

IT ALWAYS ACHIEVES the OBJECTIVE

Urofosfabol® (fosfomycin)



Unique antibiotic for the treatment of moderate and serious infections in different localization:

- infections of **CNS**, including bacterial meningitis and ventriculitis
- lower respiratory tract infections
- bacterial endocarditis
- uncomplicated and complicated urinary tract infections
- uncomplicated and complicated intra-abdominal infections
- septicemia caused by *Enterobacteriaceae*
- soft tissue infections
- bone and joint infections, including acute and chronic osteomyelitis both in adult and children

ABOLMED
PHARMACEUTICAL COMPANY

Urofofab[®]

(fosfomicin)

DESCRIPTION

Urofofab[®] (fosfomicin disodium) is a natural, broad-spectrum antibiotic with an epoxide structure and low molecular weight for intramuscular or intravenous administration.

CLINICAL PHARMACOLOGY

Clinical pharmacokinetic of **Urofofab[®]** after IV or IM administration is described with linear model. Following an intravenous (IV) infusion of 0.5 g and 1.0 g of **Urofofab[®]**, serum concentrations were 28 mcg/mL and 46 mcg/mL at 40 minutes, correspondingly. After slow IV infusion of 4 gm of **Urofofab[®]** every 6 h serum concentration exceeds 250 mcg/mL and maintains above 20 mcg/mL in inter-dosing interval. **Urofofab[®]** does not bind to plasma proteins and has a good distribution volume, reaching high concentrations in the interstitial fluid and tissues, including CSF, kidneys and bone. It is excreted by the kidneys in its active form without metabolites and is dialyzable. The half-life after an intravenous administration is 90 to 120 minutes. Following an intramuscular (IM) injection of 0.5 gm and 2.0 gm of **Urofofab[®]**, serum concentrations were 17.1 mcg/mL and 45.5 mcg/mL at 60 minutes, correspondingly. Dosing regimen 1 gm IM every 6h maintains stable serum concentration of **Urofofab[®]** above 8 mcg/mL. As additional effects it has the capacity to favor phagocytosis, act as an immunomodulator and protect human cells from cisplatin, cyclosporin, aminoglycoside, vancomycin, amphotericin B and polymyxin toxicity.

SPECTRUM OF ACTIVITY

Urofofab[®] acts in the first stage of peptidoglycan synthesis of the bacterial wall. It has a rapid bactericide effect, and a wide spectrum of antimicrobial activity, including methicillin-resistant *S. aureus* and intermediate glycopeptide-susceptible or glycopeptide-resistant enterococci. **Urofofab[®]** is effective against the following microbes: *S. aureus*, *S. epidermidis* (including MRSA and MRSE), *Str. pyogenes*, *Str. viridans*, streptococci Group C, F, G, *Str. pneumoniae*, *B. anthracis*, *Actinomyces* spp., *N. gonorrhoeae*, *H. influenzae*, *E. coli*, *K. pneumoniae*, *S. marcescens*, *Citrobacter* spp., *P. mirabilis*, *P. vulgaris*, *Salmonella* spp., *Shigella* spp., *A. hydrophila*, *C. jejuni*, *Y. enterocolitica*, *Peptococcus* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., *Veillonella* spp. Most strains of *S. haemolyticus*, *S. auricularis*, *S. hominis*, *S. agalactiae*, *E. faecalis*, *E. faecium*, *Stomatococcus mucilaginosus*, *Corynebacterium* spp., *N. meningitidis*, *K. oxytoca*, *Enterobacter* spp., *P. rettgeri*, *M. morgani*, *Vibrio* spp., *P. aeruginosa*, *Bartonella* spp., *T. pallidum*, *Leptospira* spp., *C. perfringens*, *Prevotella* spp. are moderately susceptible to **Urofofab[®]**. **Fosfomicin** has shown stable rates of resistance.

CONTRAINDICATIONS

Urofofab[®] is contraindicated in patients who have shown hypersensitivity to fosfomicin.

PRECAUTION

Pregnancy Category B. This drug should be used during pregnancy only if clearly needed. Caution should be exercised when **Urofofab[®]** is administered to a nursing woman.

ADVERSE REACTIONS

Urofofab[®] is generally well tolerated. The most common adverse reactions have been *local reactions* following IV or IM injection (pain, redness). Thrombophlebitis may develop with intravenous administration. *Allergic Reactions:* rash, urticaria, flushing, pruritus, eosinophilia, fever, dyspnea, and other allergic reactions including anaphylaxis. *Cardiovascular:* hypotension. *Gastrointestinal:* diarrhea, vomiting, stomatitis and nausea. *Blood:* eosinophilia, leukopenia including granulocytopenia, neutropenia, anemia, including hemolytic anemia, thrombocytopenia. *Liver function:* transient elevations in SGOT, SGPT, serum LDH, serum bilirubin and serum alkaline phosphatase may be observed. *Renal function:* transient evaluation of serum creatinine levels, proteinuria, and transient disbalance of serum electrolytes (K⁺ and Na⁺).

INDICATIONS AND USAGE

Urofofab[®] is indicated for the treatment of moderate and serious infections caused by susceptible strains of the microorganisms in different localization. There are central nervous system infection – bacterial meningitis (including post-surgery meningitis), ventriculitis; soft tissue infections – moderate and severe cellulites (especially in patients with co-morbidity like diabetes mellitus or arterial insufficiency), infections of burn wounds; bone and joint infections – acute and chronic hematogenous osteomyelitis both in adult and children, post-traumatic and post-surgery osteomyelitis, septic arthritis; lower respiratory tract infections, including community-acquired and nosocomial pneumonia, caused by resistant bacteria, pleural empyema, lung infections in patients with cystic fibrosis; bacterial endocarditis, caused by Gram-positive or Gram-negative bacteria; urinary tract infections (acute and chronic pyelonephritis), exacerbation of chronic pyelonephritis, pyelitis in patients with urolithiasis, post-surgery UTI; non-complicated and complicated intra-abdominal infections, including peritonitis and intra-abdominal abscesses; severe infections in patients with granulocytopenia and leucosis (in combination with cefoperazone/sulbactam, carbapenems of cefepime); septicemia caused by *Enterobacteriaceae* (in combination with cephalosporins, antipseudomonal penicillins, aminoglycosides of fluorquinolones); MRSA-associated infections (in combinations with glycopeptides). **Urofofab[®]** in combination with different antibiotics shows evident synergistic and additive effects. The most significant combination are: oxacillin, cefazolin, cefotaxime, imipenem and fluoroquinolones - synergistic action against *S.aureus*; glycopeptides - synergistic action against MRSA and *Enterococcus* spp.; fluoroquinolones - synergistic action against *Enterococcus* spp.; ampicillin - synergistic action against *E.coli*; ceftazidime, cefoperazone, imipenem, meropenem and aztreonam - synergistic action against *P.aeruginosa*; aminoglycosides - synergistic action against *S.aureus*, *E.faecalis* and *P.aeruginosa*.

DOSAGE AND ADMINISTRATION

The usual adult dosage range is 2.0 gm to 4.0 gm every eight hours. Dosage should be determined by susceptibility of the causative organisms, severity of infection, and the condition of the patient.

The recommended dosage in pediatric patients including newborns is 100 to 400 mg/kg of body weight per day divided into four to six equal doses.

Urofofab[®] does not possess revealed teratogenicity or embryotoxicity and so it can be used in pregnant women and newborns.

Route of administration – IV or IM. The intravenous route is preferred for patients with severe infections and newborn infants. For IM administration, 1 gram to 2 grams of **Urofofab[®]** should be diluted with 4.0 ml 1.0% lidocaine hydrochloride, or sterile water for injection. The recommended regimen is 1 to 2 grams every 6 to 8 hours.

Urofofab[®] may be used in patients with reduced renal function with the following dosage adjustments (see the table).

DOSAGES IN PATIENTS WITH RENAL IMPAIRMENT

Cl _{creat} , mL/min	50-90 mL/min	30-50 mL/min	10-30 mL/min	<10 mL/min
Adult dosage	2-4gm q8h	2-4gm q12h	2-4gm q24h	2-4gm q48h
In patients undergoing hemodialysis, 2-4gm q48h is recommended. Extra 2 to 4 grams should be given after each hemodialysis				

HOW SUPPLIED

Urofofab[®] is available in dry powder form in vials containing fosfomicin disodium as follows:

1 gram of fosfomicin for intramuscular injections in packages of 50 vials;
1 gram of fosfomicin for intravenous injections in packages of 50 vials;
4 grams of fosfomicin for intravenous injections in packages of 50 vials.
Store for 2 years at or below a room temperature of 25°C (77°F).

Urofofab[®] is manufactured by ABOLMED Ltd., Russia.