SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

ZINFORO® 600 mg Powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains ceftaroline fosamil 600 mg equivalent to ceftaroline 530 mg.

After reconstitution, 1 mL of the solution contains 30 mg of ceftaroline fosamil.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion.

A pale yellowish-white to light yellow powder, sterile and pyrogen free.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZINFORO is indicated for the treatment of patients with the following infections caused by susceptible isolates of the designated microorganisms.

Acute bacterial skin and skin structure infections

ZINFORO is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive and Gram-negative microorganisms: *Staphylococcus*

aureus (including methicillin-susceptible and resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Escherichia coli*, *Klebsiella pneumonia and Klebsiella oxytoca.*

Community-acquired bacterial pneumonia

ZINFORO is indicated for the treatment of community-acquired bacterial pneumonia (CABP) caused by susceptible isolates of the following Gram-positive and Gram-negative microorganisms: *Streptococcus pneumoniae* (including cases with concurrent bacteraemia), *Staphylococcus aureus* (methicillin-susceptible isolates only), *Haemophilus influenzae, Klebsiella pneumonia* and *Escherichia coli.*

ZINFORO is indicated in neonates, infants, children, adolescents and adults (see sections 4.4 and 5.1).

4.2 Posology and method of administration

Posology

The recommended dosage of ZINFORO is 600 mg administered every 12 hours by intravenous infusion over 5 to 60 minutes (standard dose), with appropriate reductions for paediatric patients (see Table 3). The duration of treatment should be guided by the type of infection to be treated, its severity, and the patient's clinical response.

For the treatment of patients with acute bacterial skin and skin structure infection (ABSSSI) confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ceftaroline, the dose of ZINFORO is 600 mg administered every 8 hours by intravenous infusion over 120 minutes (high dose), with appropriate reductions for paediatric patients (see Table 3).

The recommended duration of antimicrobial treatment for ABSSSI is 5 – 14 days and for community-acquired bacterial pneumonia (CABP) is 5 – 7 days.

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

Indication	**Posology (mg/ infusion)**	**Infusion time (minutes)/ frequency**

Standard dose[a]		
Acute bacterial skin and skin structure infection (ABSSSI)	600 mg	5 – 60[b]/every 12 hours
Community-acquired bacterial pneumonia (CABP)	600 mg	5 – 60[b]/every 12 hours
High dose[b]		
ABSSSI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ZINFORO[c]	600 mg	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 ZINFORO MIC is ≤ 1 mg/L, the standard dose is recommended.		

Special populations

Elderly patients

No dosage adjustment is required for the elderly with creatinine clearance (CrCL) values > 50 mL/min (see section 5.2).

Renal impairment

The dose should be adjusted when CrCL is ≤ 50 mL/min, as shown in Tables 2 and 4 (see sections 4.9 and 5.2). The recommended durations of treatment are 5 - 14 days for ABSSSI and 5 - 7 days for CABP.

Table 2: Dosage in adults with impaired renal function, CrCL ≤ 50 mL/min

Indications	**CrCL (mL/min)[a]**	**Posology (mg/infusion)**	**Infusion time (minutes)/ frequency**
Standard dose			
ABSSSI CABP	> 30 to ≤ 50	400 mg	5 – 60[c]/every 12 hours
	≥ 15 to ≤ 30	300 mg	
	End-stage renal disease (ESRD), including haemodialysis[b]	200 mg	
High dose[c]			
ABSSSI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ZINFORO[d]	> 30 to ≤ 50	400 mg	120/every 8 hours
	≥ 15 to ≤ 30	300 mg	
	ESRD, including haemodialysis[b]	200 mg	

[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 haemodialysable; thus ZINFORO 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 ZINFORO 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 5.2).

Paediatric population

Dose recommendations for neonates, infants and children and adolescents are based on pharmacokinetic (PK) modelling.

*Table 3: Dosage in paediatric patients with normal renal function, CrCL > 50 mL/min**

Indications	**Age group**	**Posology (mg/infusion)**	**Infusion time (minutes)/ Frequency**
Standard dose[a]			
ABSSSI CABP	Adolescents aged from 12 to < 18 years with bodyweight ≥ 33 kg	600 mg	5 – 60[b]/every 12 hours

	Adolescents aged from 12 years to < 18 years bodyweight < 33 kg and children ≥ 2 years to < 12 years	12 mg/kg to a maximum of 400 mg	5 – 60[b]/every 8 hours
	Infants ≥ 2 months to < 2 years	8 mg/kg	5 – 60[b]/every 8 hours
	Neonates from birth to < 2 months[b]	6 mg/kg	60/every 8 hours
High dose[b]			
ABSSSI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ZINFORO[c]	Children and adolescents aged from ≥ 2 years to < 18 years	12 mg/kg to a maximum of 600 mg	120/every 8 hours
	Infants ≥ 2 months to < 2 years	10 mg/kg	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, neonatal 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.

[*] Calculated using the Schwartz formula (in mL/min/1,73 m^2) for paediatric patients.

There is insufficient information to recommend dosage adjustments in adolescents aged from 12 to < 18 years with bodyweight < 33 kg and in children aged from 2 to 12 years with end-stage renal disease (ESRD).

There is insufficient information to recommend dosage adjustments in paediatric patients < 2 years with moderate or severe renal impairment or ESRD.

Table 4: Dosage in paediatric patients with impaired renal function, CrCL ≤ 50 mL/min

Indications	**Age group**	**CrCL (mL/min)[a]**	**Posology (mg/ infusion)**	**Infusion time (minutes)/ Frequency**
Standard dose				
ABSSSI CABP	Adolescents aged from 12 to < 18 years with bodyweight ≥ 33 kg	> 30 to ≤ 50	400 mg	5 - 60[c]/ every 12 hours
		≥ 15 to ≤ 30	300 mg	
		ESRD, including haemo-dialysis[b]	200 mg	
	Adolescents aged from 12 years to < 18 years	> 30 to ≤ 50	8 mg/kg to a maximum of 300 mg	5 – 60[c]/ every 8 hours

	bodyweight < 33 kg and children ≥ 2 years to < 12 years	≥ 15 to ≤ 30	6 mg/kg to a maximum of 200 mg	
High dose[c]				
ABSSSI confirmed or suspected to be caused by *S. aureus* with an MIC = 2 mg/L or 4 mg/L to ceftaroline[d]	Children and adolescents aged from ≥ 2 years to < 18 years	> 30 to ≤ 50	10 mg/kg to a maximum of 400 mg	120/every 8 hours
		≥ 15 to ≤ 30	8 mg/kg to a maximum of 300 mg	

[a] Calculated using the Schwartz formula for paediatric patients (in mL/min/1,73 m^2). Dose is based on CrCL. CrCL should be closely monitored and the dose adjusted according to changing renal function.

[b] ZINFORO is haemodialysable; thus ZINFORO 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 ZINFORO MIC is ≤ 1 mg/L, the standard dose is recommended.

Method of administration

For intravenous use.

ZINFORO solution for infusion can be administered in a 50 mL, 100 mL or 250 mL intravenous bag or bottle.

Once the intravenous solution is prepared in the intravenous bag or bottle it should be administered within 6 hours of preparation.

For instructions on reconstitution and dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to ceftaroline fosamil or to any of the excipients of ZINFORO (listed in section 6.1).
- Hypersensitivity to the cephalosporin class of antibacterials.
- Immediate and severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial medicine (e.g., penicillins or carbapenems).

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Serious and fatal hypersensitivity reactions have been reported in patients receiving beta-lactam antibacterials, such as ZINFORO (see sections 4.3 and 4.8).

Severe cutaneous adverse reactions (SCARs), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in patients taking beta-lactam antibiotics.

Patients who have a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibacterials may also be hypersensitive to ZINFORO. Before initiating therapy with ZINFORO, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibacterials. If a severe allergic reaction or SCAR occurs, ZINFORO should be discontinued and appropriate measures taken (see section 4.3).

Clostridium difficile-associated diarrhoea

Antibacterial-associated colitis and pseudomembranous colitis have been reported with ZINFORO 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 ZINFORO (see section 4.8). 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.

Non-susceptible organisms

Superinfections may occur during or following treatment with ZINFORO.

Patients with pre-existing seizure disorder

Convulsions have been reported with ZINFORO. Clinical study experience with ZINFORO 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 ZINFORO. The incidence of DAGT seroconversion in patients receiving ZINFORO was 11,2 % in the five 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 ZINFORO every 8 hours (600 mg administered over 120 minutes every 8 hours). There was no evidence of haemolysis in any patient receiving ZINFORO who developed a positive DAGT.

ABSSSI caused by S. aureus with an MIC > 1 mg/L to ZINFORO

There are limited clinical trial data on the use of ZINFORO to treat ABSSSI caused by *S. aureus* with an MIC of > 1 mg/L. The recommended dosages of ZINFORO shown in Tables 1 to 4 for the treatment of ABSSSI caused by *S. aureus* with ZINFORO MIC of 2 or 4 mg/L are based on pharmacokinetic-pharmacodynamic modelling and simulation (see section 4.2).

Paediatric population

Paediatric patients < 2 months of age

The recommended dosage of ZINFORO shown in Table 3 for paediatric patients < 2 months of age are based on pharmacokinetic-pharmacodynamic modelling and simulation.

4.5 Interaction with other medicines and other forms of interaction

No clinical medicine interaction studies have been conducted with ZINFORO.

The interaction potential of ZINFORO on medicines metabolised by CYP450 enzymes is expected to be low, since ZINFORO 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*. ZINFORO is not metabolised by CYP450 enzymes *in vitro*, so co-administered CYP450 inducers or inhibitors are unlikely to influence the pharmacokinetics of ZINFORO.

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

4.6 Fertility, pregnancy and lactation

The safety of ZINFORO in pregnancy and lactation has not been established.

Pregnancy

No clinical data on pregnancies are available for ZINFORO. ZINFORO should not be used during pregnancy.

Breastfeeding

It is not known whether ZINFORO is excreted in human milk, but because many beta-lactams are excreted in breast milk, women who are breastfeeding their infants should not be treated with ZINFORO.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Undesirable effects may occur which may have an effect on the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

The 4 clinical trials (2 in ABSSSI and 2 in CABP) included 1 305 adult patients treated with ZINFORO (600 mg administered over 60 minutes every 12 hours).

The incidence of treatment emergent adverse events in the pooled ABSSSI and CABP studies was 45,7 %. The most common adverse reactions occurring in ≥ 3 % of patients treated with ZINFORO were diarrhoea, headache, nausea, and pruritus and were generally mild or moderate in severity.

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

Tabulated summary of adverse reactions

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 are derived from the adverse events observed in the pooled and CABP studies and are defined 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).

Frequency of adverse reactions in clinical trials

System organ class	**Frequency**	**Adverse event**
Infections and infestations	Uncommon	*Clostridium difficile* colitis (see section 4.4)

Blood and lymphatic system disorders	Uncommon	Anaemia, leukopenia, thrombocytopenia
Immune system disorders	Uncommon	Hypersensitivity/ anaphylaxis (see section 4.3 and section 4.4)
Nervous system disorders	Common	Headache, dizziness
Vascular disorders	Common	Phlebitis
Gastrointestinal disorders	Common	Diarrhoea, nausea, vomiting, abdominal pain
Hepato-biliary disorders	Common	Increased transaminases
Skin and subcutaneous tissue disorders	Common	Rash, pruritus
	Uncommon	Urticaria
Renal and urinary disorders	Uncommon	Increased blood creatinine
General disorders and administration site conditions	Common	Pyrexia, infusion site reactions (erythema, phlebitis, pain)
Investigations	Very common	Positive Coombs direct test (see section 4.4)
	Uncommon	Prolonged prothrombin time,

		increased international normalised ratio

Post- marketing experience

Blood and lymphatic system disorders	Agranulocytosis, neutropenia, eosinophilia
Nervous system disorders	Encephalopathy
Respiratory, thoracic and mediastinal disorders	Eosinophilic pneumonia

Description of selected adverse reactions

Rash

Rash was observed at a common frequency in the pooled Phase III studies in ABSSI with administration of ZINFORO every 12 hours (600 mg administered over 60 minutes every 12 hours) and the study in ABSSSI 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 ZINFORO every 8 hours was very common (18,5 %).

Paediatric population

The safety assessment in paediatric patients is based on the safety data from 2 trials in which 227 patients aged from 2 months to 17 years with ABSSSI or CABP received ZINFORO. Overall, the safety profile in these 227 patients was similar to that observed in the adult population.

In addition, the safety assessment in neonates is based on the safety data from 2 trials in which 34 patients (age range from birth to less than 60 days) received ZINFORO; 23 of these patients received only a single dose of ZINFORO. Overall, the adverse events reported in these studies were consistent with the known safety profile for ZINFORO.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Limited data in patients receiving higher than recommended ZINFORO dosages show similar adverse reactions as observed in the patients receiving recommended dosages.

Patients with renal impairment

Relative overdosing can occur particularly 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).

Treatment should be symptomatic and supportive.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 20.1.1 Broad and medium spectrum antibiotics

Mechanism of action

Ceftaroline is a cephalosporin with *in vitro* 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 active against methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-non-susceptible *Streptococcus pneumoniae* (PNSP) due to its affinity for the altered PBPs found in these organisms.

Pharmacokinetic/pharmacodynamic relationship

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.

Most isolates of *Enterococcus faecium*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Pseudomonas putida*, *Acinetobacter baumannii*, *Acinetobacter* spp, *Stenotrophonomas maltophilia*, *Burkholderia cepacia*, *Bacteroides fragilis* and *Bacteroids thetaiotamicron* are intrinsically resistant to ceftaroline.

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

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 (see section 4.1).

Interpretations of test results should be made in accordance with local infectious diseases and clinical microbiology guidelines.

5.2 Pharmacokinetic properties

The C_{max} and AUC of ceftaroline increase approximately in proportion to dose within the single dose range of 50 - 1 000 mg. No appreciable accumulation of ceftaroline is observed following multiple intravenous infusions of 600 mg administered over 60 minutes every 8 or 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 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

Elderly

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 33 % increase in $AUC_{0-\infty}$ in the elderly that was mainly attributable to age-related changes in renal function.

Dose adjustment is not required in elderly patients with creatinine clearance (CrCl) above 50 mL/min.

Renal impairment

Dosage adjustments are required in adults, adolescents and children with CrCL ≤ 50 mL/min (see section 4.2).

There is insufficient information to recommend dosage adjustments in adolescents with ESRD aged from 12 to < 18 years and with bodyweight < 33 kg and in children with ESRD aged from 2 to < 12 years. There is insufficient information to recommend dosage adjustments in paediatric patients aged < 2 years with moderate or severe renal impairment or ESRD.

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.

Paediatric population

Dose adjustments are required for neonates, infants, children and adolescents with bodyweight < 33 kg (see section 4.2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-arginine

6.2 Incompatibilities

ZINFORO must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf-life

36 months.

Chemical and physical in-use stability has been demonstrated for 6 hours at 25 ºC and 24 hours at 2 to 8 ºC. From a microbiological point of view, the medicine should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ºC, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 °C.

For storage conditions of the reconstituted and diluted medicine, see section 6.3.

6.5 Nature and contents of container

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

Supplied in packs of 10 vials.

6.6 Special precautions for disposal and other handling

The powder must be reconstituted with water for injections and the resulting concentrate must then be immediately diluted prior to use.

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

Reconstitution

ZINFORO powder for solution for infusion should be reconstituted with 20 mL of sterile water for injections. The reconstitution time of the powder should not be more than 120 seconds. The resulting reconstituted solution must then be immediately diluted prior to use. One mL of the reconstituted solution contains 30 mg of ceftaroline fosamil.

Dilution

The contents of the vial should be transferred to an infusion bag or bottle for further dilution. The resulting solution should be shaken prior to being transferred to an intravenous bag or bottle. Compatibility has been demonstrated with 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) or
- lactated Ringer's solution.

A 50 mL, 100 mL or 250 mL infusion bag can be used to prepare the infusion. The total time interval between starting reconstitution and completing preparation of the intravenous infusion should not exceed 30 minutes.

Infusion volumes for paediatric patients will vary according to the weight of the child. The infusion solution concentration during preparation and administration should not exceed 12 mg/mL ZINFORO.

ZINFORO must not be mixed with any other diluents except those mentioned above.

For storage conditions of the reconstituted and diluted medicine (see section 6.3).

Each vial is for single use only.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pfizer Laboratories (Pty) Ltd

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Sandton 2196

South Africa

Tel: +27(0)11 320 6000 / 0860 734 937 (Toll-free South Africa)

8. REGISTRATION NUMBER

46/20.1.1/0628

9. DATE OF FIRST AUTHORISATION

26 November 2015

10. DATE OF REVISION OF THE TEXT

03 July 2023

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