ZINFORO® 600mg (ceftaroline fosamil) POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION

Prescribing Information:

Please refer to the Summary of Product Characteristics (SmPC) before prescribing Zinforo. **Indications:** Zinforo is indicated for treatment of complicated skin and soft tissue infections (cSSTI) and community-acquired pneumonia (CAP) in neonates, infants, children, adolescents and adults. **Presentation:** 600mg ceftaroline fosamil powder for concentrate for solution for injection containing 600mg ceftaroline fosamil. After reconstitution, 1ml of solution contains 30mg of ceftaroline fosamil. **Dosage and administration:** Zinforo 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 50mL, 100mL or 250mL. Please consult SmPC for further information. Infusion volumes for paediatric patients will vary according to weight of child. The infusion solution concentration should not exceed 12mg/ml ceftaroline fosamil. The recommended intravenous dose for adults and adolescents aged from 12 to < 18 years with bodyweight ≥ 33kg with creatinine clearance (CrCL) > 50mL/min is 600mg every 12 hours over 5 to 60 minutes. Based on pharmacokinetic (PK) and pharmacodynamic (PD) analyses the recommended dose for treatment of cSSTI due to *S. aureus* for which ceftaroline MIC is 2 or 4 mg/L is 600 mg every 8 hours using 2hour infusions. The recommended dose in children and adolescents aged from ≥ 2 years to < 18 years with bodyweight < 33kg with CrCL > 50mL/min is 12mg/kg every 8 hours over 5 to 60 minutes. The dose administered should not exceed 400mg. For infants aged ≥ 2 months to < 2 years with CrCL > 50mL/min, the recommended dose is 8mg/kg every 8 hours over 5 to 60 minutes. For neonates from birth to < 2 months CrCL > 50mL/min, the recommended dose is 6mg/kg every 8 hours over 60 minutes. The dose recommendations are applicable to treatment of *S. aureus* for which the ceftaroline MIC is ≤ 1 mg/L. Duration of treatment for cSSTI is 5-14 days and for CAP is 5-7 days. **Special populations: Elderly:** No dose adjustment required with CrCL values > 50mL/min. **Renal impairment:** The dose should be adjusted when creatinine clearance is ≤ 50 ml/min. The recommended durations of treatment are the same as for patients with CrCL > 50mL/min. The recommended dose for adults and adolescents aged from 12 to < 18 years with bodyweight ≥ 33kg for cSSTI and CAP with CrCL > 30 to ≤ 50 is 400mg every 12 hours over 5 to 60 minutes. For CrCL ≥ 15 to ≤ 30, the recommended dose is 300mg every 12 hours over 5 to 60 minutes. For end-stage renal disease (ESRD) including haemodialysis, the recommended dose is 200mg every 12 hours over 5 to 60 minutes. Please consult SmPC for further information. Based on PK and PD analyses the recommended dose for treatment of cSSTI due to *S. aureus* for which the ceftaroline MIC is 2 or 4 mg/L is the dose recommended by renal function category administered every 8 hours using 2-hour infusions. Please consult SmPC for further information. The recommended dose for children aged from 2 to < 12 years and adolescents aged from 12 to < 18 years with bodyweight < 33kg with CrCL > 30 to ≤ 50 is 8mg/kg every 8 hours over 5 to 60 minutes. The dose administered should not exceed 300mg. For CrCL ≥ 15 to ≤ 30, for children aged from 2 to < 12 years and adolescents aged from 12 to < 18 years with bodyweight < 33kg, the recommended dose is 6mg/kg every 8 hours over 5 to 60 minutes. The dose administered should not exceed 200mg. For CrCL > 30 to ≤ 50, for children and adolescents aged from > 2 to < 18 years the recommended dose is 10mg/kg every 8 hours over 120 minutes. The dose administered should not exceed 400mg.

For CrCL ≥ 15 to ≤ 30, for children and adolescents aged from > 2 to < 18 years the recommended dose is 8mg/kg every 8 hours over 120 minutes. The dose administered should not exceed 300mg. The dose recommendations are applicable to treatment of *S. aureus* for which the ceftaroline MIC is ≤ 1 mg/L. For ESRD, there is insufficient information to recommend dosage adjustments in adolescents aged from 12 to < 18 years with bodyweight < 33kg and in children aged from 2 to 12 years. There is insufficient information to recommend dosage adjustments in children aged from 2 months to < 2 years with moderate or severe renal impairment or ESRD. **Hepatic impairment:** No dose adjustment necessary. **Contraindications:** Hypersensitivity to the active substance or to any of the 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). **Warnings and precautions: Hypersensitivity reactions:** Severe cutaneous adverse reactions (SCARs), including 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 association with beta-lactam antibiotics (including cephalosporins) treatment. Patients who have a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibacterials may also be hypersensitive to ceftaroline fosamil. Zinforo 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 with Zinforo occurs, discontinue use and take appropriate measures. ***Clostridium difficile*-associated diarrhoea:** Antibacterial-associated colitis and pseudomembranous colitis have been reported and may range from mild to life threatening. Therefore, it is important to consider this diagnosis in patients with diarrhoea during or subsequent to the administration of ceftaroline fosamil. In such circumstance, consider discontinuation of therapy and use supportive measures together with the administration of specific treatment for *Clostridium difficile*. **Non-susceptible organisms:** Superinfections may occur during or following treatment with Zinforo. **Patients with pre-existing seizure disorder:** Use with caution in this patient population. **Direct antiglobulin test (Coombs test) seroconversion and potential risk of haemolytic anaemia:** A positive direct antiglobulin test (DAGT) may occur during treatment with cephalosporins and the possibility that haemolytic anaemia may occur cannot be ruled out. Patients experiencing anaemia during or after treatment with Zinforo should be investigated for this possibility. **Limitations of clinical data:** No experience with ceftaroline in treatment of CAP in the following patient groups: the immunocompromised, patients with severe sepsis/septic shock, severe underlying lung disease, 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 advised when treating such patients. No experience with ceftaroline in 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. Limited experience in treating patients with diabetic foot infections. Caution advised when treating such patients. Limited data on use of ceftaroline to treat cSSTI caused by *S. aureus* with an MIC of > 1mg/mL. The recommended dosages of Zinforo for the treatment of cSSTI caused by *S. aureus* with ceftaroline MIC of 2 or 4 mg/L are based on PK-PD modelling and simulation. Zinforo should not be used to treat cSSTI due to *S. aureus* for which ceftaroline MIC is > 4mg/mL.

Drug interactions: Co -administered CYP450 inducers or inhibitors are unlikely to influence the pharmacokinetics of ceftaroline. Interactions with substrates or inhibitors (e.g. probenecid) of renal uptake transporters (OCT2, OAT1 and OAT3) would not be expected. **Pregnancy and lactation:** Avoid using during pregnancy unless the clinical condition of the woman requires treatment. Unknown whether ceftaroline fosamil or ceftaroline is excreted in human milk. Risk to the newborns/ infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Zinforo therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Ability to drive and use machines:** Dizziness may occur. **Undesirable events:** Consult SmPC for full list of side effects. **Very Common:** Coombs direct test positive. **Common:** Rash, pruritus, headache, dizziness, phlebitis, diarrhoea, nausea, vomiting, abdominal pain, increased transaminases, pyrexia, infusion site reactions (erythema, phlebitis, pain). **Uncommon:** *Clostridium difficile* colitis, anaemia, leucopenia, neutropenia, thrombocytopenia, prothrombin time (PT) prolonged, activated partial thromboplastin time (aPTT) prolonged, international normalised ratio (INR) increased, anaphylaxis, hypersensitivity (e.g. urticaria, lip and face swelling), encephalopathy, blood creatinine increased. **Rare:** Agranulocytosis, Eosinophilia. Paediatric safety profile was similar to that observed in adults. **Legal category:** POM. **Marketing Authorisation number and basic NHS price:** ZINFORO 600 mg, powder for concentrate for solution for infusion (20 mL vial), supplied in packs of 10 vials.

£375.00 **Marketing Authorisation Holder:** Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom. **Further information is available on request from:** Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS.

Last revised: September 2020

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Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161.

Pfleet No: 2019-0054989 & 2020-0057795

ABBREVIATED PRESCRIBING INFORMATION NI

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Ringaskiddy, County Cork, Ireland. **Further information is available on request from:** Pfizer Limited, Walton Oaks, Dorking Road, Tadworth,

Surrey, KT20 7NS.

Last revised: January 2021

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