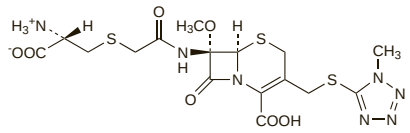
Cefminox Sodium *(pINNM)*

Cefminox sódico; Cefminox Sodique; MT-141; Natrii Cefminoxum. Sodium 7-{2-[(*S*)-2-amino-2-carboxyethyl]thioacetamido}-7-methoxy-3-(1-methyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylate.

Натрий Цефминокс

$C_{16}H_{20}N_7NaO_7S_3$ = 541.6.

CAS — 75481-73-1 (cefminox).



(cefminox)

Pharmacopoeias. *Jpn* includes the heptahydrate.

Profile

Cefminox sodium is a cephamycin antibacterial with properties similar to those of cefoxitin (p.230) but with an *N*-methylthiotetrazole side-chain like cefamandole (p.220). It is given intravenously as the sodium salt but doses are expressed in terms of cefminox; 1.04 g of cefminox sodium is equivalent to about 1 g of cefminox. A usual dose is 2 to 4 g daily given in divided doses.

◊ References.

1. Watanabe S, Omoto S. Pharmacology of cefminox, a new bactericidal cephamycin. *Drugs Exp Clin Res* 1990; **16:** 461–7.
2. Soriano F, *et al.* Comparative susceptibility of cefminox and cefoxitin to β-lactamases of Bacteroides spp. *J Antimicrob Chemother* 1991; **28:** 55–60.
3. Aguilar L, *et al.* Cefminox: correlation between in-vitro susceptibility and pharmacokinetics and serum bactericidal activity in healthy volunteers. *J Antimicrob Chemother* 1994; **33:** 91–101.
4. Mayama T, *et al.* Postmarketing surveillance on side-effects of cefminox sodium (Meicelin). *Int J Clin Pharmacol Ther* 1995; **33:** 149–55.
5. Hoellman DB, *et al.* In vitro activities of cefminox against anaerobic bacteria compared with those of nine other compounds. *Antimicrob Agents Chemother* 1998; **42:** 495–501.
6. Torres AJ, *et al.* Cefminox versus metronidazole plus gentamicin in intra-abdominal infections: a prospective randomized controlled clinical trial. *Infection* 2000; **28:** 318–22.

Sodium content. Each g of cefminox sodium contains about 1.84 mmol of sodium.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Meicelin; ***Port.:*** Tencef; ***Spain:*** Tencef; ***Thai.:*** Meicelin.

Cefodizime Sodium *(BANM, rINNM)*

Cefodizima sódica; Céfodizime Sodique; HR-221; Natrii Cefodizimum; S-771221B; Sefodizim Disodyum; THR-221; TRH-221. (*Z*)-7-[2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(5-carboxymethyl-4-methylthiazol-2-ylthiomethyl)-3-cephem-4-carboxylic acid, disodium salt.

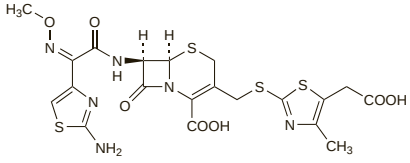
Натрий Цефодизим

$C_{20}H_{18}N_6Na_2O_7S_4$ = 628.6.

CAS — 69739-16-8 (cefodizime); 86329-79-5 (cefodizime sodium).

ATC — J01DD09.

ATC Vet — QJ01DD09.



(cefodizime)

Pharmacopoeias. In *Jpn.*

Adverse Effects and Precautions

As for Cefotaxime, p.228.

Sodium content. Each g of cefodizime sodium contains about 3.2 mmol of sodium.

Interactions

Probenecid reduces the renal clearance of cefodizime.

Antimicrobial Action

Cefodizime has similar antimicrobial activity to that of cefotaxime (p.228) although cefodizime has no active metabolite. It has variable activity against *Citrobacter* spp., and *Pseudomonas aeruginosa* and *Bacteroides fragilis* are generally resistant.

Pharmacokinetics

Cefodizime is given by injection as the sodium salt. Intramuscular injection of 1 g cefodizime produces peak plasma concentrations of about 60 to 75 micrograms/mL at about 1 to 1.5 hours. Immediately after intravenous doses of 1 or 2 g cefodizime mean peak plasma concentrations of 215 and 394 micrograms/mL, respectively, have been achieved. Cefodizime is about 80% bound to plasma proteins and is widely distributed into body tissues and fluids. It crosses the placenta and small amounts have been detected in breast milk. Plasma elimination is reported to be triphasic with a terminal elimination half-life of about 4 hours. The half-life is prolonged by renal impairment.

The majority of a dose is excreted unchanged in the urine; up to 80% of a dose has been recovered within 24 hours. Cefodizime is mainly excreted by glomerular filtration with some tubular secretion. Probenecid delays excretion. Cefodizime is removed by dialysis.

Uses and Administration

Cefodizime is a third-generation cephalosporin antibacterial with uses similar to those of cefotaxime (p.229).

Cefodizime is given as the disodium salt by intramuscular injection or intravenously by injection or infusion in the treatment of susceptible infections. Doses are expressed in terms of the equivalent amount of cefodizime; 1.08 g of cefodizime sodium is equivalent to about 1 g of cefodizime. Adults are usually given 1 to 2 g every 12 or 24 hours for lower respiratory-tract infections and upper and lower urinary-tract infections. Doses up to 4 g daily may be given in severe infection. In women with uncomplicated lower urinary-tract infections a single dose of 1 to 2 g may be sufficient. For gonorrhoea a single dose of 0.25 to 0.5 g may be given. Doses may need to be reduced in patients with renal impairment (see below).

◊ References.

1. Finch RG, *et al.*, eds. Cefodizime: a third generation cephalosporin with immunomodulating properties. *J Antimicrob Chemother* 1990; **26** (suppl C): 1–134.
2. Barradell LB, Brogden RN. Cefodizime: a review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1992; **44:** 800–834.
3. Thalhammer F, *et al.* Single-dose cefodizime as infection prophylaxis in abdominal surgery: a prospective multicenter study. *Infection* 1998; **26:** 136–8.
4. Matsumoto T, *et al.* Single dose of cefodizime completely eradicated multidrug-resistant strain of Neisseria gonorrhoeae in urethritis and uterine cervicitis. *J Infect Chemother* 2006; **12:** 97–9.
5. Matsumoto T, *et al.* Multiple doses of cefodizime are necessary for the treatment of Neisseria gonorrhoeae pharyngeal infection. *J Infect Chemother* 2006; **12:** 145–7.

Administration in renal impairment. Doses of cefodizime should be reduced in patients with renal impairment according to creatinine clearance (CC):

- CC 10 to 30 mL/minute: 1 to 2 g daily
- CC less than 10 mL/minute: 0.5 to 1 g daily

In patients undergoing dialysis, 0.5 to 1 g daily is given after dialysis.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Timecef; ***Ital.:*** Diezime; Modivid; Timecef; ***Jpn:*** Kenicef; ***Mex.:*** Modivid†; ***NZ:*** Timecef; ***Port.:*** Modivid; ***Turk.:*** Modivid.

Cefonicid Sodium *(BANM, USAN, rINNM)*

Cefonicid sódico; Cefonicide sodique; Céfonicide Sodique; Cefonicidum natricum; Natrii Cefonicidum; SKF-D-75073-Z_2; SKF-D-75073-Z (cefonicid monosodium). 7-[(*R*)-Mandelamido]-3-(1-sulphomethyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid, disodium salt.

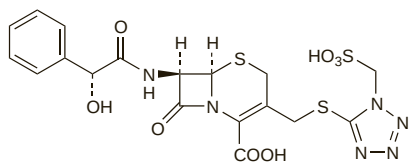
Натрий Цефоницид

$C_{18}H_{16}N_6Na_2O_8S_3$ = 586.5.

CAS — 61270-58-4 (cefonicid); 61270-78-8 (cefonicid disodium); 71420-79-6 (cefonicid monosodium).

ATC — J01DC06.

ATC Vet — QJ01DC06.



(cefonicid)

Pharmacopoeias. In *US.*

USP 31 (Cefonicid Sodium). A white to off-white solid. Freely soluble in water, in sodium chloride 0.9%, and in glucose 5%; very slightly soluble in dehydrated alcohol; soluble in methyl alcohol. pH of a 5% solution in water is between 3.5 and 6.5. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Cefonicid contains a substituted *N*-methylthiotetrazole side-chain, a structure associated with hypoprothrombinaemia.

Effects on the blood. References.

1. Riancho JA, *et al.* Life-threatening bleeding in a patient treated with cefonicid. *Ann Intern Med* 1995; **123:** 472–3.

Effects on the liver. References.

1. Famularo G, *et al.* Eosinophilic hepatitis associated with cefonicid therapy. *Ann Pharmacother* 2001; **35:** 1669–71.

Sodium content. Each g of cefonicid sodium contains about 3.4 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Antimicrobial Action

Cefonicid sodium has an antimicrobial action and pattern of resistance similar to those of cefamandole (p.221), although it is generally less active against Gram-positive cocci.

Pharmacokinetics

Cefonicid is given parenterally as the sodium salt. Peak plasma concentrations ranging from 67 to 126 micrograms/mL have been achieved 1 to 2 hours after a 1-g intramuscular dose. Cefonicid is more than 90% bound to plasma proteins. It has a plasma half-life of about 4.5 hours, which is prolonged in patients with renal impairment.

Therapeutic concentrations of cefonicid have been reported in a wide range of body tissues and fluids.

Up to 99% of a dose of cefonicid is excreted unchanged in the urine within 24 hours. Probenecid reduces excretion of cefonicid.

Uses and Administration

Cefonicid is a second-generation cephalosporin antibacterial used similarly to cefamandole (p.221) in the treatment of susceptible infections and for surgical infection prophylaxis.

It is given as the sodium salt by deep intramuscular injection, or intravenously by slow injection over 3 to 5 minutes or by infusion. Doses are expressed in terms of the equivalent amount of cefonicid; 1.08 g of cefonicid sodium is equivalent to about 1 g of cefonicid. The usual dose is cefonicid 1 g once daily. For uncomplicated urinary-tract infections, a dose of 500 mg once daily is recommended; up to 2 g once daily has been given in severe infections. More than 1 g should not be injected intramuscularly into a single site.

For surgical infection prophylaxis, a single dose of 1 g given 1 hour before surgical incision is usually sufficient, but may be given daily for a further 2 days in prosthetic arthroplasty or open-heart surgery.

◊ References.

1. Saltiel E, Brogden RN. Cefonicid: a review of its antibacterial activity, pharmacological properties and therapeutic use. *Drugs* 1986; **32:** 222–59.

Administration in renal impairment. For patients with renal impairment a loading dose equivalent to cefonicid 7.5 mg/kg is recommended, followed by reduced maintenance doses according to the creatinine clearance and the severity of the infection. A dose supplement is not required after dialysis.

Preparations

USP 31: Cefonicid for Injection.

Proprietary Preparations (details are given in Part 3)
Belg.: Monocid†; ***Israel:*** Monocef; ***Ital.:*** Abiocef†; Auricid†; Bacid†; Biocil; Bioticic; Cefobacter; Cefodie; Cefoger†; Cefok; Cefoplus; Cefosporin†; Chefir; Clastidin†; Daycef; Delsacid†; Diespor; Emidoxin; Epicef†; Fonexel†; Fonicef†; Fonicid; Fonisal†; Framecef; Ipacid†; Krucef; Lampocef†; Lisa; Maxid; Microcid†; Modicef; Modiem; Monobios; Monobiotic; Monocid†; Necid; Nokid; Pantacid†; Parecid; Praticef; Raikocef; Renbiocid†; Rocid†; Silverce†; Sintocef; Sofarcid; Unicid†; Valecid; ***Port.:*** Monocid; ***Spain:*** Monocid; Unidie; ***USA:*** Monocid†.

Cefoperazone Sodium

(BANM, USAN, rINNM)

Cefoperazon sodná sůl; Cefoperazon sodowy; Cefoperazona sódica; Céfopérazone sodique; Cefoperazonnatrium; Cefoperazon-nátrium; Cefoperazono natrio druska; Cefoperazonum natricum; CP-52640-2; CP-52640 (anhydrous cefoperazone); CP-52640-3 (cefoperazone dihydrate); Kefoperatsoninatrium; Natrii Cefoperazonum; Sefoperazon Sodyum; T-1551 (cefoperazone or cefoperazone sodium). Sodium (7*R*)-7-[(*R*)-2-(4-ethyl-2,3-dioxopiperazin-1-ylcarboxamido)-2-(4-hydroxyphenyl)acetamido]-3-[(1-methyl-1*H*-tetrazol-5-yl)thiomethyl]-3-cephem-4-carboxylate.

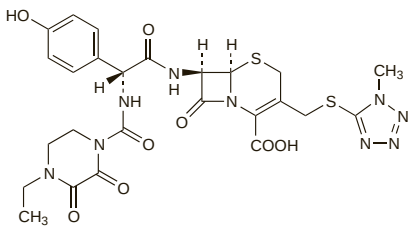
Натрий Цефоперазон

$C_{25}H_{26}N_9NaO_8S_2$ = 667.6.

CAS — 62893-19-0 (cefoperazone); 62893-20-3 (cefoperazone sodium).

ATC — J01DD12.

ATC Vet — QJ01DD12.



(cefoperazone)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Cefoperazone Sodium). A white or slightly yellow, hygroscopic, powder. If crystalline it exhibits polymorphism. Freely soluble in water; slightly soluble in alcohol; soluble in methyl alcohol. A 25% solution in water has a pH of 4.5 to 6.5. Store in airtight containers at a temperature of 2° to 8°. Protect from light.
USP 31 (Cefoperazone Sodium). A white to pale buff crystalline powder. Freely soluble in water and in methyl alcohol; slightly soluble in dehydrated alcohol; insoluble in acetone, in ether, and in ethyl acetate. pH of a 25% solution in water is between 4.5 and 6.5. Store in airtight containers.

Incompatibility. As with most beta lactams, admixture of cefoperazone sodium with aminoglycosides is not recommended because of the potential for inactivation of either drug.

There have been reports of incompatibility with other drugs including diltiazem,[1] doxorubicin,[2] pentamidine,[3] perphenazine,[4] pethidine,[5] promethazine,[6] and remifentanil.[7]

1. Gayed AA, *et al.* Visual compatibility of diltiazem injection with various diluents and medications during simulated Y-site injection. *Am J Health-Syst Pharm* 1995; **52:** 516–20.
2. Trissel LA, *et al.* Compatibility of doxorubicin hydrochloride liposome injection with selected other drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1997; **54:** 2708–13.
3. Lewis JD, El-Gendy A. Cephalosporin-pentamidine isethionate incompatibilities. *Am J Health-Syst Pharm* 1996; **53:** 1461–2.
4. Gasca M, *et al.* Visual compatibility of perphenazine with various antimicrobials during simulated Y-site injection. *Am J Hosp Pharm* 1987; **44:** 574–5.
5. Nieves-Cordero AL, *et al.* Compatibility of narcotic analgesic solutions with various antibiotics during simulated Y-site injection. *Am J Hosp Pharm* 1985; **42:** 1108–9.
6. Scott SM. Incompatibility of cefoperazone and promethazine. *Am J Hosp Pharm* 1990; **47:** 519.
7. Trissel LA, *et al.* Compatibility of remifentanil hydrochloride with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1997; **54:** 2192–6.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

Like cefotaxime (p.228), cefoperazone has the potential for colonisation and superinfection with resistant organisms. Changes in bowel flora may be more marked than with cefotaxime because of the greater biliary excretion of cefoperazone; diarrhoea may occur more often.

Cefoperazone contains an *N*-methylthiotetrazole sidechain, a structure associated with hypoprothrombinaemia. Hypoprothrombinaemia has been reported in patients treated with cefoperazone and has rarely been associated with bleeding episodes. Prothrombin time should be monitored in patients at risk of hypoprothrombinaemia and vitamin K used if necessary.

Sodium content. Each g of cefoperazone sodium contains about 1.5 mmol of sodium.

Interactions

As for Cefamandole, p.221.

Unlike many other cephalosporins, probenecid has no effect on the renal clearance of cefoperazone.

Antimicrobial Action

Cefoperazone has antimicrobial activity similar to that of ceftazidime (p.234), although it is slightly less active against some Enterobacteriaceae. It has good activity against *Pseudomonas aeruginosa*, but is less active than ceftazidime.

Cefoperazone is more susceptible than cefotaxime to hydrolysis by certain beta-lactamases.

Activity, particularly against Enterobacteriaceae and *Bacteroides* spp. has been enhanced in the presence of the beta-lactamase inhibitor sulbactam; resistant *Ps. aeruginosa* are not sensitive to the combination.

◊ References.

1. Fass RJ, *et al.* In vitro activities of cefoperazone and sulbactam singly and in combination against cefoperazone-resistant members of the family Enterobacteriaceae and nonfermenters. *Antimicrob Agents Chemother* 1990; **34:** 2256–9.
2. Clark RB, *et al.* Multicentre study on antibiotic susceptibilities of anaerobic bacteria to cefoperazone-sulbactam and other antimicrobial agents. *J Antimicrob Chemother* 1992; **29:** 57–67.

Pharmacokinetics

Cefoperazone is given parenterally as the sodium salt. With intramuscular doses equivalent to cefoperazone 1 or 2 g, peak plasma concentrations of 65 and 97 micrograms/mL have been reported after 1 to 2 hours. The plasma half-life of cefoperazone is about 2 hours, but may be prolonged in neonates and in patients with hepatic or biliary-tract disease. Cefoperazone is 82 to 93% bound to plasma proteins, depending on the concentration.

Cefoperazone is widely distributed in body tissues and fluids, although penetration into the CSF is generally poor. It crosses the placenta, and low concentrations have been detected in breast milk.

Cefoperazone is excreted mainly in the bile where it rapidly achieves high concentrations. Urinary excretion is primarily by glomerular filtration. Up to 30% of a dose is excreted unchanged in the urine within 12 to 24 hours; this proportion may be increased in patients with hepatic or biliary disease. Cefoperazone A, a degradation product less active than cefoperazone, has been found only rarely *in vivo*.

Uses and Administration

Cefoperazone is a third-generation cephalosporin antibiotic used similarly to ceftazidime (p.235) in the treatment of susceptible infections, especially those due to *Pseudomonas* spp. It is not recommended for the treatment of meningitis because of poor penetration into the CSF.

Cefoperazone is given as the sodium salt by deep intramuscular injection or intravenously by intermittent or continuous infusion. Doses are expressed in terms of the equivalent amount of cefoperazone; 1.03 g of cefoperazone sodium is equivalent to about 1 g of cefoperazone. The usual dose is 2 to 4 g daily in 2 divided doses. In severe infections, up to 12 g daily in 2 to 4 divided doses may be given.

For details of dosage in patients with hepatic and renal impairment, see below.

If cefoperazone is used with an aminoglycoside, the drugs should be given separately.

Cefoperazone has also been given with the beta-lactamase inhibitor sulbactam.

Administration in hepatic and renal impairment. In general, the dose of cefoperazone should not exceed 4 g daily in patients with liver disease or biliary obstruction or 1 to 2 g daily in those with both hepatic and renal impairment; if higher doses are used plasma concentrations of cefoperazone should be monitored.

Preparations

USP 31: Cefoperazone for Injection; Cefoperazone Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Cefobid†; ***Austria:*** Cefobid; ***Braz.:*** Cefazone†; Neoperazona†; ***Chile:*** Cefobid; ***Cz.:*** Cefobid; ***Hong Kong:*** Cefobid; ***Hung.:*** Cefobid; ***India:*** Cefomycin; Magnamycin; ***Indon.:*** Bifotik; Cefobid; Cefophar; Ceropid; Cerozon; Ferzobat; Logafox; Stabixin; ***Ital.:*** Bioperazone; Cefoneg†; Cefoper; Dardum; Farecef; Ipazone†; Novobiocyl†; Tomabef†; Zonceft; ***Jpn:*** Cefobid†; Cefoperazin; ***Malaysia:*** Cefobid; Medocef; Shinfomycin; ***Mex.:*** Cefobid; ***Philipp.:*** Bactizon; ***Pol.:*** Biocefazon; Cefobid; Dardum; ***Rus.:*** Cefobid (Цефобид); Medocef (Медоцеф); ***Singapore:*** Cefobid; Cefozone; Dardum; ***Spain:*** Cefobid†; ***Thai.:*** Cefobid; Cefozone†; Medocef; ***Turk.:*** Cefobid; ***USA:*** Cefobid†; ***Venez.:*** Cefobid†; Ortosep†.

Multi-ingredient: ***Arg.:*** Sulperazon†; ***Chile:*** Sulperazon; ***Cz.:*** Sulperazon; ***Hong Kong:*** Sulperazon; ***India:*** Lactagard; Sulbacef; Zosul; ***Indon.:*** Fosular; Stabactam; Sulperazon; ***Malaysia:*** Sulperazon; ***Philipp.:*** Sulperazone; ***Pol.:*** Sulperazon; ***Rus.:*** Sulcef (Сульцеф); Sulperason (Сульперазон); ***Thai.:*** Cebactam; Cefper; Sulcef; Sulperazon; ***Turk.:*** Primasef; Sulperazon; ***Venez.:*** Sulperazon.

Ceforanide *(BAN, USAN, rINN)*

BL-S786; Ceforanida; Céforanide; Ceforanidum. 7-[2-(α-Amino-*o*-tolyl)acetamido]-3-(1-carboxymethyl-1*H*-tetrazol-5-ylthiomethyl)-3-cephem-4-carboxylic acid.

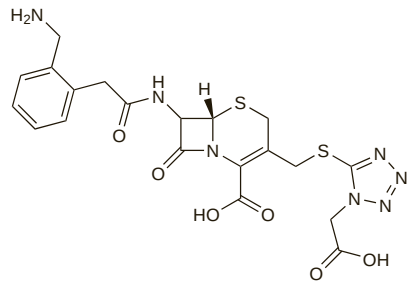
Цефоранид

$C_{20}H_{21}N_7O_6S_2$ = 519.6.

CAS — 60925-61-3.

ATC — J01DC11.

ATC Vet — QJ01DC11.



Pharmacopoeias. In *US*.
USP 31 (Ceforanide). A white to off-white powder. Practically insoluble in water, in chloroform, in ether, and in methyl alcohol; very soluble in 1N sodium hydroxide. pH of a 5% suspension in water is between 2.5 and 4.5. Store in airtight containers.

Profile

Ceforanide is a second-generation cephalosporin antibacterial with actions and uses similar to those of cefamandole (p.220), although it is reported to be less active *in vitro* against some bacteria, including staphylococci and *Haemophilus influenzae*. It is used in the treatment of susceptible infections and for surgical infection prophylaxis.

It is given as the lysine salt ($C_{26}H_{35}N_9O_8S_2$ = 665.7) but doses are expressed in terms of the equivalent amount of ceforanide; 1.28 g of ceforanide lysine is equivalent to about 1 g of ceforanide. It is given by deep intramuscular injection, or intravenously by slow injection over 3 to 5 minutes or by infusion. The usual adult dose is 1 to 2 g every 12 hours. Children may be given 20 mg/kg daily in 2 divided doses. For surgical infection prophylaxis, a dose of 1 to 2 g intravenously 1 hour before surgical incision is used in adults.

Ceforanide contains a substituted *N*-methylthiotetrazole sidechain, a structure associated with hypoprothrombinaemia and alcohol intolerance. Probenecid does not affect the renal excretion of ceforanide.

◊ References.

1. Campoli-Richards DM, *et al.* Ceforanide: a review of its antibacterial activity, pharmacokinetic properties and clinical efficacy. *Drugs* 1987; **34:** 411–37.

Preparations

USP 31: Ceforanide for Injection.

Proprietary Preparations (details are given in Part 3)

Belg.: Precef†; ***Gr.:*** Radacef.