# Ceftaroline Fosamil Powder for Concentrate for Solution for Infusion
# ZINFORO®

## 1. GENERIC NAME

Ceftaroline fosamil powder for concentrate for solution for infusion.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

**List of Excipients**

L-arginine

## 3. DOSAGE FORM AND STRENGTH

Dosage Form: Sterile powder for concentrate for solution for infusion
Strength: 600 mg/vial

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indication

Ceftaroline fosamil is indicated for the treatment of adult (≥18 years of age) patients with Community-acquired pneumonia and Complicated skin and soft tissue infections (cSSTI)

### 4.2 Posology and method of administration

Posology

The recommended durations of treatment are 5-14 days for cSSTI and 5-7 days for CAP.

® Trademark Proprietor – Forest Laboratories, LLC
Licensed User – Pfizer Limited, India

**Table 1: Dosage in adults with normal renal function, creatinine clearance (CrCL) >50 mL/min**

| Indications | Posology (mg/infusion) | Infusion time (minutes)/Frequency |
|---|---|---|
| Standard dose[a]<br><br>Complicated skin and soft tissue infections (cSSTI)<br><br>Community-acquired pneumonia (CAP) | 600 mg | 5 - 60[b] /every 12 hours |
| High dose[b]<br><br>cSSTI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ceftaroline[c] | | 120/every 8 hours |

[a] For patients with supranormal renal clearance receiving the standard dose, an infusion time of 60 minutes may be preferable.
[b] Infusion times of less than 60 minutes and high dose recommendations are based on pharmacokinetic and pharmacodynamic analyses only. See sections 4.4 and 5.1.
[c] For treatment of *S. aureus* for which the ceftaroline MIC is ≤1 mg/L, the standard dose is recommended.

Special populations

*Elderly*
No dosage adjustment is required for the elderly with creatinine clearance values >50 mL/min (see section 5.3).

*Renal impairment*
The dose should be adjusted when creatinine clearance (CrCL) is ≤50 mL/min, as shown in Tables 2 (see section 5.3). The recommended durations of treatment are 5-14 days for cSSTI and 5-7 days for CAP.

**Table 2: Dosage in adults with impaired renal function, creatinine clearance (CrCL) ≤50 mL/min**

| Indications | Creatinine clearance (mL/min)[a] | Posology (mg/infusion) | Infusion time (minutes)/Frequency |
|---|---|---|---|
| Standard dose<br><br>Complicated skin and soft tissue infections(cSSTI)<br><br>Community-acquired pneumonia (CAP) | >30 to ≤50 | 400 mg | 5–60[c]/every 12 hours |
| | ≥15 to ≤30 | 300 mg | |
| | ESRD, including haemodialysis[b] | 200 mg | |
| High dose[c]<br><br>cSSTI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ceftaroline[d] | >30 to ≤50 | 400 mg | 120/every 8 hours |
| | ≥15 to ≤30 | 300 mg | |
| | ESRD, including haemodialysis[b] | 200 mg | |

| Indications | Creatinine clearance (mL/min)[a] | Posology (mg/infusion) | Infusion time (minutes)/Frequency |
|---|---|---|---|

[a] Calculated using the Cockcroft-Gault formula for adults. Dose is based on CrCL. CrCL should be closely monitored and the dose adjusted according to changing renal function.
[b] Ceftaroline is haemodialyzable; thus ceftaroline fosamil should be administered after haemodialysis on haemodialysis days.
[c] Infusion times of less than 60 minutes and high dose recommendations are based on pharmacokinetic and pharmacodynamic analyses only. See sections 4.4 and 5.1.
[d] For treatment of *S. aureus* for which the ceftaroline MIC is ≤1 mg/L, the standard dose is recommended.

*Hepatic impairment*
No dosage adjustment is considered necessary in patients with hepatic impairment (see section 5.3).

Method of administration
Intravenous use. Ceftaroline fosamil is administered by intravenous infusion over 5 to 60 minutes for standard dose or 120 minutes for high dose (for cSSTI caused by *S. aureus* with MIC of 2 or 4 mg/L to ceftaroline) in infusion volumes of 50 mL, 100 mL or 250 mL (see section 8.4). Infusion related reactions (such as phlebitis) can be managed by prolonging the infusion duration.

For instructions on reconstitution and dilution of the medicinal product before administration, (see section 8.4).

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 2.
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).

## 4.4 Special warnings and precautions for use

**Hypersensitivity reactions**
Serious and occasionally fatal hypersensitivity reactions are possible (see sections 4.3 and 4.8).

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) which can be life-threatening or fatal, have been reported in association with ceftaroline treatment (see section 4.8)..

Acute generalised exanthematous pustulosis (AGEP) has been reported in association with beta-lactam antibiotics (including cephalosporins) treatment.

Patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, ceftaroline should be withdrawn immediately, and an alternative treatment considered.

If the patient has developed a severe skin reaction such as SJS, TEN or DRESS with the use of ceftaroline, treatment with ceftaroline must not be restarted in this patient at any time

Patients who have a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibacterials may also be hypersensitive to ceftaroline fosamil. Ceftaroline should be used with caution in patients with a history of non-severe hypersensitivity reactions to any other beta-lactam antibiotics (e.g. penicillins or carbapenems). If a severe allergic reaction or SCAR occurs during treatment with ceftaroline fosamil, the medicinal product should be discontinued and appropriate measures taken.

With other beta-lactam antibiotics there have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8).

*Clostridium difficile*-associated diarrhoea
Antibacterial-associated colitis and pseudomembranous colitis have been reported with ceftaroline fosamil and may range in severity from mild to life threatening. 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 4.8). In such circumstance, the discontinuation of therapy with ceftaroline fosamil and the use of supportive measures together with the administration of specific treatment for *Clostridium difficile* should be considered.

Non-susceptible organisms
Superinfections may occur during or following treatment with ceftaroline fosamil.

Patients with pre-existing seizure disorder
Seizures have occurred in toxicology studies at 7-25 times human ceftaroline $C_{max}$ levels (see section 6.1). Clinical study experience with ceftaroline fosamil in patients with pre-existing seizure disorders is very limited. Therefore, ceftaroline fosamil should be used with caution in this patient population.

Direct antiglobulin test (Coombs test) seroconversion and potential risk of haemolytic anaemia
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 five pooled pivotal 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), (see section 4.8). In clinical studies there was no evidence of haemolysis in patients who developed a positive DAGT on treatment. However, the possibility that haemolytic anaemia may occur in association with cephalosporins including ceftaroline fosamil treatment cannot be ruled out. Patients experiencing anaemia during or after treatment with ceftaroline fosamil should be investigated for this possibility.

Limitations of the clinical data

There is no experience with ceftaroline in the treatment of CAP in the following patient groups: the immunocompromised, patients with severe sepsis/septic shock, severe underlying lung disease (e.g. cystic fibrosis, see section 5.3), those with PORT Risk Class V, and/or CAP requiring ventilation at presentation, CAP due to methicillin-resistant *S. aureus* or patients requiring intensive care. Caution is advised when treating such patients.

There is no experience with ceftaroline in the treatment of cSSTI in the following patient groups: the immunocompromised, patients with severe sepsis/septic shock, necrotizing fasciitis, perirectal abscess and patients with third degree and extensive burns. There is limited experience in treating patients with diabetic foot infections. Caution is advised when treating such patients.

There are limited clinical trial data on the use of ceftaroline to treat cSSTI caused by *S. aureus* with an MIC of >1 mg/L. The recommended dosages of ceftaroline fosamil shown in Tables 1 to 4 for the treatment of cSSTI caused by *S. aureus* with ceftaroline MIC of 2 or 4 mg/L are based on pharmacokinetic-pharmacodynamic modelling and simulation (see sections 4.2 and 5.2). Ceftaroline fosamil should not be used to treat cSSTI due to *S. aureus* for which the ceftaroline MIC is >4 mg/L.

## 4.5 Drugs interactions

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

The interaction potential of ceftaroline or ceftaroline fosamil on medicinal products metabolised by CYP450 enzymes is expected to be low since they are not inhibitors nor inducers of CYP450 enzymes *in vitro*. Ceftaroline or ceftaroline fosamil are not metabolised by CYP450 enzymes *in vitro*, therefore co-administered CYP450 inducers or inhibitors are unlikely to influence the pharmacokinetics of ceftaroline.

Ceftaroline is neither a substrate, nor an inhibitor of renal uptake transporters (OCT2, OAT1, and OAT3) *in vitro*. Therefore, interactions of ceftaroline with medicinal products that are substrates or inhibitors (e.g. probenecid) of these transporters would not be expected.

## 4.6 Use in special populations

Pregnancy

There are no or limited amount of data from the use of ceftaroline fosamil in pregnant women. Animal studies conducted in rat and rabbit do not indicate harmful effects with respect to reproductive toxicity at exposures similar to therapeutic concentrations. Following administration throughout pregnancy and lactation in the rat, there was no effect on pup birth weight or growth, although minor changes in foetal weight and delayed ossification of the interparietal bone were observed when ceftaroline fosamil was administered during organogenesis (see section 6.1).

As a precautionary measure, it is preferable to avoid the use of ceftaroline fosamil during pregnancy unless the clinical condition of the woman requires treatment with an antibiotic with ceftaroline fosamil's antibacterial profile.

Breast-feeding
It is unknown whether ceftaroline fosamil or ceftaroline is excreted in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from ceftaroline fosamil therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
The effects of ceftaroline fosamil on fertility on humans have not been studied. Animal studies with ceftaroline fosamil do not indicate harmful effects with respect to fertility (see section 6.1).

## 4.7 Effects on ability to drive and 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 4.8).

## 4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions occurring in ≥3% of approximately 3242 patients treated with ceftaroline fosamil in clinical studies were diarrhoea, headache, nausea, and pruritus, and were generally mild or moderate in severity. *Clostridium difficile*-associated disease (CDAD) and severe hypersensitivity reactions may also occur.

A greater incidence of rash in Asian patients (see below) and a greater incidence of DAGT seroconversion (see section 4.4) were observed in a study of adult patients with cSSTI conducted with ceftaroline fosamil 600 mg administered over 120 minutes every 8 hours.

Tabulated list of adverse reactions

The following adverse reactions have been identified during clinical trials and post-marketing experience with ceftaroline fosamil. Adverse reactions are classified according to System Organ Class and frequency. Frequency categories are derived according to the following conventions: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), not known (cannot be estimated from the available data).

**Table 3: Frequency of adverse reactions by system organ class from clinical trials and post-marketing experience**

| System organ class | Very common | Common | Uncommon | Rare | Not known |
|---|---|---|---|---|---|
| Infections and infestations | | | *Clostridium difficile* colitis (see section 4.4) | | |
| Blood and lymphatic system disorders | | | Anaemia, leucopenia, neutropenia, * thrombocytopenia, prothrombin time (PT) prolonged, activated partial thromboplastin time (aPTT) prolonged, international normalized ratio (INR) increased | Agranulocytosis, * eosinophilia* | |
| Immune system disorders | | Rash, pruritus | Anaphylaxis, hypersensitivity (e.g. urticaria, lip and face swelling) (see sections 4.3 and 4.4) | | |
| Nervous system disorders | | Headache, dizziness | Encephalopathy *,+ | | |
| Vascular disorders | | Phlebitis | | | |
| Respiratory, thoracic and mediastinal disorders | | | | | Eosinophilic pneumonia* |
| Gastrointestinal disorders | | Diarrhoea, nausea, vomiting, abdominal pain | | | |
| Hepatobiliary disorders | | Increased transaminases | | | |

| System organ class | Very common | Common | Uncommon | Rare | Not known |
|---|---|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | | | Stevens-Johnson syndrome (SJS)*, Toxic epidermal necrolysis (TEN)*, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)* (see section 4.4) |
| Renal and urinary disorders | | | Blood creatinine increased | | |
| General disorders and administration site conditions | | Pyrexia, infusion site reactions (erythema, phlebitis, pain) | | | |
| Investigations | Coombs Direct Test Positive (see section 4.4) | | | | |

***** Adverse Drug Reaction (ADR) identified post-marketing.

[+] Risk of encephalopathy is higher in patients with renal impairment in whom the dose of ceftaroline has not been appropriately reduced (see sections 4.2 and 4.9).

Description of selected adverse reactions

*Kounis Syndrome*
Acute coronary syndrome associated with an allergic reaction (Kounis syndrome) has been reported with other beta-lactam antibiotics.

*Rash*
Rash was observed at a common frequency in both 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 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 was very common (18.5%).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

## 4.9 Overdose

Limited data in patients receiving higher than recommended ceftaroline fosamil dosages show similar adverse reactions as observed in the patients receiving recommended dosages. Treatment of overdose should follow standard medical practice.

Patients with renal impairment

Relative overdosing could occur in patients with moderate 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 4.2).

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

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Mechanism of action

Ceftaroline is a cephalosporin antibacterial with *in vitro* activity against Gram-positive and -negative bacteria. The bactericidal action of ceftaroline is mediated through binding to essential penicillin-binding proteins (PBPs). Biochemical studies have shown that ceftaroline has high affinity for PBP2a of methicillin-resistant *Staphylococcus aureus* (MRSA) and PBP2x of penicillin non-susceptible *Streptococcus pneumoniae* (PNSP). As a result, minimum inhibitory concentrations (MICs) of ceftaroline against a proportion of these organisms tested fall into the susceptible range (see Resistance section below).

## 5.2 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, other cephalosporins and penems, ATC code: J01DI02.

The active moiety after ceftaroline fosamil administration is ceftaroline.

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. Organisms that express these enzymes and which are therefore resistant to ceftaroline occur at very variable rates between countries and between healthcare facilities within countries. If ceftaroline is commenced before susceptibility test results are available then local information on the risk of encountering organisms that express these enzymes should be taken into consideration. Resistance may also be mediated by bacterial impermeability or drug efflux pump mechanisms. One or more of these mechanisms may co-exist in a single bacterial isolate.

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 breakpoints

MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for ceftaroline fosamil and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

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 be the parameter that best correlates with the efficacy of ceftaroline.

Clinical efficacy against specific pathogens

Efficacy has been demonstrated in clinical studies against the pathogens listed under each indication that were susceptible to ceftaroline *in vitro*.

Complicated skin and soft tissue infections

Gram-positive micro-organisms

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

- *Streptococcus agalactiae*
- *Streptococcus anginosus* group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*)
- *Streptococcus dysgalactiae*

Gram-negative micro-organisms
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Klebsiella oxytoca*
- *Morganella morganii*

*Community-acquired pneumonia*
No cases of CAP due to MRSA were enrolled into the studies. The available clinical data cannot substantiate efficacy against penicillin non-susceptible strains of *S. pneumoniae*.

Gram-positive micro-organisms
- *Streptococcus pneumoniae*
- *Staphylococcus aureus* (methicillin-susceptible strains only)

Gram-negative micro-organisms
- *Escherichia coli*
- *Haemophilus influenzae*
- *Haemophilus parainfluenzae*
- *Klebsiella pneumoniae*

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:

*Anaerobic micro-organisms*
*Gram-positive micro-organisms*
- *Peptostreptococcus* spp.

*Gram-negative micro-organisms*
- *Fusobacterium* spp.

*In vitro* data indicate that the following species are not susceptible to ceftaroline:
- *Chlamydophila* spp.
- *Legionella* spp.
- *Mycoplasma* spp.
- *Proteus* spp.
- *Pseudomonas aeruginosa*

## 5.3 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 every 8 or 12 hours in healthy adults with CrCL >50 mL/min.

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 radiolabelled ceftaroline fosamil was 20.3 L, similar to the volume of extracellular fluid.

Biotransformation

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.

Elimination

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 radiolabelled ceftaroline fosamil to healthy male adults, approximately 88% of radioactivity was recovered in urine and 6% in faeces.

Special populations

*Renal impairment*
Dosage adjustments are required in adults with CrCL $\leq$50 mL/min (see section 4.2).

*Hepatic impairment*
The pharmacokinetics of ceftaroline in patients with hepatic impairment has 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.

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

*Patients with cystic fibrosis*
Cystic fibrosis patients were excluded from CAP clinical trials.

Some case reports and published studies suggest the need for a higher dose of ceftaroline fosamil in cystic fibrosis patients due to possibility of altered ceftaroline pharmacokinetics leading to sub therapeutic levels. Results from a population pharmacokinetic study, based on data pooled from various studies, overall showed no significant, clinically relevant differences in ceftaroline pharmacokinetic parameters in cystic fibrosis patients. Ceftaroline clearance was similar between cystic fibrosis patients and patients with CAP or cSSTI while ceftaroline central volume was similar to healthy subjects.

## 6. NONCLINICAL PROPERTIES

### 6.1 Animal Toxicology or Pharmacology

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 ceftaroline $C_{max}$ 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 test, 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

Overall, no adverse effects on fertility or post-natal development were observed in the rat at up to 5 times the observed clinical exposure. When ceftaroline was administered during organogenesis, minor changes in foetal weight and delayed ossification of the interparietal bone were observed in the rat at exposures below that observed clinically. However, when ceftaroline was administered throughout pregnancy and lactation, there was no effect on pup weight or growth. Ceftaroline administration to pregnant rabbits resulted in an increased foetal incidence of angulated hyoid alae, a common skeletal variation in rabbit fetuses, at exposures similar to those observed clinically.

## 7. DESCRIPTION

A pale yellowish-white to light yellow powder.

## 8. PHARMACEUTICAL PARTICULARS

### 8.1 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 8.4.

### 8.2 Shelf-life

36 months

After constitution:

The constituted vial should be used immediately.

After dilution:

The chemical and physical in-use stability has been demonstrated for up to 12 hours at 2-8°C and 6 hours at 25 °C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination the medicinal product should be used immediately If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

### 8.3 Packaging information

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.

## 8.4 Storage and handling instructions

Store in a dry, well-ventilated place at a temperature not exceeding 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 8.2.

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.

Ceftaroline fosamil 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

A 250 mL, 100 mL or 50 mL infusion bag can be used to prepare the infusion. 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 ceftaroline fosamil.

For storage conditions of the constituted and diluted medicinal product, see section 6.3.

Each vial is for single use only.
Any unused product or waste material should be disposed of in accordance with local requirements.

## 9. PATIENT COUNSELLING INFORMATION

No data available

## 10. DETAILS OF MANUFACTURER

**Manufactured By**

M/s. ACS Dobfar S.p.A. Via A. Fleming 2 NA - 37135 Verona (Italy)

**Marketed in India by**

M/s Pfizer Limited
The Capital – A Wing, 1802, 18th Floor Plot No C-70,
G Block, Bandra Kurla Complex Bandra (East), Mumbai 400 051

## 11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

IMP-ND-68/2016 dated 09 May 2016
IMP/SND/20/000053 dated 06 July 2020

## 12. DATE OF REVISION

January 2026