Nivador®
(Ceftazidime)

1. NAME OF THE PRODUCT
Nivador®(Ceftazidime) 250mg Injection
Nivador®(Ceftazidime) 500mg Injection
Nivador®(Ceftazidime) 1g Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Nivador®**250mg Injection:**
Each vial contains:
Sterile Ceftazidime pentahydrate equivalent to Ceftazidime……..250mg

Nivador®**500mg Injection:**
Each vial contains:
Sterile Ceftazidime pentahydrate equivalent to Ceftazidime…….....500mg

Nivador®**1g Injection:**
Each vial contains:
Sterile Ceftazidime pentahydrate equivalent to Ceftazidime…….....1g

3. PHARMACEUTICAL FORM
Powder for injection/infusion

Appearance:
Nivador®**250mg Injection:** White or almost white crystalline powder.
Nivador®**500mg Injection:** White or almost white crystalline powder.
Nivador®**1g Injection:** White or almost white crystalline powder.

4. CLINICAL PARTICULARS
4.1. THERAPEUTIC INDICATIONS:
Nivador®is indicated for the treatment of the infections listed below in adults and children including neonates (from birth).

- Nosocomial pneumonia
- Broncho-pulmonary infections in cystic fibrosis
- Bacterial meningitis
- Chronic suppurative otitis media
- Malignant otitis externa
- Complicated urinary tract infections
- Complicated skin and soft tissue infections
- Complicated intra-abdominal infections
- Bone and joint infections

- Peritonitis associated with dialysis in patients on CAPD.

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above. Nivador® may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection. Nivador® may be used in the peri-operative prophylaxis of urinary tract infections for patients undergoing trans-urethral resection of the prostate (TURP). The selection of ceftazidime should take into account its antibacterial spectrum, which is mainly restricted to aerobic Gram-negative bacteria. Ceftazidime should be co-administered with other antibacterial agents whenever the possible range of causative bacteria would not fall within its spectrum of activity. Consideration should be given to official guidelines on the appropriate use of antibacterial agents.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:

Adults and children ≥ 40kg:

<table>
<tr><td colspan="2">Intermittent Administration</td></tr>
<tr><td>Infection</td><td>Dose to be administered</td></tr>
<tr><td>Broncho-pulmonary infections in cystic fibrosis</td><td>100 to 150mg/kg/day every 8h, maximum 9g per day</td></tr>
<tr><td>Febrile neutropenia</td><td rowspan="4">2g every 8h</td></tr>
<tr><td>Nosocomial pneumonia</td></tr>
<tr><td>Bacterial meningitis</td></tr>
<tr><td>Bacteraemia*</td></tr>
<tr><td>Bone and joint infections</td><td rowspan="4">1-2g every 8h</td></tr>
<tr><td>Complicated skin and soft tissue infections</td></tr>
<tr><td>Complicated intra-abdominal infections</td></tr>
<tr><td>Peritonitis associated with dialysis in patients on CAPD</td></tr>
<tr><td>Complicated urinary tract infections</td><td>1-2g every 8h or 12h</td></tr>
<tr><td>Peri-operative prophylaxis for transuretheral resection of prostate (TURP)</td><td>1g at induction of anaesthesia, and a second dose at catheter removal</td></tr>
<tr><td>Chronic suppurative otitis media</td><td rowspan="2">1g to 2g every 8h</td></tr>
<tr><td>Malignant otitis externa</td></tr>
<tr><td colspan="2">Continuous infusion</td></tr>
<tr><td>Infection</td><td>Dose to be administered</td></tr>
<tr><td>Febrile neutropenia</td><td rowspan="2"></td></tr>
<tr><td>Nosocomial pneumonia</td></tr>
</table>

Broncho-pulmonary infections in cystic fibrosis	Loading dose of 2g followed by a continuous infusion of 4 to 6g every 24h[1]
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	
[1]In adults with normal renal function 9g/day has been used without adverse effects.	
*When associated with, or suspected to be associated with, any of the infections listed.	

Children < 40kg:

Infants and toddlers >2 months and children <40kg	**Infection**	**Usual dose**
Intermittent Administration		
	Complicated urinary tract infections	100-150mg/kg/day in three divided doses, maximum 6g/day
	Chronic suppurative otitis media	
	Malignant otitis externa	
	Neutropenic children	150mg/kg/day in three divided doses, maximum 6g/day
	Broncho-pulmonary infections in cystic fibrosis	
	Bacterial meningitis	
	Bacteraemia*	
	Bone and joint infections	100-150mg/kg/day in three divided doses, maximum 6g/day
	Complicated skin and soft tissue infections	
	Complicated intra-abdominal infections	
	Peritonitis associated with dialysis in patients on CAPD	

Continuous Infusion		
	Febrile neutropenia	Loading dose of 60-100mg/kg followed by a continuous infusion 100-200mg/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**
Intermittent Administration		
	Most infections	25-60mg/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 3g, 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. 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 1g should be given. Maintenance doses should be based on creatinine clearance as shown in:

Recommended maintenance doses of Ceftazidime in renal insufficiency-intermittent infusion:

Adults and children ≥ 40kg:

Creatinine clearance ml/min	Approx. serum creatinine µmol/l (mg/dl)	Recommended unit dose of Nivador (g)	Frequency of dosing (hourly)
50-31	150-200 (1.7-2.3)	1	12
30-16	200-350 (2.3-4.0)	1	24
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 < 40kg:

Creatinine clearance (ml/min) **	Approx. serum creatinine* µmol/l (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.			

Close clinical monitoring for safety and efficacy is advised.

Recommended maintenance doses of Ceftazimidime in renal impairment – continuous infusion: ***Adults and children ≥ 40kg:***

Creatinine clearance (ml/min)	Approx. Serum creatinine µmol/l (mg/dl)	Frequency of dosing (hourly)
50-31	150-200 (1.7-2.3)	Loading dose of 2g followed by 1g to 3g /24 hours

30-16	200-350 (2.3-4.0)	Loading dose of 2g followed by 1g /24 hours
≤15	>350 (>4.0)	Not evaluated

Caution is advised in dose selection. Close clinical monitoring for safety and efficacy is advised.

Children < 40kg: The safety and effectiveness of Ceftazidime administered as continuous infusion in renally impaired children < 40kg has not been established. Close clinical monitoring for safety and efficacy is advised. If continuous infusion is used in children with renal impairment, the creatinine clearance should be adjusted for body surface area or lean body mass.

Haemodialysis: The serum half-life during haemodialysis ranges from 3 to 5 hours. Following each haemodialysis period, the maintenance dose of Ceftazidime recommended in the above table should be repeated.

Peritoneal dialysis: Ceftazidime may be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD). In addition to IV use, Ceftazidime can be incorporated into the dialysis fluid (usually 125 to 250mg for 2 litres of dialysis solution). For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units; 1g 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:

Ceftazidime 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. Ceftazidime 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.

DIRECTION FOR RECONSTITUTION:

Vial Size	Route of Administration	Amount to be Added of Diluent (ml)	Approximate Conc. (mg/ml)
250mg	Intramuscular	1.0ml	210
	Intravenous	2.5ml	90
500mg	Intramuscular	1.5ml	260
	Intravenous	5ml	90
1g	Intramuscular	3ml	260
	Intravenous	10ml	90

Preparation of solution for IM or IV bolus Injection:

- Introduce the syringe needle through the vial closure and inject the recommended volume of diluent.
- Withdraw the needle and shake the vial to give a clear solution.
- 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.

4.3. CONTRAINDICATIONS:

Hypersensitivity to the active substance, to other cephalosporins or to any of the excipients. History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (penicillins, monobactams and carbapenems).

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

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 Ceftazidime 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 Ceftazidime at the recommended dose levels. There is no evidence that Ceftazidime 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. 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 Ceftazidime therapy. When clinically appropriate during therapy of such infections, periodic susceptibility testing should be considered. Elevated levels of ceftazidime in patients with renal insufficiency can lead to seizures, nonconvulsive status epilepticus (NCSE), encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia. Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal and hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated. Distal necrosis can occur after inadvertent intra-arterial administration of ceftazidime. The development of a positive Coombs' test associated with the use of ceftazidime in about 5% of patients may interfere with the cross-matching of blood. This medicinal product contains 12.5mg sodium per 250mg vial, 25mg sodium per 500mg vial, 50mg sodium per 1g vial. The sodium content must be taken into account in patients requiring sodium restriction.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS:

Concurrent use of high doses with nephrotoxic drugs may adversely affect renal function. Chloramphenicol is antagonistic in vitro with ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but if concurrent administration of Ceftazidime 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.

4.6. FERTILITY, PREGNANCY AND LACTATION:

Fertility and Pregnancy: Ceftazidime should be administered with caution during the early months of pregnancy and early infancy.

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

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Undesirable effects may occur (e.g. dizziness), which may influence the ability to drive and use machines.

4.8. UNDESIRABLE EFFECTS:

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 ≥1/10, common ≥1/100 to <1/10, uncommon ≥1/1,000 to <1/100, rare ≥1/10,000 to <1/1,000, very rare <1/10,000.

Infections and infestation: ***Uncommon:*** Candidiasis (including vaginitis and oral thrush).

Blood and lymphatic system disorders: ***Common:*** Eosinophilia and thrombocytopenia. ***Uncommon:*** Leucopenia, neutropenia, and thrombocytopenia. ***Very rare:*** Lymphocytosis, haemolytic anemia, 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 Ceftazidime has not been appropriately reduced.

Vascular disorders: ***Common:*** Phlebitis or thrombophlebitis with IV administration.

Gastrointestinal disorders: ***Common:*** Diarrhoea. ***Uncommon:*** Nausea, vomiting, abdominal pain and antibacterial agent associated diarrhoea and colitis. ***Very rare:*** Bad taste.

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, urticaria, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

Renal and urinary disorders: ***Uncommon:*** Transient elevations of blood urea, blood urea nitrogen and/or serum creatinine. ***Very rare:*** Interstitial nephritis, acute renal failure.

General disorders and administration site conditions: ***Common:*** Pain and /or inflammation after IM 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.

4.9. OVERDOSE:

Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Antibacterials for systemic use. Third-generation cephalosporins.

ATC code: J01DD02

Mechanism of action: Ceftazidime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

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

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

5.2. PHARMACOKINETICS:

Absorption: After intramuscular administration of 500mg and 1g of ceftazidime, peak plasma levels of 18 and 37mg/l, respectively, are achieved rapidly. Five minutes after intravenous bolus injection of 500mg, 1g or 2g, plasma levels are 46, 87 and 170mg/l, respectively. The kinetics of ceftazidime are linear within the single dose range of 0.5 to 2g following intravenous or intramuscular dosing.

Distribution: The serum protein binding of ceftazidime is low at 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 CSF in the absence of inflammation. However, concentrations of 4 to 20mg/l or more are achieved in the CSF when the meninges are inflamed.

Metabolism: Ceftazidime is not metabolised in the body.

Elimination: After parenteral administration plasma levels decrease with a half-life of about 2h. Ceftazidime is excreted unchanged into the urine by glomerular filtration; approximately 80 to 90% of the dose is recovered in the urine within 24h. Less than 1% is excreted via the bile.

5.3. PRECLINICAL SAFETY DATA:

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeat dose toxicity, genotoxicity, toxicity to reproduction. Carcinogenicity studies have not been performed with ceftazidime.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

Nivador®**250mg Injection:** Sodium carbonate
Nivador®**500mg Injection:** Sodium carbonate
Nivador®**1g Injection:** Sodium carbonate

6.2. INCOMPATIBILITIES:

Ceftazidime is less stable in Sodium Bicarbonate Injection than other intravenous fluids. It is not recommended as a diluent. Ceftazidime and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation has been reported when vancomycin has been added to ceftazidime in solution. It is recommended that giving sets and intravenous lines are flushed between administration of these two agents.

Ceftazidime at concentrations between 1mg/ml and 40mg/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 0.05mg/ml and 0.25mg/ml is compatible with Intra-peritoneal Dialysis Fluid (Lactate). Both components retain satisfactory potency when ceftazidime at 4mg/ml is mixed with:

- Hydrocortisone (hydrocortisone sodium phosphate) 1mg/ml in 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
- Cefuroxime (cefuroxime sodium) 3mg/ml in 0.9% Sodium Chloride Injection.
- Cloxacillin (cloxacillin sodium) 4mg/ml in 0.9% Sodium Chloride Injection.
- Heparin 10 IU/ml or 50 IU/ml in 0.9% Sodium Chloride Injection.
- Potassium Chloride 10mEq/l or 40mEq/l in 0.9% Sodium Chloride Injection.

6.3. SHELF LIFE:

Unopened vial: See expiry on the pack.

Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 8 hours at 25°C and 24 hours at 4°C. From a microbiological

point of view, once opened, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.
Keep out of reach of children.

6.5. NATURE AND CONTENTS OF CONTAINER:

Nivador®**250mg Injection:**
Powder for Injection: Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal.
Water for Injection: Clear 3ml glass ampoule (USP Type-I).
Pack size is 1 vial and 1 ampoule.
Nivador®**500mg Injection:**
Powder for Injection: Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal.
Water for Injection: Clear 5ml glass ampoule (USP Type-I).
Pack size is 1 vial and 1 ampoule.
Nivador®**1g Injection:**
Powder for Injection: Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal.
Water for Injection: Clear 10ml glass ampoule (USP Type-I).
Pack size is 1 vial and 1 ampoule.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

This medicinal product is for single use only. Reconstitute immediately before use. Any unused product or waste material should be disposed of in accordance with local requirements. Effervescence occurs on addition of Water for Injection.

6.7. DRUG PRODUCT SPECIFICATION:

Nivador®**250mg Injection:** USP Specs.
Nivador®**500mg Injection:** USP Specs.
Nivador®**1g Injection:** USP Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured for:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharma.com

by:
Healthtek (Pvt.) Limited
Plot No. 14, Sector 19, Korangi
Industrial Area Karachi - Pakistan

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

Nivador® **250mg Injection:** 037548
Nivador® **500mg Injection:** 037549
Nivador® **1g Injection:** 037550

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Nivador® **250mg Injection:** 1st March, 2005
Nivador® **500mg Injection:** 1st March, 2005
Nivador® **1g Injection:** 1st March, 2005

10. DATE OF REVISION OF THE TEXT

نیواڈور انجکشن
(سیفٹازیڈیم)

(برائے عضلاتی یا وریدی استعمال)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

صرف ایک مرتبہ استعمال کے لئے ہے غیر استعمال شدہ دوا کو ضائع کر دیں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،

گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔