SMPC of TRIJECT 1 g IM/IV Injection

1. Name of the Finished Pharmaceutical Product

Triject 1 g IM/IV Injection

2. Qualitative and quantitative composition

Each vial contains 1 g ceftriaxone (as hydrated disodium) equivalent to 1.197 g Ceftriaxone Sodium.

3. Pharmaceutical Form

IV Injection

TRIJECT 1g IM/IV Injection is a preparation of Sterile Ceftriaxone Sodium USP. Ceftriaxone Sodium is a white to yellowish orange crystalline powder. The color of the constituted solution will be light to dark yellow.

4. Clinical particulars

4.1 Therapeutic indications

Ceftriaxone is indicated for the treatment of the following infections when caused by micro-organisms that are susceptible to ceftriaxone and if parenteral treatment is necessary.

- sepsis
- bacterial meningitis
- infections of bones or joints
- infections of skin or soft tissues
- pneumonia

Ceftriaxone is indicated for perioperative prophylaxis in patients with a certain risk of severe postoperative infections. Depending on the mode of surgery and the expected spectrum of pathogens ceftriaxone should be combined with an appropriate antimicrobial agent with additional anaerobic coverage. Consideration should be given to official local guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Route and method of administration
Triject 1 g IM/IV injection may be administered by intravenous injection after reconstitution of the solution according to the directions given in leaflet.

Dosage and mode of administration should be determined by the severity and site of infection, susceptibility of the causative micro-organism and the patient's age and condition.

An intravenous injection should be administered over at least 2 – 4 minutes directly into the vein or via the tubing of an intravenous infusion.

Normal dosage

Adults and adolescents aged over 12 years with a body weight ≥ 50 kg:

The usual dose is 1 to 2 g of ceftriaxone, administered once a day (every 24 hours). In cases of serious infections or infections caused by moderately sensitive micro-organisms the dose can be raised up to 4 g, administered once a day intravenously.

Newborn infants (age 0 – 14 days):
20 – 50 mg per kg bodyweight intravenously once daily (24-hour intervals). In severe infections the daily dose of 50 mg per kg bodyweight must not be exceeded.

Children 15 days-12 years of age with a body weight of < 50 kg:

20-80 mg per kg bodyweight intravenously once daily (24-hour intervals). In severe infections the daily dose of 80 mg per kg bodyweight must not be exceeded, except in meningitis. Children with a bodyweight of 50 kg or more receive the usual adult dosage once daily.

Elderly:

For elderly patients the dosage recommendations are the same as for adults – without modification.

Age group	Normal dosage	Frequency
Newborn infants (age 0 – 14 days)	20 – 50 mg/kg maximum: 50 mg/kg	once daily
Children 15 days - 12 years of age < 50 kg	20 - 80 mg/kg maximum: 80 mg/kg	once daily
Adolescents over 12 - 17 years ≥ 50 kg	1 - 2 g maximum: 4 g	once daily
Adults ≥ 17 years	1 - 2 g maximum: 4 g	once daily
Elderly	1 - 2 g maximum: 4 g	once daily

Special dosage recommendations

Meningitis:

Treatment is initiated with 100 mg per kg bodyweight once daily – not exceeding 4 g daily. After determining the sensitivity of the pathogen the dose may be reduced accordingly. In newborns 0 – 14 days of age the dose should not exceed 50 mg/kg/24 h.

Perioperative prophylaxis:

The normal daily dose of ceftriaxone should be administered 30-90 minutes prior to surgery. One single administration is usually sufficient.

Renal insufficiency:

In patients with impaired renal function, adjustment of the ceftriaxone dose is not necessary if the hepatic function is normal. In renal insufficiency with a reduced creatinine clearance of < 10 ml/min the daily dose of ceftriaxone should not exceed 2 g in adult patients.

Hepatic insufficiency:

The dose does not need to be altered in patients with a liver disease provided that the renal function is normal. In simultaneous severe renal and hepatic insufficiency the serum ceftriaxone concentrations should be monitored regularly and the dosage adjusted appropriately for children and adults.

Haemodialysis or peritoneal dialysis

As ceftriaxone is dialysable only to a very minor extent there is no need for an additional dose of ceftriaxone after the dialysis. Serum concentrations should be monitored, however, to determine whether dosage adjustments are necessary, since the elimination rate in these patients may be reduced. In patients on continuous ambulatory peritoneal dialysis (CAPD), ceftriaxone may be administered either intravenously or in case of CAPD associated infections may be added directly to the dialysis solution (e.g. 1-2 g ceftriaxone in the first dialysis fluid of the respective day of treatment)

Duration of therapy

The normal duration of therapy depends on the characteristics of the infection. Generally, the administration of ceftriaxone should be continued for at least 48 to 72 hours beyond the

normalization of body temperature and evidence of bacterial eradication has been obtained. Dosage recommendations for special indications should be taken into account.

4.3 Method of administration

Reconstituted solution is given through the vein over 2-4 min intervals.

4.4 Contraindication

Hypersensitivity to the active substance, 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. Hyperbilirubinemia newborns and preterm newborns should not be treated with ceftriaxone. In vitro studies have shown that ceftriaxone can displace bilirubin from its binding to serum albumin and bilirubin encephalopathy can possibly develop in these patients. Calcium treatment because of the risk of precipitation of ceftriaxone-calcium salt in term newborns. Intramuscular injection of the medicinal product is contraindicated:

• in infants < 2 years of age

• during pregnancy and lactation.

1.5.1.4.5 Special warnings and precautions for use

In suspected or proven infections with Pseudomonas aeruginosa, high resistance rates (> 60 %) for ceftriaxone in at least some European countries should be taken into consideration.

In infections caused by Pseudomonas aeruginosa with proven sensitivity to ceftriaxone a combination with amino-glycosides is warranted to avoid secondary resistance.

In infections caused by other bacteria in patients with neutropenic fever interventional treatment with ceftriaxone should be combined with an aminoglycoside.

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 ceftriaxone as well (crossallergy).

Hypersensitivity reactions against ceftriaxone are more likely in patients with any other type of hypersensitivity reaction or asthma bronchiale. Injections with ceftriaxone should be used with special caution in patients with allergic diathesis, because hypersensitivity reactions emerge faster and proceed more severely after intravenous injection

Hypersensitivity reactions may occur in all degrees of severity up to anaphylactic shock.
In severe renal impairment accompanied by hepatic insufficiency, dosage reduction is required. In case of simultaneous impairment of renal and liver function, serum-level of ceftriaxone should be monitored in regular intervals.

Each administration of antibiotics can lead to multiplication of pathogens resistant to the active substance used. Signs of consecutive secondary infections with such pathogens (including candida and fungi) are to be heeded. Secondary infections are to be treated accordingly.

Pseudomembranous colitis has been reported with almost all antibiotics, including ceftriaxone. This diagnosis should be considered in patients who develop diarrhoea during or following treatment with ceftriaxone .

Monitoring of renal and hepatic function and haematological parameters at regular intervals are indicated during long-term treatment. Ceftriaxone may precipitate in the gallbladder and kidneys and then be detectable as shadows on ultrasound. This can happen in patients of any age, but is more likely in infants and small children who are usually given a larger dose of ceftriaxone on a body weight basis. In children, doses greater than 80mg/kg body weight should be avoided – except for meningitis – because of the increased risk of biliary precipitates. There is no clear evidence of gallstones or of acute cholecystitis developing in children or infants treated with ceftriaxone, and conservative management of Ceftriaxone precipitate in the gallbladder is recommended.

Patients with risk factors for biliary stasis/sludge, e.g. preceding major therapy, severe illness and total parenteral nutrition, have increased risk of pancreatitis. Trigger role of ceftriaxone-related biliary precipitation cannot be ruled-out.

Cephalosporins as a class tend to be absorbed onto the surface of the red cell membranes and react with antibodies directed against the medicinal product to produce a positive Coombs' test and occasionally a rather mild haemolytic anaemia. In this respect, there may be some cross-reactivity with penicillins.

This medicinal product contains 3.6 mmol (or 83 mg) sodium per dose which should be taken into consideration for patients on a controlled sodium diet.

4.6 Interaction with other medicinal products and other forms of interaction

Amino glycosides:

In case of concomitant administration of cephalosporins and aminoglycosides there has been reported an increased risk of oto- and nephrotoxicity. Dose adjustment may be necessary. Furthermore, these medicinal products must be administered separately to avoid physicochemical incompatibility between ceftriaxone and the aminoglycoside. Bacteriostatic antibiotics, such as chloramphenicol and tetracycline, may antagonise the activity of ceftriaxone, especially in acute infections accompanied by rapid proliferation of micro-organisms. Simultaneous use of ceftriaxone and bacteriostatic antibiotics is, therefore, not recommended.

Ceftriaxone / probenecid:

Contrary to other cephalosporins, probenecid does not impede tubular secretion of ceftriaxone.

Oral contraceptives:

Ceftriaxon may adversely affect the efficacy of hormonal contraceptives Consequently, it is advisable to use supplementary non-hormonal contraceptive measures.

Other:

Laboratory-diagnostic tests

The Coombs test may be false-positive in rare cases during treatment with ceftriaxone

Non-enzymatic methods for glucose determinations in urine may yield false-positive results. For this reason, urine glucose determination during therapy with ceftriaxone should be carried out enzymatically. Ceftriaxone may lead to false-positive results of galactose determination in blood.

4.7 Pregnancy and lactation

There are no data on the use of ceftriaxone in pregnant women. Ceftriaxone crosses the placenta. Animal studies indicate no reproductive toxicity. As a precautionary measure, ceftriaxone should only be used during pregnancy after benefit/risk assessment by the physician in charge, especially during the first trimester. Ceftriaxone is excreted in low concentrations in breast milk. Caution should be exercised when prescribing to breastfeeding women. Diarrhoea and fungal infection of the mucous membrane could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitisation should be borne in mind.

Powder for solution for injection – intramuscular administration: The use of ceftriaxone and lidocaine is contraindicated during pregnancy and lactation.

4.8 Effects on ability to drive and use machines

Ceftriaxone has no or negligible influence on the ability to drive and use machines. However, undesirable effects such as hypotension or vertigo should be taken into account.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Undesirable effects

Rarely severe adverse reactions have been reported in preterm and full-term newborns. These reactions have caused death in some cases. These newborns had been treated with intravenous ceftriaxone and calcium. Some of them had received ceftriaxone and calcium at different times and on different intravenous lines. Precipitations of ceftriaxone – calcium salt have been observed in lungs and kidneys of these dead preterm newborns. The high risk of precipitation is due to the low blood volume of the newborns. Moreover half-life is longer than in adults.

The following adverse reactions, that reverse spontaneously or after treatment discontinuation, have been observed in association with ceftriaxone use. In this section undesirable effects are defined as follows:

very common	*(>1/10)*
common	*(>1/100, <1/10)*
uncommon	*(>1/1000, <1/100)*
rare	*(>1/10 000, <1/1000)*
very rare, including isolated reports	*(<1/10 000)*

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Infections and Infestations

Uncommon:

Mycosis of the genital tract.

Superinfections with non- susceptible micro-organisms.

Blood and lymphatic system disorders

Rare:

Eosinophilia, leucopenia, granulocytopenia.

Very rare including isolated reports:

Agranulocytosis (<500/mm3) mostly after 10-day treatment and a total dose of 20 g ceftriaxone and more; Coagulation disorders, Thrombocytopenia. Minor prolongation in the prothrombin time has been described.

Anaemia (including haemolytic anaemia)

Immune system disorders

Common:

Allergic skin reactions (e.g. dermatitis, urticaria, exanthema), pruritus, oedematous swelling of skin and joints.

Rare:

Severe acute hypersensitivity reactions up to anaphylactic shock.

Lyell syndrome/toxic epidermolysis, Stevens-Johnson syndrome or Erythema multiforme. Severe acute hypersensitivity reactions and anaphylactic shock require immediate discontinuation of the administration of ceftriaxon and the initiation of appropriate emergency measures.

Nervous system disorders

Uncommon:

Headache, dizziness, vertigo.

Gastrointestinal disorders

Uncommon:

Stomatitis, glossitis, anorexia, nausea, emesis, abdominal pain, loose stool or diarrhoea.

These undesirable effects are mostly mild and frequently subside during, otherwise after discontinuation of therapy.

Very rare:

Pseudomembranous enterocolitis.

If severe, persistent diarrhoea occurs during or after treatment, pseudomembranous colitis which is a serious, even life-threatening complication mostly caused by clostridium difficile, should be considered,. Discontinuation of therapy with ceftriaxone depending on the indication should be considered and appropriate treatment measures should be initiated: e.g. intake of specific antibiotics/chemotherapeutics with clinically proven efficacy. Antiperistaltics are contraindicated.

Hepato-bilary disorders

Very common

Symptomatic precipitation of ceftriaxone calcium salt in the gallbladder of children/reversible cholelithiasis in children. This disorder is rare in adults

Common:

Elevated liver enzymes in serum (AST, ALT, alkaline phosphatase).

Rare:

Pancreatitis. Increase in liver enzymes. Symptomatic precipitation of ceftriaxone calcium salt in the gallbladder of adults, which disappeared after discontinuation or cessation of therapy with ceftriaxone. These opacities usually occurred only after administration of higher doses than the recommended standard doses. In the rare cases in which the precipitates are accompanied by

clinical symptoms such as pain, symptomatic measures are recommended. Discontinuation of treatment should be considered too.

Renal and urinary disorders
Uncommon:
Oliguria, increase in serum creatinine.
Rare:
Precipitates of ceftriaxone in the kidneys in paediatric patients, mostly in children older than 3 years
treated either with high daily doses (e.g. 80 mg/kg BW per day and more) or with total doses above 10 g ceftriaxone and who presented several risk factors (e.g. restricted fluid supply). However, this symptomatology is reversible after discontinuation of ceftriaxone. General disorders and administration site conditions.

Common
Phlebitis following intravenous administration. This can be minimised by slow injection (over 2-4 minutes). Pain at the site of injection. In rapid intravenous injection intolerability reactions in the form of sensation of heat or nausea may occur. This can be avoided by slow injection (2-4 minutes). Pain and induration of tissue at the site of injection occur after intramuscular injection.

4.10 Overdose
No case of overdose has been reported.

Symptoms of intoxication
Typical signs of overdose can be expected to correspond to the adverse reaction profile. Colics occurred very rarely in the presence of nephropathy or cholelithiasis when using high doses administered more frequently and more rapidly than recommended.

Therapy of intoxication

Excessive serum concentration of ceftriaxone cannot be reduced by haemodialysis or peritoneal dialysis. There is no specific antidote. Symptomatic therapeutic measures are indicated.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cephalosporins and related substances

Mechanism of action

Ceftriaxone has bactericidal activity that results from the inhibition of bacterial cell wall synthesis. Ceftriaxone has a high degree of stability in the presence of β-lactamases produced by Gram-negative and Gram-positive bacteria. Synergistic effects of ceftriaxone and aminoglycosides on certain Gram-negative bacteria have been noted in vitro. Ceftriaxone is active against organisms producing some types of beta-lactamase, for example TEM-1.However, it is inactivated by beta-lactamases that can efficiently hydrolyse cephalosporins, such as many of the extended-spectrum beta-lactamases and chromosomal cephalosporinases, such as AmpC type enzymes. Ceftriaxone cannot be expected to be active against the majority of bacteria with penicillin-binding proteins that have reduced affinity for beta-lactam medicinal products. Resistance may also be mediated by bacterial impermeability or by bacterial drug efflux pumps. More than one of these four means of resistance may be present in the same organism.

Breakpoints

The minimum inhibitory concentration (MIC, according to the German Institute for Standardization DIN 58940) are 4 mg/l, – (sensitive) and 32 mg/l (resistant). The MIC breakpoints according to the Clinical and Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards are 8 µg/ml (sensitive), 16-32 µg/ml (intermediate) and 64 µg/ml (resistant) for Enterobacteriaceae and Staphylococcus spp.The respective values for Streptococcus pneumoniae are 0.5 µg/ml (sensitive), 1 µg/ml (intermediate) and 2 µg/ml (resistant). The breakpoints for sensitivity are 2 µg/ml for Haemophilus spp. and 0.25 µg/ml for Neisseria

gonorrhoea. The respective values for anaerobes are 16 µg/ml (sensitive), 32 µg/ml (intermediate) and 64 µg/ml (resistant).

Microbiology

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such, that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Gram positive aerobes

Staphylococcus aureus(MSSA)*

Streptococcus agalactiae

Streptococcus bovis

*Streptococcus pyogenes**

Streptococcus pneumoniae

Gram-positive anaerobes

Peptococcus niger

Peptostreptococcus spp.

Gram-negative aerobes

Citrobacter koseri1

*Escherichia coli*1*

*Haemophilus influenzae**

*Haemophilus parainfluenzae**

Klebsiella pneumoniae 1*

Klebsiella oxytoca 1*

*Moraxella catarrhalis**

Morganella morganii1

*Neisseria meningitidis**

*Proteus mirabilis*1*

Proteus vulgaris1

Providencia spp.1

Salmonella spp.1

Serratia spp.1

Shigella spp

5.2 Pharmacokinetic properties

Ceftriaxone is a cephalosporin for parenteral administration. Ceftriaxone is not absorbed after oral application.

After a dose of 1–2 g, concentrations have been shown to remain above the MIC values for most infection-causing pathogens for over 24 hours in over 60 different tissues (including lungs, heart, bile ducts, liver, tonsils, middle ear, nasal mucosa, bones) and in many tissue fluids (including cerebrospinal fluid, pleural fluid as well as prostatic and synovial fluid).

Absorption

Ceftriaxone is completely absorbed following intramuscular administration with peak plasma concentrations (about 80 mg/l) occurring between 2 and 3 hours after dosing.

Distribution

Ceftriaxone distributes well in various compartments and also passes the placental barrier. The mean volume of distribution in healthy adults is 0.13 l/kg. Ceftriaxone is reversibly bound to albumin. The binding is 95 % at plasma concentrations less than 100 mg/l with the binding percentage decreasing as the concentration increases (to 85 % at ceftriaxone plasma concentrations of 300 µg/ml).

Serum levels

Following the intravenous infusion of 1 g of ceftriaxone for 30 minutes, serum levels immediately after cessation of the infusion process were at 123.2 µg/ml, and at 94.81, 57.8, 20.2 and 4.6 µg/ml, respectively, 1.5, 4, 12 and 24 hours after the onset of infusion.

Subsequent to an intramuscular injection of 1 g of ceftriaxone the serum concentration amounted to 79.2 µg/ml after 1.5 hours, and afterwards 58.2, 35.5 and 7.8 µg/ml at the respective time-points 4, 12 and 24 hours after injection. Ceftriaxone penetrates the inflamed meninges of newborn, infants and children. In CSF the peak concentrations of 18 mg/l are achieved, after a 50–100 mg/kg intravenous dose, in about four hours. In adult patients with meningitis, therapeutic concentrations are achieved within 2–24 hours with the dose of 50 mg/kg. Ceftriaxone crosses the placenta and is excreted in human milk at low concentrations.

Biotransformation

Ceftriaxone does not undergo systemic metabolism but it is broken down in the small intestine by bacterial action.

Elimination

Over a 0.15 to 3 g dose range, the values of elimination half-life range from 6 to 9 hours, total plasma clearance from 0.6–1.4 l/h and renal clearance from 0.3–0.7 l/h. 50–60 % of ceftriaxone is eliminated as an unchanged active substance in the urine whilst the remainder is excreted via the bile into the faeces as microbiologically inactive metabolites.

Ceftriaxone concentrates in the urine. The urine concentrations are 5–10 times higher than those found in the plasma. Ceftriaxone cannot be removed by dialysis. This applies to both haemodialysis and peritoneal dialysis. Urinary excretion is via glomerular filtration. No tubular secretion takes place. For this reason, no increase in the serum levels is to be expected in coincident administration of probenecid and is actually - even at higher dosage e.g. with 1-2 g probenecid - not found.

Non-Linearity

The pharmacokinetics of ceftriaxone are non-linear with respect to the dose. This nonlinearity is explained by a concentration dependent decrease of binding to plasma proteins which leads to a respective increase in distribution and elimination. With the exception of elimination half-life, all pharmacokinetic parameters are dose-dependent. Repeat dosing of 0.5 to 2 g results in 15 % –36

% accumulation above single dose values The plasma elimination half-life of ceftriaxone is about 2 - 3 fold increase compared to young adults.

Special patient groups

Elderly above 75 years:

The plasma elimination half-life of ceftriaxone is about 2 - 3-fold increase compared to young adults.

In newborn infants of 3 days of age, the half-life of ceftriaxone in the serum amounts to approximately 16 hours, and approximately 9 hours in newborn infants aged from 9 to 30 days.

Patients with impaired renal and/or liver function:

Patients with an impaired renal function have an increased excretion of ceftriaxone into the bile. Patients with an impaired liver function have an increased renal excretion of ceftriaxone. The plasma elimination half-life of ceftriaxone is almost not increased in these patient groups. Patients with an impaired renal function, as well as an impaired liver function, may have an increased ceftriaxone

plasma elimination half-life.

In case of terminal renal insufficiency, the half-life is distinctively higher and reaches approximately 14 hours.

5.3 Preclinical safety data

The adverse reactions (e.g. gastrointestinal disturbances and nephrotoxicity) associated with high parenteral doses of cephalosporins have been shown to be reversible in animals during repeat dosing. After high doses of ceftriaxone diarrhoea, formation of biliary caliculi in the gallbladder and nephropathy were observed in monkeys and dogs.

Ceftriaxone has no effect on fertility or reproduction. It has not been shown to possess any mutagenic activity.

6 Pharmaceutical particulars

6.1 List of excipients

None.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6. In particular, ceftriaxone is not compatible with calcium-containing solutions such as Hartmann's solution and Ringer's solution. Based on literature reports, ceftriaxone is not compatible with amsacrine, vancomycin, fluconazole, aminoglycosides and labetalol.

6.3 Shelf life

24 Months

Opened & after reconstitution:

Chemical and physical in-use stability has been demonstrated for 24 hours at 2°C to 8°C.

From a microbiological point of view, 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 not be longer than 24 hours at 2° to 8°C, otherwise any unused portion must be discarded.

6.4 Special precautions for storage

Do not store above 30°C temperature. Keep away from light and wet place. Keep out of reach of children. Reconstituted solution is stable for 6 hours at controlled room temperature (20-25°C) and for 24 hours in a refrigerator (2-8°C temperature)

6.5 Nature and contents of container

The IV Injection is given in a 15 mL Glass clear Vial (Type I) having Grey Bromobutyl Rubber Stopper & Flip Off Seal 20 mm (Orange Colored & Blue text) along with a pre-printed ampoule (10Ml) for sterile water for injection.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

Instructions for use and handling

Intravenous injection

Ceftriaxone 1 g powder for solution for injection should be dissolved in 10 ml of water for injections (resulting volume 10.8 ml, concentration 93 mg/ml). The injection should be administered over at least 2 – 4 minutes directly into the vein or via the tubing of an intravenous infusion.

Ceftriaxone should not be mixed in the same syringe with any medicinal product other than 1% w/v lidocaine hydrochloride solution (for intramuscular injection only)
The reconstituted solution should be shaken up to 60 seconds to ensure complete dissolution of ceftriaxone.

When reconstituted for intramuscular or intravenous injection, the white to yellowish crystalline powder gives a pale yellow to amber solution.

Reconstituted solutions should be inspected visually. Only clear solutions free of visible particles should be used. The reconstituted product is for single use only and any unused solution must be discarded.

7. Marketing Authorization Holder

Company Name: Eskayef Pharmaceuticals Limited

Address:
Plant: 400 Tongi Industrial Area, Squibb Road, Tongi, Gazipur, Bangladesh
e-mail: motiar@skf.transcom.com
Web: www.skfbd.com

8. Marketing authorization number(s)

CTD4873

9. Date of first authorization/renewal of the authorization

06.01.2014

10 Date of revision of the text

28/06/2026