For the use of a Registered Medical Practitione

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Ceftazidime 2 gm and Avibactam 0.5 gm (As Sodium salt) powder for concentrate for solution for infusion Infegam®



Sterile Powder For Intravenous use Single use vial

h vial contains ceftazidime pentahydrate equivalent to 2 g ceftazidime and avibactam sodium vivalent to 0.5 g avibactam. After reconstitution, 1 mL of solution contains 167mg of ceftazidime and 42mg of avibactam.

4 Clinical particulars

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4.1 Therapeutic indications
Ceftazidime and Avibactam is indicated in adults for the treatment of the following infections:

• Complicated intra-abdominal infection (clAl)
• Complicated uniary tract infection (clTI), including pyelonephritis
• Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP) with susceptible gram negative microorganisms
Treatment of patients with bacteraemia that occurs in association with, or is suspected to be essociated with anout the infections (listed above

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and Method of Administration

Dosage in adults with creatinine clearance (CrCL) > 50 ml /min.

ended intravenous dose for adults with estimated creatinine clearance (CrCL) > 50

Type of infection	Dose of Ceftazidime and Avibactam	Frequency	Infusion time	Duration of treatment
cIAI 23	2 g/0.5 g	Every 8 hours	2 hours	5-14 days
cUTI, including pyelonephritis ³	2 g/0.5 g	Every 8 hours	2 hours	5-10 days ⁴
HAP/VAP ³	2 g/0.5 g	Every 8 hours	2 hours	7-14 days
Bacteraemia associated with, or suspected to be associated with any of the above infections	2 g/0.5 g	Every 8 hours	2 hours	Duration of treatment should be in accordance with the site of infection.

CrCL estimated using the Cockcroft-Gault formula.

- Crt.L estimated using the Cockcroft-Gault formula.

 To be used in combination with metronidazole when anaerobic pathogens are known or suspected to be contributing to the infectious process.

 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.

 The total duration shown may include intravenous Ceftazidime and Avibactam followed by annormate and therapy.

lo dosage adjustment is required in elderly patients.

No dosage adjustment is required in patients with mild renal impairment (estimated CrCL > 50 -< 80 ml /min)

Table shows the recommended dose adjustments for adults with estimated CrCL ≤ 50 mL/min.
Dosage in adults with CrCl < 50 ml /min

DUS	JOSAGE II Addits Will CICL S 30 IIIL/IIIII						
	Age Group	Estimated CrCL	Dose of Ceftazidime and Avibactam 24	Frequency	Infusion time		
		(mL/min)	Certazidime and Avibactam				
	Adults 31-50 16-30		1 g/0.25 g	Every 8 hours			
				Every 12 hours			
		6-15	0.75 a/0.1875 a	Every 24 hours	2 hours		
	End Stage Renal Disease including on haemodialysis 3		0.10 g/0.1010 g	Every 48 hours			

1 CrCL estimated using the Cockcroft-Gault formula.

Dose recommendations are based on pharmacokinetic modelling.

Ceftazidime and avibactam are removed by haemodialysis. Dosing of Ceftazidime and vibactam on haemodialysis days should occur after completion of haemodialysis. Ceftazidime and Avibactam is a combination product in a fixed 4:1 ratio and dosage ecommendations are based on the ceftazidime component only.

No dosage adjustment is required in patients with hepatic impairment.

Method of Administration

Intravenous use Ceftazidime and Avibactam is administered by intravenous infusion over 120 minutes in an

appropriate infusion volume. Preparation of the Ceftazidime and Avibactam Solution for Administration Ceftazidime and Avibactam Solution for Administration Ceftazidime and Avibactam is supplied as a dry powder, which must be constituted and subsequently diluted, using aseptic technique prior to intravenous infusion.

a) Constitute the powder in the Ceftazidime and Avibactam vial with 10 mL of one of the following solutions:

Sterile water for injections IP

0.9% of sodium chloride injection IP (normal saline)

- So of dextrose injection IP
 all combinations of dextrose injection and sodium chloride injection IP, containing up to 2.5% dextrose IP, and 0.45% sodium chloride IP, or lactated Ringer's injection IP
- Mix gently. The constituted Ceftazidime and Avibactam solution will have an approximately to the constituted Ceftazidime. b) Mix gently. The constituted Ceftazidime and Avibactam solution will have an approximate ceftazidime concentration of 42 mg/mL. The final volume is approximately 12 mL. The constituted solution must be diluted before intravenous intustions of the constituted solution must be diluted before intravenous intustions.
 Prepare the required dose for intravenous infusion by withdrawing the appropriate volume determined from below Table from the constituted vial. Use these concentrations to calculate the volume of ceftazidime avibactam required to prepare the prescribed dose.

Ceftazidime-avibactam	Volume to Withdraw from Constituted Vial for Further Dilution to 50 to 250 * mL		
2.5 grams (2 grams and 0.5 grams)	12 mL (entire contents)		
1.25 grams (1 gram and 0.25 grams)	6 mL		
0.94 grams (0.75 grams and 0.19 grams)	4.5 mL		
a. Dilution to 250 mL should only be used for	the 2.5gram dose		

d) Before infusion, dilute the withdrawn volume of the constituted ceftazidime and avibactam solution further with the same diluent used for constitution of the powder (except sterile water for injection), to achieve a ceftazidime concentration of 8 to 40 mg/mL and an avibactam concentration of 2 to 10 mg/mL in an infusion bag, ifsterile water for in je ct i on was used for constitution, use any of the other appropriate constitution diluents for dilution. Mix gently and ensure that the contents are dissolved completely. Visually inspect the diluted Ceftazidime and Avibactam solution (for administration) for particulate matter and discoloration prior to administration the color of the Ceftazidime and Avibactam infusion solution for administration ranges from clear to light yellor.

1) Use the diluted Ceftazidime and Avibactam solution in the infusion bags within 12 hours when stored at room temperature.

2) The diluted Ceftazidime and Avibactam solution in the infusion bags may be stored under refrigeration at 2 to 8°C (361 de 8°F) up to 24 hours following dilution and used within 12 hours of subsequent storage at room temperature.

hours of subsequent storage at room temperature.
From a microbiological point of view, the medicinal product should be used immediately. If

not used immediately, in-use storage times and conditions prior to use is the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution/dilution bas taken place in controlled and validated respons conditions.

4.3 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. one picillism, smoophactams or carbanenems).

Hypersensitivity reactions
Serious and occasionally fatal hypersensitivity reactions are possible. In case of hypersensitivity reactions, treatment with Ceftazidime and Avibactam must be discontinued immediately and

Before beginning treatment, it should be established whether the patient has a history of before beginning dearment, it sindou be established whether the patient has a mistory or hypersensitivity reactions to certazidime, to other cephalosporins or to any other type of the lactar antibacterial agent. Caution should be used if Certazidime and Avibactam is given to patients with a history of non-severe hypersensitivity to penicillins, monobactams or carbapenems. Clostridioides difficile - associated diarrhoea

Clostridioldes difficile - associated diarrhoea

Clostridioldes difficile - associated diarrhoea

Clostridioldes difficile - associated diarrhoea has been reported with Ceftazidime and Avibactam, and can range in severity from mild to life-threatening. This diagnosis should be considered in patients who present with diarrhoea during or subsequent to the administration of Ceftazidime and Avibactam. Discontinuation of therapy with Ceftazidime and Avibactam and the administration of specific treatment for Clostridioldes difficile should be considered. Medicinal products that inhibit peristals is should not be given.

Renal impairment retrait impariment.

Ceffazidime and avibactam are eliminated via the kidneys, therefore, the dose should be reduced according to the degree of renal impairment. Neurological sequelae, including tremor, mycolonus, non-convulsive status epilepticus, convulsion, encephalopathy and coma, have occasionally been reported with ceffazidime when the dose has not been reduced in patients with

In patients with renal impairment, close monitoring of estimated creatinine clearance is advised.

tment with high doses of cephalosporins and nephrotoxic medicinal products plycosides or potent diuretics (e.g. furosemide) may adversely affect renal

Direct antiglobulin test (DAGT or Coombs test) seroconversion and potential risk of haemolytic

certain and 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 haemolytic anaemia. While DAGT seroconversion in patients receiving Ceffazidime and Avibactam was very common in clinical studies (the estimated range of seroconversion across Phase 3 studies was 3.2% to 20.3% in patients with a negative Coombs seroconversion across Frase 3 studies was 3.2% to 20.3% in patients with a negative Coombs test at baseline and at least one follow-up test), there was no evidence of haemolysis in patients who developed a positive DAGT on treatment. However, the possibility that haemolytic anaemia could occur in association with Ceftazidime and Avibactam treatment cannot be ruled out. Patients experiencing anaemia during or after treatment with Ceftazidime and Avibactam should be investigated for this possibility. nectrum of activity of Ceftazidime and Avibactan

Spectrum of activity of certazionine and avribational certazionine and specific defazidime 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.

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-factamases and class C β-factamases. Avibactam does not inhibi class B enzymes (metallo-β-factamases) 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.

rungy, winch may require interruption of treatment of 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

Controlled sodium diet ... This medicinal product contains approximately 148 mg sodium per vial, equivalent to 7.3% of the WHO recommended maximum daily intake (RDI) of 2 g sodium for an adult. The maximum daily dose of this product is equivalent to 22% of the WHO recommended maximum daily intake for sodium. Ceftaclidime and Avibactam is considered high in sodium. This should be considered when administering Ceftazidime and Avibactam to patients who are on a controlled sodium diet.

Ceffazidime and Avihactam may be diluted with sodium-containing solutions and this should be

4.5 Interaction with other medicinal products and other forms of interaction

4.5 Interaction with other medicinal products and other forms of interaction In vitro, avilactam is a substrate of OAT1 and OAT3 transporters which might contribute to the active uptake of avibactam from the blood compartment and, therefore, affect its excretion. Probenecid (a potent OAT inhibitor) inhibits this uptake by 56% to 70% in vitro and, therefore, has the potential to after the elimination of avibactam. Since a clinical interaction study of avibactam and probenecid has not been conducted, co-administration of avibactam with probenecid is not recommended. Avibactam showed no significant inhibition of cytochrome P450 enzymes in vitro. Avibactam and celtrazidime showed no in vitro cytochrome P450 induction at clinically relevant concentrations. Avibactam and celtrazidime do not inhibit the major real of hepatic transporters in the clinically relevant exposure range, therefore the interaction potential via these mechanisms.

is considered to be low. Clinical data have demonstrated that there is no interaction between ceftazidime and avibactam, and between Ceftazidime and Avibactam and metronidazole. Other types of interaction
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 centralosporins. The clinical vance of this finding is unknown, but due to the possibility of antagonism in vivo this drug

4.6 Special Populations

nimal studies with ceftazidime do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Animal studies with avibactam have shown reproductive toxicity without evidence of teratogenic effects. Ceftazidime and Avibactam should only be used during pregnancy if the potential benefit outweighs the possible risk.

Breast-feeding
Ceftazidime is excreted in human milk in small quantities. It is unknown whether avibactam is excreted in human milk. A risk to newborns/infants cannot be excluded. A decision must be made excreted in human milk. A risk to newborns/infants cannot be excluded. A decision must be made

eALIFECTURI HIMMAN MIK. A risk to newborns/infants cannot be excluded. A decision must be made whether to discontinue breast feeding or to discontinue/abstain from Ceftazidime and Avibactam therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Undesirable effects may occur (e.g. dizariess), which may influence the ability to drive and use machines following administration of Ceftazidime and Avibactam.

4 8 Undesirable Effects

is of the state the cut of the control of the cont iarrhoea were usually mild or moderate in intensity.

Uncommon

Very rare Unknown

<u>Fabulated list of adverse reactions</u>

The following adverse reactions have been reported with ceftazidime alone and/or identified during the Phase 2 and Phase 3 trials with Ceftazidime / avibactam. Adverse reactions are classified according to frequency and System Organ Class. Frequency categories are derived from adverse reactions and/or potentially clinically significant laboratory abnormalities, and are Fabulated list of adverse reactions

- Uncommon (≥1/1.000 and <1/100)
- Rare (≥1/10.000 and <1/1000)</p>

System Organ Very Common

 Unknown (cannot be estimated from the available data) Frequency of adverse reactions by system organ class

Class	common	Common	oncommon.	very raic	0
Infections and infestations		Candidiasis (including Vulvovaginal candidiasis and Oral candidiasis)	Clostridioides difficile colitis Pseudomembranous colitis		
Blood and lymphatic system disorders	Coombs direct test positive	Eosinophilia Thrombocytosis Thrombocytopenia	Neutropenia Leukopenia Lymphocytosis		Agranulocytosis Haemolytic anaemia
Immune system disorders					Anaphylactic reaction
Nervous system disorders		Headache Dizziness	Paraesthesia		
Gastrointestinal disorders		Diarrhoea Abdominal pain Nausea Vomiting	Dysgeusia		
Hepatobiliary disorders		Alanine aminotransferase increased Aspartate aminotransferase increased Blood alkaline phosphatase increased Gamma - glutamyltransferase increased Blood lactate dehydrogenase increased			Jaundlice
Skin and subcutaneous tissue disorders		Rash maculo - papular Urticaria Pruritus			Toxic epidermal necrolysis Stevens "Johnsor syndrome Erythema multiforme Angioedema Drug Reaction w Eosinophilia and Systemic Symptoms (DRES
Renal and urinary disorders			Blood creatinine increased Blood urea increased	Tubulointerstitial nephritis	
General disorders and administration site conditions		Infusion site thrombosis Infusion site phlebitis Pyrexia			

4-3 User ususage Overdose with Ceftazidime and 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.

 1.Pharmacotogram roperties & Mechanism of action.

Pharmacotherapeutic group: Antibacterials for systemic use, other beta-lactam antibacterials third-generation cephalosporins, ATC code: J010D52 Mechanism of action

dime inhihits hacterial nentidoglycan cell wall synthesis following hinding to nenicillin Centazulime timilus bacerial peptiologiycari cell wail syntiessis bioliumig biturili pi opericimi binding proteins (PBPs), which leads to bacterial cell lysis and death. Avibactam is a non Falcatam, F-lactamase inhibitor that acts by forming a covalent adduct with the enzyme that is stable to hydroysis. It timibitors both Ambler class A and class C g-lactamases and some class D enzymes, including extended-spectrum g-lactamases (ESBLs), KPC and 0XA-48 cardapenemases, and AmpC enzymes. Avibactam does not inhibit class B enzymes (metallo-2).

Bacterial resistance mechanisms that could potentially affect Ceftazidime and Avibactam include

mutant or acquired PBPs, decreased outer membrane permeability to either compound, active efflux of either compound, and β-lactamase enzymes refractory to inhibition by avibactam and albe to hydrolyse celtaridine

able to hydroryse cettazdidme.

Antibacterial activity in combination with other antibacterial agents

No synergy or antagonism was demonstrated in in vitro drug combination studies with
Ceftazidime and Avibactam and metronidazole, tobramycin, levofloxacin, vancomycin, linezolid,

Suscentibility testing breakpoints

Minimum Inhibitory Concentration (MIC) breakpoints established by the European Committee or

icrobial Susceptibility Testing (EUCAST) for Ceftazidime and Avibactam are as follo					
rganisms	Susceptible	Resistant			
nterobacteriales	≤8 mg/L	>8 mg/L			
aaridamanaa aasislaaaa	<0 ma/l	>9 ma/l			

Pharmacokinetic/pharmacodynamic relationship
The antimicrobial activity of ceftazidime against specific pathogens has been shown to best correlate with the percent time of free-drug concentration above the Ceftazidime and Avibactam inhibitory concentration over the dose interval (% TT >MIC of Ceftazidime and Avibactam). For avibactam the PK-PD index is the percent time of the free drug concentration

Clinical efficacy against specific pathogens
Efficacy has been demonstrated in clinical studies against the following pathogens that were susceptible to Ceftazidime and Avibactam in vitro

Complicated intra-abdominal infections Gram-negative micro-organisms

- Citrobacter freundi
- Klebsiella oxytoca
- Klebsiella pneumoniae
- Pseudomonas aeruginosa
- Complicated urinary-tract infection: Gram-negative micro-organisms
- Escherichia coli
- Klebsiella pneumoniae Proteus mirabilis

Hospital-acquired pneumonia including ventilator-associated pne

- Enterobacter cloaca
- Escherichia coli Klebsiella pneumoniae
- Proteus mirabilis
- Serratia marcescens Clinical efficacy has not been established against the following pathogens that are relevant to the approved indications although *in vitro* studies suggest that they would be susceptible to Ceftazidime and Avibactam in the absence of acquired mechanisms of resistance.
- Gram-negative micro-organisms
- Citrobacter koseri
- Enterobacter aerogenes
- Proteus vulgaris
- In-vitro data indicate that the following species are not susceptible to Ceftazidime and
- Staphylococcus aureus (methicillin-susceptible and methicillin-resistant)
- Enterococcus spp. Stenotrophomonas maltophiliaAcinetobacter spp.

5.2 Pharmacokinetic Properties

Distribution
The human protein binding of both ceftazidime and avibactam is approximately 10% and 8%, the human protein binding of both ceftazidime and avibactam were about respectively. The steady-state volumes of distribution of cefts administration and volumes of the volumes of volumes of the volu

etration of ceftazidime into the intact blood-brain barrier is poor. Ceftazidime concentrations of 4 to 20 mg/L or more are achieved in the CSF when the meninges are inflamed. Avibactam penetration of the blood brain barrier has not been studied clinically, however, in rabbits with inflamed meninges, CSF exposures of ceftazidime and avibactam were 43% and 38% of plasma AUC, respectively. Ceftazidime crosses the placentar readily, and is excreted in the breast milk.

<u>Biotransformation</u>

Ceffazidime is not metabolised. No metabolism of avibactam was observed in human liver preparations (microsomes and hepatocytes). Unchanged avibactam was the major drug-related component in human plasma and urine following dosing with [14C]-avibactam. infiliation The terminal half-life (t½) of both ceftazidime and avibactam is about 2 h after intra

The terminal nati- (It's) of born certaizonine and avulacitam is about 2 h after intravenous administration. Ceftazidime is excreted unchanged into the urine by glomerular lititation; approximately 80-90% of the dose is recovered in the urine with 1624 h. Avibactam is excreted unchanged into the urine with a renal clearance of approximately 158 mL/min. suggesting active tubular secretion in addition to glomerular filtration. Approximately 97% of the avibactam dose is recovered in the urine, 95% within 12 h. Less than 1% of ceftazidime is excreted via the bile and less than 0.25% of avibactam is excreted into faces. The pharmacokinetics of both ceftazidime and avibactam are approximately linear across the dose range studied (0.05 g to 2 g) for a single intravenous administration. No appreciable accumulation of ceftazidime are avibactam was observed following multiple intravenous infusions of 2 g/0.5 g of Ceftazidime and Avibactam administered every 8 hours for up to 11 days in healthy adults with normal renal function.

Special populations

Trenta impairment
Elimination of celtazidime and avibactam is decreased in patients with moderate or severe renal impairment. The average increases in avibactam AUC are 3.8-fold and 7-fold in subjects with moderate and severe renal impairment.

Mild to moderate henatic impairment had no effect on the pharmacokinetics of ceftazidime in Mild to moderate hepatic impairment had no effect on the pharmacokinetics of ceftazidime in individuals administered 2 gintravenously every 8 hours for 5 days, provided renal function was not impaired. The pharmacokinetics of ceftazidime in patients with severe hepatic impairment has not been established. The pharmacokinetics of avibactam in patients with any degree of hepatic impairment has not been studied. As ceftazidime and avibactam do not appear to undergo significant hepatic metabolism, the systemic clearance of either active substance is not expected to be significantly altered by

Elderly patients (>65 years)

Elderly patients (2-65 years)

Reduced clearance of ceftazidime was observed in elderly patients, which was primarily due to age-related decrease in renal clearance of ceftazidime. The mean elimination half-life of ceftazidime ranged from 3.5 to 4 hours following intravenous bolus dosing with 2 g every 1.2 hours in elderly patients aged 80 years or older. Following a single intravenous administration of 500 mg avibactam as a 30-minute IV infusion, the elderly had a slower terminal half-life of avibactam, which may be attributed to age related decrease in renal clearance.

The pharmacokinetics of Ceftazidime and Avibactam is not significantly affected by gender or race

6 Non-clinical Properties

Characteristics of the content of th

Avioaciam

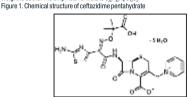
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity or genotoxicity. Carcinogenicity studies have not been conducted with avibactam.

conducted with avibactam. Begroduction toxicity. In pregnant rabbits administered avibactam at 300 and 1000 mg/kg/day, there was a dose-related lower mean foetal weight and delayed ossification, potentially related to maternal toxicity. Plasma exposure levels at maternal and foetal no-observed-adverse-effect-level (NOAEL) (100 mg/kg/day) indicate moderate to low margins of safety. In the rat, no adverse effects were observed on embryofetal development or ferfility. Following administration of avibactam throughout pregnancy and lactation in the rat, there was no effect on pup survival, growth or development, however there was an increase in incidence of dilation of the renal pelvis and ureters in less than 10% of the rat pups at maternal exposures greater than or equal to prepresentative. 15 times human tharanelitic exposures.

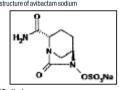
7. Description

Cetazidime and Avibactam is an antibacterial combination product consisting of the semisynthetic cephalosporin ceftazidime pentahydrate and the beta-lactamase inhibitor avibactam sodium for intravenous administration.

Certazidime is a semisynthetic, beta-lactam antibacterial drug. It is the pentahydrate (6B,7R,2)-7-(2-(2aminothiazol-4-yl)-2-(2-carboxypropan-2-yloxyimino)acetamido)-8-oxo-(pyridinium-1-ylmethyl)-5-thia-1aza-bicyclo[4.2.0]oct-2-ene-2-carboxylate. Its molecu weight is \$36.6. The empirical formula is \$C_xH_xN_0,0.5_x\$.



Avibactam sodium chemical name is sodium [(2S,5R)-2-carbamoyl-7-oxo-1,6-diazabicyolo[3,2.1]octan-6-yi] sulfate. Its molecular weight is 287.23. The empirical formula is C,H_N,O,SNa.
Figure 2. Chemical structure of avibactam sodium



urug Lompatibility
The Ceftazidime and Avibactam solution for administration at the range of diluted concentrations of ceftazidime 8 mg/mL and avibactam 2 mg/mL to ceftazidime 40 mg/mL and avibactam 11 mg/mL is compatible with the more commonly used intravenous infusion fluids in infusion bags such as:

5% dextrose injection IP all combinations of dextrose injection and sodium chloride injection IP, containing up to 2.5% dextrose IP, and 0.45% sodium chloride IP

Lactated ringer's injection IP, and 0.9% sodium chloride injection or 5% dextrose injection

0.9% sodium chloride injection IP

Intravenous Line Compatibility

Compatible Drugs for use with 0.9% Sodium Chloride, 5% Dextrose or Lactated Ringer's Injection as Diluents

Compatible Drugs for use with 0.9% Sodium Chloride or 5% Dextrose Injection as Diluents

Compatible Drugs for use with 5% Dextrose or Lactated Ringer's Injection as Diluents

Heparin Sodium Injection

Compatible Drugs for use with One Compatible Diluent

Tobramycin Injection or Tobramycin for Injection

Simulated Y-site compatibility of Ceftazidime and Avibactam admixed with other drug products in Simulated Y-site compatibility of Ceftazidime and Avibactam admixed with other drug products in a 1-1 volume ratio at room temperature was evaluated by yisual inspection, and measurement of turbidity and particulate matter at 0, 1 and 4 hours after mixing. Ceftazidime and avibactam were tested at concentrations of 20 mg/ml. and 5 mg/ml. respectively, which can be obtained by dilution of constituted Ceftazidime and Avibactam solution in a 100 ml. intravenous infusion bag. The highest recommended concentration (40 mg/ml. to ceftazidime and 10 mg/ml. of avibactamy was not tested in this study and should not be used during co-administration of Ceftazidime and Avibactam with other drugs through the same intravenous line. Compatible drugs with the corresponding compatible diluent (i.e., 0.9% Sodium Chloride Injection, 5% Dextrose Injection or Lactated Ringer's Injection) are listed in tables below. Any drug products not listed in the tables below should not be co-administered with Ceftazidime and Avibactam through the same intravenous line for cranula!

8.2 Shelf-Life: 24 Months.

8.3 Package Information
20 ml vial packed in carton along with leaflet.

8.4 Storage and Handling Instructions
Store at temperature not exceeding 30°C and protect from light.

Storage of Constituted Solutions Joon constitution with appropriate diluent, the constituted Ceftazidime and Avibactam solution may be held for no longer than 30 minutes prior to transfer and dilution in a suitable infusion bag. Following dilution of the constituted solutions with the appropriate diluents, Ceftazidime and Avibactam solutions in the infusion bags are stable for 12 hours when stored at room

temperature.

Following dilution of the constituted solutions with the appropriate diluents, Ceftazidime and Avihaciam solutions in the influsion bags may also be refrigerated at 2 to 8°C (36 to 46°F) for up to

s. Fatient consening information Serious Allergic Reactions Advise patients, their families, or caregivers that allergic reactions, including serious allergic reactions, could occur that require immediate treatment. Ask them about any previous typersensitivity reactions to Cettazidime and Avibactam, other beta-lactams (including phalosporins), or other allergens. Potentially Serious Diarrhea

Total reading serious blannead Advise patients, their families, or caregivers that diarrhea is a common problem caused by antibacterial drugs. Sometimes, frequent watery or bloody diarrhea may occur and may be a sign of a more serious intestinal infection. If severe watery or bloody diarrhea develops, tell them to contact his or her healthcare provider. contact his or her healthcare provider.

Nernous System Reactions

Advise patients, their families, or caregivers that neurological adverse reactions can occur with
Ceftazidime and Avibactam use. Instruct patients their families, or caregivers to inform a
healthcare provider at once of any neurological signs and symptoms, including encephalopathy
(disturbance of consciousness including conflusion, hallucinations, stupor, and coma),
myoclonus, and seizures, for immediate treatment, dosage adjustment, or discontinuation of
Ceftazidime and Avibactam.

Antibacterial Resistance
Counsel patients, their families, or caregivers that antibacterial drugs including Ceftazidime and
Avibactam should only be used to treat bacterial infections. They do not treat viral infections (e.g.,
the common cold). When Ceftazidime and Avibactam is prescribed to treat a bacterial infection,
patients should be told that although it is common to feel better early in the course of therapy, the
medication should be taken exactly as directed. Skipping doses or not compileting the full course
of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the
likelihood that bacteria will develop resistance and will not be treatable by Ceftazidime and
Avibactam or other antibacterial drugs in the future.

10. Details of Manufacturer

At: Plot No. 04, Village Kunjhal, Nr. Jharmajri Baddi, Dstt. Solan, Himachal Pradesh - 173 Marketed by: Biocon Biologics Limited,

Electronic City, Phase - II, Bengaluru - 560 100. India.

11. Details of Permission or License number with date: $Mfg.\,Lic.\,No.\,L/15/1688/MB\,,17/01/2023$ ® - Registered trademark

To report adverse events and/or product complaints visit our website www.biocon.com or call toll free No: 1800 102 9465 or e mail us at

ARTWORK DETAILS

WANUFACTURER	dulle biosciences Ellinted		ACTUAL SIZE			
PRODUCT	INFEGAM®		DESIGN / STYLE	60 GSM Maplitho Paper.		
PACK	2/0.5g		SPECIFICATIONS	After fold Size – L120 x H25 mm 3 Vertical folds		
COMPONENT	Leaflet		COLOUR SCHEME	3 COLORS		
ITEM CODE	BF/LL/4515/01		PANTONE CODE	032 C 7402 C B 6 C		
SPECIAL INSTRUCTIONS (IF ANY)						
CHECKED & APPROVED BY:						
MARCOMM	PKG. DEVELOPMENT	MARKETING	PRODUCTION	MEDICAL	REGULATORY	QA

D:\Jobs G Drive Data\GLOBE DESIGN BBL\CCD\INFEGAM\110523



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