ABBREVIATED PRESCRIBING INFORMATION

ZAVICEFTA®(ceftazidime and avibactam) 2g/0.5g powder for concentrate for solution for infusion.

Prescribing Information:

Please refer to the Summary of Product Characteristics (SmPC) before prescribing Zavicefta. **Indications:** Zavicefta is indicated in adults and paediatric patients aged 3 months and older for treatment of complicated intra-abdominal infection (cIAI), complicated urinary tract infection (cUTI), including pyelonephritis, and hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP). Treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above. Also indicated for the treatment of infections due to aerobic Gram-negative organisms in adult patients and paediatric patients aged 3 months and older with limited treatment options. **Presentation:** 2g ceftazidime (as ceftazidime pentahydrate) and 0.5g avibactam (as avibactam sodium) powder for concentrate for solution for infusion. After reconstitution, 1mL of solution contains 167.3mg of ceftazidime and 41.8mg of avibactam. **Dosage and administration:** Zavicefta is administered by intravenous infusion over 120 minutes in an infusion – please refer to sections 4.2 & 6.6 of SmPC. The recommended intravenous dose for adult patients with estimated creatinine clearance (CrCL) > 50mL/min is 2g ceftazidime and 0.5g avibactam every 8 hours, for a duration of 5 to 14 days, depending on severity of infection, pathogen and clinical progress. *Special populations*: *Elderly*: No dose adjustment required. *Hepatic impairment*: No dose adjustment required. *Renal impairment*: Mild (estimated CrCL > 50-≤ 80mL/min): No dose adjustment. CrCL 31-50mL/min (estimated): 1g ceftazidime and 0.25g avibactam, every 8 hours. CrCL 16-30mL/min (estimated): 0.75g ceftazidime and 0.1875g avibactam, every 12 hours. CrCL 6-15mL/min (estimated): 0.75g ceftazidime and 0.1875g avibactam, every 24 hours. ESRD including on haemodialysis: 0.75g ceftazidime and 0.1875g avibactam, every 48 hours. *Dosage in paediatric patients: Paediatric patients aged 2 years to <18 years:* CrCL > 50mL/min/1.73 m^2 (estimated): 50mg/kg ceftazidime and 12.5mg/kg avibactam to a maximum of 2g/0.5g, every 8 hours. CrCL 31-50mL/min/1.73 m^2 (estimated): 25mg/kg ceftazidime and 6.25mg/kg avibactam to a maximum of 1g/0.25g, every 8 hours. CrCL 16-30mL/min/1.73 m^2 (estimated): 18.75mg/kg ceftazidime and 4.75mg/kg avibactam to a maximum of 0.75g/0.1875g, every 12 hours. CrCL 6-15mL/min/1.73 m^2 (estimated): 18.75mg/kg ceftazidime and 4.75mg/kg avibactam to a maximum of 0.75g/0.1875g, every 24 hours. ESRD including on haemodialysis: 18.75mg/kg ceftazidime and 4.75mg/kg avibactam to a maximum of 0.75g/0.1875g, every 48 hours. *Paediatric patients aged 6 months to < 2 years:* CrCL > 50mL/min/1.73 m^2 (estimated): 50mg/kg ceftazidime and 12.5mg/kg avibactam to a maximum of 2g/0.5g, every 8 hours. CrCL 31-50mL/min/1.73 m^2 (estimated): 25mg/kg ceftazidime and 6.25mg/kg avibactam, every 8 hours. CrCL 16-30mL/min/1.73 m^2 (estimated): 18.75mg/kg ceftazidime and 4.7mg/kg avibactam, every 12 hours. *Paediatric patients aged 3 months to < 6 months:* CrCL > 50mL/min/1.73 m^2 (estimated): 40mg/kg ceftazidime and 10mg/kg avibactam, every 8 hours. CrCL 31-50mL/min/1.73 m^2 (estimated): 20mg/kg ceftazidime and 5mg/kg avibactam, every 8 hours. CrCL 16- 30mL/min/1.73 m^2 (estimated): 15mg/kg ceftazidime and 3.75mg/kg avibactam, every 12 hours. There is insufficient data to recommend dosage for patients < 2 years of age that have a CrCL < 16 mL/min/1.73 m^2. The safety and efficacy of Zavicefta in paediatric patients < 3 months old have not been established. **Contraindications:** Hypersensitivity to the active substances, any of the excipients or to any cephalosporin antibacterial agent. Severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of β-lactam antibacterial agent (e.g. penicillins, monobactams or carbapenems). **Warnings and precautions:** *Hypersensitivity reactions*: Treatment with Zavicefta must be discontinued immediately and adequate emergency measures must be initiated. Before beginning treatment, it should be established whether the patient has a history of hypersensitivity reactions to ceftazidime, to other cephalosporins or to any other type of β-lactam antibacterial agent. Caution should be used if ceftazidime/avibactam is given to patients with a history of non-severe hypersensitivity to penicillins, monobactams or carbapenems. *Clostridioides difficile -associated diarrhoea*: Discontinuation of Zavicefta and the administration of specific treatment for *Clostridioides difficile* should be considered in patients who present with diarrhoea during or subsequent to the administration of Zavicefta. Medicinal products that inhibit peristalsis should not be given. *Renal impairment*: Dose should be reduced according to the degree of renal impairment. Neurological sequelae, including tremor, myoclonus, non-convulsive status epilepticus, convulsion, encephalopathy and coma have occasionally been reported with ceftazidime when the dose has not been reduced in patients with renal impairment. Close monitoring of estimated creatinine clearance is advised. *Nephrotoxicity*: Concurrent treatment with high doses of cephalosporins and nephrotoxic medicinal products such as aminoglycosides or potent diuretics (e.g. furosemide) may adversely affect renal function. *Direct antiglobulin test (DAGT or Coombs test) seroconversion and potential risk of haemolytic anaemia:* Ceftazidime/avibactam use may cause development of a positive direct antiglobulin test, which may interfere with the cross-matching of blood and/or may cause drug induced immune haemolytic anaemia. Patients experiencing anaemia during or after treatment with Zavicefta should be investigated for this possibility. *Spectrum of activity*: Ceftazidime has little or no activity against the majority of Gram-positive organisms and anaerobes. Additional antibacterial agents should be used when these pathogens are known or suspected to be contributing to the infectious process. The inhibitory spectrum of avibactam includes many of the enzymes that inactivate ceftazidime, including Ambler class A β-lactamases and class C β-lactamases. Avibactam does not inhibit class B enzymes (metallo-β-lactamases) and is not able to inhibit many of the class D enzymes. *Non-susceptible organisms*: Prolonged use may result in the overgrowth of non-susceptible organisms (e.g. enterococci, fungi), which may require interruption of treatment or other appropriate measures. *Interference with laboratory tests*: Ceftazidime may interfere with copper reduction methods (Benedict's, Fehling's, Clinitest) for detection of glycosuria leading to false positive results. Ceftazidime does not interfere with enzyme-based tests for glycosuria. *Controlled sodium diet*: There is a potential risk of overdosing, particularly for paediatric patients aged less than 12 months of age. Care should be taken when calculating the volume of administration of the dose and dilution with sodium-containing solutions should be considered in relation to the total sodium from all sources that will be administered to the patient (see section 6.6 of SmPC). Consideration should be given to patients who are on a controlled sodium diet. **Drug interactions:** Co-administration with probenecid may affect elimination of avibactam and is therefore not recommended. Avibactam and ceftazidime do not inhibit the major renal or hepatic transporters in the clinically relevant exposure range, therefore the interaction potential via these mechanisms is considered to be low. No interaction between ceftazidime and avibactam, or between ceftazidime/avibactam and metronidazole have been demonstrated. Concurrent treatment with high doses of cephalosporins and aminoglycosides or potent diuretics (e.g. furosemide) may adversely affect renal function. Chloramphenicol should be avoided, due to the possibility of antagonism *in vivo*. **Pregnancy and lactation:** Zavicefta should only be used during pregnancy if the potential benefit outweighs the possible risk. Ceftazidime is excreted in human milk in small quantities. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breast feeding. **Ability to drive and use machines:** Undesirable effects may occur (e.g. dizziness). **Undesirable events:** *Very common*: Coombs direct test positive. *Common*: Candidiasis (including vulvovaginal candidiasis and oral candidiasis), eosinophilia, thrombocytosis, thrombocytopenia, headache, dizziness, diarrhoea, abdominal pain, nausea, vomiting, alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, gamma-glutamyltransferase increased, blood lactate dehydrogenase increased, rash maculo-papular, urticaria, pruritus, infusion site thrombosis, infusion site phlebitis, pyrexia. *Uncommon*: *Clostridium difficile* colitis, pseudomembranous colitis, neutropenia, leukopenia, lymphocytosis, paraesthesia, dysgeusia, blood creatinine and urea increased, acute kidney injury. *Very rare*: Tubulointerstitial nephritis. *Unknown*: Agranulocytosis, haemolytic anaemia, anaphylactic reaction, jaundice, toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, angioedema, jaundice, drug reaction with eosinophilia and systemic symptoms (DRESS). Refer to SmPC for further information on side effects. **Overdose:** Overdose with ceftazidime/avibactam can lead to neurological sequelae including encephalopathy, convulsions and coma. **Package quantities, Marketing Authorisation number and basic NHS price:** ZAVICEFTA (ceftazidime and avibactam) 2g/0.5g powder for concentrate for solution for infusion (20 mL vial), supplied in packs of 10 vials. EU/1/16/1109/001 £857.00. **Legal category:** POM. **Marketing Authorisation Holder:** Pfizer Ireland Pharmaceuticals, Operations Support Group, Ringaskiddy, County Cork, Ireland. **Further information is available on request from:** Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Tel: +44 (0) 1304 616161.

Last revised: February 2021
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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.

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

Ref: ZI 9_0

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

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 (e.g. cystic fibrosis), 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 degreeand 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 accountthe 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. EU/1/12/785/001, £375.00 **Marketing Authorisation Holder:** Pfizer Ireland Pharmaceuticals, Operations Support Group

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

Ref: ZI 10_0

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Pfleet No: 2020-0062283 & 2020-0063371

Meronem IV 500 mg and 1 g
Prescribing Information
Please refer to the SPC before prescribing Meropenem.
Presentation: Each vial contains meropenem trihydrate equivalent to 500 mg or 1 g anhydrous meropenem. Each 500 mg vial contains 104 mg sodium carbonate which equates to approximately 2 mEq of sodium (approximately 45 mg). Each 1 g vial contains 208 mg sodium carbonate which equates to approximately 4 mEq of sodium (approximately 90 mg). A white to light yellow powder for solution for injection or infusion. **Indications and dosage (for adults and adolescents)**: Severe pneumonia including hospital and ventilator-associated pneumonia (500 mg or 1 g every 8 hours), Broncho-pulmonary infections in cystic fibrosis (2 g every 8 hours), Complicated urinary tract infections (500 mg or 1 g every 8 hours), Complicated intra-abdominal infections (500 mg or 1 g every 8 hours), Intra- and post-partum infections (500 mg or 1 g every 8 hours), Complicated skin and soft tissue infections (500 mg or 1 g every 8 hours), Acute bacterial meningitis (2 g every 8 hours), Management of febrile neutropenic patients (1 g every 8 hours). Meropenem is usually given by intravenous infusion over approximately 15 to 30 minutes. Alternatively, doses up to 1 g can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection. **Indications and dosage (Children from 3 months to 11 years of age and up to 50 kg body weight)**: Severe pneumonia including hospital and ventilator-associated pneumonia (10 or 20 mg/kg every 8 hours), *Broncho-pulmonary* infections in cystic fibrosis (40 mg/kg every 8 hours), Complicated urinary tract infections (10 or 20 mg/kg every 8 hours), Complicated intra-abdominal infections (10 or 20 mg/kg every 8 hours), Complicated skin and soft tissue infections (10 or 20 mg/kg every 8 hours), Acute bacterial meningitis (40 mg/kg every 8 hours), Management of febrile neutropenic patients (20 mg/kg every 8 hours). Children over 50 kg body weight the adult dose should be administered. The safety and efficacy of meropenem in children under 3 months of age have not been established and the optimal dose regimen has not been identified. However, limited pharmacokinetic data suggest that 20 mg/kg every 8 hours may be an appropriate regimen. **Administration and dosage:** Meropenem is usually given by intravenous (IV) infusion over approximately 15 to 30 minutes at a usual dose of 500 mg/1 g every 8 hours. Alternatively, doses up to 1 g can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection. The dose of Meropenem administered and the duration of treatment should take into account the type of infection to be treated, including its severity, and the clinical response. For paediatric dosing, see SPC. **Renal Impairment:** Dose adjustment required to the degree of renal impairment (see SPC). Meropenem is cleared by haemodialysis and haemofiltration. The required dose should be administered after completion of the haemodialysis cycle. **Hepatic impairment:** No dose adjustment. **Elderly:** No dose adjustment if renal function normal or creatinine clearance above 50 ml/min. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed in the SPC section 6.1. Hypersensitivity to any other carbapenem antibacterial agent. Severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins or cephalosporins). **Warnings and precautions:** The selection of meropenem to treat an individual patient should take into account the appropriateness of using a carbapenem antibacterial agent based on factors such as severity of the infection, the prevalence of resistance to other suitable antibacterial agents and the risk of selecting for carbapenem-resistant bacteria. Resistance to penems of *Enterobacteriaceae*, *Pseudomonas aeruginosa, Acinetobacter* spp. varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in these bacteria to penems. As with all beta-lactam antibiotics, serious and occasionally fatal hypersensitivity reactions have been reported. Patients who have a history of hypersensitivity to carbapenems, penicillins or other beta-lactam antibiotics may also be hypersensitive to meropenem. Before initiating therapy with meropenem, careful enquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. If a severe allergic reaction occurs, the medicinal product should be discontinued and appropriate measures taken. Severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme (EM) and acute generalised exanthematous pustulosis (AGEP) have been reported in patients receiving meropenem (see section 4.8). If signs and symptoms suggestive of these reactions appear, meropenem should be withdrawn immediately and an alternative treatment should be considered. Antibiotic-associated colitis and pseudomembranous colitis have been reported with nearly all anti-bacterial agents, including meropenem, 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 meropenem. Discontinuation of therapy with meropenem and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given. Seizures have infrequently been reported during treatment with carbapenems, including meropenem. Hepatic function should be closely monitored during treatment with meropenem due to the risk of hepatic toxicity (hepatic dysfunction with cholestasis and cytolysis). Use in patients with liver disease: patients with pre-existing liver disorders should have liver function monitored during treatment with meropenem, there is no dose adjustment necessary. A positive direct or indirect Coombs test may develop during treatment with meropenem. The concomitant use of meropenem and valproic acid/ sodium valproate/valpromide is not recommended. Meropenem is licensed for children over 3 months of age. There is no evidence of an increased risk of any adverse drug reaction in children based on the limited available data. All reports received were consistent with events observed in the adult population. Meropenem contains sodium. Meronem 500 mg: This medicinal product contains 45 mg sodium per 500 mg vial, equivalent to 2.25% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Meronem 1 g: This medicinal product contains 90 mg sodium per 1 g vial, equivalent to 4.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult. **Drug interactions:** No specific medicinal product interaction studies other than probenecid have been conducted. Probenecid inhibits the renal excretion of meropenem increasing the elimination half-life and plasma concentration of meropenem. Caution is required if probenecid is co-administered with meropenem. The potential effect of meropenem on the protein binding of other medicinal products or metabolism has not been studied. However, the protein binding is so low that no interactions with other compounds would be expected on the basis of this mechanism. Decreases in blood levels of valproic acid have been reported when it is co-administered with carbapenem agents resulting in 60-100% decrease in valproic acid levels in about two days and therefore should be avoided. Simultaneous administration of antibiotics with warfarin may augment its anti-coagulant effects. It is recommended that the INR should be monitored frequently during and shortly after co-administration of antibiotics with an oral anti-coagulant agent. **Pregnancy and lactation:** There are no or limited amount of data from the use of meropenem in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of meropenem during pregnancy. Small amounts of meropenem have been reported to be excreted in human milk. Meropenem should not be used in breast-feeding women unless the potential benefit for the mother justifies the potential risk to the baby. **Effects on driving:** No studies. **Side effects:** *Common (≥1/100 to <1/10)*: thrombocythaemia, headache, diarrhoea, abdominal pain, vomiting, nausea, transaminases increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, rash, pruritis, inflammation, pain. *Serious adverse reactions: Uncommon (≥1/1,000 to <1/100):* pseudomembranous colitis, anaphylaxis; *Rare (≥1/10,000 to <1/1,000):* delirium, toxic epidermal necrolysis, convulsions, *Not known (can not estimate from the data):* Stevens-Johnson syndrome and Drug reaction with eosinophilia and systemic symptoms. See SPC for other side effects. **Legal category:** POM. **Marketing Authorisation Number and Basic NHS cost:** Meronem IV 500 mg PL 0057/1535: £103.14, Meronem IV 1 g PL 00057/1536: £206.28. **Marketing Authorisation Holder:** Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ, United Kingdom.
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Further information is available on request from: Medical Information, Pfizer Limited, Walton Oaks, Dorking Road, Walton-on-the-Hill, Surrey KT20 7NS. www.pfizermedicalinformation.co.uk

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.