5) Hematological Disorders
On rare occasions, agranulocytosis may develop, and occasionally patients develop signs of anemia, eosinophilia, granulocytopenia and thrombocytopenia.
6) Gastrointestinal Tract
Such side effects as stomatitis, nausea, vomiting, abdominal pain, diarrhea and anorexia may occasionally develop.
7) Skin
Rarely develop eruption, urticaria, erythema, and itching.
8) Injection Site
Phlebitis develops on rare occasions, and angialgia may occasionally occur.
9) Others
There are occurrences of dull headache, oral dryness, vertigo and chest discomfort, and occasionally patients may experience a feeling of pressure on the chest.

(3) Usage in Pregnancy
The safety of this drug for administration during the course of pregnancy has not yet been established. Therefore, it is desirable to avoid the use of this drug in females who are, or may be pregnant.

(4) Precautions in Application
1) FOSMICIN FOR I.V. USE should be administered only by the intravenous route. In addition, it is desirable for the administration to be performed by intravenous drip infusion whenever possible.
2) It is known that phlebitis and angialgia may occur following the intravenous administration of this drug. Therefore, sufficient care should be taken with regard to the selection of the injection site and the technique to be employed for the administration, and the rate at which the drug solution is injected should be as slow as possible.

(5) Other Precautions
1) In the case of patients who are put on longterm therapy using this drug, it is desirable to periodically perform liver and kidney function tests, as well as hematological tests.
2) FOSMICIN FOR I.V. USE contains 14.5 mEq of sodium per g (Potency) ; accordingly, care should be taken when administering it to patients who need to reduce their sodium intake due to heart failure, kidney failure, hypertension, etc.

CAUTIONS

When FOSMICIN FOR I.V. USE is dissolved, heat is released ; this has no detrimental effect on the drug or its activity, and is therefore no cause for worry.

STORAGE CONDITION

Store below 30°C and the drug should be used before expiration date stated on the label. After reconstitution, the solution stable at 30±2°C and 5±3°C for 24 hours.

HOW SUPPLIED

FOSMICIN 1 g, Reg. No. DKL9715302444A1
FOSMICIN 2 g, Reg. No. DKL9715302444B1

ON MEDICAL PRESCRIPTION ONLY

HARUS DENGAN RESEP DOKTER

meiji

PT MEIJI INDONESIAN
PHARMACEUTICAL INDUSTRIES
Bangil - Pasuruan, Jawa Timur - Indonesia

Licensed by
Meiji Seika Pharma Co., Ltd.
Tokyo, Japan

(FOM, FOL 0122 J)

New Broad-Spectrum Antibiotic with Unique Action Mechanism

FOSMICIN®

FOR I.V. USE
(Fosfomycin Sodium)

FOSFOMYCIN is a new antibiotic, first discovered in 1967 in a culture of *Streptomyces fradiae* which was isolated from a Spanish soil sample. Now it is produced by chemical synthesis.

Fosfomycin is quite different from other antibiotics in that it has a very simple and unique chemical structure and a unique mode of action. Cross resistance between fosfomycin and other antibiotics has not been demonstrated. No binding to serum proteins has been reported. In animal studies, there has been no evidence of fosfomycin's possessing antigenicity.

FOSMICIN FOR I.V. USE contains fosfomycin sodium and is given by intravenous administration. It is effective against infections due to *Pseudomonas aeruginosa, Proteus sp., Serratia marcescens* and multi-drug resistant strains of *Staphylococcus aureus* and *E. coli.*

COMPOSITION and PROPERTIES

Composition
* FOSMICIN for Injection 1 g / vial :
each vial contains 1 g (Potency) of fosfomycin sodium
* FOSMICIN for Injection 2 g / vial :
each vial contains 2 g (Potency) of fosfomycin sodium

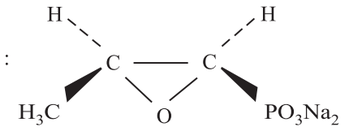
pH and Osmotic Pressure Ratio

pH	Osmotic Pressure Ratio	Concentration
7.4 - 7.5	1.2 - 1.3	20 mg (Potency)/ml (Distilled water for Injection)
7.4 - 7.5	3.1	50 mg (Potency)/ml (Distilled water for Injection)
7.4 - 7.5	2.3	20 mg (Potency)/ml (5 % Glucose solution)
7.4 - 7.5	4.1 - 4.2	50 mg (Potency)/ml (5 % Glucose solution)

Osmotic pressure ratio : determined by cryoscopy using physiological saline as a control.

Fosfomycin sodium is a white crystalline powder having a slightly salty taste. It is very soluble in water, sparingly soluble in methanol, and practically insoluble in acetone, ethyl acetate, ether and chloroform. Its decomposition point is over 300°C.

Chemical structure :



Generic name : Fosfomycin sodium
Abbreviation : FOM
Chemical name : Disodium (–) – (IR,2S) – (1,2 – epoxypropyl) phosphonate
Molecular formula : $C_3H_5Na_2O_4P$
Molecular weight : 182.02

Nama Produk	Brosur Fosmicin Universal (Page 1)	Tanggal Desain	Keterangan
Ukuran	220 x 270 mm	- 05 Maret 2012 - 15 Desember 2021	- Perubahan logo Meiji dan nama lisensor - Perubahan suhu penyimpanan menjadi Store below 30°C dan penambahan penyimpanan pasca rekonstitusi
Bahan	HVS 60 g		
Warna	Black		

1. Fosfomycin belongs to an entirely new group of antibiotics ; in addition, fosfomycin has a low molecular weight and a simple chemical structure.
2. It acts bactericidally on Gram-positive and Gram-negative pathogens.
3. Fosfomycin shows no cross resistance with other groups of antibiotics, and it is also effective against pathogens that are resistant to multiple drugs.
4. A synergistic effect has been reported between fosfomycin and other antibiotics such as β -lactam antibiotics, aminoglycosides, macrolide, tetracyclin, chloramphenicol, rifampicin, and lincomycin.
5. Fosfomycin has a unique mode of action, i.e., it is taken into bacterial cells in high concentration via the active transport system and inhibits the initial stage of bacterial cell wall synthesis. In contrast, β-lactam antibiotics inhibit the final stage.
6. It diffuses efficiently to the organs and tissues and is excreted in the urine in an active unchanged form.
7. Fosfomycin has not been observed to show any antigenicity in animal studies.
8. It has low toxicity and exerts no influence on the audiovisual organs.
9. Fosfomycin is chemically stable.
10. Large-scale clinical trials have confirmed that fosfomycin provides a high therapeutic efficacy, yet causes few side effects.

ACTIONS

(1) Antibacterial Activity

Fosfomycin acts bactericidally on gram-positive and gram-negative pathogens. It is especially highly active against *Pseudomonas aeruginosa*, *Proteus sp.*, *Serratia marcescens*, and multi-drug resistant strains of *Staphylococcus aureus* and *E. coli.*

(2) Mode of Action

The mode of action of fosfomycin is very unique. It is taken into bacterial cells in high concentration via the active transport system against a concentration gradient, and inhibits the initial stage of cell wall synthesis. (β -lactam antibiotics inhibit the final stage of cell wall synthesis).

(3) Absorption and Excretion

In adult patients, intravenous injection of 1 g dissolved in 20 ml of 20 % glucose solution produced a mean peak blood concentration of 74 μg/ml at 30 minutes after injection, which gradually declined to 8 μg/ml by 6 hours after injection. In healthy adult volunteers receiving one-hour intravenous drip infusion of 2 g dissolved in 300 ml of 5 % glucose solution, a mean peak blood concentration of 157.3 μg/ml was attained at the time of completion of the infusion. This gradually decreased thereafter, reaching a level of 2.6 μg/ml at 12 hours after infusion. The serum half-life was 1.8 hours. The urinary recovery rate was 96 % on an average within the first 12 hours.

(4) Tissue Concentrations

In patients with respiratory tract infections, intravenous injection of 1 g produced a mean sputum concentration of 7.0 μg/ml over the first 3 hours after injection.

Distribution to the cerebrospinal fluid was observed in patients with meningitis after intravenous injection or continuous intravenous drip infusion.

In rabbits, good distribution to the kidney, liver, lung, pancreas, heart, spleen, thymus, aqueous humor, etc., was confirmed.

(5) Toxicity

1) Acute Toxicity

LD_{50} of Fosfomycin Sodium (FOM-Na) (mg/kg)

Route of Administration	Mice		Rats	
	Male	Female	Male	Female
i.v.	1,230	1,225	1,650	1,560
i.p.	2,175	2,467	2,060	2,000
i.m.	2,625	2,662	2,630	2,460
s.c.	5,100	6,150	5,100	4,320
p.o.	8,020	7,300	4,700	4,550

(Litchfield-Wilcoxon method)

(2) Subacute and Chronic Toxicities

Subacute toxicity tests revealed that the maximum non-toxic dose is 500 mg/kg/day in rats and 400 mg/kg/day in rabbits.

Chronic toxicity tests in rats and dogs indicated the maximum nontoxic dose to be 250 mg/kg/day for both animals.

(6) Others

In animal studies, no adverse effects were observed in audiovisual tests or in teratogenicity tests. No antigenicity of fosfomycin sodium has been found in experiments on the induction of IgG and IgE antibodies.

INDICATIONS

Prevention of infections in abdominal surgery.

ADMINISTRATION and DOSAGE

Intravenous Drip Infusion

The usual daily dosage of FOSMICIN FOR I.V. USE is 2 to 4 g (Potency) for adults and 100 to 200 mg (Potency)/kg for children; both of these are given by intravenous drip infusion in 2 divided doses. Each dose is dissolved in 100 to 500 ml of intravenous fluid and infused over a period of one to 2 hours.
For acute and elektiv abdominal surgery.
Adults and children over 12 years : 8 g as a single dose infused intravenous 0,5 - 1 hour preoperative.
Depending on the level of contamination and the length of the surgery, this dose can be repeated.
Fosmicin should be given in combination with an aerobic antibiotics.
Renal insufficiency.
Repeated doses should not be given at creatinin clearance below 20 ml/minute.
The dose interval should be 16 hours at 20 - 40 ml/ minute. 8 g of Fosmicin to be mixed with 500 ml isotonic glucose infusion liquid and to be given at an infusion rate 10 -15 ml/minute. Heat is generated when Fosmicin is resolved. Other Antibiotics or medicaments shall not be added.

PRECAUTIONS

(1) This drug should be administered with care to patients with liver disorders.

(2) Side Effects

1) Liver
Occasionally the values for S-GOT, S-GPT and ALP, LDH, gamma-GTP and bilirubin may increase.
2) Kidney
Proteinuria and abnormalities in the Fishberg test develop in rare cases, and occasionally an elevated BUN value and edema may develop.
3) Respiratory Organs
A cough and asthma attacks may develop on rare occasions.
4) Central and Peripheral Nervous Systems
Occasionally patients may experience headaches and a feeling of numbness of the lips following the use of this drug. Moreover, in the case of administration of large doses, spasms may occasionally occur.

Nama Produk	Brosur Fosmicin Universal (Page 1)	Tanggal Desain	Keterangan
Ukuran	220 x 270 mm	- 05 Maret 2012 - 15 Desember 2021	- Perubahan logo Meiji dan nama lisensor - Perubahan suhu penyimpanan menjadi Store below 30°C dan penambahan penyimpanan pasca rekonstitusi
Bahan	HVS 60 g		
Warna	Black		