Summary of Prescribing Information_Ceftazidime- Avibactam

Generic Name: Ceftazidime Pentahydrate and Avibactam Sodium **Brand name**: Zavicefta ™Trademark Proprietor: Pfizer Ireland Pharmaceuticals **Indication:** For the treatment of the following infections in adults with Complicated intra-abdominal infection (cIAI), Complicated urinary tract infection (cUTI), including pyelonephritis, Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP) with susceptible gram negative microorganisms **Pharmaceutical Form, Dosage and Method of Administration :** Powder for concentrate for solution for infusion (powder for concentrate). A white to yellow powder. Recommended intravenous dose for patients with estimated CrCL ≥51 mL/min: 2.5 gm every 8 hourly as a 2 hour infusion for 5-14 days in cIAI (To be used in combination with metronidazole when anaerobic pathogens are known or suspected to be contributing to the infectious process), 5-10 days for cUTI with pyelonephritis & 7-14 days for HAP/VAP. To be used in combination with an antibacterial agent active against Gram-positive pathogens when these are known or suspected to be contributing to the infectious process. For patients with cUTI including pyelonephritis, The total duration shown may include intravenous Zavicefta followed by appropriate oral therapy. No dosage adjustment is required in **elderly** patients. No dosage adjustment is required in patients with mild renal impairment (estimated CrCL ≥51 - ≤80 mL/min). **Dosage for Cr CL ≤ 51 mg/mL**: 1g/0.25 g every 8 hours by 2 hour infusion for Cr CL 31-50 mL/min, 0.75g/0.1875g every 12 hours by 2 hr infusion for Cr CL 16-30mL/min, 0.75g/0.1875g every 24 hours by 2 hr infusion for Cr CL 6- 15mL/min and 0.75g/0.1875g every 48 hours by 2 h infusion for ESRD including on hemodialysis. Ceftazidime and avibactam are removed by haemodialysis. Dosing of Zavicefta on haemodialysis days should occur after completion of haemodialysis.No dosage adjustment is required in patients with hepatic impairment. Safety and efficacy in children and adolescents below 18 years of age have not yet been established. Zavicefta is administered by intravenous infusion over 120 minutes in an infusion volume of 100 mL. **Contraindications** : Hypersensitivity to the active substances or to any of the excipients, hypersensitivity 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, including special population:** Serious and occasionally fatal hypersensitivity reactions are possible. In case of hypersensitivity reactions, treatment with Zavicefta must be discontinued immediately and adequate emergency measures must be initiated. Clostridium difficile-associated diarrhoea has been reported with ceftazidime/avibactam, and can range in severity from mild to life-threatening. Discontinuation of therapy with Zavicefta and the administration of specific treatment for Clostridium difficile should be considered. 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. In patients with renal impairment, close monitoring of estimated creatinine clearance is advised. 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. Ceftazidime/avibactam use may cause development of a positive direct antiglobulin test (DAGT, or Coombs test), which may interfere with the cross-matching of blood and/or may cause drug-induced immune hemolytic anemia. Patients experiencing anemia during or after treatment with Zavicefta should be investigated or this possibility. **Adverse Reactions:** 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 glutamyl transferase increased;Blood lactate dehydrogenase increased, Rash maculo-papular; Urticaria; Pruritus; Infusion site thrombosis; Infusion site phlebitis; Pyrexia **Drug Interactions:** Co-administration of avibactam with probenecid is not recommended as Probenecid (a potent OAT inhibitor) inhibits this uptake by

56% to 70% in vitro and, therefore, has the potential to alter the elimination of avibactam. Avibactam showed no significant inhibition and avibactam & ceftazidime showed no induction (at clinically relevant concentrations) of CYP P450 enzymes in vitro. 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. There is no interaction between ceftazidime and avibactam, and between ceftazidime/avibactam and metronidazole. 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. Chloramphenicol is antagonistic in vitro with ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but due to the possibility of antagonism in vivo this drug combination should be avoided. **Overdose** : Overdose with ceftazidime/avibactam can lead to neurological sequelae including encephalopathy, convulsions and coma, due to the ceftazidime component. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis. During a 4-hour haemodialysis period, 55% of the avibactam dose was removed. **Storage condition**: Store below 30°C in the original package. Protect from light. The reconstituted vial should be used immediately. After dilution, the chemical and physical in-use stability has been demonstrated for up to 24 hours at 2 - 8°C, followed by up to 12 hours at not more than 25°C.

Adapted from Zavicefta. Local Product Document. Version LPDZAVIC032020.

Please refer to the complete prescribing information for complete details