% and 10%. BMI of subjects in the analysis ranged from 18 kg/m^2 to 36 kg/m^2. This change is not considered clinically meaningful.

Pediatric use information is approved for Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s Emend (fosaprepitant) for injection. However, due to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information.

Drug Interactions Studies

Fosaprepitant, given as a single 150-
mg dose, is a weak inhibitor of CYP3A4, with no evidence of inhibition or induction of CYP3A4 observed on Day 4. The weak inhibition of CYP3A4 continues for 2 days after single dose administration of fosaprepitant. Aprepitant is a substrate, an inhibitor, and an
inducer of CYP3A4. Aprepitant is also an inducer of CYP2C9.Fosaprepitant or aprepitant is unlikely to interact with drugs that are substrates for the P glycoprotein transporter.

Effects of Fosaprepitant/Aprepitant on the Pharmacokinetics of Other Drugs

CYP3A4 Substrates

Midazolam:

Fosaprepitant 150 mg administered as a single intravenous dose on Day 1 increased the $AUC_{0-\infty}$ of midazolam by approximately 1.8-fold on Day 1 and had no effect on Day 4
when midazolam was coadministered as a singleoral dose of 2 mg on Days 1 and 4. [see Drug interactions (7.1)].

Corticosteroids:

Dexamethasone: Fosaprepitant administered as a single 150 mg intravenous dose on Day 1 increased the AUC_{0-24hr} of dexamethasone, administered as a single 8-mg oral dose on Days 1, 2,
and 3, by approximately 2-
foldon Days 1 and 2 [see Dosageand Administration (2.1),Drug Interactions (7.1)].

Methylprednisolone: When oral aprepitant as a 3-day regimen (125-mg/80-mg/80-mg) was administered with intravenous methylprednisolone 125 mg on Day 1 and oral methylprednisolone 40 mg on Days 2 and 3, the AUC of methylprednisolone was increased by 1.34-fold on Day 1 and by 2.5-fold on Day 3 [see Drug Interactions (7.1)].Chemotherapeutic agents:Docetaxel: In a pharmacokinetic study, oral aprepitant administered as a 3-day regimen (125 mg/80-mg/80-mg) did not influence the pharmacokinetics of docetaxel.

Vinorelbine:

In a pharmacokinetic study,oral aprepitant administered as a 3-day regimen (125 mg/80-mg/80-
mg) did not influence the pharmacokinetics of vinorelbine to a clinically significant degree.Oral contraceptives: When oral aprepitant was administered as a 3-day regimen (125-mg/80-mg/80 mg) with ondansetron and dexamethasone, and coadministered with an oral contraceptive containing ethinyl estradiol and norethindrone, the trough concentrations of both ethinyl estradiol and norethindrone were reduced by as much as 64% for 3 weeks post-
treatment [see Drug Interactions (7.1)].

CYP2C9 substrates (Warfarin, Tolbutamide):Warfarin: A single125-
mg dose of oral aprepitant was administered on Day 1 and 80 mg/day on Days 2 and 3 to subjects who were stabilized on chronic warfarin therapy. Although there was no
effect of oral aprepitant on the plasma AUC of R(+) or S(-
) warfarindetermined on Day 3, there was a 34% decrease in S(-) warfarin trough concentration accompanied by a 14% decrease in the prothrombin time (reported as International Normalized Ratio or INR) 5 days after completion of dosing with oral aprepitant [see Drug Interactions (7.1)].

Tolbutamide:

Oral aprepitant, when given as 125 mg on Day 1 and 80 mg/day on Days 2 and 3, decreased the AUC of tolbutamide by 23% on Day 4, 28% on Day 8, and 15% on Day 15, when
a single dose of tolbutamide 500 mg was administered prior to the administration of the 3-
day regimen of oral aprepitant and on Days 4, 8, and 15. This effectwas not considered clinically important.

Other Drugs

P-glycoprotein substrates: Aprepitant is unlikely to interact with drugs that are substrates for the P-
glycoprotein transporter, as demonstrated by the lack of interaction of oral aprepitant with digoxin in a clinical drug interaction study.

5-HT_3 antagonists: In clinicaldrug interaction studies,aprepitant did not have clinically important effects on the pharmacokinetics of ondansetron, granisetron, or hydrodolasetron (the active metabolite of dolasetron).

Effect of Other Drugson the Pharmacokinetics of Fosaprepitant/Aprepitant

Rifampin:

When a single 375-mgdose of oral aprepitant was administered on Day 9 of a 14-day regimen of 600 mg/day of rifampin, a strong CYP3A4 inducer, the AUC of aprepitant decreased approximately 11-fold and the mean terminal half-life decreased approximately 3-fold [see Drug Interactions (7.2)]..

Ketoconazole:

When a single 125-mg dose of oral aprepitant was administered on Day 5 of a 10-day regimen of 400 mg/day of ketoconazole, a strong CYP3A4 inhibitor, the AUC of aprepitant increased approximately 5-
foldand the mean terminal half-life of aprepitant increased approximately 3-fold [see Drug Interactions (7.2)].

Diltiazem: In a study in 10 patients with mild to moderate hypertension, administration of 100 mg of fosaprepitant as an intravenous infusion with 120 mg of diltiazem, a moderate CYP3A4 inhibitor administered three times daily, resulted in a 1.5-fold increase in the aprepitant AUC and a1.4-fold increase in the diltiazem AUC.

When fosaprepitant was administered with diltiazem, the mean maximum decrease in diastolic blood pressure was significantly greater than that observed with diltiazem alone [24.3 ± 10.2 mm Hg with fosaprepitant versus 15.6 ± 4.1 mm
Hg without fosaprepitant]. The mean maximumdecrease in systolic blood pressure was also greater after co-administration of diltiazem with fosaprepitant than administration of diltiazem alone [29.5 ± 7.9 mm Hg with fosaprepitant versus 23.8 ± 4.8 mm Hg without fosaprepitant]. Co-administration of fosaprepitant and diltiazem; however, did not result in any additional clinically significant changes in heart rate or PR interval, beyond those changes observed with diltiazem alone [see Drug Interactions (7.2)].

Paroxetine: Coadministration of once daily doses of oral aprepitant 170 mg, with paroxetine 20 mg once daily, resulted in a decrease in AUC by approximately 25% and C_{max} by approximately 20% of both aprepitant and paroxetine. This effect was not considered clinically important.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment Of Fertility

Carcinogenesis

Carcinogenicity studieswere conducted in Sprague-Dawley rats and in CD-
1 mice for 2 years. In the rat carcinogenicity studies, animals were treated with oral doses ranging from 0.05 to 1,000 mg/kg twice daily. The highest dose produced systemic exposuresto aprepitant approximately equivalent to (female rats) or less than (male rats) the adulthuman exposure at the RHD of 150 mg. Treatment with aprepitant at doses of 5 to 1,000 mg/kg twicedaily caused an increase in the incidences of thyroid follicular cell adenomas and carcinomas in male rats. In female rats, it produced hepatocellular adenomas at 5 to 1,000 mg/kg twicedaily and hepatocellular carcinomas and thyroidfollicular cell adenomasat 125 to 1000mg/kg twice daily. In the mouse carcinogenicity studies,the animals were treated with oral doses ranging from 2.5 to 2,000 mg/kg/day. The highest dose produced a systemic exposureapproximately 2
times the adult human exposure at the RHD of 150 mg. Treatment with aprepitant
produced skin fibrosarcomas
at 125 and 500 mg/kg/day doses in male mice. Carcinogenicity studies were not conducted with fosaprepitant.

Mutagenesis

Aprepitant and fosaprepitant were not genotoxicin the Ames test, the human lymphoblastoid cell (TK6) mutagenesis test, the rat hepatocyte DNA strand break test, the Chinese hamster ovary (CHO) cell chromosome aberration test and the mouse micronucleustest.

Impairment of Fertility

Fosaprepitant, when administered intravenously, is rapidly convertedto aprepitant. In the fertilitystudies conducted with fosaprepitant and aprepitant, the highest systemic exposures to aprepitant were obtained following oral administration of aprepitant. Oral aprepitant did not affectthe fertility or general reproductive performance of male or female rats at doses up to the maximum feasible dose
of 1,000 mg/kg twice daily (providingexposure in male rats lower than the exposure at the recommended adult human dose of 150 mg and exposurein female rats approximately equivalent to the adult human exposure).

14 CLINICAL STUDIES

14.1 Prevention of Nausea and Vomiting Associated with HEC in Adults

In a randomized, parallel,double-blind, active-controlled study, fosaprepitant for injection 150 mg as a single intravenous infusion(N=1147) was comparedto a 3-day oral aprepitant regimen (N=1175) in patientsreceiving a HEC regimen that included cisplatin (≥70 mg/m^2). All patients in both groups received
dexamethasone and ondansetron (see Table 11). Patient demographics were similar betweenthe two treatment groups. Of the total 2322 patients, 63% were men, 56% White,26% Asian, 3% American Indian/Alaska Native,2% Black, 13% Multi-Racial, and 33% Hispanic/Latino ethnicity. Patient ages ranged from 19 to 86 years of age, with a mean age of 56 years.Other concomitant chemotherapy agents commonly administered were fluorouracil (17%),gemcitabine (16%), paclitaxel (15%), and etoposide (12%).

Table 11: Treatment Regimens in Adult HEC Trial*

	Day 1	Day 2	Day 3	Day 4
	Fosaprepitant Regimen			
Fosaprepitant for injection	150 mg intravenously over 20 to 30 minutes approximately 30 minutes priorto chemotherapy	none	none	none
Oral dexamethasone†	12 mg	8 mg	8 mg twice daily	8 mg twice daily
Ondansetron	Ondansetron‡	none	none	none
	Oral Aprepitant Regimen			
Aprepitant capsules	125 mg	80 mg	80 mg	none
Oral dexamethasone§	12 mg	8 mg	8 mg	8 mg
Ondansetron	Ondansetron‡	none	none	none

* fosaprepitant for injection placebo, aprepitant capsules placebo and dexamethasone placebo (in the evenings on Days 3 and 4) were used to maintain blinding.

†Dexamethasone was administered 30 minutes prior to chemotherapy treatment on Day 1 and in the morning on Days 2 through 4. Dexamethasone was also administered in the evenings on Days 3 and 4. The 12 mg dose of dexamethasone on Day 1 and the 8 mg once daily dose on Day 2 reflects a dosage adjustment to account for a drug interaction with the fosaprepitant for injection regimen [see Clinical Pharmacology (12.3)].

‡Ondansetron 32 mg intravenous was used in the clinical trials of fosaprepitant. Although this dose was used in clinical trials, this is no longer the currently recommended dose. Refer to the ondansetron prescribing information for the current recommended dose.

§Dexamethasone was administered 30 minutes prior to chemotherapy treatment on Day 1 and in the morning on Days 2 through 4. The 12 mg dose of dexamethasone on Day 1 and the 8 mg once daily dose on Days 2 through 4 reflects a dosage adjustment to account for a drug interaction with the oral aprepitant regimen [see Clinical Pharmacology(12.3)].

The efficacy of fosaprepitant for injection was evaluated based on the primary and secondary endpoints listed in Table 12 and was shown to be non-inferior to that of the 3-day oral aprepitant regimen with regard to complete response in each of the evaluated phases. The pre-specified non-inferiority margin for complete response in the overall phase was 7%. The pre-specified non-inferiority margin for complete response in the delayedphase was 7.3%. Thepre-specified non-inferiority margin for no vomiting in the overall phase was 8.2%.

Table 12Percent of Adult Patients Receiving HEC Responding by Treatment Group and Phase — Cycle 1

ENDPOINTS	Fosaprepitant for Injection Regimen (N = 1106) *%	Oral Aprepitant Regimen (N = 1134) *%	Difference†(95% CI)
PRIMARY ENDPOINT			
Complete Response‡			
Overall§	71.9	72.3	-0.4 (-4.1, 3.3)
SECONDARYENDPOINTS			
Complete Response‡			
Delayedphase¶	74.3	74.2	0.1 (-3.5, 3.7)
No Vomiting			
Overall§	72.9	74.6	-1.7 (-5.3, 2.0)

*N: Number of patients included in the primary analysis of completeresponse.

†Difference and Confidence interval (CI) were calculated using the method proposed by Miettinen and Nurminen and adjusted for Gender.

‡Complete Response = no vomiting and no use of rescue therapy.

§Overall = 0 to 120 hours post-initiation of cisplatin chemotherapy.

¶Delayed phase = 25 to 120 hours post-initiation of cisplatin chemotherapy.

14.2 Prevention of Nausea and Vomiting Associated with MEC in Adults

In a randomized, parallel, double-blind, active comparator-controlled study, fosaprepitant for injection 150 mg as a single intravenous infusion (N=502) in combination with ondansetron and dexamethasone (fosaprepitant dimeglumine regimen) was compared with ondansetron and dexamethasone alone (standard therapy) (N=498) (see Table 13) in patients receiving a MEC regimen. Patient demographics were similar between the two treatment groups. Of the total 1,000 patients included in the efficacy analysis, 41% were men, 84% White, 4% Asian, 1% American Indian/Alaska Native, 2% Black, 10% Multi-Racial, and 19% Hispanic/Latino ethnicity. Patient ages ranged from 23 to 88 years of age, with a mean age of 60 years. The most commonly administered MEC chemotherapeutic agents were carboplatin (51%), oxaliplatin (24%), and cyclophosphamide (12%).

Table 13 Treatment Regimens in Adult MEC Trial*

	Day 1	**Day 2**	**Day 3**
Fosaprepitant Regimen			
Fosaprepitant for Injection	150 mg intravenously over 20 to 30 minutes approximately 30 minutes prior to chemotherapy	none	none
Oral Dexamethasone†	12 mg	none	none
Oral Ondansetron‡	8 mg for 2 doses	none	none
Standard Therapy			
Oral Dexamethasone	20 mg	none	none
Oral Ondansetron‡	8 mg for 2 doses	8 mg twice daily	8 mg twice daily

*Fosaprepitant for injection placebo and dexamethasone placebo (on Day 1) were used to maintain blinding.

†Dexamethasone was administered 30 minutes prior to chemotherapy treatment on Day 1. The 12 mg dose reflects a dosage adjustment to account for a drug interaction with the Fosaprepitant for injection regimen [see Clinical Pharmacology (12.3)].

‡The first ondansetron dose was administered 30 to 60 minutes prior to chemotherapy treatment on Day 1 and the second dose was administered 8 hours after first ondansetron dose.

The primary endpoint was complete response (defined as no vomiting and no rescue therapy) in the delayed phase (25 to 120 hours) of chemotherapy-induced nausea and vomiting. The results by treatment group are shown in Table 14.

Table 14 Percent of Adult Patients Receiving MEC Responding by Treatment Group

ENDPOINTS	**Fosaprepitant for Injection Regimen (N = 502)*%**	**Standard Therapy Regimen (N = 498)* %**	**P-Value**	**Treatment Difference (95% CI)**
PRIMARYENDPOINT				
Complete Response†				
Delayed phase‡	78.9	68.5	<0.001	10.4 (5.1, 15.9)

*N: Number of patients included in the intention to treat population.

†Complete Response = no vomiting and no use of rescue therapy.

‡Delayed phase = 25 to 120 hours post-initiation of chemotherapy.

16 HOW SUPPLIED/STORAGE AND HANDLING

Single-dose glass vial containing 150 mg of fosaprepitant as a white to off white lyophilized cake or powder for reconstitution. Supplied as follows:

NDC- 16714-929-0 1 vial per carton

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDAapproved patientlabeling (Patient Information).

Hypersensitivity

Advise patientsthat hypersensitivity reactions, including anaphylaxis and anaphylactic shock, have been reported in patients taking fosaprepitant. Advisepatients to seek immediate medical attention if they experience signs or symptoms of a hypersensitivity reaction, such as hives, rash and itching, skin peeling or sores, flushing, difficulty in breathingor swallowing, or dizziness, rapid or weak heartbeat or feeling faint [see warnings and precautions (5.2)].

Infusion Site Reactions

Advise patients to seek medical attention if they experience new or worsening signs or symptoms of an infusion site reaction, such as erythema, edema, pain, necrosis, vasculitis, or thrombophlebitis at or near the infusion site [see Warnings and Precautions (5.3)].

Drug Interactions

Advise patients to discuss all medications they are taking, including other prescription, non-prescription medication or herbal products[see Contraindications (4), Warnings and Precautions (5.1)].

Warfarin:

Instruct patientson chronic warfarintherapy to follow instructions from their healthcare provider regarding blood draws to monitor their INR during the 2-week period, particularly at 7 to 10 days, followinginitiation of fosaprepitant with each chemotherapy cycle [see Warningsand Precautions (5.4)].

Hormonal Contraceptives:

Advise patients that administration of fosaprepitant may reduce the efficacy of hormonal contraceptives. Instruct patients to use effectivealternative or back-upmethods of contraception (such as condomsand spermicides) during treatment with fosaprepitant and for 1 month following administration of fosaprepitant [see Warnings and Precautions (5.5),Use in Specific Populations (8.3)].

Mfd. for: Northstar Rx LLC

Memphis, TN 38141

Mfd. by: MSN Laboratories Pvt. Ltd,

Telangana - 509 228 , India.

Issued: 0320

Patient Information

Fosaprepitant (FOS a PREP i tant) for Injection

Read this patientinformation before you start receivingfosaprepitant for injection and each time you are scheduled to receive fosaprepitant for injection. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is fosaprepitant for injection?

Fosaprepitant for injection is a prescription medicine used with other medicines that treat nausea and vomiting in patients 18 years of age and older to prevent nausea and vomiting caused by certain anti-cancer (chemotherapy) medicines.

Fosaprepitant for injection is not used to treat nausea and vomiting that you already have.

It is not known if fosaprepitant for injection is safe and effective in children less than 6 months of age.

Who should not recieve fosaprepitant for injection?

Do not receive fosaprepitant for injection if you:are allergic to fosaprepitant, aprepitant, or any of the ingredients in fosaprepitant for injection. See the end of this leaflet for a complete list of the ingredients in fosaprepitant for injection.are taking pimozide (ORAP®)

What should I tell my healthcare provider before receiving fosaprepitant for injection?

Before receiving fosaprepitant for injection, tell your healthcare provider if you:

have liver problems

are pregnant or plan to become pregnant. It is not known if fosaprepitant for injection can harm your unborn baby.

Women who use birth control medicines containing hormones to prevent pregnancy (birth control pills, skin patches, implants, and certain IUDs) should also use a backup method of birth control that does not contain hormones, such as condoms and spermicides, during treatment with fosaprepitant for injection and for 1 month after receiving fosaprepitant for injection.

are breastfeeding or plan to breastfeed. It is not known if fosaprepitant for injection passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you receive fosaprepitant for injection.

Tell your healthcare provider about all the medicinesyou take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.Fosaprepitant for injection may affect the way other medicines work, and other medicines may affect the way fosaprepitant for injection works, causing serious side effects.Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How will I receive fosaprepitant for injection?

Adults 18 years of age and older:Fosaprepitant for injection will be given on Day 1 of chemotherapy treatment. It will be given to you by intravenous (IV) infusion in your vein about 50 to 60 minutes before you start your chemotherapy treatment.If you take the blood thinner medicine warfarin sodium (COUMADIN®, JANTOVEN®), your healthcare provider may do blood tests after you receive fosaprepitant for injection to check your blood clotting.

What are the possible side effectsof fosaprepitant for injection?

Fosaprepitant for injection may cause serious side effects, including:

Serious allergic reactions. Allergic reactions can happen with fosaprepitant for injection and may be serious. Tell your doctor or nurse right away if you have hives, rash, itching, flushing or redness of your face or skin, trouble breathing or swallowing, dizziness, a rapid or weak heartbeat, or you feel faint during or soon after you receive fosaprepitant for injection, as you may need emergency medical care.

Severe skin reactions, which may include rash, skin peeling, or sores, may occur.

Infusion site reactions (ISR) at or near the infusion site have happened with fosaprepitant for injection.

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. Most ISR can happen with the first, second, or third dose and some can last up to 2 weeks or longer. Tell your healthcare provider right away if you get any infusion site side effects.

In adults, the most common side effects of fosaprepitant for injection include:

tiredness	feeling weak or numb in your arms and legs
diarrhea	painful, difficult, or changes in your digestion (dyspepsia)
low white blood cell and red blood cell counts	urinary tract infection
weakness	pain in your arms and legs

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all of the possible side effects of fosaprepitant for injection. For more information ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of fosaprepitant for injection?

If you would like more information about fosaprepitant for injection, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about fosaprepitant for injection that is written for health professionals. For more information about fosaprepitant for injection call 1-844-375-6847.

What are the ingredients in fosaprepitant for injection?

Active ingredient: fosaprepitant dimeglumine

Inactive ingredients: edetate disodium, lactose anhydrous, polysorbate 80, sodium hydroxide and/ or hydrochloric acid (for pH adjustment).The brands listed are trademarks or registered trademarks of their respective owners and are not affiliated with and do not endorse MSN Pharmaceuticals Inc.

Pediatric use information is approved for Merck Sharp & Dohme Corp., a subsidiary of Merck & Co.,Inc.'s Emend (fosaprepitant) for injection. However, due to Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.'s marketing exclusivity rights, this drug product is not labeled with that pediatric information

This Patient Information has been approved by the U.S. Food and Drug Administration.

Mfd. for: Northstar Rx LLC

Memphis, TN 38141

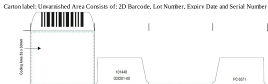
Mfd. by: MSN Laboratories Pvt. Ltd,

Telangana - 509 228 , India.

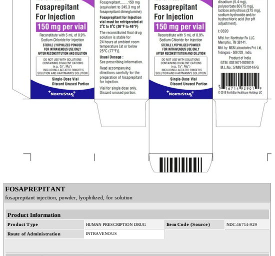
Issued: 0320

PACKAGE LABEL PRINCIPAL DISPLAY PANEL SECTION

Vial Label:



Carton label: Unvarnished Area Consists of: 2D Barcode, Lot Number, Expiry Date and Serial Number



FOSAPREPITANT fosaprepitant injection, powder, lyophilized, for solution			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:16714-929
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Fosaprepitant Dimeglumine (UNII: D35FM8T64X) (Aprepitant - UNII:1NF15YR6UY)	Fosaprepitant	150 mg in 5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Edetate Sodium (UNII: MP1J8420LU)	5.4 mg in 5 mL

Sulpiride Lactose (UNII: 5VVXL8P9MR)	375 mg in 5 mL
Polysorbate 80 (UNII: 6OZP39ZG8H)	75 mg in 5 mL
Sodium Hydroxide (UNII: 55X04QC32I)	
Hydrochloric Acid (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16714-929-01	5 in 1 CARTON	03/20/2020	
1		5 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA207999-5	03/20/2020	

Labeler - NorthStar RxLLC (830914643)

Establishment

Name	Address	ID/FEI	Business Operations
MPA Laboratories Lab.		918178419.52	analysis(16714-929) , manufacture(16714-929)