

Generic Name: Ceftaroline fosamil
Trade Name: ZINFORO™
CDS Effective Date: March 03, 2020
Supersedes: August 11, 2016
Approved by BPOM:

PT PFIZER INDONESIA
Local Product Document

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Qualitative and quantitative composition

Each vial contains ceftaroline fosamil acetic acid solvate monohydrate equivalent to 600 mg ceftaroline fosamil that equivalent to 530 mg ceftaroline.

For excipients, see section *List of excipients*.

Pharmaceutical form

Powder for concentrate for solution for infusion

A pale yellowish-white to light yellow powder

Therapeutic indication

ZINFORO™ is indicated for the treatment of adult (≥ 18 years of age) patients with complicated skin and soft tissue infections (cSSTI) caused by susceptible isolates of the designated microorganism: *Staphylococcus aureus* (including methicillin-susceptible and –resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Escherichia coli*, *Klebsiella pneumonia* and *Klebsiella oxytoca*.

Usage:

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftaroline and other antibacterial drugs, ceftaroline should be used to treat only cSSTI that are proven or strongly suspected to be caused by susceptible bacteria. Appropriate specimens for microbiological examination should be obtained in order to isolate and identify the causative pathogens and to determine their susceptibility to ceftaroline. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Posology and method of administration

The recommended dosage of ZINFORO™ is 600 mg administered every 12 hours by intravenous infusion over 60 minutes in patients ≥ 18 years of age for duration of 5-14 days. The duration of treatment should be guided by the severity of infection and the patient's clinical response.

Special populations

Patients with renal impairment

The following dose adjustment is recommended in patients with renal impairment (see sections *Special warnings and special precautions for use* and *Pharmacokinetic properties*):

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Estimated creatinine clearance (mL/min)	Recommended dosage regimen
>30 to ≤50	400 mg intravenously (over 60 minutes) every 12 hours
≤30 and End-stage renal disease	Insufficient information to make specific dosage adjustment recommendations for patients with severe renal impairment and end-stage renal disease, including patients undergoing haemodialysis

Patients with hepatic impairment

No dosage adjustment is considered necessary in patients with hepatic impairment (see section *Pharmacokinetic properties*).

Elderly patients

No dosage adjustment is required for the elderly with creatinine clearance (CrCL) values >50 mL/min (see section *Pharmacokinetic properties*).

Paediatric patients

Safety and efficacy in paediatric patients have not been established (see section *Pharmacokinetic properties*).

Constitution and compatibility

See section *Instructions for use, handling and disposal*.

Contraindications

Hypersensitivity to the active substance or to any of its excipients.

Hypersensitivity to the cephalosporin class of antibacterials.

Immediate and severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins or carbapenems).

Special warnings and special precautions for use

Hypersensitivity reactions

As with all beta-lactam antibacterials, serious and occasionally fatal hypersensitivity reactions are possible (see sections *Contraindications* and *Undesirable effects*).

Patients who have a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibacterials may also be hypersensitive to cefataroline fosamil. Before initiating therapy with ZINFORO™, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibacterials. If a patient developed an immediate and severe hypersensitivity (e.g. anaphylactic reaction) previously to any type of beta-lactam antibacterial, cefataroline fosamil should not be administered (see section *Contraindications*).

If a severe allergic reaction occurs, the medicinal product should be discontinued and appropriate measures taken.

Clostridium difficile-associated diarrhoea

Antibacterial-associated colitis and pseudomembranous colitis have been reported with nearly all antibacterial agents, including ZINFORO™, and may range in severity from mild to life threatening.

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Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of ceftaroline fosamil (see section *Undesirable effects*). In such circumstance, the discontinuation of therapy with ZINFORO™ and the use of supportive measures together with the administration of specific treatment for *Clostridium difficile* should be considered.

Patients with pre-existing seizure disorder

As with other cephalosporins, seizures have occurred in ceftaroline toxicology studies at 7-25 times human C_{max} levels (see section *Preclinical safety data*). Clinical study experience with ceftaroline in patients with pre-existing seizure disorders is limited. Therefore, ZINFORO™ should be used with caution in this patient population.

Direct antiglobulin test (Coombs test) seroconversion

The development of a positive direct antiglobulin test (DAGT) may occur during treatment with cephalosporins. The incidence of DAGT seroconversion in patients receiving ceftaroline fosamil was 11.2% in the pooled Phase 3 studies with administration every 12 hours (600 mg administered over 60 minutes every 12 hours) and 32.3% in a study in patients receiving ceftaroline fosamil every 8 hours (600 mg administered over 120 minutes every 8 hours). There was no evidence of haemolysis in any patient receiving ceftaroline fosamil who developed a positive DAGT.

Patients with renal impairment

Clinical study experience with ceftaroline in patients with severe renal impairment and ESRD is limited. Therefore, use of ZINFORO™ is not recommended in these patient populations (see section *Pharmacokinetic properties*).

Non-susceptible organisms

Superinfections may occur as with other antibacterial agents.

Interaction with other medicinal products and other forms of interaction

No clinical drug-drug interaction studies have been conducted with ceftaroline.

The interaction potential of ceftaroline on drugs metabolised by CYP450 enzymes is expected to be low, since ceftaroline is not an inhibitor (CYP1A1, CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4) nor an inducer (CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP3A4/5) of CYP450 enzymes *in vitro*. Ceftaroline is not metabolised by CYP450 enzymes *in vitro*, so co-administered CYP450 inducers or inhibitors are unlikely to influence the pharmacokinetics of ceftaroline.

In vitro, ceftaroline is not transported by efflux transporters P-gp or BCRP. Ceftaroline does not inhibit P-gp, therefore an interaction with substrates, such as digoxin, is not expected. Ceftaroline is a weak inhibitor of BCRP, but the effect is too small to be clinically relevant. *In vitro* studies demonstrated that ceftaroline is not a substrate of, nor did it inhibit the renal uptake transporters OCT2, OAT1, and OAT3; drug-drug interactions with drugs that inhibit active renal secretion (e.g. probenecid) or with drugs that are substrates of these transporters would therefore not be expected.

Pregnancy and lactation

Pregnancy

No clinical data on pregnancies are available for ceftaroline. Animal studies with ceftaroline fosamil do not indicate harmful effects with respect to fertility, pregnancy, parturition or postnatal development (see section *Preclinical safety data*). ZINFORO™ should not be used during pregnancy unless clearly necessary and only if the potential benefit outweighs the possible risk.

Lactation

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It is not known whether ceftaroline is excreted in human milk, but because many beta-lactams are excreted in breast milk, women who are breast-feeding should be treated with ZINFORO™ only if clearly indicated. Interruption of breast-feeding is recommended.

Effects on ability to drive and to use machines

Undesirable effects e.g. dizziness may occur and this may have an effect on the ability to drive and use of machines (see section *Undesirable effects*).

Undesirable effects

Pooled Phase III studies

The incidences of treatment emergent adverse events were similar in ceftaroline and comparator groups (45.7% versus 46.7%, respectively). The most common adverse reactions occurring in $\geq 3\%$ of patients treated with ceftaroline were diarrhoea, headache, nausea, and pruritus, and were generally mild or moderate in severity.

Additional Phase III studies

A study (COVERS) was conducted of 506 adult patients with cSSTI treated with ceftaroline fosamil (600 mg administered over 120 minutes every 8 hours). The most common adverse reactions occurring in $\geq 3\%$ of patients treated with ceftaroline fosamil were nausea, headache, and rash. The safety profile of ceftaroline fosamil was similar to that observed in previous pooled Phase III studies with the exception of both a greater incidence of rash in Asian patients (see below) and a greater incidence of DAGT seroconversion (see section *Special warnings and special precautions for use*).

The following adverse reactions have been identified during clinical trials with ZINFORO. Adverse reactions are classified according to frequency and System Organ Class. Frequency categories for the adverse events are defined according to the following conventions: Very common ($\geq 1/10$), Common ($\geq 1/100, < 1/10$), Uncommon ($\geq 1/1000, < 1/100$), Rare ($\geq 1/10000, < 1/1000$).

Table 1 Frequency of adverse reactions in clinical trials

Frequency	System organ class	Event
Very common ($\geq 10\%$)	Investigations	Coombs Direct Test Positive (see section <i>Special warnings and special precautions for use</i>)
Common ($\geq 1\%$ and $< 10\%$)	Gastrointestinal disorders	Diarrhoea, nausea, vomiting, abdominal pain
	Nervous system disorders	Headache, dizziness
	Skin and subcutaneous tissue disorders	Rash, pruritus
	Hepatobiliary disorders	Increased transaminases
	Vascular disorders	Phlebitis
	General disorders and administration site conditions	Pyrexia Infusion site reactions (erythema, phlebitis, pain)
Uncommon ($\geq 0.1\%$ and $< 1\%$)	Blood and lymphatic system disorders	Anaemia, neutropenia*, leucopenia, thrombocytopenia
	Immune system disorders	Hypersensitivity/anaphylaxis (see sections <i>Contraindications</i> and <i>Special warnings and special precautions for use</i>)
	Nervous system disorders	Encephalopathy*

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Frequency	System organ class	Event
	Skin and subcutaneous tissue disorders	Urticaria
	Infections and infestations	<i>Clostridium difficile</i> colitis (see section <i>Special warnings and special precautions for use</i>)
	Investigations	Prothrombin time prolonged, international normalized ratio increased
	Renal and urinary disorders	Blood creatinine increased
Rare ($\geq 0.01\%$ and $< 0.1\%$)	Blood and lymphatic system disorders	Agranulocytosis*
Not known (cannot be estimated from the available data).	Blood and lymphatic system disorders	Eosinophilia*
	Respiratory, thoracic and mediastinal disorders	Eosinophilic pneumonia*

* Adverse Drug Reaction (ADR) identified post marketing.

Description of selected adverse reactions

Rash

Rash was observed at a common frequency in the pooled Phase III studies in cSSTI with administration of ceftaroline fosamil every 12 hours (600 mg administered over 60 minutes every 12 hours) and the COVERS study in cSSTI with administration every 8 hours (600 mg administered over 120 minutes every 8 hours). However, the frequency of rash in the subgroup of Asian patients receiving ceftaroline fosamil every 8 hours (COVERS) was very common (18.5%).

Overdose

Intentional overdosing of ceftaroline fosamil is unlikely. Limited data in patients receiving higher than recommended ceftaroline fosamil dosages show similar adverse reactions as observed in the patients receiving recommended dosages. Treatment under such circumstances should follow local standard medical practice.

Patients with renal impairment

Relative overdosing could occur in patients with moderate to severe renal impairment. Neurological sequelae, including encephalopathy, have been noted in cases where beta-lactam antibiotics (including cephalosporins) have been given to patients with impaired renal function without reducing the dose (see section *Posology and method of administration*).

Ceftaroline can be removed by haemodialysis; over a 4-hour dialysis session, approximately 74% of a given dose was recovered in the dialysate.

Pharmacological properties

Pharmacodynamic properties

Mechanism of action

Ceftaroline is a cephalosporin with activity against Gram-positive and Gram-negative bacteria. *In-vitro* studies have shown that ceftaroline is bactericidal, due to inhibition of bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs). Ceftaroline is also active against methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-nonsusceptible *Streptococcus pneumoniae* (PNSP) due to its high affinity for the altered PBPs found in these organisms.

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Pharmacokinetic/pharmacodynamic relationship

As with other beta-lactam antimicrobial agents, the percent time above the minimum inhibitory concentration (MIC) of the infecting organism over the dosing interval (%T >MIC) has been shown to best correlate with the antimicrobial activities for ceftaroline.

Mechanisms of resistance

Ceftaroline is not active against strains of *Enterobacterales* producing extended-spectrum beta-lactamases (ESBLs) from the TEM, SHV or CTX-M families, serine carbapenemases (such as KPC), class B metallo-beta-lactamases or class C (AmpC cephalosporinases). Resistance may also be mediated by bacterial impermeability or drug efflux pump mechanisms. One or more of these mechanisms may co-exist in the same bacterium.

Cross-resistance

Unlike other cephalosporins, ceftaroline is active against most MRSA and PNSP due to its ability to bind to the altered PBPs in these organisms that commonly confer insusceptibility to other beta-lactam agents.

Interaction with other antibacterial agents

In vitro studies have not demonstrated any antagonism between ceftaroline in combination with other commonly used antibacterial agents (e.g., amikacin, azithromycin, aztreonam, daptomycin, levofloxacin, linezolid, meropenem, tigecycline, and vancomycin).

Susceptibility testing

The prevalence of acquired resistance may vary geographically and with time for selected species. Local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent is questionable.

The susceptibility to ceftaroline of a given clinical isolate should be determined by standard methods. Interpretations of test results should be made in accordance with local infectious diseases and clinical microbiology guidelines.

Clinical efficacy against specific pathogens

Efficacy has been demonstrated in clinical studies against pathogens that were susceptible to ceftaroline *in vitro*.

Complicated skin and soft tissue infections

Gram-positive organisms

- *Staphylococcus aureus* (including methicillin-resistant strains)
- *Streptococcus pyogenes*
- *Streptococcus agalactiae*

Gram-negative organisms

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Klebsiella oxytoca*

Antibacterial activity against other relevant pathogens

Clinical efficacy has not been established against the following pathogens although *in vitro* studies suggest that they would be susceptible to ceftaroline in the absence of acquired mechanisms of resistance:

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Anaerobic Gram-positive organisms

Peptostreptococcus species

Anaerobic Gram-negative organisms

Fusobacterium species

Clinical efficacy and safety

Complicated skin and soft tissue infections

A total of 1396 adults with documented complicated skin and soft tissue infections were enrolled in two identical randomised, multi-centre, multinational, double-blind studies (CANVAS 1 and CANVAS 2) comparing ceftaroline fosamil (600 mg administered intravenously over 60 minutes every 12 hours) to vancomycin plus aztreonam (1 g vancomycin administered intravenously over 60 minutes followed by 1 g aztreonam administered intravenously over 60 minutes every 12 hours). Patients with deep/extensive cellulitis, a major abscess, a wound infection (surgical or traumatic), infected bites, burns or ulcers, or any lower extremity infection in patients with either pre-existing diabetes mellitus or peripheral vascular disease, were eligible for the studies. Treatment duration was 5 to 21 days. The modified intent-to-treat (MITT) population included all patients who received any amount of study drug according to their randomised treatment group. The clinically evaluable (CE) population included patients in the MITT population with sufficient adherence to the protocol.

The primary efficacy endpoint was the clinical response at the Test of Cure (TOC) visit in the co-primary populations of the CE and MITT patients in the table below.

Table 2 Clinical cure rates at TOC from two Phase 3 studies in cSSTI after 5 to 21 days of therapy

	Ceftaroline n/N (%)	Vancomycin/Aztreonam n/N (%)	Treatment difference (2-sided 95% CI)
CANVAS 1			
CE	288/316 (91.1)	280/300 (93.3)	-2.2 (-6.6,2.1)
MITT	304/351 (86.6)	297/347 (85.6)	1.0 (-4.2,6.2)
CANVAS 2			
CE	271/294 (92.2)	269/292 (92.1)	0.1 (-4.4,4.5)
MITT	291/342 (85.1)	289/338 (85.5)	-0.4 (-5.8,5.0)

Clinical cure rates at TOC by pathogen in the microbiologically evaluable patients are presented below.

Table 3 Clinical cure rates by infecting pathogen from microbiologically evaluable patients with cSSTI (data from two integrated Phase 3 studies)

Organism	Ceftaroline N/N (%)	Vancomycin/Aztreonam n/N (%)
<u>Gram-positive organisms</u>		
<i>Staphylococcus aureus</i>	352/378 (93.1)	336/356 (94.4)
MSSA (methicillin-susceptible strains)	212/228 (93.0)	225/238 (94.5)
MRSA (methicillin-resistant strains)	142/152 (93.4)	115/122 (94.3)
<i>Streptococcus pyogenes</i>	56/56 (100.0)	56/58 (96.6)
<i>Streptococcus agalactiae</i>	21/22 (95.5)	18/18 (100.0)
<i>Streptococcus dysgalactiae</i>	13/13 (100.0)	15/16 (93.8)
<i>Streptococcus anginosus</i> group ^a	12/13 (92.3)	15/16 (93.8)
<u>Gram-negative organisms</u>		
<i>Escherichia coli</i>	20/21 (95.2)	19/21 (90.5)

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Organism	Ceftaroline N/N (%)	Vancomycin/Aztreonam n/N (%)
<i>Klebsiella pneumoniae</i>	17/18 (94.4)	13/14 (92.9)
<i>Morganella morganii</i>	11/12 (91.7)	5/6 (83.3)
<i>Klebsiella oxytoca</i>	10/12 (83.3)	6/6 (100.0)

^a Includes *S. aninosus*, *S. intermedius*, and *S. constellatus*

Pharmacokinetic properties

The C_{max} and AUC of ceftaroline increase approximately in proportion to dose within the single dose range of 50 to 1000 mg. No appreciable accumulation of ceftaroline is observed following multiple intravenous infusions of 600 mg administered over 60 minutes every 12 hours for up to 14 days in healthy adults with normal renal function.

Distribution

The plasma protein binding of ceftaroline is low (approximately 20%) and ceftaroline is not distributed into erythrocytes. The median steady-state volume of distribution of ceftaroline in healthy adult males following a single 600 mg intravenous dose of radiolabeled ceftaroline fosamil was 20.3 L, similar to the volume of extracellular fluid.

Metabolism

Ceftaroline fosamil (prodrug), is converted into the active ceftaroline in plasma by phosphatase enzymes and concentrations of the prodrug are measurable in plasma primarily during intravenous infusion. Hydrolysis of the beta-lactam ring of ceftaroline occurs to form the microbiologically inactive, open-ring metabolite, ceftaroline M-1. The mean plasma ceftaroline M-1 to ceftaroline AUC ratio following a single 600 mg intravenous infusion of ceftaroline fosamil in healthy subjects is approximately 20-30%.

In pooled human liver microsomes, metabolic turnover was low for ceftaroline, indicating that ceftaroline is not metabolised by hepatic CYP450 enzymes.

Excretion

Ceftaroline is primarily eliminated by the kidneys. Renal clearance of ceftaroline is approximately equal, or slightly lower than the glomerular filtration rate in the kidney, and *in vitro* transporter studies indicate that active secretion does not contribute to the renal elimination of ceftaroline.

The mean terminal elimination half-life of ceftaroline in healthy adults is approximately 2.5 hours.

Following the administration of a single 600 mg intravenous dose of radiolabeled ceftaroline fosamil to healthy male adults, approximately 88% of radioactivity was recovered in urine and 6% in faeces.

Special populations

Patients with renal impairment

Dosage adjustment is required in patients with moderate renal impairment (CrCL >30 to 50 mL/min).

There is insufficient data to make specific dosage adjustment recommendations for patients with severe renal impairment (CrCL ≤30 mL/min) and end-stage renal disease (ESRD), including patients undergoing haemodialysis.

Patients with hepatic impairment

The pharmacokinetics of ceftaroline in patients with hepatic impairment have not been established. As ceftaroline does not appear to undergo significant hepatic metabolism, the systemic clearance of ceftaroline is not expected to be significantly affected by hepatic impairment. Therefore, no dosage adjustment is recommended for patients with hepatic impairment.

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Elderly patients

Following administration of a single 600 mg intravenous dose of ceftaroline fosamil, the pharmacokinetics of ceftaroline was similar between healthy elderly subjects (≥ 65 years of age), and healthy young adult subjects (18-45 years of age). There was a slight 33% increase in $AUC_{0-\infty}$ in the elderly that was mainly attributable to age-related changes in renal function. Ceftaroline dose adjustment is not required in elderly patients with creatinine clearance above 50 mL/min.

Paediatric patients

The safety and efficacy of ceftaroline in paediatric patients have not been established.

Gender

The pharmacokinetics of ceftaroline were similar between males and females. No dose adjustment is required based on sex.

Race

Race was evaluated as a covariate in a population pharmacokinetic analysis on data from the clinical studies. No significant differences in ceftaroline pharmacokinetics were observed in Caucasian, Hispanic, Black, or other patients. No dosage adjustment is recommended based on race.

Preclinical safety data

The kidney was the primary target organ of toxicity in both the monkey and rat. Histopathologic findings included pigment deposition and inflammation of the tubular epithelium. Renal changes were not reversible but were reduced in severity following a 4 week recovery period.

Convulsions have been observed at relatively high exposures during single and multi-dose studies in both the rat and monkey (≥ 7 times to the estimated C_{max} level of a 600 mg twice a day).

Other important toxicologic findings noted in the rat and monkey included histopathologic changes in the bladder and spleen.

Genetic toxicology

Ceftaroline fosamil and ceftaroline were clastogenic in an *in vitro* chromosomal aberration assay, however there was no evidence of mutagenic activity in an Ames, mouse lymphoma and unscheduled DNA synthesis assay. Furthermore, *in vivo* micronucleus assays in rat and mouse were negative. Carcinogenicity studies have not been conducted.

Reproductive toxicology

Reproductive studies in pregnant rabbits resulted in an increased foetal incidence of angulated hyoid alae, a common skeletal variation in rabbit foetuses, at exposures similar to 600 mg twice daily in humans. In the rat, no adverse effects were observed on embryofoetal development, fertility or postnatal development.

List of excipients

L-arginine

Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section Instructions for use, handling and disposal.

Shelf life

Dry powder: 3 years

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After constitution:

The constituted vial should be used immediately (within 30 minutes).

After dilution:

Once the intravenous solution is prepared with diluents listed in section *Instructions for use, handling and disposal* it should be administered within 6 hours of preparation. The chemical and physical in-use stability has been demonstrated for up to 24 hours at 2-8°C. Once removed from refrigeration to room temperature, the diluted product must be used within 6 hours.

From a microbiological point of view, the medicinal product should be used immediately unless constitution and dilution has taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

Special precautions for storage

Store below 30°C

Store in the original package in order to protect from light.

For storage conditions of the constituted and diluted medicinal product, see section *Shelf life*.

Nature and contents of container

20 mL glass vial (Type 1) closed with a rubber (halobutyl) stopper and aluminium seal with flip-off cap.

The medicinal product is supplied in packs of 10 vials.

Instructions for use, handling and disposal

The powder must be constituted with water for injections and the resulting constituted solution must then be immediately diluted prior to use. The constituted solution is a pale yellow solution that is free of any particles.

Standard aseptic techniques should be used for solution preparation and administration.

ZINFORO™ powder should be constituted with 20 mL sterile water for injections. The resulting constituted solution should be shaken prior to being transferred to an infusion bag or bottle containing one of the following diluents:

- sodium chloride 9 mg/mL (0.9%) solution for injection
- dextrose 50 mg/mL (5%) solution for injection
- sodium chloride 4.5 mg/mL and dextrose 25 mg/mL solution for injection (0.45% sodium chloride and 2.5% dextrose)
- Lactated Ringer's solution

Routinely, a 250 mL infusion bag should be used to prepare the infusion and only in exceptional patients for whom there could be great concern over volumes infused should a 50 mL or 100 mL infusion bag be used. The total time interval between starting constitution and completing preparation of the intravenous infusion should not exceed 30 minutes.

One mL of the constituted solution contains 30 mg of ceftriaxone fosamil.

For storage conditions of the constituted and diluted medicinal product, see section *Shelf life*.

Each vial is for single use only.

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

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Supply

Box of 10 vials @ 600 mg (Reg. No.: DKI1843900280A1)

HARUS DENGAN RESEP DOKTER

Manufactured by:

ACS Dobfar S.p.A.
Viale Addetta, 2a/12 – 3/5
20067 Tribiano, Milan – Italy

Packed and released by:

ACS Dobfar S.p.A.
Nucleo Industriale S. Atto
64100 Teramo – Italy

Imported by:

PT Pfizer Indonesia
Jakarta, Indonesia

Leaflet kemasan: Informasi untuk Pasien

ZINFORO™ **Ceftaroline fosamil** **Serbuk untuk konsentrat untuk larutan infus 600 mg**

Bacalah seluruh isi leaflet ini dengan seksama sebelum anda mulai menggunakan obat ini karena leaflet ini berisi informasi penting untuk anda.

- Simpanlah leaflet ini. Anda mungkin memerlukannya di kemudian hari.
- Apabila anda memiliki pertanyaan lebih lanjut, hubungi dokter atau perawat anda.
- Apabila anda mengalami efek samping, komunikasikanlah dengan dokter atau perawat anda. Hal ini termasuk efek samping yang mungkin timbul yang tidak disebutkan dalam leaflet ini.

Informasi yang terkandung dalam leaflet ini:

1. ZinfoTM dan kegunaannya
2. Hal yang perlu anda ketahui sebelum menggunakan ZinfoTM
3. Cara penggunaan ZinfoTM
4. Efek samping yang mungkin terjadi
5. Cara penyimpanan ZinfoTM
6. Isi kemasan dan informasi lainnya

1. ZinfoTM dan kegunaannya

ZinfoTM adalah obat antibiotik yang mengandung zat aktif ceftaroline fosamil yang merupakan golongan obat ‘antibiotik sefalosporin’

ZinfoTM digunakan untuk mengobati infeksi kulit dan jaringan di bawah kulit pada orang dewasa.

ZinfoTM bekerja membunuh jenis bakteri tertentu yang dapat menyebabkan infeksi serius.

2. Hal yang perlu anda ketahui sebelum menggunakan ZinfoTM

Jangan gunakan ZinfoTM apabila:

- Anda memiliki alergi terhadap ceftaroline fosamil atau bahan-bahan lain yang terkandung dalam obat ini.
- Anda memiliki alergi terhadap antibiotik sefalosporin lainnya.
- Anda pernah mengalami reaksi alergi berat terhadap antibiotik lainnya seperti penisilin atau carbapenem.

Jangan gunakan ZinfoTM apabila anda memiliki salah satu atau lebih dari kondisi diatas. Apabila anda ragu, komunikasikan dengan dokter atau perawat anda sebelum anda menggunakan ZinfoTM.

Peringatan dan pencegahan

Komunikasikanlah dengan dokter atau perawat sebelum menggunakan obat apabila:

- Anda memiliki gangguan ginjal (dokter anda dapat menentukan apakah obat ini cocok untuk anda atau dapat diberikan dalam dosis yang lebih rendah).
- Anda pernah mengalami kejang.
- Anda pernah mengalami reaksi alergi ringan terhadap antibiotik jenis lain seperti penisilin atau carbapenem.
- Anda pernah mengalami diare berat saat mengonsumsi antibiotik sebelumnya.

Anda dapat menderita infeksi yang disebabkan oleh bakteri lain selama atau setelah pengobatan dengan ZinfoTM.

Tes laboratorium

Anda dapat mengalami hasil tes laboratorium yang abnormal (tes Coombs) yang mendeteksi

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antibodi tertentu yang dapat bereaksi terhadap sel darah merah anda.

Apabila anda mengalami salah satu kondisi di atas (atau anda tidak yakin), komunikasikanlah dengan dokter atau perawat anda sebelum menggunakan Zinforo™.

Anak-anak dan remaja

Zinforo™ sebaiknya tidak digunakan untuk anak-anak dan remaja karena terbatasnya data penggunaan obat pada populasi ini.

Zinforo™ dan obat-obatan lain

Komunikasikanlah dengan dokter anda apabila anda sedang atau baru saja atau pernah menggunakan obat-obatan lain. Hal ini termasuk obat-obatan yang didapat tanpa resep dan obat-obatan herbal.

Kehamilan dan menyusui

Komunikasikan dengan dokter sebelum menggunakan Zinforo™ apabila anda sedang hamil. Jangan menggunakan obat ini saat hamil kecuali telah diresepkan oleh dokter.

Komunikasikan dengan dokter anda sebelum menggunakan Zinforo™ apabila anda sedang atau berencana untuk menyusui. Dokter anda dapat meminta anda untuk berhenti menyusui selama pengobatan dengan Zinforo™.

Mintalah nasihat dari dokter anda sebelum mengkonsumsi obat jenis apa pun apabila anda sedang hamil atau menyusui.

Mengemudi dan menjalankan mesin

Efek yang tidak diinginkan seperti dapat terjadi pusing dan ini mungkin memiliki efek pada kemampuan untuk mengemudi dan menggunakan mesin (efek yang tidak diinginkan).

3. Cara penggunaan Zinforo™

Zinforo™ akan diberikan kepada anda oleh dokter atau perawat.

Jumlah yang harus digunakan

Dosis yang umum digunakan untuk orang dewasa adalah 600 mg setiap 12 jam. Obat ini diberikan dalam tetesan melalui pembuluh darah vena dalam waktu 60 menit. Pengobatan biasanya berlangsung antara 5 sampai 14 hari.

Pasien dengan gangguan ginjal

Apabila anda menderita gangguan ginjal, dokter anda dapat menurunkan dosis obat anda hingga 400 mg setiap 12 jam karena Zinforo™ dibersihkan dari tubuh anda melalui ginjal.

Apabila anda menggunakan Zinforo™ melebihi dosis yang seharusnya

Apabila anda merasa diberikan Zinforo™ dalam jumlah terlalu banyak, segera beritahu dokter anda.

Apabila anda melewatkan satu dosis Zinforo™

Apabila anda merasa telah melewatkan satu dosis pemberian obat, segera beritahu dokter atau perawat anda.

Apabila anda memiliki pertanyaan lebih lanjut mengenai penggunaan produk ini, tanyakan pada dokter atau perawat.

4. Efek samping yang mungkin terjadi

Seperti obat-obatan lainnya, Zinforo™ dapat menimbulkan efek samping walaupun tidak semua orang akan mengalaminya. Berikut adalah efek samping yang mungkin timbul dari pemberian obat ini.

Beritahu dokter anda segera apabila anda mengalami gejala-gejala berikut ini karena anda mungkin memerlukan pertolongan medis segera:

- Pembengkakan tiba-tiba pada bibir, wajah, tenggorokan atau lidah; ruam parah; kesulitan menelan atau bernafas. Hal-hal ini merupakan tanda reaksi alergi berat (anafilaksis) yang dapat mengancam nyawa.
- Diare yang menjadi berat atau tidak kunjung sembuh atau tinja yang mengandung darah atau lendir selama atau setelah pengobatan dengan Zinforo™. Dalam situasi ini, anda harus menghentikan konsumsi semua obat yang menghentikan atau melambatkan pergerakan usus.

Efek samping sangat umum (dialami oleh lebih dari 1 dari 10 pasien)

Perubahan dari tes darah yang bernama “tes Coombs” sering ditemui pada pasien yang mendapatkan antibiotik jenis ini. Tes ini mendeteksi antibodi tertentu yang dapat bereaksi terhadap sel darah merah anda.

Efek samping umum (dialami oleh 1 dari 10 pasien)

- Demam
- Sakit kepala
- Pusing
- Gatal, ruam kulit
- Diare, nyeri perut
- Mual atau muntah
- Peningkatan enzim liver (ditunjukkan melalui tes darah)
- Nyeri dan iritasi pada pembuluh darah vena
- Kemerahan, nyeri, atau bengkak pada lokasi penyuntikan obat.

Efek samping tidak umum (dialami oleh kurang dari 1 dari 100 pasien)

- Anemia
- Ruam yang gatal
- Peningkatan kadar kreatinin darah. Kreatinin menunjukkan kinerja ginjal anda.
- Perdarahan atau memar lebih daripada biasanya. Hal ini mungkin disebabkan oleh penurunan platelet dalam tubuh anda.
- Perubahan hasil tes darah yang mengukur pembekuan darah.
- Penurunan jumlah sel darah putih dalam tubuh anda (leukopenia).
- Perubahan kondisi mental Anda seperti kebingungan, penurunan tingkat kesadaran, gerakan yang abnormal, atau kejang (ensefalopati).
- Rendahnya konsentrasi sel darah putih dalam tubuh Anda (neutropenia).

Jarang (dialami oleh kurang dari 1 dari 1000 pasien)

- Penurunan signifikan jumlah sel darah putih dalam darah Anda (agranulositosis). Anda dapat mengalami demam, gejala menyerupai flu, sakit tenggorokan, atau infeksi lainnya yang dapat bersifat serius.

Frekuensi tidak diketahui (tidak dapat diperkirakan dari data yang tersedia)

- Suatu bentuk penyakit paru-paru yang ditandai dengan munculnya eosinofil (salah satu bentuk sel darah putih) di dalam paru-paru dalam jumlah yang meningkat (pneumonia eosinofilik).

Apabila efek samping tersebut diatas bertambah berat, atau apabila anda merasakan efek samping yang tidak disebutkan diatas, harap beritahukan dokter atau perawat anda.

5. Cara penyimpanan Zinforo™

Jauhkan dari jangkauan anak-anak.

Jangan gunakan Zinforo™ setelah tanggal kadaluarsa yang tertera pada kemasan obat. Tanggal kadaluarsa yang dimaksud adalah hari terakhir dari bulan yang tercantum.

Generic Name: Ceftriaxone fosamil
Trade Name: **ZINFORO™**
CDS Effective Date: 3 Maret 2020
Supersedes: August 11, 2016
Approved by BPOM:

Simpan dibawah suhu 30°C.

Simpan dalam kemasan aslinya agar terlindung dari sinar matahari.

Obat sebaiknya tidak dibuang melalui pembuangan air atau sampah rumah tangga. Tanyakanlah kepada apoteker anda bagaimana cara membuang obat yang sudah tidak digunakan lagi. Hal ini dapat membantu anda melindungi lingkungan.

Kedaluwarsa: Serbuk kering: 3 tahun.

6. Isi kemasan dan informasi lainnya

Zinforo™ mengandung:

- Setiap vial mengandung 600 mg ceftriaxone fosamil
- Komposisi lainnya adalah arginine

Bentuk sediaan dan isi kemasan:

Zinforo™ merupakan bubuk berwarna putih kekuningan untuk konsentrasi untuk larutan infus dalam sebuah vial. Obat ini tersedia dalam kemasan yang berisi 10 vial. **No. Reg.:**

DKI1843900280A1.

HARUS DENGAN RESEP DOKTER

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