15-02-2023
1st Copy

"Unfold Leaflet"
Revised due to change in size (100mm x 160mm)

160mm

Neucef®
Capsules / Suspension / Paediatric Drops
(Cefadroxil)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Neucef® 500mg Capsules
Each capsule contains:
Cefadroxil Monohydrate USP
equivalent to Cefadroxil.....500mg

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

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

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

PHARMACEUTICAL FORM
Capsules / Suspension / Paediatric Drops

CLINICAL PARTICULARS
THERAPEUTIC INDICATIONS: Treatment of following infections caused by cefadroxil-susceptible organisms, when an oral therapy is indicated:
● Streptococcal pharyngitis and tonsillitis. ● Bronchopneumonia, bacterial pneumonia. ● **Uncomplicated urinary tract infections:** Pyelonephritis, cystitis. ● **Skin and soft tissue infections:** Abscesses, furunculosis, impetigo, erysipelas, pyoderma, lymphadenitis.

POSOLOGY AND METHOD OF ADMINISTRATION: The dosage depends on the susceptibility of the pathogens, the severity of the disease and on the clinical status of the patient (renal and hepatic function).

Indication	Adults and adolescents >40kg with normal renal function	Children (< 40 kg) with normal renal function
Streptococcal pharyngitis/ tonsillitis	Dosage may be decreased to1000mg once a day over at least 10 days	30mg/kg/day once a day over at least 10 days
Bronchopneumonia, bacterial pneumonia	1000mg twice a day	30 - 50mg/kg/day divided into two daily doses
Urinary tract infections	1000mg twice a day	30 - 50mg/kg/day divided into two daily doses
Skin & soft tissue infections	1000mg twice a day	30 - 50mg/kg/day divided into two daily doses

Children may benefit of increased posology up to 100mg/kg/day. Depending on the severity of the infection, adults may require increased posology. The dosage maximum is 4g per day. Chronic urinary tract infection may require a prolonged and intensive treatment with continued testing of susceptibility and clinical monitoring. Cefadroxil 500mg capsules is not recommended for infants and children under 6 years. For younger children and children with a body weight <40kg, liquid oral forms (cefadroxil 250mg/5ml or 125mg/5ml suspension) are available. **Renal impairment:** The dosage should be adjusted according to creatinine clearance rates to prevent accumulation of cefadroxil. In patients with creatinine clearance of 50ml/min or less, the following reduced dosage schedule is recommended as a guideline for adults:

Creatinine clearance (ml/min/ 1.73m²)	Serum Creatinine (mg/100ml)	Initial dose	Following dose	Dosage interval
50 - 25	1.4 - 2.5	1000mg	500mg - 1000mg	every 12 hours
25 - 10	2.5 - 5.6	1000mg	500mg - 1000mg	every 24 hours
10 - 0	> 5.6	1000mg	500mg - 1000mg	every 36 hours

Children: The recommended dosage for children is 25 to 50mg/kg/day in two equally divided doses (every 12 hour) asindicated. For pharyngitis, tonsillitis and impetigo the recommended daily dosage may be administered as a single dose or in two equally divided doses (every 12 hour).

Child's weight (kg)	Oral Suspension 125mg/5ml	Oral Suspension 250mg/5ml	Oral Drops (100mg/ml)
4	-	-	0.5 - 1 drop per full
5	2.5 - 5ml	-	-
10	5 - 10ml	2.5 - 5ml	-
15	7.5 - 15ml	3.75 - 7.5ml	-
20	10 - 20ml	5 - 10ml	-
25	12.5 - 25ml	5.25 - 12.5ml	-

Children (<40kg) with renal impairment: Cefadroxil is not indicated in children suffering from renal insufficiency and children requiring haemodialysis. **Dosage for haemodialysis patients:** Haemodialysis eliminates 63% of 1000mg of cephalosporin after 6 to 8 hours of haemodialysis. Elimination half-time of cephalosporin is about 3 hours during dialysis. Patients with haemodialysis receive one additional dose of 500mg-1000mg at the end of the haemodialysis. **Hepatic impairment:** No adjustment of posology is necessary. **Elderly:** As cefadroxil is excreted by renal route, the dosage should be adjusted if necessary. **Mode of administration:** Bioavailability is not affected by food and cefadroxil may be taken with meals or on an empty stomach. In case of gastro-intestinal disturbances, it may be administered with food. The capsules are taken unchewed with a liberal quantity of fluid. **Duration of therapy:** Treatment should be applied for 2 to 3 further days after regression of the acute clinical symptoms or evidence of bacterial eradication has been obtained. In infections caused by Streptococcus pyogenes up to 10 days treatment may be considered.

CONTRAINDICATIONS: ● Hypersensitivity to cefadroxil, to any of the cephalosporins. ● History of severe reactions to penicillin's or to any other beta-lactam drugs.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE: ● 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. ● Special caution should be exercised in patients with history of severe allergies or asthma. ● In patients with a history of non-severe hypersensitivity to penicillin, or other non-cephalosporin beta-lactam drugs, cefadroxil should be used with special caution as cross allergies occur (incidence 5-10%). ● Caution is necessary in patients with renal impairment; the dosage must be adjusted according to the grade of renal impairment. ● Cefadroxil should be used with caution in patients with a history of gastro-intestinal disturbances, particularly colitis. ● The occurrence of diarrhoea may impair the resorption of other medicaments and therefore lead to an impairment of their efficacy. ● 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). ● 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. ● 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. Antiperistaltics are contraindicated. ● 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. This also applies to Coombs tests carried out in newborns whose mothers received treatment with cephalosporins before delivery. ● Forced diuresis leads to a decrease of cefadroxil blood levels. ● Urinary sugar should be determined enzymatically (e.g. with test strips)

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during treatment with cefadroxil since reduction tests can furnish falsely elevated values.
Cefadroxil contains sodium: This medicinal product contains less than 1mmol (23mg) sodium per hard capsule, that is to say essentially 'sodium-free'.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: 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:** ● Cefadroxil binds to cholestyramine which may lead to reduced bioavailability of cefadroxil. ● 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.

FERTILITY, PREGNANCY AND LACTATION: ● Although animal studies and clinical experience have not shown any evidence of teratogenicity, the safe use during pregnancy has not been established. ● Cefadroxil is present 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Cefadroxil may cause headache, dizziness, nervousness, sleeplessness and fatigue, therefore the ability to drive and use machines may be influenced.

UNDESIRABLE EFFECTS: Common: Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, glossitis, pruritus, rash, allergic exanthema, urticaria. **Uncommon:** Clinical pictures due to a growth of opportunistic organisms (fungi), such as vaginal mycoses, thrush. **Rare:** Eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis: rare cases during prolonged used, which subside upon discontinuation of therapy, serum sickness-like reactions, cholestase and idiosyncratic hepatic failure have been reported. Minor elevation of serum transaminases (ASAT, ALAT) and alkaline phosphatases, angioneurotic oedema, arthralgia, interstitial nephritis, drug fever. **Very Rare:** Haemolytic anemia of immunologic origin, immediate allergic reaction (anaphylactic shock), headache, sleeplessness, dizziness, nervousness, pseudomenbranous colitis has been reported (may range in severity from mild to life threatening), Stevens-Johnson syndrom and erythema multiforma have been reported, fatigue, direct and indirect positive Coombs tests.

OVERDOSE: Induce vomiting at once or gastric lavage, if necessary haemodialysis. Monitor and if necessary, correct the water and electrolyte balance, monitor renal function.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties: ATC classification. **ATC-Code:** J01DB05. **Pharmacotherapeutic group:** Other beta-lactam antibacterials. First generation cephalosporins. **Mode 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. **Mechanisms of resistance:** Cefadroxil may be active against organisms producing some types of beta-lactamase, for example TEM-1, in low to moderate quantities. Cefadroxil cannot be expected to be active against bacteria with penicillin-binding proteins that have reduced affinity for beta-lactam drugs. 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 following breakpoint recommendations for cefadroxil according to the European Committee on Antimicrobial Susceptibly Testing (EUCAST) have been defined (Breakpoint tables for interpretation of MICs and zone diameters, Version 1.0, December 2009):

Cefadroxil (EUCAST Clinical Breakpoint Table)	MIC breakpoints	
	S ≤	R >
Enterobacteriaceae (uncomplicated UTI only)	16	16
Staphylococcus spp.	Note[1]	Note[1]
Streptococcus groups A, B, C, and G	Note[2]	Note[2]
Non-species related breakpoints	IE	IE

Note[1]: Susceptibility of staphylococci to cephalosporins is inferred from the methicillin susceptibility except for ceftazidime and cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections. **Note[2]:** The beta-lactam susceptibility of beta-haemolytic streptococci groups A, B, C and G is inferred from the penicillin susceptibility. **IE:** Indicates that there is insufficient evidence that the species in question is a good target for therapy with the drug.
Susceptibility: The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. **Species:** ***Commonly susceptible species:*** Gram-positive aerobes, Streptococci Group B, C and G, Streptococcus pyogenes*, Gram-negative aerobes, Moraxella catarrhalis*. ***Species for which acquired resistance may be a problem:*** Gram-positive aerobes: Staphylococcus aureus (methicillin-susceptible)*, Staphylococcus epidermidism, Streptococcus pneumoniae*. ***Gram-negative aerobes:*** Citrobacter diversus[§], Escherichia coli[§], Haemophilus influenzae[§], Klebsiella pneumoniae[§], Klebsiella oxytoca[§], Proteus mirabilis[§,*]. ***Inherently resistant species:*** Gram-positive aerobes: Enterococcus spp., Staphylococcus aureus (methicillin-resistant) Staphylococcus epidermidis (methicillin-resistant), Streptococcus pneumoniae (penicillin-resistant). ***Gram-negative aerobes:*** Acinetobacter spp, Citrobacter freundii, Enterobacter spp, Morganella morganii, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Pseudomonas aeruginosa, Serratia marcescens. **Other species:** Chlamydia spp, Mykoplasma spp, Legionella spp. *Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications. [§]Species with natural intermediate susceptibility.

PHARMACOKINETIC PROPERTIES: Absorption: After oral administration cefadroxil is practically completely absorbed. Simultaneous intake of food has practically no effect on absorption (AUC). **Distribution:** After oral doses of 500mg (1000mg) peak plasma concentrations of about 16 (30) µg/ml are obtained after 1-1,3 hours. Between 18 and 20% of cefadroxil is bound to plasma proteins. Cephalosporins do not penetrate in the CSF and should not be used for treatment of meningitis. **Biotransformation:** Cefadroxil is not metabolized. **Elimination:** Cefadroxil is eliminated far more slowly than comparable oral cephalosporins (half-life: about 1,4h to 2,6h) so that intervals between doses can be prolonged to 12-24 hours. Roughly 90% of the substance is eliminated in unchanged form through the kidneys within 24 hours. Cefadroxil may be eliminated from the organism through haemodialysis. Characteristics in patients with reduced creatinine clearance, a sign for renal functional impairment; Elimination is retarded, so that interval between doses must be prolonged.

DIRECTION FOR RECONSTITUTION: For Neucef® Suspension/Drops: 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.

SHELF LIFE: See expiry on the pack.

AVAILABILITY

Neucef® 500mg capsules in a pack of 12's.
Neucef® suspension (125mg/5ml) in a pack of 60ml.
Neucef® DS suspension (250mg/5ml) in a pack of 60ml.
Neucef® paediatric drops (100mg/ml) in a pack of 10ml.

INSTRUCTIONS: Dosage: As advised by the physician.
Only to be sold on the prescription of a registered medical practitioner.
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.
For Suspension / Paediatric Drops: The reconstituted suspension should be kept at 2 - 8°C, so that potency of the product remains stable and be used within 7 days.

Manufactured for:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com
by:
Healthtek (Pvt.) Limited
Plot No.14, Sector 19, Korangi
Industrial Area Karachi - Pakistan

نیوسیف کیپسول/سسپینشن/پیڈیاٹرک ڈراپس
(سیفاڈروکسل)
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۔
برائے سسپینشن/پیڈیاٹرک ڈراپس: تیار شدہ سسپینشن کو ۲ سے ۸ ڈگری سینٹی گریڈ پر رکھیں تاکہ دوا کی تاثیر برقرار رہے اور ۷ یوم کے اندر استعمال کر لیں۔

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