SUMMARY OF PRODUCT CHARACTERISTIC

1. Name of the Medicinal Product:
EFECTAL

2. Quality and Quantitative Composition:
Ceftriaxone Sodium (Sterile) equivalent to Ceftriaxone BP1000 mg
Water for Injections BP

For a full list of excipients, see section 6.1

3. Pharmaceutical form:
Almost white or yellowish, crystalline, slightly hygroscopic Powder for Injection

4. Clinical Particulars:

4.1 Therapeutic indications

Before instituting treatment with ceftriaxone sodium, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ceftriaxone and other antibacterial drugs, ceftriaxone should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Ceftriaxone is indicated for the treatment of the following infections when caused by susceptible organisms:

-Acute Bacterial Otitis Media caused by Streptococcus pneumoniae, Hemophilus influenzae (including beta-lactamase producing strains) or Moraxella catarrhalis (including beta-lactamase producing strains).
-Lower respiratory Tract infection
-Skin and Skin Structure infections
-Urinary Tract infections (complicated and uncomplicated)
-Uncomplicated Gonorrhea – Cervical/Urethral/Rectal
-Pelvic inflammatory Disease
-Bacterial Septicemia
-Bone and joint infections
-Intra-abdominal infections
-Meningitis
-Surgical Prophylaxis, prophylaxis of meningococcal meningitis

4.2 Posology and method of administration

Ceftriaxone may be administered intravenously or intramuscularly.

Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Ceftriaxone vials or to further dilute

a reconstituted vial for IV administration because a precipitate can form. Precipitation of Ceftriaxone-calcium can also occur when Ceftriaxone is mixed with calcium-containing solutions in the same IV administration line.
Ceftriaxone must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, Ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid.
Adult: The usual adult dose is 1-2 g.o.d. /b.d. Total daily dose should not exceed 4g.

Neonates: By intravenous infusion over 60 minutes, 20 - 50 mg/kg daily (max. 50mg/kg daily). Hyperbilirubinemia neonates, especially prematures, should not be treated with Ceftriaxone. Ceftriaxone is contraindicated in neonates if they require (or are expected to require) treatment with calcium-containing IV solutions, including continuous calcium-containing infusions such as parenteral nutrition because of the risk of precipitation of ceftriaxone calcium.

Infant and child under 50 kg: By deep intramuscular injection, or by intravenous injection over 2-4 minutes or by intravenous infusion, 20-50 mg/kg daily; upto 80 mg/kg daily in severe infections; doses of 50 mg/kg and over by intravenous infusion only.

Child 50 kg and over: adult dose.

In Gonorrhea: A single intramuscular dose of 250 mg is recommended. Ceftriaxone regimen should be continued for 72 hours after fever abates or after evidence of bacterial eradication.
Ceftriaxone for intramuscular injection should be given in 1% lignocaine and administered by a deep intragluteal injection to minimize pain).
For the treatment of serious infections in children other than meningitis the recommended total daily dose is 50-75 mg/kg body wt. (not to exceed 2 g) given in 2 divided doses.
For preoperative use (surgical prophylaxis) a single dose given 1/2to 2 hours before surgery is recommended. For Strep. pyogenes infections 10 day regimen is required.
No dose adjustment is required in renal or hepatic dysfunction but serum levels should be monitored in patients with other severe renal impairment (eg. Dialysis patients) or in patients suffering from both renal and hepatic malfunction.

RECONSTITUTION
Intramuscular Injection:
For IM injection, Ceftriaxone 1g in 3.6 ml of sterilized Water for Injection BP or 1% Lidocaine solution. Ceftriaxone dissolved in a 1% Lidocaine solution can reduce pain at the site of injection. Ceftriaxone must be

injected well within the body of a relatively large muscle. It is recommended that not more than 1 g be injected on either side. Reconstitution with 1% Lidocaine (without adrenaline) has no effect on the absorption or the elimination of Ceftriaxone.
The Lidocaine solution (Reconstituted) must never be administered intravenously.

Intravenous Injection:
For IV injection, Ceftriaxone 1 g dissolved in 9.6 ml of Sterilized Water for Injections BP. The intravenous administration should be given over two to four minutes.

4.3 Contra-indications

Ceftriaxone Sodium for Injection is contraindicated in patients with known allergy to Cephalosporin group of antibiotics. It is also contraindicated in neonates with jaundice, hypoalbuminemia, acidosis or impaired bilirubin binding.
Ceftriaxone is contraindicated in neonates if they require (or are expected to require) treatment with calcium-containing IV solutions, including continuous calcium- containing infusions such as parenteral nutrition because of the risk of precipitation of Ceftriaxone - calcium.

A small number of cases of fatal outcomes in which a crystalline material was observed in the lungs and kidneys at autopsy have been reported in neonates receiving Ceftriaxone and calcium-containing fluids.

In some of these cases, the same intravenous infusion line was used for both Ceftriaxone and calcium-containing fluids and in some a precipitate was observed in the intravenous infusion line.

At least one fatality has been reported in a neonate in whom Ceftriaxone and calcium- containing fluids were administered at different time points via different intravenous lines; no crystalline material was observed at autopsy in this neonate. There have been no similar reports in patients other than neonates.

4.4 Special warning and precautions for use Warning

Before therapy with ceftriaxone sodium is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs.
This product should be given cautiously to Penicillin sensitive patients. Antibiotics should be given cautiously to patients with any of kind allergy particularly to drugs.

Serious hypersensitivity reactions may require use of subcutaneous epinephrine and other emergency measures.

Pseudomembranous colitis has been reported with use of Cephalosporin's and other broad-spectrum antibiotics. Therefore, it is

important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.
Treatment with broad spectrum antibiotics can alter normal flora of colon and promote growth of Clostridia.

As with other cephalosporin's, anaphylactic reactions with fatal outcome have been reported, even if a patient is not known to be allergic or previously exposed.

Interaction with Calcium-Containing Products:
Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Ceftriaxone vials or to further dilute reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone calcium can also occur when Ceftriaxone is mixed with calcium-containing solutions in the same IV administration line.
Ceftriaxone must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, Ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid. In vitro studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium.
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including ceftriaxone, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.
C. difficile toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, surgical evaluation should be instituted as clinically indicated.

Hemolytic Anemia:
An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class antibacterial including Ceftriaxone. Severe cases of hemolytic anemia, including fatalities, have been reported during treatment in both adults and children. If a patient develops anemia while on Ceftriaxone, the diagnosis of a cephalosporin associated anemia should be considered and Ceftriaxone stopped until the etiology

is determined.

Precautions:
There have been reports of sonographic abnormalities in the gallbladder of patients treated with Ceftriaxone sodium; some of these patients also had symptoms of gallbladder disease. The condition appears to be transient and reversible upon discontinuation of Ceftriaxone and institution of conservative management.

In renal failure no adjustment may be necessary but serum levels should be monitored periodically and the dosage reduced if required.
Dosage adjustment is similarly not essential in hepatic failure but in patients with both, hepatic and significant renal malfunction. Ceftriaxone Sodium for Injection doses should not exceed 2 g/day without close serum monitoring.
Rarely, alterations in Prothrombin time have occurred and may require co- administration of vitamin K (10 mg weekly).

Prolonged use may cause overgrowth of non-susceptible organisms and cause hyperinfection.
Administer with caution to patients with history of G.I. diseases, especially, colitis.

Carcinogenesis, Mutagenesis and Impairment of Fertility:
No evidence seen in doses up to 20 times the clinical dose.

Pregnancy:
No evidence of embryotoxicity, fetotoxicity or teratogenicity seen up to 20 times the usual human dose given to mice. As there are no adequate trials in pregnant women, administer only if clearly necessary.

Nursing Mothers:
Low concentrations of Ceftriaxone are excreted in human milk. Caution should be exercised when Ceftriaxone is administered to a nursing woman.

Pediatric Use:
With reference to literature the in vitro studies have shown that Ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Ceftriaxone should not be administered to hyperbilirubinemia neonates, especially premature.

4.5 Interaction with other drugs, other forms of interactions
Interaction with Calcium-Containing Products:
Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Ceftriaxone vials or to further dilute reconstituted vial for IV administration because a precipitate can form. Precipitation of ceftriaxone calcium can also occur when Ceftriaxone is mixed with calcium-containing solutions in the same IV administration

line.
Ceftriaxone must not be administered simultaneously with calcium-containing IV solutions, including continuous calcium containing infusions such as parenteral nutrition via a Y-site. However, in patients other than neonates, Ceftriaxone and calcium-containing solutions may be administered sequentially of one another if the infusion lines are thoroughly flushed between infusions with a compatible fluid. In vitro studies using adult and neonatal plasma from umbilical cord blood demonstrated that neonates have an increased risk of precipitation of ceftriaxone-calcium.
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C. difficile toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, surgical evaluation should be instituted as clinically indicated.

Hemolytic Anemia
An immune mediated hemolytic anemia has been observed in patients receiving cephalosporin class antibacterial including Ceftriaxone. Severe cases of hemolytic anemia, including fatalities, have been reported during treatment in both adults and children. If a patient develops anemia while on Ceftriaxone, the diagnosis of a cephalosporin associated anemia should be considered and Ceftriaxone stopped until the etiology is determined.

4.6 Pregnancy and Lactation Pregnancy:
No evidence of embryotoxicity, fetotoxicity or teratogenicity seen up to 20 times the usual human dose given to mice. As there are no adequate trials in pregnant women, administer only if clearly necessary.

Nursing Mothers:
Low concentrations of Ceftriaxone are excreted in human milk. Caution should be exercised when Ceftriaxone is administered to a nursing woman.

Paediatric Use:
With reference to literature the in vitro studies have shown that

Ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Ceftriaxone should not be administered to hyperbilirubinemic neonates, especially prematures.

4.7 Effects on ability to drive and use machine

Ceftriaxone has been associated with dizziness, which may affect the ability to drive or operate machines.

4.8 Undesirable effects

Ceftriaxone Sodium for Injection is generally well tolerated. In clinical trials following reactions were encountered which may or may not be related to Ceftriaxone Sodium for Injection therapy.

1) **Local reactions** : Pain, induration, tenderness at si te of injection less frequently phlebitis was seen after intravenous doses. The incidence of warmth, tightness or induration was (3/17) after IM administration of 350 mg/mL and (1/20) after IM administration of 250 mg/ml.

2) **Hypersensitivity** : Rash, Pruritus, fever, chills.

3) **Haematological** : Eosinophilia, thrombocytosis and leukopenia. Less frequently reported were anemia, hemolytic anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

4) **G.I.T.** : Diarrhea, nausea, vomiting, dysgeusia. The onset of pseudo membranous colitis symptoms may occur during or after antibacterial treatment.

5) **Hepatic** : SGOT elevation SGPT elevation Alkaline phosphatase/bilirubin elevation

6) **Renal** : BUN elevation Creatinine elevation Casts in urine

7) **C.N.S.** : Headache/dizziness

8) **Genitourinary** : Moniliasis/Vaginitis

4.9 Overdoses

In overdose, the symptoms of nausea, vomiting and diarrhea can occur. Ceftriaxone concentrations cannot be reduced by hemodialysis or peritoneal dialysis. There is no specific antidote. Treatment is symptomatic.

5. Pharmacological properties:

5.1 Pharmacodynamic Properties Mechanism of action

Ceftriaxone 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.

Resistance

Bacterial resistance to ceftriaxone may be due to one or more of the following mechanisms:

- Hydrolysis by beta-lactamases, including extended-spectrum beta-lactamases (ESBLs), carbapenemases and Amp C enzymes that may be induced or stably derepressed in certain aerobic Gram-negative bacterial species.
- Reduced affinity of penicillin-binding proteins for ceftriaxone.
- Outer membrane impermeability in Gram-negative organisms.
- Bacterial efflux pumps.

5.2 Pharmacokinetic Properties Absorption:

Ceftriaxone is completely absorbed following intramuscular administration with mean maximum plasma concentrations occurring 2-3 hours post dosing.

Distribution:

Apparent volume of distribution of Ceftriaxone is 5.78 – 13.5 L.
Ceftriaxone is reversibly bound to plasma proteins.
Concentrations of Ceftriaxone inhibitory for most Gram-negative bacteria are attained in the meninges, in purulent sputum and in synovial, prostatic and pleural fluid. Ceftriaxone also reaches high concentrations in the blister and peritoneal fluid, bone, myometrium, endometrium and salpinges tissue.
Ceftriaxone is excreted in breast milk (AUC in milk is 3-4% of AUC in serum). High concentrations are also seen in bile. Elimination half-life of Ceftriaxone is 6-9 hours.

Excretion:

Major excretory pathway is urine (40-60%) by glomerular filteration.
Some amount is eliminated via bile (11-65%).

In infants and Children:

Elimination half-life in neonates is prolonged (almost equal to adults) but decreases with increasing postnatal age. In patients with renal failure, non-renal elimination may compensate.

5.3 Preclinical Safety Data

Not Available

6. Pharmaceutical particulars:

6.1 List of excipients

None

6.2 Incompatibilities

Ceftriaxone has been shown to be compatible with Metronidazole Hydrochloride IV. The concentration should not exceed 5 to 7.5 mg/mL metronidazole hydrochloride with ceftriaxone 10 mg/mL as an admixture. The admixture is stable for 24 hours at room temperature only in 0.9%w/v sodium chloride injection or 5% w/v dextrose in water (D5W). Metronidazole at concentrations greater than 8 mg / mL will precipitate. Do not refrigerate the admixture as precipitation will occur. Vancomycin, amsacrine, aminoglycosides, and fluconazole are physically incompatible with ceftriaxone in admixtures. When any of these drugs are to be administered concomitantly with ceftriaxone by intermittent intravenous infusion, it is recommended that they be given sequentially, with thorough flushing of the intravenous lines (with one of the compatible fluids) between the administrations.

Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Efectal vials or to further dilute a reconstituted vial for IV administration. Particulate formation can result. Efectal solutions should not be physically mixed with or piggybacked into solutions containing other antimicrobial drugs or into diluent solutions other than those listed above, due to possible incompatibility. After reconstitution, protection from normal light is not necessary. The color of solutions ranges from light yellow to amber, depending on the length of storage, concentration and diluent used.

6.3 Shelf – life

24 Months.

6.4 Special precautions for storage

Store below 30°C, protected from light.

6.5 Nature and contents of container

10 ml flint USP-type III EROS, stoppered with 20 mm grey butyl rubber stopper, and sealed with 20 mm flip-off orange 'NEON' embossed aluminium seal and one 10 ml plastic ampoule of diluent – Sterilized water for injection BP are packed in a combi pack carton along with package insert.

6.6 Special Precautions for Handling and Disposal

Ceftriaxone should not be mixed in the same syringe with any drug other than 1% Lidocaine Injection BP (for intramuscular injection only).

7. Marketing authorization holder:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,

28, Mahal Industrial Estate, M. Caves
Road, Andheri (E), Mumbai – 400 093.
INDIA

8. Marketing Authorization Number (s):
14995

9. Date of first authorization/renewal of the authorization:
March, 2026.

10. Date of revision of the text: March, 2025