Summary of Product Characterstics

Neucef® Capsules

Neucef® Suspension / Drops

Neucef®
(Cefadroxil)

1. NAME OF THE PRODUCT
Neucef® (Cefadroxil) 500mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Neucef® 500mg Capsules
Each capsule contains:
Cefadroxil Monohydrate equivalent to Cefadroxil.....500mg

3. PHARMACEUTICAL FORM
Capsule

Appearance: White to off-white powder in hard gelatin capsules having light green cap with **Neucef®** 500 printed & translucent body with SAMI logo printed in black color.

4. CLINICAL PARTICULARS
4.1. THERAPEUTIC INDICATIONS:
Neucef® is a cephalosporin antibiotic bactericidal in vitro against a wide range of Gram-positive and Gram-negative microorganisms. **Neucef®** is indicated in the treatment of the following infections when due to susceptible microorganisms.
Respiratory tract infections: Tonsillitis, pharyngitis, lobar and bronchopneumonia, acute and chronic bronchitis, pulmonary abscess, empyema, pleurisy, sinusitis, laryngitis, otitis media.
Skin and soft-tissue infections: Lymphadenitis, abscesses, cellulitis, decubitus ulcers, mastitis, furunculosis, erysipelas.
Genitourinary tract infections: Pyelonephritis, cystitis, urethritis, gynaecological infections.
Other infections: Osteomyelitis, septic arthritis.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:
Posology:
Adults and children weighing more than 40kg: One to two capsules (500mg to 1g) twice a day, depending upon the severity of infection. Alternatively, in skin and soft tissue and uncomplicated urinary tract infections, 1g once a day.

In the treatment of beta-haemolytic streptococcal infections, **Neucef**® should be administered for at least 10 days.

Adults and children (7years & above) weighing less than 40 kg): One capsule (500mg) twice a day.

Elderly: No specific dosage recommendations or precautions for use in the elderly except to monitor those patients with impaired renal function. The bioavailability and consequent chemotherapeutic effects of cefadroxil are unaffected by food. It may, therefore, be taken with meals or on an empty stomach.

Renal Impairment: In patients with renal impairment, the dosage should be adjusted according to creatinine clearance rates to prevent drug accumulation and serum levels should be monitored. A modified dosage schedule is unnecessary in patients with creatinine clearance rates of greater than 50ml/min. In those patients with creatinine clearance rates of 50ml/min or less, the following reduced dosage schedule is recommended as a guideline, based upon the creatinine clearance rate (ml/min/1.73m^2). Patients with renal insufficiency may be treated with an initial dose of 500mg to 1000mg of **Neucef**®. Subsequent doses may be administered according to the following table:

Creatinine Clearances	Dose	Dosage Interval
0-10mL/min/1.73m^2	500-1000mg	36 hours
11-25mL/min/1.73m^2	500-1000mg	24 hours
26-50mL/min/1.73m^2	500-1000mg	12 hours

Cefadroxil can be removed from the body by haemodialysis.

Method of administration:

For oral use only.

4.3. CONTRAINDICATIONS:

Cefadroxil is contraindicated in patients with:

- History of hypersensitivity to cefadroxil, to any other cephalosporin or to any of the excipients of this product.
- History of severe reactions to penicillins or to any other beta-lactam drugs.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Pseudomembranous colitis: As with other broad-spectrum antibiotics, pseudomembranous colitis has been reported. In case of severe and persistent diarrhoea, an antibiotic-associated pseudomembranous colitis should be considered. In that case Cefadroxil must be discontinued immediately and a suitable therapy should be started (e.g. oral vancomycin, 250mg q.i.d.). Antiperistaltics are contraindicated.

***Clostridium difficile* associated diarrhoea (CDAD):** *Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefadroxil, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile. C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause 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 diarrhoea 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* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

History of gastro-intestinal disturbances: Cefadroxil should be used with caution in patients with a history of gastro-intestinal disturbances particularly colitis. Cefadroxil does not penetrate in the CSF and is not indicated for the treatment of meningitis. Penicillin is the first drug of choice for the treatment of the Streptococcus pyogenes and for the prevention of rheumatic fever. Data for cefadroxil are not sufficiently substantial for prophylaxis therapy. As experience in premature infants and neonates is limited, the use of cefadroxil in these patients should only be undertaken with caution.

Patients with history of allergies: Special caution should be exercised in patients with history of severe allergies or asthma. In patients with a history of non-severe hypersensitivity to penicillins, or other non-cephalosporin beta–lactam drugs, cefadroxil should be used with special caution as cross allergies occur (incidence 5-10%). There is evidence of partial crossallergenicity between the penicillins and the cephalosporins. Should an allergic reaction to cefadroxil occur, the drug should be discontinued and the patient treated with the usual agents (pressor amines, corticosteroids and/or antihistamines), depending on the severity of the reaction.

Allergic reactions: Treatment must be discontinued at once if allergic reactions occur (urticaria, exanthema, pruritus, fall of blood pressure and increased heart rate, respiratory disturbances, collapse, etc.) and suitable countermeasures should be taken (sympathomimetics, corticosteroids and/or antihistaminics).

Renal impairment: Caution is necessary in patients with renal impairment; the dosage must be adjusted according to the grade of renal impairment.

Prolonged use: Particularly on prolonged use frequent checks on the blood count and regular hepatic and renal function tests are advisable. Superinfections with fungi (e.g., candida) can occur on prolonged treatment with cefadroxil. Severe life-threatening infections or those which require higher

posology or repetitive administrations per day may benefit of parenteral cephalosporins. The result of the Coombs' test can be transiently positive during or after treatment with cefadroxil. In haematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Neurotoxicity: Neurotoxicity with cephalosporins are mainly characterized by seizures. Seizures associated with cephalosporins may present as either convulsive or non-convulsive. A disruption in the neurotransmitter gamma-aminobutyric acid (GABA) function is proposed to be a possible mechanism for such events. Symptoms of neurotoxicity have been reported to develop within several days after starting treatment and to resolve following discontinuation.

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

Contraindication of concomitant use: Cefadroxil should not be combined with bacteriostatic antibiotics (e.g., tetracycline, erythromycin, sulfonamides, chloramphenicol) since an antagonistic effect is possible. Treatment with Cefadroxil in combination with aminoglycoside antibiotics, polymyxin B, colistin or high-dose loop diuretics should be avoided since such combinations can potentiate nephrotoxic effects.

Concomitant use not recommended: Frequent checks on coagulation parameters are necessary during concomitant long-term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications.

Precautions to be exercised: The concomitant administration of probenecid can produce higher and sustained concentrations of cefadroxil in the serum and in the bile. The occurrence of diarrhoea may impair the resorption of other medicaments and therefore lead to an impairment of their efficacy. Forced diuresis leads to a decrease of cefadroxil blood levels. Cefadroxil may attenuate the effect of oral contraceptives. Cefadroxil binds to cholestyramine which may lead to reduced bioavailability of cefadroxil.

Laboratory tests: The result of the direct Coombs' test can be transiently positive during or after treatment with cefadroxil. This also applies to Coombs' tests carried out in newborns whose mother received treatment with cephalosporins before delivery. Urine from patients treated with cefadroxil may give a false-positive glycosuria reaction when tested with Benedict's or Fehling's solutions. This does not occur with enzyme-based tests. Urinary sugar should be determined enzymatically (e.g., with test strips) during treatment with cefadroxil.

4.6. FERTILITY, PREGNANCY AND LACTATION:

Fertility: The human dose and have revealed no evidence of impaired fertility or harm to the foetus due to Cefadroxil.

Pregnancy: No adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Breast-feeding: Cefadroxil is excreted in low concentrations in breast milk sensitization, diarrhoea or colonization of the infants' mucosa with fungi are possible. The use of cefadroxil during pregnancy and in lactating mothers should therefore be handled very strictly.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

There is no evidence to suggest that cefadroxil has any effect on the ability to drive and/or use machines.

4.8. UNDESIRABLE EFFECTS:

The most commonly reported side-effects are gastrointestinal disturbances and hypersensitivity phenomena. Undesirable effects reported are listed per System Organ Class and per frequency. Very common: (>1/10) Common: (>1/100, <1/10), Uncommon: (>1/1000, <1/100), Rare: (>1/10000,<1/1000), Very rare: (<1/10000), including isolated cases.

Infections and Infestations:

Uncommon: Clinical pictures due to a growth of opportunistic organisms (fungi), such as vaginal mycoses (genital candidiasis), thrush.

Blood and Lymphatic system disorders:

Rare: Eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis: rare cases during prolonged use, which subside upon discontinuation of therapy.

Very rare: Isolated cases of haemolytic anaemia of immunologic origin.

Immune system disorders:

Rare: Serum sickness-like reactions.

Very rare: Immediate allergic reaction (anaphylactic shock).

Nervous and Psychiatric system disorders:

Very rare: Dizziness, headache, nervousness, sleeplessness. Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment, when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.

Gastrointestinal disorders:

Common: Nausea, vomiting, diarrhoea, dyspepsia, abdominal discomfort, abdominal pain, glossitis.

Very rare: Isolated cases of pseudo-membranous colitis.

Unknown frequency: Colitis has been reported.

Hepatobiliary disorders:
Rare: Minor elevations of serum transaminases (ASAT, ALAT) and alkaline phosphatase.
Cases of cholestasis and idiosyncratic hepatic failure have been reported.
Skin and Subcutaneous tissues disorders:
Common: Rash, pruritus, allergic exanthema, urticaria
Rare: Angioneurotic oedema.
Very rare: Stevens Johnson syndrome and erythema multiforma have been reported.
Musculoskeletal and Connective tissue disorders:
Rare: Arthralgia.
Renal and Urinary disorders:
Rare: Interstitial nephritis.
General disorders and Administration site conditions:
Rare: Drug fever.
Very rare: Fatigue.
Investigations:
Very rare: Direct and indirect positive Coombs' tests.

4.9. OVERDOSE:

No clinical reports are as yet available on cefadroxil in this respect. However, in view of experience gained with other cephalosporins the following symptoms are possible: nausea, hallucinations, hyperreflexia, extrapyramidal symptoms, clouded consciousness, or even coma and renal functional impairment. First aid after intake of toxic doses: induce vomiting at once or gastric lavage, if necessary, haemodialysis. Monitor and if necessary, correct the water and electrolyte balance, monitor renal function. Ingestion of <250mg/kg in children under six years of age was not associated with significant outcomes. The patient should be observed and treated symptomatically. For amounts >250mg/kg, gastric lavage or stimulation of vomiting is appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Other beta-lactam antibacterial. First generation cephalosporins.
ATC-Code: J01DB05
Mechanism of action: Cefadroxil is a cephalosporin for oral administration which inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins. The result is formation of a defective cell wall that is osmotically unstable, and bacterial cell lysis.

5.2. PHARMACOKINETICS PROPERTIES:

Absorption: Cefadroxil is rapidly absorbed after oral administration. The bioavailability is unaffected by food.

Distribution: Following single doses of 500mg and 1000mg average peak serum levels were approximately 16 and 28g/ml respectively. Measurable levels were present 12 hours after administration.

Biotransformation: Increases in dose generally produce a proportionate increase in cefadroxil urinary concentration. Oral dosing produces effective tissues penetration in lungs, tonsil, liver, gall bladder, bile duct, prostate, bone, muscle and synovial fluid.

Elimination: Over 90% of the drug is excreted unchanged in the urine within 24 hours. Peak urine concentrations are approximately 1,800g/ml after a 500mg dose. The half-life is approximately 80 – 120 minutes, and protein binding is approximately 20%. Cefadroxil can be removed from the body by haemodialysis.

5.3. PRECLINICAL SAFETY DATA:

Preclinical data reveal no special hazard for humans on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction. Although, tests for mutagenicity and carcinogenicity of cefadroxil in animals have not been reported, there is no published evidence to suggest that potential carcinogenicity and mutagenicity is a concern with the cephalosporin-class of compounds.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

- Sodium Starch Glycolate
- Magnesium Stearate
- Hard Gelatin Capsule

6.2. INCOMPATIBILITIES:

Not applicable.

6.3. SHELF LIFE:

See expiry on pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

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

6.5. NATURE AND CONTENTS OF CONTAINER:

Alu/PVC blister, pack size is 12's.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

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

6.7. DRUG PRODUCT SPECIFICATION:

USP Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured for:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharma.com
ML No. 000072

by:
Healthtek (Pvt.) Limited
Plot No. 14, Sector 19, Korangi Industrial Area Karachi – Pakistan
ML No. 000618

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

011670

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10th October, 1990

10. DATE OF REVISION OF THE TEXT

نیوسیف کیپسول
(سیفاڈروکسِل)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

Neucef®
(Cefadroxil)

1. NAME OF THE PRODUCT

Neucef® (Cefadroxil) Suspension (125mg/5ml)
Neucef®DS (Cefadroxil) Suspension (250mg/5ml)
Neucef® (Cefadroxil) Paediatric Drops (100mg/ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Neucef® Suspension (125mg/5ml)
Each 5ml of reconstituted suspension contains:
Cefadroxil Monohydrate equivalent to Cefadroxil.....125mg

Neucef®DS Suspension (250mg/5ml)
Each 5ml contains (reconstituted):
Cefadroxil Monohydrate equivalent to Cefadroxil.....250mg

Neucef® Paediatric Drops (100mg/ml)
Each ml of reconstituted suspension contains:
Cefadroxil Monohydrate equivalent to Cefadroxil.....100mg

3. PHARMACEUTICAL FORM

Suspension / Paediatric Drops

Appearance:
Neucef® Suspension (125mg/5ml): White to light orange colored, granular free flowing powder having no lumps and foreign particle with characteristic odor of banana & pineapple flavor.
Neucef®DS Suspension (250mg/5ml): White to yellowish colored, granular free flowing powder having no lumps and foreign particle with characteristic odor of banana & pineapple flavor.
Neucef® Paediatric Drops (100mg/ml): White to pale yellow colored, granular free flowing powder having no lumps and foreign particle with characteristic odor of raspberry flavor.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS:

Neucef® is indicated for the treatment of patients with infection caused by susceptible strains of the designated organisms in the following diseases:

- Urinary tract infections caused by *E. coli, P. mirabilis,* and *Klebsiella species.*
- Skin and skin structure infections caused by *staphylococci* and/or *streptococci*.
- Pharyngitis and/or tonsillitis caused by *Streptococcus pyogenes* (Group A beta-haemolytic streptococci)

Note: Neucef® is generally effective in the eradication of streptococci from the oropharynx. However, data establishing the efficacy of **Neucef®** for the prophylaxis of subsequent rheumatic fever are not available.
Note: Culture and susceptibility tests should be initiated prior to and during therapy.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of **Neucef®** for oral suspension and other antibacterial drugs, **Neucef®** for oral suspension 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.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:

Adults:

Urinary Tract Infections: For uncomplicated lower urinary tract infections (i.e., cystitis) the usual dosage is 1 or 2g per day in a single (q.d.) or divided doses (b.i.d.). For all other urinary tract infections the usual dosage is 2g per day in divided doses (b.i.d.).

Skin and Skin Structure Infections: For skin and skin structure infections the usual dosage is 1g per day in single (q.d.) or divided doses (b.i.d.).

Pharyngitis and Tonsillitis: Treatment of group A beta-haemolytic streptococcal pharyngitis and tonsillitis — 1g per day in single (q.d.) or divided doses (b.i.d.) for 10 days.

Children:

For urinary tract infections, the recommended daily dosage for children is 30mg/kg/day in divided doses every 12 hours. For pharyngitis, tonsillitis, and impetigo, the recommended daily dosage for children is 30mg/kg/day in a single dose or in equally divided doses every 12 hours. For other skin and skin structure infections, the recommended daily dosage is 30mg/kg/day in equally divided doses every 12 hours. In the treatment of beta-haemolytic streptococcal infections, a therapeutic dosage of **Neucef®** should be administered for at least 10 days.

DAILY DOSAGE OF Neucef® SUSPENSION / PAEDIATRIC DROPS:

Child's Weight		Dosage		
lbs	**Kg**	**125mg/5ml**	**250mg/5ml**	**100mg/ml**
10	4.5	1 tsp	½ tsp	
20	9.1	2 tsp	1 tsp	
30	13.6	3 tsp	1 ½ tsp	
40	18.2	4 tsp	2 tsp	1 tsp
50	22.7	5 tsp	2 ½ tsp	1 ¼ tsp
60	27.3	6 tsp	3 tsp	1 ½ tsp
70 & above	31.8+	-	-	2 tsp

Renal Impairment: In patients with renal impairment, the dosage of **Neucef®** should be adjusted according to creatinine clearance rates to prevent drug accumulation. The following schedule is suggested. In adults, the initial dose is 1000mg of **Neucef®** and the maintenance dose (based on the creatinine clearance rate [mL/min/1.73m^2]) is 500mg at the time intervals listed below

Creatinine Clearances	Dosage Interval
0 to 10mL/min	36 hours
10 to 25mL/min	24 hours
25 to 50mL/min	12 hours

Patients with creatinine clearance rates over 50mL/min may be treated as if they were patients having normal renal function.

Direction for Reconstitution for Neucef® Suspension / Paediatric Drops:

Brand name with pack size	Direction for Reconstitution
Neucef® Suspension (125mg/5ml) 60ml (After reconstitution)	Shake bottle to loosen the mass. Add freshly boiled and cooled water below the mark given on bottle label then shake to make homogeneous suspension. Add further same water up to the mark of bottle label and shake vigorously to form uniform suspension.
Neucef® DS Suspension (250mg/5ml) 60ml (After reconstitution)	Shake bottle to loosen the mass. Add freshly boiled and cooled water below the mark given on bottle label then shake to make homogeneous suspension. Add further same water up to the mark of bottle label and shake vigorously to form uniform suspension.

Neucef® **Paediatric Drops** **100mg/ml** **10ml** **(After reconstitution)**	Shake bottle to loosen the mass. Add freshly boiled and cooled water below the mark given on bottle label then shake to make homogeneous suspension. Add further same water upto the mark of bottle label and shake vigorously to form uniform suspension.
The reconstituted suspension should be kept at 2-8°C, so that potency of the product remains stable and be used within 7 days.	

Method of administration:
Cefadroxil is acid-stable and may be administered orally without regard to meals. Administration with food may be helpful in diminishing potential gastrointestinal complaints occasionally associated with oral Cephalosporin therapy.

4.3. CONTRAINDICATIONS:

Cefadroxil is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Warnings:
Before therapy with Cefadroxil is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to Cefadroxil, Cephalosporins, Penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-sensitivity among beta-lactam antibiotics has been clearly documented and may occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to Cefadroxil occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.
Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including Cefadroxil for oral suspension, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C.difficile. C.difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C.difficile* cause 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 diarrhoea 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* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C.difficile*, and surgical evaluation should be instituted as clinically indicated.

Neurotoxicity with cephalosporins are mainly characterized by seizures. Seizures associated with cephalosporins may present as either convulsive or non-convulsive. A disruption in the neurotransmitter gamma-aminobutyric acid (GABA) function is proposed to be a possible mechanism for such events. Symptoms of neurotoxicity have been reported to develop within several days after starting treatment and to resolve following discontinuation.

Precautions:

General: Cefadroxil should be used with caution in the presence of markedly impaired renal function (creatinine clearance rate of less than 50mL/min/1.73m^2). In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy. Prescribing Cefadroxil for oral suspension in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. Prolonged use of Cefadroxil may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken. Cefadroxil should be prescribed with caution in individuals with history of gastrointestinal disease, particularly colitis.

Information for Patients: Patients should be counseled that antibacterial drugs including Cefadroxil for oral suspension should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Cefadroxil for oral suspension is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may:

- decrease the effectiveness of the immediate treatment
- increase the likelihood that bacteria will develop resistance and will not be treatable by Cefadroxil for oral suspension or other antibacterial drugs in the future.

Diarrhoea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Drug/Laboratory Test Interactions: Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In haematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

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

- The occurrence of diarrhoea may impair the absorption of other medicaments and therefore lead to an impairment of their efficacy.
- Forced diuresis leads to a decrease of Cefadroxil blood levels.
- Cefadroxil should not be combined with bacteriostatic antibiotics (e.g., tetracycline, erythromycin, sulfonamides, and chloramphenicol) since an antagonistic effect is possible.
- Treatment with Cefadroxil in combination with aminoglycoside antibiotics, polymyxin B, vancomycin, colistin or high-dose loop diuretics should be avoided since such combinations can potentiate nephrotoxic effects.
- The concomitant administration of probenecid reduces the renal elimination of Cefadroxil; therefore, plasma concentrations of Cefadroxil may be increased when given in combination with probenecid.
- As with other cephalosporins (in high doses) frequent checks on coagulation parameters are necessary during concomitant long-term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications.

4.6. FERTILITY, PREGNANCY AND LACTATION:

Fertility: Not known.

Pregnancy: A large number of exposed pregnancies did not appear to reveal any malformative or foetotoxic effect specifically related to cefadroxil. Consequently, Cefadroxil can be prescribed during pregnancy, if necessary.

Breast-feeding: Low levels of Cefadroxil are excreted in breast milk and the ingested quantities are lower than therapeutic doses. Consequently, breast-feeding is possible when taking this antibiotic. However, breast-feeding (or treatment) should be discontinued if the infant develops diarrhoea, candidosis or a skin eruption.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

No effects have been observed.

4.8. UNDESIRABLE EFFECTS:

The adverse effects are presented according to the frequency of the cases, 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), not known (cannot be estimated from the available data).

Infections and Infestations:

Uncommon: Clinical pictures due to a growth of opportunistic organisms (fungi) such as vaginal mycoses (genital candidiasis) or thrush

Not Known: Fever, genital pruritus, genital moniliasis, moderate transient neutropaenia, vaginitis

Blood and Lymphatic system disorders:

Rare: Eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis occur during prolonged use but subside upon discontinuation of therapy

Not Known: Haemolytic anaemia, aplastic anaemia, haemorrhage, prolonged prothrombin time, positive Coombs' test, pancytopenia

Nervous system disorders:

Very rare: Dizziness, headache, nervousness, sleeplessness, fatigue.

Not known: Neurotoxicity, seizures

Gastrointestinal disorders:

Common: Nausea, vomiting, diarrhoea, dyspepsia, abdominal discomfort, abdominal pain, glossitis

Not known: Pseudomembranous colitis has been reported

Hepatobiliary disorders:

Rare: Minor elevations of serum transaminases (ASAT, ALAT) and alkaline phosphatase

Not Known: Idiosyncratic hepatic failure, elevated bilirubin, elevated LDH, cholestasis

Skin and Subcutaneous tissues disorders:

Common: Rash, pruritus, allergic exanthema, urticaria

Rare: Angioneurotic oedema, drug fever, serum sickness-like reactions

Very rare: Immediate allergic reaction (anaphylactic shock).

Not known: Stevens Johnson syndrome, toxic epidermal necrolysis and erythema multiforme have been reported

Musculoskeletal and Connective tissue disorders:

Rare: Arthralgia

Renal and Genital Urinary disorders:

Rare: Interstitial nephritis

Not Known: Renal dysfunction, toxic nephropathy, increased BUN, increased creatinine, genital pruritus, genital moniliasis, vaginitis

4.9. OVERDOSE:

Toxicity: Acute toxicity varies for different substances but generally speaking appears low. In cases of impaired kidney function, parenteral administration of high doses has given rise to neurological symptoms.

Symptoms: In exceptional cases, anaphylactic shock may occur within 20-40 minutes; a fall in blood pressure with tachycardia or bradycardia, breathing difficulties, nausea, vomiting, exanthema, oedema.
Toxic reactions: Nausea, vomiting, diarrhoea, electrolytic disorders, reduced consciousness, muscular fasciculations, myoclonia, cramps, coma.
Haemolytic reactions: Kidney insufficiency, acidosis. Possibly coagulopathy and impairment of already impaired kidney function.
Treatment: When justified; ventricle emptying, charcoal. Symptomatic treatment. Possibly dialysis in toxic reactions and impaired kidney function.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Antibacterials for systemic use, other beta-lactam antibacterials, first generation Cephlasporins.
ATC-Code: J01DB05
Mechanism of action: Cefadroxil is a semisynthetic cephalosporin derivative for oral administration which inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins. The result is formation of a defective cell wall that is osmotically unstable. Cefadroxil exhibits time-dependent bactericidal activity.

5.2. PHARMACOKINETICS PROPERTIES:

Absorption: Cefadroxil is stable in an acid environment, and is absorbed just as well in conjunction with food as without. Maximal serum concentration (approx. 16µg/ml after a single dose of 500mg Cefadroxil) is attained about 1.5 hours after ingestion.
Distribution: About 20% of Cefadroxil is bound to serum proteins.
Elimination: Cefadroxil is excreted via glomerular filtration and tubular secretion. After 24 hours, approx. 90% of the active substance will have been excreted in the urine. In people with normally functioning kidneys, the half-life of Cefadroxil in serum is about 1 hour 20 minutes. After a single dose of 1g of Cefadroxil, sufficient concentrations of Cefadroxil are present in the urine after 24 hours to combat the most commonly occurring urinal tract pathogens.

5.3. PRECLINICAL SAFETY DATA:

There is no preclinical data of relevance for the safety-judgement beyond what has already been considered in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

Neucef® Suspension (125mg/5ml):

- Sucrose (White Refined Cane Sugar)
- Sodium Benzoate

- Silicon Dioxide Fumed
- Xanthan Gum
- Sodium Saccharin
- Banana Flavour
- Sunset Yellow Color
- Pineapple Flavour

Neucef® DS Suspension (250mg/5ml):

- Sucrose (White Refined Cane Sugar)
- Sodium Benzoate
- Silicon Dioxide Fumed
- Xanthan Gum
- Sodium Saccharin
- Banana Flavour
- Tartrazine Yellow Color
- Pineapple Flavour

Neucef® Paediatric Drops (100mg/ml):

- Silicon Dioxide Fumed
- Sucrose (White Refined Cane Sugar)
- Sodium Benzoate
- Neotame Powder
- Raspberry Flavor
- Xanthan Gum

6.2. INCOMPATIBILITIES:

Not applicable

6.3. SHELF LIFE:

See expiry on pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Keep out of reach of children.
Do not store over 30°C and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.
After reconstitution:
The reconstituted suspension should be kept at 2 - 8°C, so that potency of the product remains stable and be used within 7 days.

6.5. NATURE AND CONTENTS OF CONTAINER:

Neucef® Suspension (125mg/5ml): Amber glass bottle with tamper-proof aluminium cap with conical plug, contains 5ml measuring spoon. Pack size is 60ml.

Neucef® DS Suspension (250mg/5ml): Amber glass bottle with tamper-proof aluminium cap with conical plug, contains 5ml measuring spoon. Pack size is 60ml.
Neucef® Paediatric Drops (100mg/ml): Amber glass bottle with tamper-proof aluminium cap with conical plug, contains 1ml measuring dropper. Pack size is 10ml.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

Tightly close the cap after use.
Any unused products or waste material should be disposed of in accordance with local requirements.

6.7. DRUG PRODUCT SPECIFICATION:

Neucef® Suspension (125mg/5ml): USP Specs.
Neucef® DS Suspension (250mg/5ml): USP Specs.
Neucef® Paediatric Drops (100mg/ml): USP Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured for:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharma.com
ML No. 000072

by:
Healthtek (Pvt.) Limited
Plot No. 14, Sector 19, Korangi Industrial Area Karachi – Pakistan
ML No. 000618

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

Neucef® Suspension (125mg/5ml): 011247
Neucef® DS Suspension (250mg/5ml): 018094
Neucef® Paediatric Drops (100mg/ml): 039058

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Neucef® Suspension (125mg/5ml): 30th June, 1990
Neucef® DS Suspension (250mg/5ml): 5th October, 1995
Neucef® Paediatric Drops (100mg/ml): 19th May, 2005

10. DATE OF REVISION OF THE TEXT

نیوسیف سسپینشن / پیڈیاٹرک ڈراپس
(سیفاڈروکسِل)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

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۔

تیار شدہ سسپینشن کو ۲ سے ۸ ڈگری سینٹی گریڈ پر رکھیں تا کہ

دوا کی تاثیر برقرار رہے اور ۷ یوم کے اندر استعمال کر لیں۔