Carfecillin Sodium (BANM, pINNM)

BRL-3475; Carbenicillin Phenyl Sodium (USAN); Carfecilina sódica; Carfécilline Sodique; Natrii Carfecillinum. Sodium (6R)-6-(2-phenoxycarbonyl-2-phenylacetamido)penicillanate.

Натрий Карфециллин

 $C_{23}H_{21}N_2NaO_6S = 476.5.$

CAS — 27025-49-6 (carfecillin); 21649-57-0 (carfecillin sodium).

ATC — GO I AAO8.

ATC Vet - QG01AA08.

Profile

Carfecillin is the phenyl ester of carbenicillin (p.216) to which it is hydrolysed after absorption from the gastrointestinal tract. Its use has been restricted to the treatment of urinary-tract infections due to Pseudomonas spp. and other sensitive bacteria including Proteus spp.

Carindacillin Sodium (BANM, pINNM)

Carbenicillin Indanyl Sodium (USAN); Carindacilina sódica; Carindacilline Sodique; CP-15464-2; Natrii Carindacillinum. Sodium (6R)-6-[2-(indan-5-yloxycarbonyl)-2-phenylacetamido]penicillanate.

Натрий Кариндациллин

 $C_{26}H_{25}N_2NaO_6S = 516.5.$

CAS — 35531-88-5 (carindacillin); 26605-69-6 (carindacillin sodium).

ATC - 101 CA05.

ATC Vet - QJ01CA05.

Pharmacopoeias. In US.

USP 31 (Carbenicillin Indanyl Sodium). A white to off-white powder. Soluble in water and in alcohol. pH of a 10% solution in water is between 5.0 and 8.0. Store in airtight containers.

Carindacillin is the indanyl ester of carbenicillin (p.216) to which it is hydrolysed after absorption from the gastrointestinal tract. Its use is restricted to the treatment of urinary-tract infections due to Pseudomonas spp. and other sensitive bacteria including Proteus

Carindacillin is given orally as the sodium salt; 535 mg of carindacillin sodium is equivalent to about 382 mg of carbenicillin. Usual doses, expressed in terms of carbenicillin, are 382 to 764 mg four times daily.

Sodium content. Each g of carindacillin sodium contains about 1.9 mmol of sodium.

Preparations

USP 31: Carbenicillin Indanyl Sodium Tablets.

Proprietary Preparations (details are given in Part 3) USA: Geocillin†

Carumonam Sodium (BANM, USAN, rINNM)

AMA-1080 (carumonam); Carumonam sódico; Carumonam Sodique; Natrii Carumonamum; Ro-17-2301 (carumonam); Ro-17-2301/006 (carumonam sodium). (Z)-(2-Aminothiazol-4yl){[(2S,3S)-2-carbamoyloxymethyl-4-oxo-1-sulphoazetidin-3yl]carbamoyl}methyleneamino-oxyacetic acid, disodium salt.

Натрий Карумонам

 $C_{12}H_{12}N_6Na_2O_{10}S_2 = 510.4.$

CAS — 87638-04-8 (carumonam); 86832-68-0 (caru-

CONH₂ SO₃H NaOOC

(carumonam)

Pharmacopoeias. In Jpn.

Profile

Carumonam is a monobactam antibacterial with a spectrum of antimicrobial action in vitro similar to that of aztreonam (p.209). It is given by intramuscular or intravenous injection as the sodium salt and doses are expressed in terms of carumonam; 1.09 g of carumonam sodium is equivalent to about 1 g of carumonam. The usual dose is 1 to 2 g daily in two divided doses.

Sodium content. Each g of carumonam sodium contains about 3.92 mmol of sodium.

Preparations

Proprietary Preparations (details are given in Part 3)

Cefacior (BAN, USAN, DINN)

Céfaclor; Cefaclorum; Cefaclorum Monohydricum; Cefaklór; Cefaklor; Cefaklor monohydrát; Cefakloras; Compound 99638; Kefakloori; Sefaklor. (7R)-3-Chloro-7-(α-D-phenylglycylamino)-3cephem-4-carboxylic acid monohydrate.

Цефаклор

 $C_{15}H_{14}CIN_3O_4S,H_2O = 385.8.$

CAS — 53994-73-3 (anhydrous cefaclor); 70356-03-5

(cefaclor monohydrate). ATC — J0 I DC04.

ATC Vet - QJ01DC04.

Pharmacopoeias. In Chin., Eur. (see p.vii), and US. Jpn includes the anhydrous substance.

Ph. Eur. 6.2 (Cefaclor). A white or slightly yellow powder. Slightly soluble in water; practically insoluble in dichloromethane and in methyl alcohol. A 2.5% suspension in water has a pH

USP 31 (Cefaclor). A white to off-white crystalline powder. Slightly soluble in water; practically insoluble in chloroform, in methyl alcohol, and in benzene. pH of a 2.5% suspension in water is between 3.0 and 4.5. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalexin, p.218.

Hypersensitivity. Serum-sickness-like reactions may be more common with cefaclor than several other oral antibacterials1 especially in young children who have received a number of courses of cefaclor;2 typical features include skin reactions and arthralgia. A relatively high incidence of anaphylactic reactions has been reported from Japan.3

There has been a report of myocarditis that developed as a hypersensitivity reaction to cefaclor in a 12-year-old child.4

- McCue JD. Delayed detection of serum sickness caused by oral antimicrobials. Adv Therapy 1990; 7: 22–7.
 Vial T, et al. Cefaclor-associated serum sickness-like disease:
- eight cases and review of the literature. Ann Pharmacother 1992; **26:** 910–14
- 3. Hama R, Mori K. High incidence of anaphylactic reactions to
- cefaclor. *Lancet* 1988; i: 1331.

 4. Beghetti M, *et al.* Hypersensitivity myocarditis caused by an allergic reaction to cefaclor. J Pediatr 1998; 132: 172-3

Interactions

As for Cefalexin, p.218.

Anticoagulants. UK licensed product information recommends that monitoring of prothrombin time should be considered in patients receiving cefaclor and warfarin after rare reports of increased prothrombin times. It is not known whether this interaction is related to the vitamin K-related hypoprothrombinaemia observed with some cephalosporins (see Adverse Effects of Cefamandole, p.221), but cefaclor does not contain the sidechain usually implicated in this reaction.

Antimicrobial Action

Cefaclor is bactericidal and has antimicrobial activity similar to that of cefalexin (p.218) but is reported to be more active against Gram-negative bacteria including Escherichia coli, Klebsiella pneumoniae, Neisseria gonorrhoeae, and Proteus mirabilis, and especially against Haemophilus influenzae. It is active against some beta-lactamase-producing strains of H. influenzae. It may be less resistant to staphylococcal penicillinase than cefalexin or cefradine and a marked inoculum effect has been reported in vitro.

Pharmacokinetics

Cefaclor is well absorbed from the gastrointestinal tract. Oral doses of 250 mg, 500 mg, and 1 g produce peak plasma concentrations of about 7, 13, and 23 micrograms/mL respectively after 0.5 to 1 hour. The presence of food may delay the absorption of cefaclor, but the total amount absorbed is unchanged. A plasma half-life of 0.5 to 1 hour has been reported; it may be slightly prolonged in patients with renal impairment. About 25% is bound to plasma proteins.

Cefaclor appears to be widely distributed in the body; it crosses the placenta and low concentrations have been detected in breast milk. It is rapidly excreted by the kidneys; up to 85% of a dose appears unchanged in the urine within 8 hours, the greater part within 2 hours. High concentrations of cefaclor are achieved in the urine within 8 hours of a dose; peak concentrations of 600, 900, and 1900 micrograms/mL have been reported after doses of 0.25, 0.5, and 1 g respectively. Probenecid delays excretion. Some cefaclor is removed by haemodialysis.

- 1. Wise R. The pharmacokinetics of the oral cephalosporins-a re-
- view. J Antimicrob Chemother 1990; 26 (suppl E): 13–20.
 2. Sourgens H, et al. Pharmacokinetic profile of cefaclor. Int J Clin Pharmacol Ther 1997; 35: 374–80.

Uses and Administration

Cefaclor is a cephalosporin antibacterial given orally similarly to cefalexin in the treatment of susceptible infections including upper and lower respiratory-tract infections, skin infections, and urinary-tract infections. Some classify cefaclor as a second-generation cephalosporin and its greater activity against Haemophilus influenzae makes it more suitable than cefalexin for the treatment of infections such as otitis media. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Cefaclor is given as the monohydrate. Doses are expressed in terms of the equivalent amount of anhydrous cefaclor; 1.05 g of cefaclor monohydrate is equivalent to about 1 g of anhydrous cefaclor. The usual adult dose is 250 to 500 mg every 8 hours; up to 4 g daily has been given. A suggested dose for children over 1 month of age is 20 mg/kg daily in three divided doses, increased if necessary to 40 mg/kg daily, but not exceeding a total daily dose of 1 g. A common dosage regimen is: children over 5 years, 250 mg three times daily; 1 to 5 years, 125 mg three times daily; under 1 year, 62.5 mg three times daily.

Modified-release formulations of cefaclor are available in some countries.

Preparations

BP 2008: Cefaclor Capsules; Cefaclor Oral Suspension; Prolonged-release

USP 31: Cefaclor Capsules; Cefaclor Chewable Tablets; Cefaclor Extended-Release Tablets; Cefaclor for Oral Suspension.

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Arg.: Cecţ. Cefalkonţ; Cefalţ Kwizaŋɨ; Austral: Aclor; Cedor; Cefkor;
Karlor; Keflor; Ozcef; Austria: Cec; Ceclor; Cefastad; Cefax; Lanacefţ;
Belg.: Ceclor; Doccefaclo; Braz.: Ceclorţ; Cefacloren; Clorcin-Ped;
Faclorţ; Piecorţ; Reflaxţ Canada: Ceclor; Chile: Keflorţ; Cz.: Cecţ-Ceclor; Serviclor; Vercef; Fin.: Kefolor; Fr.: Alfatii; Alphexineţ; Haxifal; Ger.:
Cec; Cecloretat: Cef-Diolan; Cefa-Wolffţ; Cephalodo; Hefaclorţ; InfectoCef; Panoral; Sigacefalţ; Gr.: Afecton; Camirox; Ceclor; Cefacloril; Fredyren; Hetaclox; Makovan; Pandor; Phacotrex; Ufoxillinţ; Hong Kong;
Castal; Ceclor; Cefalor; Medoclor; Qualicector; Qualiporo; Soficior Vercef;
Hung.: Ceclor; Cecloretta; Vercef; India: Halocef; Keflor; Indon.: Capabi-

The symbol † denotes a preparation no longer actively marketed

otic; Cedor; Cloracef; Especior; Forifek; Medikoncef; Sodor; Irl.: Cefager; Distaclor; Keftid; Pinaclor; Israel: Ceclor†; Cefalor; Ital.: Altaclor; Bacticef; Bactigram; Cefulton; Citiclor†; Clorad; Clorazer; Dorf; Erredor†; Eurocefix†; Fuclode†; Geniclor; Kliacef; Lafarclor; Macovan; Necloral; Omaspic, Oralcef; Panacef, Performer; Selanir†; Selviclor; Takeef; Tibiror; Valeclor; Valeclor; Selviclor†; Siracef; Tibiror; Valeclor; Malaysia: Distaclor†; Sifaclor; Soficior†; Vercef; Mex.: Arcefal; Cec; Ceclor; Cefalan; Ceflacid; Fasiclor; Fermed; Ranclor; Serviclor; Teraclox; Neth.: Ceclor; NZ: Clorotir; Philipp.: Aczebn; Brelox; Ceclobid; Ceclori; Celor; Cloracef†; Pandor; Serviclor; Vercef; Port.: Ceclor; Rol.: Ceclor; Clerox; Cloracef†; Pandor; Serviclor; Vercef; Port.: Ceclor; NZ: Ceclor; Clexox; Orotir; Distaclor; Soficlor; Vercef; Spain: Ceclor; Switz.: Ceclor; Thuk: Celco; Clorotir; Distaclor; Kefalor†; Sidaclor; Tefaclor; Vercef; Ver

Multi-ingredient: Mex.: Ceclordox.

Cefadroxil (BAN, USAN, DINN)

BL-S578; Cefadroksilis monohidratas; Cefadroksyl jednowodny; Céfadroxil; Cefadroxil monohydrát; Céfadroxil monohydraté; Cefadroxilmonohydrat; Cefadroxilo; Cefadroxilum; Cefadroxilum monohydricum: Cephadroxil: Kefadroksiili: Kefadroksiilimonohydraatti; MIF-11567-3; Sefadroksil. (7R)-7-(α-D-4-Hydroxyphenylglycylamino)-3-methyl-3-cephem-4-carboxylic acid monohydrate.

Цефадроксил

 $C_{16}H_{17}N_3O_5S,H_2O = 381.4.$

CAS — 50370-12-2 (anhydrous cefadroxil); 119922-85-9 (cefadroxil hemihydrate); 66592-87-8 (cefadroxil monohy-

ATC - 101 DB05. ATC Vet - QJ01DB05.

Pharmacopoeias. In Chin., Eur. (see p.vii), and US. Jpn includes the anhydrous substance.

Ph. Eur. 6.2 (Cefadroxil Monohydrate). A white or almost white powder. Slightly soluble in water; very slightly soluble in alcohol. A 5% suspension in water has a pH of 4.0 to 6.0. Protect from light.

USP 31 (Cefadroxil). A white to off-white crystalline powder. Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a 5% suspension in water is between 4.0 and 6.0. Store in airtight containers

Adverse Effects and Precautions

As for Cefalexin, p.218.

Breast feeding. Although higher concentrations of cefadroxil were reported in breast milk compared with cefalexin, cefalotin, cefapirin, and cefotaxime, ¹ no detectable cefadroxil would be expected in breast-fed infants and no adverse effects have been seen in infants whose mothers were receiving cefadroxil. Accordingly, the American Academy of Pediatrics considers2 that cefadroxil is usually compatible with breast feeding.

- Kafetzisi DA, et al. Passage of cephalosporins and amoxicillin into the breast milk. Acta Paediatr Scand 1981; 70: 285–8.
 American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. Pediatrics 2001; 108: 776–89.
- Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Interactions

As for Cefalexin, p.218.

Antimicrobial Action

As for Cefalexin, p.218.

Pharmacokinetics

Cefadroxil is almost completely absorbed from the gastrointestinal tract. After oral doses of 500 mg and 1 g, peak plasma concentrations of about 16 and 30 micrograms/mL respectively are obtained after 1.5 to 2 hours. Although peak concentrations are similar to those of cefalexin, plasma concentrations are more sustained. Dosage with food does not appear to affect the absorption of cefadroxil. About 20% of cefadroxil is reported to be bound to plasma proteins. The plasma half-life of cefadroxil is about 1.5 hours and is prolonged in patients with renal impairment.

Cefadroxil is widely distributed to body tissues and fluids. It crosses the placenta and appears in breast milk.

More than 90% of a dose of cefadroxil may be excreted unchanged in the urine within 24 hours by glomerular filtration and tubular secretion; peak urinary concentrations of 1.8 mg/mL have been reported after a dose of 500 mg. Cefadroxil is removed by haemodialysis.

- 1. Tanrisever B, Santella PJ. Cefadroxil: a review of its antibacterial, pharmacokinetic and therapeutic properties in comparisor with cephalexin and cephradine. *Drugs* 1986; **32** (suppl 3): 1–16.
- Wise R. The pharmacokinetics of the oral cephalosporins—a review. J Antimicrob Chemother 1990; 26 (suppl E): 13–20.
- 3. Garrigues TM, et al. Dose-dependent absorption and elimination of cefadroxil in man. Eur J Clin Pharmacol 1991; 41: 179–83.

Uses and Administration

Cefadroxil is a first-generation cephalosporin antibacterial that is the para-hydroxy derivative of cefalexin (p.219), and is used similarly in the treatment of mild to moderate susceptible infections. It is given orally, and doses are expressed in terms of the anhydrous substance; 1.04 g of cefadroxil monohydrate is equivalent to about 1 g of anhydrous cefadroxil. The usual adult dose is 1 to 2 g daily as a single dose or in two divided doses. The following doses are used in children weighing less than 40 kg: 500 mg twice daily for those over 6 years of age, 250 mg twice daily for those aged 1 to 6 years, and 25 mg/kg daily in divided doses for infants under 1 year. For details of reduced doses of cefadroxil in patients with renal impairment, see below.

Cefadroxil has also been used as the lysine derivative.

Administration in renal impairment. Following an initial loading dose of 0.5 to 1 g, dosage of cefadroxil should be adjusted in patients with renal impairment according to creatinine clearance (CC):

- CC 26 to 50 mL/minute per 1.73 m²: 0.5 to 1 g every 12 hours
- CC 11 to 25 mL/minute per 1.73 m²: 0.5 to 1 g every 24 hours
- CC 10 mL/minute per 1.73 m² or less: 0.5 to 1 g every 36 hours.

Preparations

BP 2008: Cefadroxil Capsules; Cefadroxil Oral Suspension; USP 31: Cefadroxil Capsules; Cefadroxil for Oral Suspension; Cefadroxil

Proprietary Preparations (details are given in Part 3)

Arg.: Cefabiot+; Cefacar; Cefacilina; Cefadrox; Cefamar; Cefasin; Cefatenk; Arg.: Cetabiot†; Cetacar; Cetaclina; Cetadrox; Cetamar; Cetasni; Cetatenis; Croxili Kandicin; Klonadrovili†; Versatic; Austria; Biodroxil; Duracef; Belg.: Duracef; Moxacef†; Braz.: Cefadroxon; Cefamox; Celoxin†; Drofaxil†; Neo Cefadni; Canad.: Duricef; Chile: Adroxef; Biodroxil†; Cefamox; Sedafex; Cz.: Biodroxil; Cedrox†; Cefadrox†; Duracef; Fin:: Duracef; Fin: Oracefix; Hong Kong: Amben; Androxyl; Biodroxil; Mouracef; Qualidrox; Soldrox†; Hung.: Biodroxil†; Duracef; India: Cefadrox; Cefadur; Lactocef; Lydroxil; Odoxil; Pendrox; Vepan; Vistadrox; Indon.: Alxil; Ancefa; Bidicef; Biodroxil; Cefat; Dexacef; Doxef; Duricef; Erphadrox; Ethicef; Keljec; Lapicef; Librocef; Longcef; Opicef; Osadrox; Pyricef; Q Cef; Qidrox; Renasistin; Roksicap; Sedrofen; Stafoni; Tisacef; Widrox; Int.: Ultracef; Israel: Biodroxil: Duracef; Ital): Cefaditi; Ceoxil†: Cebnos: Foxil: Oradroxil; Malovsici. Roksicap; Sedrofen; Statonn; Tisacet; Widrox; fir.: Ultracet; Israel: Biodrox-it; Duracet; Ital.: Cefadin; Ceoxit; Cephos; Foxi; Oradroxi; Malaysia: Kefloxin; Sofidrox; Mex.: Cefamox; Cepotec; Duracef; Teroxina; Philipp.: Drolex; Drozid; Lexipad; Pol.: Biodroxi; Duracef; Port.: Biofaxit; Cefacite; Ceforal; Cefra; S.Afr.: Cipadur; Dacef; Duracef; Singapore: Duricef; Sofidrox; Spain: Usracef; Swed.: Cefamox; Thal.: Cefadin; Turk.: Cefra-dur; Duricef; UK: Baxan; USA: Duricef; Venez.: Bidroxyt; Cedroxim; Ce-fadril; Cefaval; Cefonax; Drocef; Droxifan; Grunicef; Sanodril.

Multi-ingredient: Arg.: Cefacar Mucolitico†; Cefacilina Bronquial; Mex.:

Cefalexin (BAN, pINN)

66873; Cefaleksinas monohidratas; Cefaleksyna; Cefalexin monohydrát; Cefalexina; Céfalexine; Céfalexine monohydratée; Cefalexinmonohydrat; Cefalexinum; Cefalexinum monohydricum; Cephalexin (USAN); Kefaleksiini; Kefaleksiinimonohydraatti; Sefaleksin. (7R)-3-Methyl-7-(α -D-phenylglycylamino)-3-cephem-4-carboxylic acid monohydrate.

Цефалексин

 $C_{16}H_{17}N_3O_4S,H_2O = 365.4.$

CAS — 15686-71-2 (anhydrous cefalexin); 23325-78-2 (cefalexin monohydrate).

ATC - JOIDBOI.

ATC Vet — QJ01DB01; QJ51DA01.

Pharmacopoeias. In Chin., Eur. (see p.vii), Jpn, US, and Viet. Ph. Eur. 6.2 (Cefalexin Monohydrate). A white or almost white crystalline powder. Sparingly soluble in water; practically insoluble in alcohol. A 0.5% solution in water has a pH of 4.0 to 5.5. Protect from light.

USP 31 (Cephalexin). A white to off-white crystalline powder. Slightly soluble in water; practically insoluble in alcohol, in chloroform, and in ether. pH of a 5% suspension in water is between 3.0 and 5.5. Store in airtight containers.

Cefalexin Hydrochloride (BANM, pINNM)

Céfalexine. Chlorhydrate de: Cefalexini Hydrochloridum: Cephalexin Hydrochloride (USAN); Hidrocloruro de cefalexina; LY-061188

Цефалексина Гидрохлорид $C_{16}H_{17}N_3O_4S,HCI,H_2O = 401.9.$ CAS — 105879-42-3. ATC — JOIDBOI. ATC Vet — QJ01DB01.

Pharmacopoeias. In US.

USP 31 (Cephalexin Hydrochloride). A white to off-white crystalline powder. Soluble 1 in 100 in water, in acetone, in acetonitrile, in alcohol, in dimethylformamide, and in methyl alcohol; practically insoluble in chloroform, in ether, in ethyl acetate, and in isopropyl alcohol. pH of a 1% solution in water is between 1.5 and 3.0. Store in airtight containers.

Adverse Effects and Precautions

As for Cefalotin Sodium, p.219.

The most common adverse effects of cefalexin and other oral cephalosporins are generally gastrointestinal disturbances and hypersensitivity reactions. Pseudomembranous colitis has been reported.

- Dave J, et al. Cephalexin induced toxic epidermal necrolysis. J Antimicrob Chemother 1991; 28: 477–8.
- Baran R, Perrin C. Fixed-drug eruption presenting as an acute paronychia. Br J Dermatol 1991; 125: 592–5.
- Clark RF. Crystalluria following cephalexin overdose. Pediatrics 1992; 89: 672–4.
- rics 1992; 89: 672–4.
 Murray KM, Camp MS. Cephalexin-induced Stevens-Johnson syndrome. Ann Pharmacother 1992; 26: 1230–3.
 Czechowicz RT, et al. Bullous pemphigoid induced by cephalexin. Australas J Dermatol 2001; 42: 132–5.
 Longstreth KL, et al. Cephalexin-induced acute tubular necrosis. Pharmacotherapy 2004; 24: 808–11.
 Skoog SM, et al. Cephalexin-induced cholestatic hepatitis. J Clin Gastroenterol 2004; 38: 833.
 Partilia Let al. Policium in an edulocopt nation during typic.

- Penttilä J, et al. Delirium in an adolescent patient during treatment with cephalexin. J Adolesc Health 2006; 39: 782–3.

Porphyria. Cefalexin is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Interactions

The renal excretion of cefalexin, and many other cephalosporins, is delayed by probenecid.

Hormonal contraceptives. There have been isolated reports of cefalexin decreasing the efficacy of oestrogen-containing oral contraceptives.1 For a discussion of decreased efficacy of oral contraceptives and the need for additional contraceptive methods in patients taking broad-spectrum antibacterials, see under Hormonal Contraceptives, p.2068.

Friedman M, et al. Cephalexin and Microgynon-30 do not go well together. J Obstet Gynaecol 1982; 2: 195–6.

Antimicrobial Action

As for Cefalotin Sodium, p.220, although cefalexin is generally less potent. Some strains of Gram-negative bacteria may be inhibited only by the high concentrations achievable in the urinary tract. Haemophilus influenzae is moderately resistant to cefalexin.

Pharmacokinetics

Cefalexin is almost completely absorbed from the gastrointestinal tract and produces a peak plasma concentration of about 18 micrograms/mL 1 hour after a 500mg oral dose. If cefalexin is taken with food, absorption may be delayed, but the total amount absorbed is