PATIENT INFORMATION LEAFLET

FOSEMAZON 150 mg Powder For Concentrate Solution For I.V. Infusion

Administrated Intravenously

Sterile

- ***Active Substance:*** Each vial contains 245,32 mg fosaprepitant dimeglumin equivalent to 150 mg fosaprepitant.
- ***Excipient:*** Disodium edetate, polysorbate 80, lactose anhydrus, sodium hydroxide, hydrochloric acid, water for injection.

Before using this medicine, read all of this PATIENT INFORMATION LEAFLET carefully. Because, this leaflet includes important information for you.

- *Keep this PATIENT INFORMATION LEAFLET. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow these instructions exactly as written. Do not use **higher or lower** dose other than your recommended dose.*

The following subjects are covered herein:

1. What FOSEMAZON is and what it is used for?

FOSEMAZON contains the active substance fosaprepitant that is converted into aprepitant in your body. Fosaprepitant is a prodrug of aprepitant, and when administered intravenously, it is quickly turns into aprepitant. Aprepitant belongs to a group of drugs called" neurokinin 1 (NK_1) receptor antagonists". There is a special area in the brain that controls nausea and vomiting. FOSEMAZON works preventing signals in that area, thus reducing nausea and vomiting.

FOSEMAZON is used with other drugs to prevent nausea and vomiting caused by chemotherapy (cancer treatment), which is the trigger of strong and moderate nausea and vomiting by adults, adolescents and children aged 6 months or older.

FOSEMAZON lyophilized powder for infusion is white and almost white lyophilized powder in colorless glass vial.

2. What you need to know before you use FOSEMAZON?

DO NOT USE ASİMPLEX under the following circumstances

If;

- You are allergic to Fosaprepitanta, aprepitanta, polysorbate 80 or any of the other ingredients,
- Do not use Fossazone if you are using any of the following drugs:
  -Pimozide (used to treat psychiatric illnesses)
  -Terfenadine, astemizole (used for hay fever and other allergic conditions) and
  -Sisaprid (used in the treatment of digestive problems).

Before you start using FOSEMAZON, inform your doctor, your doctor may change your treatment.

USE FOSEMAZON CAREFULLY in the following situations

Before the medical treatment, If you have liver disease, inform your physician because liver is important that metabolizing medication in your body. Your doctor will need to follow condition of your liver.

Before using FOSEMAZON, talk with your physician, pharmacist or nurse.

Children and adolescents

Since it has not been studied in this population, FOSEMAZON should not be used in children younger than 6 months or less than 6 kg.

If these warnings are valid for you, even at any time in the past, please consult your doctor.

Using FOSEMAZON with food and drink

It has no interaction with food and drinks due to the route of administration.

Pregnancy

Please consult your physician or pharmacist before taking the medicine.

You should not use this medicine during pregnancy unless absolutely necessary. If you are pregnant or breastfeeding, if you are thinking of becoming pregnant or having a baby, consult your doctor before taking this medicine.

See the section on 'Use in combination with other drugs' for information on birth control.

If you realize that you are pregnant during your treatment, immediately consult your physician or pharmacist.

Lactation

Please consult your physician or pharmacist before taking the drug.

It is not known whether FOSEMAZON is excreted in human milk, therefore, breastfeeding is not recommended while using this medicine. It is important to inform your doctor if you are breastfeeding or planning to breastfeed before taking this medicine.

Ability to drive and use machines
It should be consider that some patients experience dizziness or sleepiness after FOSEMAZON treatment. If you feel dizziness or sleepiness after FOSEMAZON treatment, avoid to drive and use machines. (See possible side effects section)

Important information about some of the excipient contained in FOSEMAZON

This medical product contains less from 1 mmol (23 mg) each vial; so it can be considered essentially free of sodium.

Use in combination with other drugs
FOSEMAZON may affect other medicines during and after treatment. FOSEMAZON should not be used in combination with certain drugs such as pimozide, terfenadine, astemizole and cisapride, or dose adjustment may be required. (See Do not use FOSEMAZON in the following situations)

When FOSEMAZON is used with the following drugs, the effect of FOSEMAZON or other drugs may change. If you are using any of the drugs listed below, consult your physician or pharmacist:

- Birth control drugs (birth control pills, skin patches, vaccination, and some hormone-containing intrauterine devices) may not work as well when taken with FOSEMAZON. Another method of contraception (one or more hormone-free forms of birth control) should be used during FOSEMAZON treatment and up to 2 months after using FOSEMAZON.
- Cyclosporine, tacrolimus, sirolimus, everolimus (immune system suppressants),
- Alfentanil, fentanyl (used to treat pain),
- Quinidine (used to treat irregular heartbeat),
- Irinotecan, etoposide, vinorelbine, ifosfamide (drugs used in cancer treatment),
- Medicines containing ergot alkaloid derivatives such as ergotamine and diergotamine (used in the treatment of migraine)
- Warfarin, acenocoumarol (blood thinners; blood tests may need to be done),
- Rifampicin, clarithromycin, telithromycin (antibiotics used to treat infections),
- Phenytoin (used to treat seizures)
- Carbamazepine (used in the treatment of depression and epilepsy),
- Midazolam, triazolam, phenobarbital (calm and sleep aid drugs),
- St. John’s Wort (herbal preparation used in the treatment of depression),
- Protease inhibitors (used in the treatment of HIV infection),
- Ketoconazole other than shampoo (used to treat Cushing's syndrome - when the body supplies excessive amounts of cortisol),
- Itraconazole, voriconazole, posaconazole (antifungals),
- Nefazodone (used to treat depression),
- Diltiazem (a medicine used to treat high blood pressure),
- Corticosteroids (such as dexamethasone),

- Anti-anxiety medications (such as alprazolam),
- Tolbutamide (used to treat diabetes).

If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.

3. How to use FOSEMAZON?

- **Instructions regarding correct use and dosage/administration frequency:**

Your physician will determine the dose of your medicine depending on your illness and will apply it to you.

The recommended dose of FOSEMAZON in adults (18 years and over) is 150 mg fosaprepitant on the 1st day (chemotherapy day). The recommended dose should be administered approximately 30 minutes before chemotherapy on day 1, at least within 20-30 minutes.

The recommended dosage of FOSEMAZON in children and adolescents (6 months to 17 years old) depends on the age and weight of the patient. Depending on the chemotherapy treatment, there are two ways FOSEMAZON can be applied:

- FOSEMAZON is given only on the 1st day (a single chemotherapy day).

- FOSEMAZON is given on the 1st, 2nd and 3rd days (single or multiple chemotherapy days).

FOSEMAZON is administered intravenously for more than 30 minutes and the infusion is completed approximately 30 minutes before chemotherapy for pediatric patients 12 years and older. The infusion is completed approximately 30 minutes before chemotherapy, FOSEMAZON is administered intravenously for longer than 60 minutes for children younger than 12 years.

- **Administration route and method**

FOSEMAZON vial content is injected into the vial with 5 mL of sodium chloride (0.9%) solution over the wall of the vial to prevent foam formation and the vial is slowly dissolved without shaking. After the contents of the vial are completely dissolved, the contents of the vial (5mL) are diluted by transferring them into the infusion bag containing 145 mL of sodium chloride (0.9%) solution. Ready-to-use solution for infusion contains 1mg / mL fosaprepitant.

About 30 minutes before starting chemotherapy treatment in adults or about 30-60 minutes before starting chemotherapy treatment in children and adolescents, the infusion solution is given to you by an intravenous infusion (drip) by a healthcare professional such as a doctor or nurse. Your physician will ask you to take corticosteroids (eg dexamethasone) and other medicines containing "5-HT3 antagonists" (such as ondansetron) to prevent nausea and vomiting. If you are not sure, consult your doctor or pharmacist.

- **Different age groups:**

Use in children:

FOSEMAZON should not be used in children younger than 6 months or less than 6 kg.

Use in the elderly:

Dose adjustment is not required for elderly patients.

- **Special use cases:**

Kidney failure:

No dose adjustment is required for patients with renal insufficiency or end-stage renal failure patients undergoing hemodialysis.

Liver failure:

No dose adjustment is required for patients with mild hepatic impairment. There are limited data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment. FOSEMAZON should be used with caution in these patients.

If you have an impression that the effect of FOSEMAZON is too strong or too weak, talk to your physician or pharmacist.

If you have taken FOSEMAZON than you should have:

Since this medicine will be administered by specialist healthcare professionals, it is unlikely that you will be given more or less medication than is necessary.

If you have used FOSEMAZON more than you should have or more than prescribed consult a physician or a pharmacist.

If you forget to take FOSEMAZON:

Since this medicine will be administered by specialist healthcare professionals, its use is unlikely to be forgotten.

Do not take a double dose to make up for forgotten doses.

Effects that may occur when treatment with FOSEMAZON is terminated

Your physician will tell you when the medicine will be given to you as long as it is designed and when it will be stopped.

If you have any other questions on the use of this medicine, ask your physician or pharmacist.

4. Possible side effects

People who are sensitive to the ingredients of FOSEMAZON may have side effects, like all medicines.

If you experience any of the effects listed below, cease using FOSEMAZON and IMMEDIATELY consult your physician or go to the nearest emergency room:
- Hives, rash, itching, difficulty breathing or swallowing, or a severe drop in blood pressure (frequency not known, cannot be estimated from available data); these are signs of an allergic reaction.
- Infusion site reactions (IBR) at or near the infusion site. The most serious IBR has occurred with certain chemotherapy drugs (vesiccants) that burn or blister your skin, with side effects including pain, swelling, and redness. Death (necrosis) of skin tissue has been observed in some people receiving this type of chemotherapy medication.

These are all very serious side effects. If you have one of them, it means you have a serious allergy to FOSEMAZON. You may need urgent medical attention or hospitalization.

All of these very serious side effects are very rare.

The other adverse effects are as follows:

Side effects are classified following below levels of frequency.

Very common (may affect more than 1 in 10 people)
Common (may affect less than 1 in 100 people)
Uncommon (may affect less than 1-10 in 1000 people)
Rare (may affect less than 1-10 in 10,000 people)
Very Rare (may affect less than 1 in 10,000 people)
Not known (Cannot be estimated from the available data)

Common:
- Constipation, dyspepsia,
- Headache,
- Tiredness,
- Loss of appetite,
- Hiccup,
- An increase in the amount of liver enzymes in the blood.

Uncommon:
- Dizziness, sleepiness,
- Acne, rash,
- Restlessness,
- Burping, nausea, vomiting, heartburn, stomach pain, dry mouth, burping,
- Increase in pain and burning during urination,
- Weakness, generally feeling unwell,
- Redness of the face / body, hot sweating,
- Fast or irregular heartbeat, increased blood pressure,
- High fever with risk of infection, decrease in red blood cell count,
- Pain at the infusion site, redness at the infusion site, itching at the infusion site, infusion site vascular inflammation.

Rare:
- Difficulty thinking, lack of energy, taste disturbance
- Sun sensitivity of the skin, excessive sweating, oily skin, skin sores, itchy rash, Stevens Johnson syndrome / toxic epidermal necrolysis (a rare and severe skin reaction),
- Euphoric mood (feeling of extreme happiness), disorientation (disorientation),
- Bacterial infection, fungal infection,
- Severe constipation, stomach ulcer, inflammation of the small intestine and large intestine, mouth sores, swelling,
- Frequent urination, excessive urine production, sugar or blood in the urine,
- Chest discomfort, swelling, change in gait,
- Cough, sputum, throat irritation, sneezing, sore throat,
- Eye irritation and itching
- Tinnitus,

- Muscle spasms, muscle weakness,
- Excessive thirst,
- Slow heartbeat, cardiovascular disease,
- Decrease in white blood cells, decrease in the amount of sodium in the blood, weight loss,
- The infusion site has hardened.

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

5. How to store FOSEMAZON?

Keep FOSEMAZON out of the sight and reach of children, and in its original packaging.

Store in a refrigerator (2° C - 8° C).

After dissolution and dilution, its chemical and physical stability in use is 24 hours at 25 ° C.

The product must be immediately used due to microbiological reasons. If not used immediately used, the storage duration and conditions during application are under the responsibility of the user and should normally not be longer than 24 hours at 2 to 8 ° C.

Use in compliance with the expiry date.

Do not use FOSEMAZON after the expiration date printed on its packaging. If you notice any irregularities in the product and/or its packaging, do not use FOSEMAZON.

Do not put in trash if the product is expired or out of use! Give it to collection system specified by Ministry of Environment and Urbanization.

Marketing Authorization Holder:

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This patient information leaflet was last approved on 25/06/2020.

INFORMATION PROVIDED HERE AFTER IS INTENDED FOR THE MEDICAL PERSONNEL APPLYING THE DRUG PRODUCT

Posology and method of administration

Adults

The recommended dose is 150 mg administered as an infusion over 20-30 minutes on Day 1, initiated approximately 30 minutes prior to chemotherapy.

FOSEMAZON should be administered in conjunction with a corticosteroid and a 5-HT3 antagonist as specified in the tables below.

The following regimens are recommended to prevent nausea and vomiting associated with emetogenic cancer chemotherapy.

High Emetogenic Chemotherapy Regimen

	1st Day	2nd Day	3rd Day	4th Day
FOSEMAZON	150 mg intravenously	None	None	None
Dexamethasone	12 mg orally	8 mg orally	8 mg orally twice daily	8 mg orally twice daily
5-HT_3 antagonists	Standard dose of 5-HT3 antagonists. See the product information of the selected 5-HT3 antagonist for appropriate dosage information.	None	None	None

Dexamethasone should be administered 30 minutes before chemotherapy treatment on day 1 and in the morning from day 2 to day 4. Dexamethasone should be applied in the evening on the 3rd and 4th days. Dexamethasone dose explains the interactions of the active substance interactions.

Moderate Emetogenic Chemotherapy Regimen

	Day 1
FOSEMAZON	150 mg intravenously
Dexamethasone	12 mg orally
5-HT_3 antagonists	Standard dose of 5-HT3 antagonists. See the product information of the selected 5-HT3 antagonist for appropriate dosage information.

Dexamethasone should be administered 30 minutes before chemotherapy treatment on day 1. The dose of dexamethasone accounts for active substance interactions

The Pediatric Population

Pediatric patients 6 months old and older and not less than 6 kg:

The recommended dose regimen of IVEMEND, to be administered with a 5-HT3 antagonist, with or without a corticosteroid, for the prevention of nausea and vomiting associated with administration of single or multi-day chemotherapy regimens of Highly Emetogenic Chemotherapy (HEC) or Moderately Emetogenic Chemotherapy (MEC), is shown in Table 1. Single day chemotherapy regimens include those regimens in which HEC or MEC is administered for a single day only. Multi-day chemotherapy regimens include chemotherapy regimens in which HEC or MEC is administered for 2 or more days.

An alternative dosage regimen that can be used in one-day chemotherapy regimens is shown in table 2.

Dosing for Single or Multi-Day Chemotherapy Regimens

FOSEMAZON is administered as an intravenous infusion via a central venous catheter on days 1, 2, and 3 for pediatric patients receiving single or multi-day HEC or MEC regimens.

Table 1. Recommended dosing for the prevention of nausea and vomiting due to single or multi-day regimens of HEC or MEC in paediatric patients

	Population	**1st Day**	**2nd Day**	**3rd Day**
FOSEMAZON*	Pediatric patients 12 years of age or older	115 mg intravenously	80 mg intravenously	80 mg intravenously
	Pediatric patients aged 6 months to 12 years and not less than 6 kg	3 mg/kg intravenously Maximum Dose 115 mg	2 mg/kg intravenously Maximum Dose 80 mg	2 mg/kg intravenously Maximum Dose 80 mg
Dexamethasone**	All pediatric patients	When a corticosteroid such as dexamethasone is co-administered, administer 50% of the recommended corticosteroid dose between days 1 and 4.		
5-HT_3 antagonists	All pediatric patients	See selected 5-HT3 antagonist prescribing information for recommended dose.		

* FOSEMAZON is administered intravenously for more than 30 minutes and the infusion is completed approximately 30 minutes before chemotherapy for pediatric patients 12 years and older. The infusion is completed approximately 30 minutes before chemotherapy, FOSEMAZON is administered intravenously for longer than 60 minutes for children younger than 12 years.

** Dexamethasone should be administered 30 minutes before chemotherapy treatment on day 1.

Alternative Dosing for Single Day Chemotherapy Regimens
FOSEMAZON is administered as an intravenous infusion via a central venous catheter on day 1 for pediatric patients receiving single day HEC or MEC regimens.

Table 2. Alternative dosing for the prevention of nausea and vomiting due to single day regimens of HEC or MEC in paediatric patients

	Population	**1st Day**
FOSEMAZON*	Pediatric patients 12 years of age or older	150 mg intravenously
	Pediatric patients between 2 and 12 years old	4 mg/kg intravenously Maximum Dose 150 mg
	Pediatric patients between 6 months and 2 years of age and not less than 6 kg	5 mg/kg intravenously Maximum Dose 150 mg
Dexamethasone**	All pediatric patients	When a corticosteroid such as dexamethasone is co-administered, administer 50% of the recommended corticosteroid dose between days 1 and 2.
5-HT_3 antagonists	All pediatric patients	See selected 5-HT3 antagonist prescribing information for recommended dose.

* FOSEMAZON is administered intravenously for more than 30 minutes and the infusion is completed approximately 30 minutes before chemotherapy for pediatric patients 12 years and older. The infusion is completed approximately 30 minutes before chemotherapy, FOSEMAZON is administered intravenously for longer than 60 minutes for children younger than 12 years.
** Dexamethasone should be administered 30 minutes before chemotherapy treatment on day 1.

The safety and efficacy of fosaprepitant dimeglumine in infants younger than 6 months have not been established. No data available.

General
Efficacy data in combination with other corticosteroids and 5-HT3 antagonists are limited. See Section 4.5 for additional information on co-administration with corticosteroids. See Summary of Product Characteristics for co-administered 5-HT3 antagonist medicinal products.

Method of Administration:

FOSEMAZON should be administered intravenously only and should not be given by the intramuscular and subcutaneous route. Intravenous administration in adults occurs preferably through a running intravenous infusion over 20-30 minutes. Intravenous administration in pediatric patients 6 months and older is recommended through central venous catheter and should be administered over 30 minutes in patients 12 years of age or older, or over 60 minutes in pediatric patients younger than 12 years. FOSEMAZON is not for use as a bolus injection or undiluted solution.

Instructions for reconstituting and diluting FOSEMAZON:

1. Inject 5 mL of sodium chloride 9 mg / mL (0.9%) solution for injection into the vial over the wall of the vial to prevent foaming. Solve slowly turning the vial and make sure that it is completely dissolved, avoid shaking the vial.
2. Prepare the infusion bag with 145 mL of sodium chloride 9 mg / mL (0.9%) solution for injection; for example, removing 105 mL from the infusion bag containing 250 mL of sodium chloride 9 mg / mL (0.9%) solution for injection.
3. Withdraw all solution from the vial and transfer to an infusion bag containing 145 mL of sodium chloride 9 mg / mL (0.9%) solution for injection to obtain a total volume of 150 mL. Gently invert the bag 2-3 times (See How to use FOSEMAZON?).
4. Determine the volume to be administered according to the recommended dose, from this infusion bag prepared. (See Summary of Product Characteristics, Section 4.2).

Adults

The entire volume of the prepared infusion bag (150 mL) can be applied.

Pediatric Patients

The volume to be administration in patients aged 12 years and over is calculated as follows:

- Administration volume (mL) is equivalent to recommended dose (mg).

The volume to be administered in patients aged 6 months to 12 years is calculated as follows:

- Administration volume (mL)= recommended dose (mg/kg) x weight (kg)

- **Note: Maximum doses should not exceed. (See Summary of Product Characteristics, Section 4.2)**

5. If necessary, for volumes less than 150 ml, the calculated volume prior to administration in an appropriate size can be transferred into the infusion bag or syringe.

   After reconstitution and dilution, the final solution is stable for 24 hours at 25 ° C.

   Parenteral drugs should be visually inspected for particulate matter and discoloration to verify the suitability of solution and package prior to administration.

   The sight of the diluted solution should be the same as the sight of the solvent.

   Discard all remaining solutions and waste materials. Unused medical products or waste materials should be disposed of in accordance with local requirements.

   The medicinal product should not be reconstituted or mixed with solutions in which physical and chemical compatibility is not achieved (see Summary of Product Characteristics, section 6.2).