Biodroxil®

125 mg/250 mg/500 mg/5 ml – granules for oral suspension
500 mg – capsules
1000 mg – film-coated tablets

SANDOZ

Composition

Biodroxil 125mg/5ml granules for oral suspension:
5ml (1 measuring spoonful) of the reconstituted suspension contain:
Cefadroxil, 125mg (as Cefadroxil monohydrate); Saccharin, 3.5mg; Sucrose, appr. 3.5g

Biodroxil 250mg/5ml granules for oral suspension:
5ml (1 measuring spoonful) of the reconstituted suspension contain:
Cefadroxil, 250mg (as Cefadroxil monohydrate); Saccharin, 3.5mg; Sucrose, appr. 3.4g

Biodroxil 500mg/5ml granules for oral suspension:
5ml (1 measuring spoonful) of the reconstituted suspension contain:
Cefadroxil, 500mg (as Cefadroxil monohydrate); Saccharin, 3.5mg; Sucrose, appr. 3.1g

Biodroxil 500mg capsules:
1 capsule contains: Cefadroxil, 500mg (as Cefadroxil monohydrate);

Biodroxil 1000 mg film-coated tablets:
1 tablet contains: Cefadroxil, 1000mg (as Cefadroxil monohydrate);

Properties

Cefadroxil, the active ingredient of Biodroxil, has a bactericidal action in that it suppresses synthesis of the bacterial cell wall. The following organisms are highly sensitive to cefadroxil: b-haemolytic streptococci (= Streptococcus pyogenes), pneumococci and staphylococci (coagulase-positive and coagulase-negative and penicillinase-producing strains). Klebsiellae, Escherichia coli, Proteus mirabilis, Haemophilus influenzae, Salmonella spp. and Shigella spp. are partly sensitive to cefadroxil. Cefadroxil has no activity against most strains of enterobacter, proteus and pseudomonas and against Streptococcus faecalis.

Pharmacokinetics

After oral administration cefadroxil is absorbed practically completely in the upper segment of the small intestine and peak concentrations are present after 1 to 2 hours. Simultaneous intake of food has hardly any effect on absorption (AUC). Cefadroxil is eliminated far more slowly than comparable oral cephalosporins so that intervals between doses can be prolonged to 12 to 24 hours. Between 15 and 20% of cefadroxil is bound to plasma proteins. Clinically relevant cefadroxil concentrations are produced particularly in the tonsils, in tissues and secretions of the respiratory tract, in middle-ear secretion, in the skin, the eyes, muscle tissue, bones and joints, liver and bile as well as in the urine, prostate gland and in the female genital organs. Concentrations of cefadroxil reached in the fetal blood and amniotic fluid amount to approximately one third of the maternal serum concentrations. Cefadroxil, although in low concentrations, diffuses into breast milk.
Approximately 90% of the substance is eliminated in unchanged form through the kidneys. Elimination is retarded in patients with high-grade renal functional impairment so that intervals between doses must be prolonged in such patients (see "Dosage").

Indications

Biodroxil is suitable for the treatment of infections caused by cefadroxil-sensitive organisms such as:
– *Infections of the upper respiratory tract* (acute and chronic otitis media and sinusitis, pharyngitis, tonsillitis, laryngitis)
– *Infections of the lower respiratory tract* (acute and chronic bronchitis, bronchopneumonia, bacterial pneumonia)
– *Infections of the urogenital tract* (uncomplicated and complicated urinary-tract infections such as cystitis, pyelonephritis, adnexitis, urethritis, prostatitis, salpingitis)
– *Infections of the skin and soft tissues* (abscesses, furuncles, impetigo, pyodermia, erysipelas, lymphadenitis, wound infections)
– *Infections of the bones and joints* (osteomyelitis)
Biodroxil should not be used in severe systemic infections in which β-lactamase-stable cephalosporins are more effective.

Mode of application

The reconstituted suspension is taken with a liberal quantity of fluid.
The capsules and film-coated tablets are taken unchewed with a liberal quantity of fluid.
Intake with food does not influence the therapeutic effect.

Dosage

The average dosage for children with normal renal function consists of 25–50mg/kg body weight given in one single dose or in two equal divided doses (at 12-hour intervals) per day.
The dose may be increased to 100mg/kg body weight depending on the severity of the infection and the susceptibility of the causative agent. Children between 9 and 12 years of age (30–40kg body weight) receive 2 capsules of Biodroxil 500mg per day given in one single dose or in two divided doses. The dose may be increased or even doubled insevere infections.
In general, adults and juveniles weighing more than 40kg with normal renal function and mild to moderately severe infections receive 1–2g of Biodroxil in one single dose or in two equal divided doses per day.
The dose may be increased or even doubled in severe infections.

Age (weight)	Daily Biodroxil dose
Children up to 2 months (5 kg):	2 x ½ measuring spoonful 125 mg/5 ml suspension
Children between 2 and 12 months (5 – 10 kg):	2 x 1 measuring spoonful 125 mg/5 ml suspension or 2 x ½ measuring spoonful 250 mg/5 ml suspension
Children between 1 and 5 years (10 – 20 kg):	1 x 2 or 2 x 1 measuring spoonful 250 mg/5 ml suspension or 1 x 1 or 2 x ½ measuring spoonful 500 mg/5 ml suspension
Children between 5 and 12 years (20 – 40 kg):	1 x 2 or 2 x 1 measuring spoonful 500 mg/5 ml suspension
Children between 9 and 12 years (30 – 40 kg):	1 x 2 or 2 x 1 capsule 500 mg
Juveniles and adults (over 40 kg):	1 – 2 x 1 film-coated tablet 1000 mg in one single dose or in two equal divided doses

Special dosage guidelines
– Tonsillitis/pharyngitis caused by β-haemolytic streptococci (Streptococcus pyogenes):
Children: 30mg Biodroxil/kg body weight daily in one single dose or in two divided doses over at least 10 days
Adults: 1g Biodroxil daily in one single dose or in two equal divided doses over at least 10 days
– Complicated urinary tract infections (e.g. pyelonephritis):
Adults: 2x1g Biodroxil daily over 7–10 days
– Infections of the bones and/or joints, if oral therapy with cefadroxil is indicated:
Children: At least 50mg Biodroxil/kg body weight daily given in 2 to 4 divided doses at 6- to 12-hour intervals over 3 to 5 weeks (depending on clinical response)
Adults: 4x1g Biodroxil daily given at 6-hour intervals over 3 to 5 weeks (depending on clinical response)

Dosage in renal insufficiency

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

Dosage for haemodialysis patients
The patient receives 1x500mg cefadroxil 48 hours before the dialysis and 1x500mg again at the end of the dialysis. The next dose with haemodialysis two to three times per week is again given 48 hours before the next dialysis.
Duration of treatment
Treatment should be applied over 7 to 10 days but in any case for 2 to 3 further days after regression of the acute symptoms.
Treatment over at least 10 days is necessary in infections with Streptococcus pyogenes.

Contraindications

History of or suspected hypersensitivity to cephalosporins.
Due attention should be paid to the possible occurrence of cross allergies in patients hypersensitive to penicillins (incidence 5–10%).
Biodroxil should be used with special caution in persons with a history of severe allergies or asthma.
Caution is necessary in patients with renal functional impairment (see "Dosage").

Pregnancy and lactation

The following should be borne in mind if the preparation is used in women of child-bearing age:
No adequate clinical experiences are as yet available concerning use of the preparation during pregnancy and lactation to recommend safe treatment in corresponding patients. If treatment of nursing mothers is necessary their milk should be pumped off and discarded during and up to two days after treatment.

Side effects

Biodroxil, the same as all cephalosporins, is well tolerated. Undesirable effects are observed in about 6% of all treated patients. The most frequent side effects are gastrointestinal disturbances (nausea, vomiting, diarrhoea, abdominal pain, etc.) and dermatological symptoms (pruritus, allergic exanthema or rash, urticaria, drug fever, joint pain and angio-oedema «rare»). Other side effects such as glossitis, dizziness, nervousness, sleeplessness, etc. or an immediate allergic reaction (anaphylactic shock) are possible in very rare cases. Isolated cases of pseudomembranous colitis have been reported.
Symptoms due to growth of opportunistic organisms (fungi) such as vaginal mycosis, thrush, etc. can occur in isolated cases.
Stevens-Johnson syndrome and erythema multiforme have been observed in isolated cases.
Haematological changes such as eosinophilia, thrombocytopenia, leukopenia and neutropenia have been reported on prolonged therapy in rare cases which returned to normal again after discontinuation of treatment. A slight increase in serum transaminases (ALT, AST) has been observed in isolated cases.

Interactions

Biodroxil should not be combined with bacteriostatic chemotherapeutics/antibiotics such as tetracyclines, erythromycin, sulphonamides or chloramphenicol since an antagonistic effect is possible.
Higher serum concentrations of cefadroxil of longer duration can result on concomitant administration of probenecid.
The occurrence of diarrhoea can impair the absorption of other medicaments and consequently adversely affect their efficacy. The same as on treatment with other cephalosporins or penicillins falsely positive results of the Coombs test are possible. Patients treated with Biodroxil can have falsely positive tests for glucose in the urine if nonenzymatic reagents are used. Treatment with Biodroxil in combination with aminoglycoside antibiotics, polymyxin B, colistin or high-dose loop diuretics should be avoided since such combinations en potentiate the nephrotoxic effect.
The same as on treatment with all other cephalosporins (in high dose frequent checks on coagulation parameters are necessary during concomitant long-term use of anticoagulants or thrombocyte aggregation inhibitors to avoid haemorrhagic complications. The same as with all antibiotics Biodroxil may attenuate the effect of oralcontraceptives.
Interference with laboratory tests
The results of the direct Coombs test can be transiently positive during or after treatment with cefadroxil. This also applies for Coombs tests carried out in newborns whose mothers received treatment with cephalosporins before delivery.
Urinary sugar should be determined enzymatically (e.g. with test strips) during treatment with cefadroxil since reduction tests can furnish falsely elevated values.

Incompatibilities

No incompatibilities are known for oral cephalosporins.

Special warnings for safe use

Cefadroxil, the same as all other cephalosporin antibiotics should be used with special caution in patients with a history of penicillin allergy since cross allergies are possible (incidence 5–10%).
The interval between doses must be prolonged in patients with high-grade renal functional impairment in accordance with the table in the chapter "Dosage".
The same as with all other antibiotics (and particularly on prolonged use) frequent checks on the blood count and regular hepatic and renal function tests are advisable.
Treatment must be discontinued at once if allergic symptoms occur (urticaria, exanthema, pruritus, fall of blood pressure and increase in heart rate, respiratory disturbances, collapse, etc.) and suitable countermeasures should be taken by the physician (sympathicomimetics, corticosteroids and/or antihistaminics).
Antibiotic-induced pseudomembranous colitis which can be life- threatening should be borne in mind in severe and persistent diarrhoea.
In such cases use of Biodroxil should be discontinued at once and corresponding therapy instituted (e.g. oral vancomycin, 250mg q.i.d.). Antiperistaltics are contraindicated.
The same as with all other antibiotics, superinfections with fungi (e.g. candida) or vitamin K deficiency (haemorrhagia) or vitamin B deficiency (stomatitis, glossitis,

neuritis, anorexia, etc.) can occur on prolonged treatment with cefadroxil.
Patients with severe gastrointestinal disturbances should not be treated with cefadroxil.
Severe life-threatening infections should be treated initially with injectable cephalosporin.
Warning to diabetics
The sugar content of the granules (see "Composition") should be allowed for.
Measures to be taken on excessive overdose of cephalosporins
No clinical reports in this respect are as yet available on cefadroxil.
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.

Stability
If properly stored, Biodroxil granules for oral suspension, capsules and tablets retain their full potency to the date of expiration shown on the pack.

Storage conditions
Store granules, capsules and tablets below 25° C; protect from light and moisture.

Presentations
Biodroxil 125mg/250mg/500mg/5ml granules:
single packs for 60ml/100ml oral suspension, hospital packs
Biodroxil 500mg capsules:
single packs of 12 and 20 capsules, hospital packs
Biodroxil 1000mg film-coated tablets:
single packs of 10, 12 and 20 tablets, hospital packs

"Keep medicines out of the reach of children!"

Sandoz GmbH, Kundl – Austria