

FORTUM

Ceftazidime

QUALITATIVE AND QUANTITATIVE COMPOSITION

FORTUM injection contains 250 mg, 500 mg, 1 g of ceftazidime (as pentahydrate). Ceftazidime pentahydrate is formulated in a mixture with sodium carbonate. When constituted, this mixture provides a solution of ceftazidime sodium.

PHARMACEUTICAL FORM

Powder for injection/infusion

CLINICAL PARTICULARS

Indications

Treatment of single or multiple infections caused by susceptible organisms.

May be used alone as first choice drug before the results of sensitivity tests are available.

May be used in combination with an aminoglycoside or most other beta-lactam antibiotics.

May be used with an antibiotic against anaerobes when the presence of *Bacteroides fragilis* is suspected.

Susceptibility to *FORTUM* will vary with geography and time and local susceptibility data should be consulted where available (*see Pharmacological properties, Pharmacodynamic effects*).

Indications include:

- severe infections e.g.
 - septicaemia, bacteraemia, peritonitis, meningitis
 - infections in immunosuppressed patients
 - infections in patients in intensive care, e.g. infected burns
- respiratory tract infections including lung infections in cystic fibrosis
- ear, nose and throat infections
- urinary tract infections
- skin and soft tissue infections
- gastrointestinal, biliary and abdominal infections
- bone and joint infections
- infections associated with haemo- and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD)
- prophylaxis: prostatic surgery (transurethral resection).

Dosage and Administration

Adults and children ≥ 40 kg

<i>Intermittent Administration</i>	
Infection	Dose to be administered
Broncho-pulmonary infections in cystic fibrosis	100 to 150 mg/kg/day every 8 h, maximum 9 g per day ¹
Febrile neutropenia	2 g every 8 h
Nosocomial pneumonia	

Bacterial meningitis	1-2 g every 8 h
Bacteraemia*	
Bone and joint infections	
Complicated skin and soft tissue infections	
Complicated intra-abdominal infections	
Peritonitis associated with dialysis in patients on CAPD	
Complicated urinary tract infections	1-2 g every 8 h or 12 h
Per-operative prophylaxis for transurethral resection of prostate (TURP)	1 g at induction of anaesthesia, and a second dose at catheter removal
Chronic suppurative otitis media	1 g to 2 g every 8 h
Malignant otitis externa	
<i>Continuous infusion</i>	
Infection	Dose to be administered
Febrile neutropenia	Loading dose of 2 g followed by a continuous infusion of 4 to 6 g every 24 h ¹
Nosocomial pneumonia	
Broncho-pulmonary infections in cystic fibrosis	
Bacterial meningitis	
Bacteraemia*	
Bone and joint infections	
Complicated skin and soft tissue infections	
Complicated intra-abdominal infections	
Peritonitis associated with dialysis in patients on CAPD	

¹In adults with normal renal function 9 g/day has been used without adverse effects. *When associated with, or suspected to be associated with, any of the infections listed in section Indications.

Children < 40 kg

Infants and toddlers >2 months and children <40 kg	Infection	Usual dose
<i>Intermittent Administration</i>		
	Complicated urinary tract infections	100-150 mg/kg/day in three divided doses, maximum 6 g/day
	Chronic suppurative otitis media	
	Malignant otitis externa	
	Neutropenic children	150 mg/kg/day in three divided doses, maximum 6 g/day
	Broncho-pulmonary infections in cystic fibrosis	
	Bacterial meningitis	
	Bacteraemia*	
	Bone and joint infections	100 – 150 mg/kg/day in three divided doses, maximum 6 g/day
	Complicated skin and soft tissue infections	
	Complicated intra-abdominal infections	
	Peritonitis associated with dialysis in patients on CAPD	
<i>Continuous Infusion</i>		
	Febrile neutropenia	Loading dose of 60-100 mg/kg followed by a continuous infusion 100-200 mg/kg/day, maximum 6 g/day
	Nosocomial pneumonia	
	Broncho-pulmonary infections in cystic fibrosis	
	Bacterial meningitis	
	Bacteraemia*	
	Bone and joint infections	
	Complicated skin and soft tissue infections	

	Complicated intra-abdominal infections	
	Peritonitis associated with dialysis in patients with CAPD	
Neonates and infants ≤ 2 months	Infection	Usual dose
<i>Intermittent Administration</i>		
	Most infections	25-60 mg/kg/day in two divided doses ¹
¹ In neonates and infants ≤ 2 months, the serum half life of ceftazidime can be three to four times that in adults. *Where associated with, or suspects to be associated with, any of the infections listed in section Indications.		

- **Elderly**

In view of the reduced clearance of ceftazidime in acutely ill elderly patients, the daily dosage should not normally exceed 3 g, especially in those over 80 years of age.

- **Hepatic impairment**

Available data do not indicate the need for dose adjustment in mild or moderate liver function impairment. There are no study data in patients with severe hepatic impairment (see also Pharmacokinetics). Close clinical monitoring for safety and efficacy is advised.

- **Renal Impairment**

Ceftazidime is excreted unchanged by the kidneys. Therefore, in patients with impaired renal function, the dosage should be reduced.

An initial loading dose of 1 g should be given. Maintenance doses should be based on creatinine clearance as shown in:

Recommended maintenance doses of *FORTUM* in renal insufficiency -intermittant infusion.

<i>Adults and children</i> ≥ 40 kg	Approx. serum creatinine $\mu\text{mol/l(mg/dl)}$	Recommended unit dose of Fortum (g)	Frequency of dosing (hourly)
Creatinine clearance ml/min			
50-31	150-200 (1.7-2.3)	1	12
30-16	200-350	1	24

	(2.3-4.0)		
15-6	350-500 (4.0-5.6)	0.5	24
<5	>500 (>5.6)	0.5	48

In patients with severe infections the unit dose should be increased by 50% or the dosing frequency increased. In children the creatinine clearance should be adjusted for body surface area or lean body mass.

Children < 40 kg

Creatinine clearance (ml/min)**	Approx. serum creatinine* $\mu\text{mol/l}(\text{mg/dl})$	Recommended individual dose mg/kg body weight	Frequency of dosing (hourly)
50-31	150-200 (1.7-2.3)	25	12
30-16	200-350 (2.3-4.0)	25	24
15-6	350-500 (4.0-5.6)	12.5	24
<5	>500 (>5.6)	12.5	48

*The serum creatinine values are guideline values that may not indicate exactly the same degree of reduction for all patients with reduced renal function.

** Estimated based on body surface area, or measured.

Recommended maintenance doses of Fortum in renal impairment – continuous infusion

Adults and children ≥ 40 kg

Creatinine clearance (ml/min)	Approx. Serum creatinine $\mu\text{mol/l}$ (mg/dl)	Frequency of dosing (hourly)
50-31	150-200 (1.7-2.3)	Loading dose of 2 g followed by 1 g to 3 g /24 hours
30-16	200-350 (2.3-4.0)	Loading dose of 2 g followed by 1 g /24 hours
≤ 15	> 350 (>4.0)	Not evaluated

Haemodialysis

The serum half-life during haemodialysis ranges from 3 to 5 hours.

Following each haemodialysis period, the maintenance dose of *FORTUM* recommended in the above table should be repeated.

Peritoneal dialysis

FORTUM may be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD).

In addition to i.v. use, *FORTUM* can be incorporated into the dialysis fluid (usually 125 to 250 mg for 2 litres of dialysis solution).

For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units; 1 g daily either as a single dose or in divided doses. For low-flux haemofiltration, follow the dosage recommended under impaired renal function.

For patients on venovenous haemofiltration and venovenous haemodialysis, follow the dosage recommendations in the following tables.

Continuous veno-venous haemofiltration dose guidelines

Residual renal function (creatinine clearance ml/min)	Maintenance dose (mg) for an ultrafiltration rate (ml/min) of ¹ :			
	5	16.7	33.3	50
0	250	250	500	500
5	250	250	500	500
10	250	500	500	750
15	250	500	500	750
20	500	500	500	750

¹ Maintenance dose to be administered every 12 h.

Continuous veno-venous haemodialysis dose guidelines

Residual renal function (creatinine clearance in ml/min)	Maintenance dose (mg) for a dialysate in flow rate of ¹ :					
	1.0 litre/h			2.0 litre/h		
	Ultrafiltration rate (litre/h)			Ultrafiltration rate (litre/h)		
	0.5	1.0	2.0	0.5	1.0	2.0
0	500	500	500	500	500	750
5	500	500	750	500	500	750
10	500	500	750	500	750	1000
15	500	750	750	750	750	1000
20	750	750	1000	750	750	1000

¹ Maintenance dose to be administered every 12 h.

Method of administration

Fortum should be administered by intravenous injection or infusion, or by deep intramuscular injection. Recommended intramuscular injection sites are the upper outer quadrant of the *gluteus maximus* or lateral part of the thigh. Fortum solutions may be given directly into the vein or introduced into the tubing of a giving set if the patient is receiving parenteral fluids.

The standard recommended route of administration is by intravenous intermittent injection or intravenous continuous infusion. Intramuscular administration should only be considered when the intravenous route is not possible or less appropriate for the patient.

The dose depends on the severity, susceptibility, site and type of infection and on the age and renal function of the patient.

Contraindications

Hypersensitivity to the active substance (ceftazidime pentahydrate), to other cephalosporins or to any of the excipients.

Previous immediate and/or severe hypersensitivity reaction to a penicillin or to any other beta-lactam medicinal products.

Warnings and Precautions

Special caution is required to determine any other type of previous hypersensitivity reactions to penicillin or to other beta-lactam medicinal products because patients hypersensitive to these medicines may be hypersensitive to (ceftazidime pentahydrate) as well (cross- allergy).

If an allergic reaction to *FORTUM* occurs discontinue the drug. Serious hypersensitivity reactions may require epinephrine (adrenaline), hydrocortisone, antihistamine or other emergency measures.

Concurrent treatment with high doses of cephalosporins and nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. furosemide) may adversely affect renal function. Clinical experience has shown that this is not likely to be a problem with *FORTUM* at the recommended dose levels. There is no evidence that *FORTUM* adversely affects renal function at normal therapeutic doses.

Ceftazidime is eliminated via the kidneys, therefore the dosage should be reduced according to the degree of renal impairment. Neurological sequelae have occasionally been reported when the dose has not been reduced in patients with renal impairment (*see Dosage and Administration – Renal Impairment and Adverse Reactions*).

As with other broad spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms (e.g. *Candida*, *enterococci*) which may require interruption of treatment or appropriate measures. Repeated evaluation of the patient's condition is essential.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

As with other extended-spectrum cephalosporins and penicillins, some initially susceptible strains of *Enterobacter* spp. and *Serratia* spp. may develop resistance during *FORTUM* therapy. When clinically appropriate during therapy of such infections, periodic susceptibility testing should be considered.

Each 1 g of ceftazidime contains 52 mg of sodium. The sodium content must be taken into account in patients requiring sodium restriction

Interactions

Concurrent use of high doses with nephrotoxic drugs may adversely affect renal function (*see Warnings and Precautions*).

Chloramphenicol is antagonistic *in vitro* with ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but if concurrent administration of *FORTUM* with chloramphenicol is proposed, the possibility of antagonism should be considered.

In common with other antibiotics, ceftazidime may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Ceftazidime does not interfere with enzyme-based tests for glycosuria but slight interference may occur with copper reduction methods (Benedict's, Fehling's, Clinitest).

Ceftazidime does not interfere in the alkaline picrate assay for creatinine.

Pregnancy and Lactation

There is no experimental evidence of embryopathic or teratogenic effects, but as with all drugs, *FORTUM* should be administered with caution during the early months of pregnancy and early infancy.

Ceftazidime is excreted in human milk in small quantities and should be used with caution in breast-feeding.

Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines (see section 4.8).

Adverse Reactions

Data from large clinical trials (internal and published) were used to determine the frequency of very common to uncommon undesirable effects. The frequencies assigned to all other undesirable effects were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

very common $\geq 1/10$,

common $\geq 1/100$ to $< 1/10$,

uncommon $\geq 1/1,000$ to $< 1/100$,

rare $\geq 1/10,000$ to $< 1/1,000$,

very rare $< 1/10,000$.

Infections and infestations

Uncommon: Candidiasis (including vaginitis and oral thrush).

Blood and lymphatic system disorders

Common: Eosinophilia and thrombocytosis.

Uncommon: Leucopenia, neutropenia, and thrombocytopenia.

Very rare: Lymphocytosis, haemolytic anaemia, and agranulocytosis.

Immune system disorders

Very rare: Anaphylaxis (including bronchospasm and/or hypotension).

Nervous system disorders

Uncommon: Headache and dizziness.

Very rare: Paraesthesia.

There have been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy, and coma in patients with renal impairment in whom the dose of *FORTUM* has not been appropriately reduced.

Vascular disorders

Common: Phlebitis or thrombophlebitis with i.v. administration.

Gastrointestinal disorders

Common: Diarrhoea.

Uncommon: Nausea, vomiting, abdominal pain, and colitis.

Very rare: Bad taste.

As with other cephalosporins, colitis may be associated with *Clostridium difficile* and may present as pseudomembranous colitis (See *Warnings and Precautions*).

Hepatobiliary disorders

Common: Transient elevations in one or more of the hepatic enzymes, ALT (SGPT), AST (SOGT), LDH, GGT and alkaline phosphatase.

Very rare: Jaundice.

Skin and subcutaneous tissue disorders

Common: Maculopapular or urticarial rash.

Uncommon: Pruritus.

Very rare: Angioedema, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

General disorders and administration site conditions

Common: Pain and/or inflammation after i.m. injection.

Uncommon: Fever.

Investigations

Common: Positive Coombs test.

Uncommon: As with some other cephalosporins, transient elevations of blood urea, blood urea nitrogen and/or serum creatinine have been observed.

A positive Coombs test develops in about 5% of patients and may interfere with blood cross-matching.

Overdose

Symptoms and Signs

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma.

Treatment

Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Mechanism of Action

Ceftazidime is bactericidal in action. It acts by inhibiting bacterial cell wall synthesis.

Pharmacodynamic Effects

The prevalence of acquired resistance is geographically and time dependent and for select species may be very high. Local information on resistance ***and prevalence of extended spectrum beta lactamase (ESBLs) producing organisms*** is desirable, particularly when treating severe infections.

***In vitro* susceptibility of micro-organisms to Ceftazidime**

Where clinical efficacy of ceftazidime has been demonstrated in clinical trials this is indicated with an asterisk (*).

Commonly Susceptible Species

Gram-positive aerobes:

Beta-hemolytic streptococci*

Staphylococcus aureus (methicillin susceptible)*

<i>Coagulase negative staphylococcus (methicillin susceptible)</i>
<u>Gram-negative aerobes:</u> <i>Haemophilus influenzae</i> * including ampicillin-resistant strains <i>Haemophilus parainfluenzae</i> <i>Neisseria gonorrhoeae</i> <i>Neisseria meningitidis</i> * <i>Pasteurella multocida</i> <i>Proteus</i> spp.* <i>Providencia</i> spp. <i>Salmonella</i> spp. <i>Shigella</i> spp.
Species for which acquired resistance may be a problem
<u>Gram-negative aerobes:</u> <i>Acinetobacter</i> spp. <i>Burkholderia cepacia</i> <i>Citrobacter</i> spp.* <i>Enterobacter</i> spp.* <i>Escherichia coli</i> * <i>Klebsiella</i> spp. including <i>K. pneumoniae</i> * <i>Pseudomonas</i> spp. including <i>P. aeruginosa</i> * <i>Serratia</i> spp.* <i>Morganella morganii</i> <i>Yersinia enterocolitica</i>
<u>Gram-positive aerobes:</u> <i>Streptococcus pneumoniae</i> * Viridans group streptococcus
<u>Gram-positive anaerobes:</u> <i>Clostridium</i> spp. not including <i>C. difficile</i> <i>Peptostreptococcus</i> spp. <i>Propionibacterium</i> spp.
<u>Gram-negative anaerobes:</u>

<i>Fusobacterium</i> spp.
Inherently resistant organisms
<u>Gram-positive aerobes:</u> <i>Enterococcus</i> spp. including <i>E. faecalis</i> and <i>E. faecium</i> <i>Listeria</i> spp.
<u>Gram-negative aerobes:</u> <i>Campylobacter</i> spp.
<u>Gram-positive anaerobes:</u> <i>Clostridium difficile</i>
<u>Gram-negative anaerobes:</u> <i>Bacteroides</i> spp. including <i>B. fragilis</i>
<u>Others:</u> <i>Chlamydia</i> spp. <i>Mycoplasma</i> spp. <i>Legionella</i> spp.

Pharmacokinetics

Absorption

After i.m. administration of 500 mg and 1 g, peak levels of 18 and 37 mg/l, respectively, are achieved rapidly. Five minutes after i.v. bolus injection of 500 mg, 1 g or 2 g, serum levels are, respectively, 46, 87 and 170 mg/l.

Distribution

Therapeutically effective concentrations are still present in the serum 8 to 12 hours after either i.v. or i.m. administration. Serum protein binding is about 10%. Concentrations in excess of the MIC for common pathogens can be achieved in tissues such as bone, heart, bile, sputum, aqueous humour, synovial, pleural and peritoneal fluids. Ceftazidime crosses the placenta readily, and is excreted in the breast milk. Penetration of the intact blood-brain barrier is poor resulting in low levels of ceftazidime in the cerebral spinal fluid (CSF) in the absence of inflammation. However, therapeutic levels of 4 to 20 mg/l or more are achieved in the CSF when the meninges are inflamed.

Metabolism

Ceftazidime is not metabolised in the body.

Elimination

Parenteral administration produces high and prolonged serum levels, which decrease with a half-life of about 2 hours. Ceftazidime is excreted unchanged, in active form into the urine by glomerular filtration; approximately 80 to 90% of the dose is recovered in the urine within 24 hours. Less than 1% is excreted via the bile, which limits the amount entering the bowel.

Special Patient Populations

Renal impairment

Elimination of ceftazidime is decreased in patients with impaired renal function and the dose should be reduced (*see Dosage and Administration - Renal Impairment, Warnings and Precautions*).

Hepatic impairment

The presence of mild to moderate hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime in individuals administered 2 g intravenously every 8 hours for 5 days, provided renal function was not impaired (*see Dosage and Administration*).

Elderly

The reduced clearance observed in elderly patients was primarily due to age-related decrease in renal clearance of ceftazidime. The mean elimination half-life ranged from 3.5 to 4 hours following single or 7 days repeat BID dosing of 2 g IV bolus injections in elderly patients 80 years or older.

Paediatric population

The half-life of ceftazidime is prolonged in preterm and term neonates by 4.5 to 7.5 hours after doses of 25 to 30 mg/kg. However, by the age of 2 months the half-life is within the range for adults.

Pre-clinical Safety Data

No additional data of relevance.

PHARMACEUTICAL PARTICULARS

List of Excipients

Sodium carbonate (anhydrous).

Incompatibilities

FORTUM is less stable in Sodium Bicarbonate Injection than in other i.v. fluids. It is not recommended as a diluent. *FORTUM* and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported with vancomycin added to *FORTUM* in solution. Therefore, it would be prudent to flush giving sets and i.v. lines between administration of these two agents.

Shelf-Life

The expiry date is indicated on the packaging.

Special Precautions for Storage

Vials of *FORTUM* for Injection should be stored at room temperature .
Protect unconstituted vials from light.

Nature and Contents of Container

Fortum 1 gm: carton box contains 1 vial with safety cap and 2 ampoules of water for injection (5 ml) and inner leaflet.

Fortum 500 mg: carton box contains 1 vial with safety cap and 1 ampoule of water for injection (5 ml) and inner leaflet.

Fortum 250 mg: carton box contains 1 vial with safety cap and 1 ampoule of water for injection (5 ml) and inner leaflet.

Instructions for Use/Handling

FORTUM for injection/infusion is compatible with most commonly used i.v. fluids. However, Sodium Bicarbonate Injection is not recommended as a diluent (*see Incompatibilities*).

All sizes of vials of *FORTUM* Injection are supplied under reduced pressure. As the product dissolves, carbon dioxide is released and a positive pressure develops. Small bubbles of carbon dioxide in the constituted solution may be ignored.

Table 4: Instructions for reconstitution

Vial Size		Amount of Diluent to be added (ml)	Approximate Concentration (mg/ml)
250 mg	Intramuscular	1.0 ml	210
	Intravenous	2.5 ml	90
500 mg	Intramuscular	1.5 ml	260
	Intravenous	5 ml	90
1 g	Intramuscular	3 ml	260
	Intravenous bolus	10 ml	90
	Intravenous infusion	50 ml #	20

NOTE: Addition should be in two stages (*see text*)

Solutions range from light yellow to amber depending on concentration, diluent and storage conditions used. Within the stated recommendations, product potency is not adversely affected by such colour variations.

Ceftazidime at concentrations between 1 mg/ml and 40 mg/ml is compatible with:

0.9% Sodium Chloride Injection

M/6 Sodium Lactate Injection

Compound Sodium Lactate Injection (Hartmann's Solution)

5% Dextrose Injection

0.225% Sodium Chloride and 5% Dextrose Injection

0.45% Sodium Chloride and 5% Dextrose Injection

0.9% Sodium Chloride and 5% Dextrose Injection

0.18% Sodium Chloride and 4% Dextrose Injection

10% Dextrose Injection

Dextran 40 Injection 10% in 0.9% Sodium Chloride Injection

Dextran 40 Injection 10% in 5% Dextrose Injection

Dextran 70 Injection 6% in 0.9% Sodium Chloride Injection

Dextran 70 Injection 6% in 5% Dextrose Injection.

Ceftazidime at concentrations between 0.05 mg/ml and 0.25 mg/ml is compatible with Intra-peritoneal Dialysis Fluid (Lactate).

Both components retain satisfactory potency when ceftazidime at 4 mg/ml is mixed with:

Hydrocortisone (hydrocortisone sodium phosphate) 1 mg/ml in 0.9% Sodium Chloride Injection or 5% Dextrose Injection.

Cefuroxime (cefuroxime sodium) 3 mg/ml in 0.9% Sodium Chloride Injection.

Cloxacillin (cloxacillin sodium) 4 mg/ml in 0.9% Sodium Chloride Injection.

Heparin 10 IU/ml or 50 IU/ml in 0.9% Sodium Chloride Injection.

Potassium Chloride 10 mEq/l or 40 mEq/l in 0.9% Sodium Chloride Injection.

The contents of a 500 mg vial of *FORTUM* for injection, constituted with 1.5 ml Water for Injections, may be added to metronidazole injection (500 mg in 100 ml) and both retain their activity.

Preparation of solutions for i.m. or i.v. bolus injection

1. Introduce the syringe needle through the vial closure and inject the recommended volume of diluent.
2. Withdraw the needle and shake the vial to give a clear solution.
3. Invert the vial. With the syringe piston fully depressed insert the needle into the solution. Withdraw the total volume of solution into the syringe ensuring that the needle remains in the solution. Small bubbles of carbon dioxide may be disregarded.

Preparation of solutions for i.v. infusion from *FORTUM* injection (mini-bag or burette-type set)

Prepare using a total of 50 ml (for 1 g and 2 g vials) and 75 ml (for 3 g vials) of compatible diluent, added in TWO stages as below.

1 g vials for i.v. infusion:

1. Introduce the syringe needle through the vial closure and inject 10 ml of diluent for the 1 g and 2 g vials, and 15 ml for the 3 g vial.
2. Withdraw the needle and shake the vial to give a clear solution.
3. Do not insert a gas relief needle until the product has dissolved. Insert a gas relief needle through the vial closure to relieve the internal pressure.
4. Transfer the reconstituted solution to final delivery vehicle (e.g. mini-bag or burette-type set) making up a total volume of at least 50 ml (75 ml for the 3 g vial), and administer by intravenous infusion over 15 to 30 minutes.

NOTE: To preserve product sterility, it is important that the gas relief needle is not inserted through the vial closure before the product has dissolved.

Not all presentations are available in every country.

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