Enrofloxacin *(BAN, USAN, rINN)*

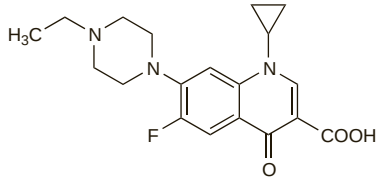
Bay-Vp-2674; Enrofloksasiini; Enrofloxacine; Enrofloxacino; Enrofloxacinum. 1-Cyclopropyl-7-(4-ethylpiperazin-1-yl)-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid.

Энрофлоксацин

$C_{19}H_{22}FN_3O_3$ = 359.4.

CAS — 93106-60-6.

ATC Vet — QJ01MA90.



Profile

Enrofloxacin is a fluoroquinolone antibacterial that is used in veterinary practice.

Ertapenem Sodium *(BANM, USAN, rINNM)*

Ertapenem sódico; Ertapénem Sodique; L-749345; MK-826; MK-0826; Natrii Ertapenemum; ZD-4433. Sodium (4*R*,5*S*,6*S*)-3-({(3*S*,5*S*)-5-[(*m*-Carboxyphenyl)carbamoyl]-3-pyrrolidinyl}thio)-6-[(1*R*)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate.

Натрий Эртапенем

$C_{22}H_{24}N_3NaO_7S$ = 497.5.

CAS — 153832-46-3 (ertapenem); 153832-38-3 (ertapenem disodium); 153773-82-1 (ertapenem sodium).

ATC — J01DH03.

ATC Vet — QJ01DH03.

Incompatibility and stability. References.

1. McQuade MS, *et al.* Stability and compatibility of reconstituted ertapenem with commonly used iv infusion and coinfusion solutions. *Am J Health-Syst Pharm* 2004; **61:** 38–45.

Adverse Effects and Precautions

As for Imipenem, p.286.

Ertapenem is more stable to renal dehydropeptidase I than imipenem and use with cilastatin, which inhibits the enzyme, is not required.

Interactions

Probenecid inhibits the renal excretion of ertapenem thereby increasing its plasma concentrations and prolonging its elimination half-life.

Antiepileptics. For reports of decreased plasma-*valproate* concentrations (sometimes with loss of seizure control) attributed to ertapenem, see p.510.

Antimicrobial Action

As for Imipenem, p.287,

Ertapenem is reported to be slightly more active *in vitro* than imipenem but has a narrower spectrum of activity and is not active against *Acinetobacter* or *Pseudomonas aeruginosa*.

Pharmacokinetics

After intravenous infusion of ertapenem 1 g over 30 minutes, a mean plasma concentration of 155 micrograms/mL is attained, falling to 9 micrograms/mL after 12 hours and 1 microgram/mL after 24 hours. After the same dose intramuscularly, a plasma concentration of 67 micrograms/mL is achieved after 2 hours. Bioavailability after intramuscular injection is about 90%.

Ertapenem is more than 90% bound to plasma proteins. It is distributed into breast milk. The plasma half-life is about 4 hours in adults and 2.5 hours in infants and in children aged 3 months to 12 years; the half-life may be prolonged in patients with renal impairment.

Ertapenem is partially metabolised via hydrolysis of its beta-lactam ring by dehydropeptidase I to an open-ringed metabolite. About 80% of a dose is excreted in the urine as both unchanged drug and metabolite. About 10% is excreted in faeces.

Ertapenem is removed by haemodialysis.

Uses and Administration

Ertapenem is a carbapenem beta-lactam antibacterial with actions and uses similar to those of imipenem (p.287). It is more stable to renal dehydropeptidase I than imipenem and need not be given with an enzyme inhibitor such as cilastatin. It is used in the treatment of susceptible infections including intra-abdominal infections, acute gynaecological infections, urinary-tract infections, skin and skin structure infections (including diabetic foot infections), and community-acquired pneumonia. It is also used prophylactically in colorectal surgery. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

Ertapenem is given as the sodium salt, but doses are expressed in terms of the base; 1.04 g of ertapenem sodium is equivalent to about 1 g of ertapenem. For treatment, it is given by intravenous infusion over 30 minutes or by intramuscular injection, in a usual adult dose of 1 g once daily. For prophylaxis, a single 1- g dose is given intravenously 1 hour before the start of surgery. For details of reduced doses in renal impairment, see below.

For details of doses in infants and children, see below.

◊ Reviews.

1. Keating GM, Perry CM. Ertapenem: a review of its use in the treatment of bacterial infections. *Drugs* 2006; **65:** 2151–78.

Administration in children. The dose of ertapenem for children aged 3 months to 12 years is 15 mg/kg twice daily (up to a maximum of 1 g daily) given by intravenous infusion over 30 minutes; if appropriate, the intramuscular route may be used.

Administration in renal impairment. Doses of ertapenem should be reduced in patients with renal impairment according to creatinine clearance (CC) and the following data are based on US prescribing information:

- CC 30 mL or less per minute (including end-stage disease where CC is 10 mL or less per minute): 500 mg daily for adults
- haemodialysis: if the 500-mg dose is given in the 6-hour period before dialysis an additional 150 mg should be given after each session.

The UK product licence, however, states that in advanced renal insufficiency and haemodialysis there are inadequate data to make recommendations and that ertapenem should not be used in these patients.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Invanz; ***Austral.:*** Invanz; ***Austria:*** Invanz; ***Belg.:*** Invanz†; ***Braz.:*** Invanz; ***Canad.:*** Invanz; ***Chile:*** Invanz; ***Cz.:*** Invanz; ***Denm.:*** Invanz; ***Fin.:*** Invanz; ***Fr.:*** Invanz; ***Ger.:*** Invanz; ***Gr.:*** Invanz; ***Hong Kong:*** Invanz; ***Hung.:*** Invanz; ***Irl.:*** Invanz; ***Israel:*** Invanz; ***Ital.:*** Invanz; ***Malaysia:*** Invanz; ***Neth.:*** Invanz; ***NZ:*** Invanz; ***Philipp.:*** Invanz; ***Pol.:*** Invanz; ***Port.:*** Invanz; ***Rus.:*** Invanz (Инванз); ***S.Afr.:*** Invanz; ***Singapore:*** Invanz; ***Spain:*** Invanz; ***Swed.:*** Invanz; ***Thai.:*** Invanz; ***UK:*** Invanz; ***USA:*** Invanz; ***Venez.:*** Invanz.

Erythromycin *(BAN, rINN)*

Eritromicin; Eritromicina; Eritromicinas; Eritromisin; Érythromycine; Erythromycinum; Erytromycin; Erytromycyna; Erytromysiini. Erythromycin A is (2*R*,3*S*,4*S*,5*R*,6*R*,8*R*,10*R*,11*R*,12*S*,13*R*)-5-(3-amino-3,4,6-trideoxy-*N*,*N*-dimethyl-β-D-*xylo*-hexopyranosyloxy)-3-(2,6-dideoxy-3-*C*,3-*O*-dimethyl-α-L-*ribo*-hexopyranosyloxy)-13-ethyl-6,11,12-trihydroxy-2,4,6,8,10,12-hexamethyl-9-oxotridecan-13-olide.

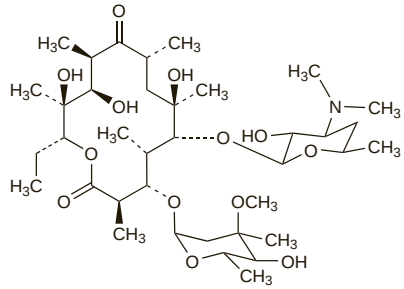
Эритромицин

$C_{37}H_{67}NO_{13}$ = 733.9.

CAS — 114-07-8.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QJ51FA01; QS01AA17.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Erythromycin). It is produced by the growth of a strain of *Streptomyces erythreus* and is a mixture of macrolide antibiotics consisting largely of erythromycin A. It occurs as a white or slightly yellow powder or colourless or slightly yellow crystals; slightly hygroscopic. Slightly soluble in water but less soluble at higher temperatures; freely soluble in alcohol; soluble in methyl alcohol. Protect from light.
USP 31 (Erythromycin). It consists primarily of erythromycin A. A white or slightly yellow, odourless or practically odourless, crystalline powder. Soluble 1 in 1000 of water; soluble in alcohol, in chloroform, and in ether. Store in airtight containers.

Erythromycin Estolate *(BAN, USAN, rINNM)*

Eritromicin-esztolát; Eritromicino estolatas; Erythromycin Propionate Lauryl Sulfate; Erythromycin Propionate Lauryl Sulphate; Érythromycine, estolate d'; Erythromycin-estolát; Erythromycini estolas; Erytromycinestolat; Erytromycyny estolan; Erytromysiini-estolaatti; Estolato de eritromicina; Propionylerythromycin Lauryl Sulphate. Erythromycin 2′-propionate dodecyl sulphate.

Эритромицина Эстолат

$C_{40}H_{71}NO_{14}$,$C_{12}H_{26}O_4S$ = 1056.4.

CAS — 3521-62-8.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Ph. Eur. 6.2 (Erythromycin Estolate). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in alcohol; soluble in acetone; practically insoluble in dilute hydrochloric acid. Protect from light.
USP 31 (Erythromycin Estolate). A white, odourless or practically odourless, crystalline powder. It has a potency equivalent to not less than 600 micrograms of erythromycin per mg, calculated on the anhydrous basis. Practically insoluble in water; soluble 1 in 20 of alcohol, 1 in 15 of acetone, and 1 in 10 of chloroform. Store in airtight containers.

Erythromycin Ethyl Succinate *(BANM)*

Eritromicina, etilsuccinato de; Eritromicin-etilszukcinát; Eritromicino etilsukcinatas; Erythromycin Ethylsuccinate; Érythromycine, éthylsuccinate d'; Erythromycin-ethylsukcinát; Erythromycini ethylsuccinas; Erytromycinetylsuccinat; Erytromycyny etylobursztynian; Erytromysiinietyylisuksinaatti. Erythromycin 2′-(ethylsuccinate).

Эритромицина Этилсукцинат

$C_{43}H_{75}NO_{16}$ = 862.1.

CAS — 41342-53-4.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

NOTE. Compounded preparations of erythromycin ethyl succinate may be represented by the following names:

- Co-erynsulfisox (*PEN*)—erythromycin ethyl succinate and acetyl sulfafurazole.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.
Ph. Eur. 6.2 (Erythromycin Ethylsuccinate; Erythromycin Ethyl Succinate BP 2008). A white or almost white, hygroscopic crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol, in acetone, and in methyl alcohol. Store in airtight containers. Protect from light.
USP 31 (Erythromycin Ethylsuccinate). A white or slightly yellow, odourless or practically odourless, crystalline powder. It has a potency equivalent to not less than 765 micrograms of erythromycin per mg, calculated on the anhydrous basis. Very slightly soluble in water; freely soluble in alcohol, in chloroform, and in macrogol 400. Store in airtight containers.

Erythromycin Gluceptate *(BANM, rINNM)*

Érythromycine, Gluceptate d'; Erythromycini Gluceptas; Gluceptato de eritromicina. Erythromycin glucoheptonate.

Эритромицина Глюцептат

$C_{37}H_{67}NO_{13}$,$C_7H_{14}O_8$ = 960.1.

CAS — 304-63-2; 23067-13-2.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

Pharmacopoeias. In *US*.
USP 31 (Sterile Erythromycin Gluceptate). It is erythromycin gluceptate suitable for parenteral use. It has a potency equivalent to not less than 600 micrograms of erythromycin per mg, calculated on the anhydrous basis. pH of a 2.5% solution in water is between 6.0 and 8.0.

Erythromycin Lactobionate *(BANM, rINNM)*

Eritromicin-laktobionát; Eritromicino laktobionatas; Érythromycine, lactobionate d'; Erythromycini lactobionas; Erythromycin-laktobionát; Erytromycinlaktobionat; Erytromycyny laktobionian; Erytromysiinilaktov; Éthylèneglycol, monostéarate d'; Lactobionato de eritromicina; Lactobionato de eritromicina. Erythromycin mono(4-*O*-β-D-galactopyranosyl-D-gluconate).

Эритромицина Лактобионат

$C_{37}H_{67}NO_{13}.C_{12}H_{22}O_{12}$ = 1092.2.

CAS — 3847-29-8.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.

Ph. Eur. 6.2 (Erythromycin Lactobionate). Salt of a product obtained by fermentation using a strain of *Streptomyces erythreus*. White or slightly yellow, hygroscopic powder. Soluble in water; freely soluble in dehydrated alcohol and in methyl alcohol; very slightly soluble in acetone and in dichloromethane. A 2% solution in water has a pH of 6.5 to 7.5. Store in airtight containers.

USP 31 (Sterile Erythromycin Lactobionate). It has a potency equivalent to not less than 525 micrograms of erythromycin per mg, calculated on the anhydrous basis. pH of a solution in water containing the equivalent of erythromycin 5% is between 6.5 and 7.5.

Erythromycin Propionate *(BANM, USAN, rINNM)*

Erythromycin Propanoate; Érythromycine, Propionate d'; Erythromycini Propionas; Propionato de eritromicina; Propionylerythromycin. Erythromycin 2′-propionate.

Эритромицина Пропионат

$C_{40}H_{71}NO_{14}$ = 790.0.

CAS — 134-36-1.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

Pharmacopoeias. In *Fr.*

Erythromycin Stearate *(BANM, rINNM)*

Eritromicino stearatas; Eritromicin-sztearát; Eritromisin Stearat; Érythromycine, stéarate d'; Erythromycini stearas; Erythromycin-stearát; Erytromycinstearat; Erytromycyny stearynian; Erytromysiinistearaatti; Estearato de eritromicina. Erythromycin octadecanoate.

Эритромицина Стеарат

$C_{37}H_{67}NO_{13}.C_{18}H_{36}O_2$ = 1018.4.

CAS — 643-22-1.

ATC — D10AF02; J01FA01; S01AA17.

ATC Vet — QD10AF02; QJ01FA01; QS01AA17.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Erythromycin Stearate). A mixture of the stearates of erythromycin and stearic acid. A white or almost white crystalline powder. Practically insoluble in water; soluble in acetone and in methyl alcohol. Solutions may be opalescent.

USP 31 (Erythromycin Stearate). The stearic acid salt of erythromycin with an excess of stearic acid. White or slightly yellow crystals or powder, odourless or may have a slight, earthy odour. Practically insoluble in water; soluble in alcohol, in chloroform, in ether, and in methyl alcohol. Store in airtight containers.

Incompatibility and stability. The stability of erythromycin derivatives is dependent upon pH, with particularly rapid degradation occurring at a pH greater than 10 or less than 5.5. Incompatibility might reasonably be expected, therefore, when erythromycin preparations are mixed with drugs or preparations that have a highly acidic or alkaline pH. In practice, reports of incompatibility are not always consistent, and other factors such as the temperature and concentration of solutions, and the diluents used, may play a role.

Solutions for infusion. For the preparation of solutions of erythromycin lactobionate for infusion, a primary solution containing not more than 5% of erythromycin should be prepared first; only water for injection should be used in preparing the primary solution. It should be further diluted with sodium chloride 0.9% or other suitable intravenous fluid before use. Acidic solutions, such as glucose, should only be used if neutralised with sodium bicarbonate.

Adverse Effects

Erythromycin and its salts and esters are generally well tolerated and serious adverse effects are rare. Gastrointestinal disturbances such as abdominal discomfort and cramp, nausea, vomiting, and diarrhoea are fairly common after both oral and parenteral use, probably because of the stimulant activity of erythromycin on the gut. Gastrointestinal effects are dose related and appear to be more common in young than in older patients. Superinfection with resistant organisms may occur and pseudomembranous colitis has been reported.

Hypersensitivity reactions appear to be uncommon, having been reported in about 0.5% of patients, and include pruritus, urticaria, and skin rash as well as occasional cases of anaphylaxis. Stevens-Johnson syndrome and toxic epidermal necrolysis have also been reported very rarely. Hypersensitivity or irritation may occur after topical application of erythromycin.

A hypersensitivity reaction is thought to be responsible for the hepatotoxicity sometimes reported in patients receiving erythromycin or its derivatives but this has been disputed by some. Most reports of cholestatic hepatitis have been in patients receiving the estolate, and it has been suggested that the propionyl ester linkage is particularly associated with hepatotoxicity, but symptoms have also been reported in patients given the base and most of the other derivatives, both orally and parenterally. Symptoms indicative of cholestasis, including upper abdominal pain (sometimes very severe), nausea and vomiting, abnormal liver function values, raised serum bilirubin, and usually jaundice, may be accompanied by rash, fever, and eosinophilia. Symptoms usually occur in patients who have been taking the drug for more than 10 days, although they may develop more quickly in patients given the drug previously. Hepatic dysfunction seems to be rare in children under 12 years of age. The effects of erythromycin on the liver are generally reversible on stopping treatment. Erythromycin may interfere with tests for serum aspartate aminotransferase, which might make diagnosis of hepatotoxicity more difficult.

A generally reversible sensorineural deafness, sometimes with tinnitus, has been reported in patients given erythromycin and appears to be related to serum concentration, with an increased likelihood of such effects in patients given doses of 4 g or more daily of base or its equivalent, in those given intravenous therapy, and in those with renal or hepatic impairment.

Other adverse effects that have been reported in patients given erythromycin include agranulocytosis, aggravation of muscular weakness in myasthenia gravis patients, and pancreatitis. Prolongation of the QT interval and other arrhythmias, sometimes fatal, including torsade de pointes have been reported particularly with intravenous use. There have also been isolated reports of transient CNS adverse effects including confusion, hallucinations, seizures, and vertigo.

Parenteral formulations of erythromycin are irritant and intravenous dosage may produce thrombophlebitis, particularly at high doses. Intramuscular injection is generally avoided as it may produce severe pain.

◊ General reviews.

1. Periti P, *et al.* Adverse effects of macrolide antibacterials. *Drug Safety* 1993; **9:** 346–64.
2. Principi N, Esposito S. Comparative tolerability of erythromycin and newer macrolide antibacterials in paediatric patients. *Drug Safety* 1999; **20:** 25–41.
3. Rubinstein E. Comparative safety of the different macrolides. *Int J Antimicrob Agents* 2001; **18** (suppl 1): S71–S76.

Effects on body temperature. A report of hypothermia associated with oral erythromycin in 2 children.[1] Symptoms resolved on stopping the drug. The children were cousins, perhaps indicating a genetic predisposition to the effect. There has also been a similar report of hypothermia in 3 children given azithromycin orally.[2]

1. Hassel B. Hypothermia from erythromycin. *Ann Intern Med* 1991; **115:** 69–70.
2. Kavukçu S, *et al.* Hypothermia from azithromycin. *J Toxicol Clin Toxicol* 1997; **35:** 225 6.

Effects on the cardiovascular system. There have been several reports[1-6] of QT prolongation or torsade de pointes associated with erythromycin, particularly with intravenous use.

A review[7] of reports of torsade de pointes received by the FDA Adverse Event Reporting System between 1987 and December 2000 identified 156 cases associated with use of the macrolides azithromycin, clarithromycin, dirithromycin, or erythromycin. Of these reports, half involved the use of other drugs known to prolong the QT interval; co-morbid diseases and physiological abnormalities, including cardiac abnormalities, were also commonly reported. A retrospective analysis[8] of a cohort of patients who suffered sudden death from cardiac causes found that the rate of sudden cardiac death was twice as high among current users of erythromycin as in those not using antibacterials; there was no such increase among former users, nor among current users of amoxicillin. The greatest increase in risk was seen in patients using erythromycin with inhibitors of the cytochrome P450 isoenzyme subfamily CYP3A; such patients had more than 5 times the risk of sudden cardiac death of patients who took neither.

1. McComb JM, *et al.* Recurrent ventricular tachycardia associated with QT prolongation after mitral valve replacement and its association with intravenous administration of erythromycin. *Am J Cardiol* 1984; **54:** 922–3.
2. Schoenenberger RA, *et al.* Association of intravenous erythromycin and potentially fatal ventricular tachycardia with Q-T prolongation (torsades de pointes). *BMJ* 1990; **330:** 1375–6.
3. Nattel S, *et al.* Erythromycin-induced long QT syndrome: concordance with quinidine and underlying cellular electrophysiologic mechanism. *Am J Med* 1990; **89:** 235–8.
4. Gitler B, *et al.* Torsades de pointes induced by erythromycin. *Chest* 1994; **105:** 368–72.
5. Gouyon JB, *et al.* Cardiac toxicity of intravenous erythromycin lactobionate in preterm infants. *Pediatr Infect Dis J* 1994; **13:** 840–1.
6. Drici M-D, *et al.* Cardiac actions of erythromycin: influence of female sex. *JAMA* 1998; **280:** 1774–6.
7. Shaffer D, *et al.* Concomitant risk factors in reports of torsades de pointes associated with macrolide use: review of the United States Food and Drug Administration Adverse Event Reporting System. *Clin Infect Dis* 2002; **35:** 197–200.
8. Ray WA, *et al.* Oral erythromycin and the risk of sudden death from cardiac causes. *N Engl J Med* 2004; **351:** 1089–96.

Effects on the gastrointestinal tract. Comparison in patients with upper respiratory-tract infections has suggested that erythromycin ethyl succinate may be associated with less abdominal pain than an equivalent dosage of erythromycin base.[1] Another study has indicated that there was no significant difference in gastrointestinal symptoms between plain and enteric-coated formulations of erythromycin base.[2] Severe nausea and vomiting after rapid intravenous infusion of erythromycin lactobionate stopped in 2 patients who transferred to oral erythromycin base or ethyl succinate.[3] However, the adverse effects may have been due to the rate of infusion, since in 2 further patients symptoms resolved when the lactobionate was given more slowly as a more dilute solution.[3]

There have been a number of studies suggesting an association between erythromycin and infantile hypertrophic pyloric stenosis.[4-6] A retrospective cohort study of 469 infants who had received erythromycin found that 43 were diagnosed with the condition including 36 male infants, although erythromycin had been prescribed almost equally for males and females.[5] All the infants in whom stenosis developed were given erythromycin in the first 2 weeks of life. In another study,[6] involving 7138 infants who received erythromycin between 3 and 90 days of life, use of the drug between 3 and 13 days of life was associated with an almost eightfold increased risk of infantile hypertrophic pyloric stenosis. However, it was believed that the evidence did not support a generalisation of this association to the whole class of macrolides[7] although pyloric stenosis has been reported in breast-fed infants associated with the use of erythromycin or several other macrolides in their mothers (see under Precautions, below).

For reference to the stimulant effects of erythromycin on the gastrointestinal tract, see Decreased Gastrointestinal Motility under Uses and Administration, below.

1. Saloranta P, *et al.* Erythromycin ethylsuccinate, base and acistrate in the treatment of upper respiratory tract infection: two comparative studies of tolerability. *J Antimicrob Chemother* 1989; **24:** 455–62.
2. Ellsworth AJ, *et al.* Prospective comparison of patient tolerance to enteric-coated vs non-enteric-coated erythromycin. *J Fam Pract* 1990; **31:** 265–70.
3. Seifert CF, *et al.* Intravenous erythromycin lactobionate-induced severe nausea and vomiting. *DICP Ann Pharmacother* 1989; **23:** 40–4.
4. Honein MA, *et al.* Infantile hypertrophic pyloric stenosis after pertussis prophylaxis with erythromycin: a case review and cohort study. *Lancet* 1999; **354:** 2101–5. Correction. *ibid.* 2000; **355:** 758.
5. Mahon BE, *et al.* Maternal and infant use of erythromycin and other macrolide antibiotics as risk factors for infantile hypertrophic pyloric stenosis. *J Pediatr* 2001; **139:** 380–4.
6. Cooper WO, *et al.* Very early exposure to erythromycin and infantile hypertrophic pyloric stenosis. *Arch Pediatr Adolesc Med* 2002; **156:** 647–50.
7. Hauben M, Amsden GW. The association of erythromycin and infantile hypertrophic pyloric stenosis: causal or coincidental? *Drug Safety* 2002; **25:** 929–42.

Effects on the neonate. For a suggestion that erythromycin or other macrolides might be associated with an increased risk of infantile hypertrophic pyloric stenosis in neonates, see under Effects on the Gastrointestinal Tract, above.

Effects on the skin. Skin reactions ranging from mild eruptions to erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have rarely been reported with macrolides.[1,2]

1. Lestico MR, Smith AD. Stevens-Johnson syndrome following erythromycin administration. *Am J Health-Syst Pharm* 1995; **52:** 1805–7.
2. Sullivan S, *et al.* Stevens-Johnson syndrome secondary to erythromycin. *Ann Pharmacother* 1999; **33:** 1369.

Overdosage. Acute pancreatitis was reported in a 12-year-old girl after ingestion of about 5 g of erythromycin base.[1] Transient pancreatitis has also been reported in another 15-year-old girl who took 5.328 g of erythromycin base.[2] Erythromycin produces contraction of the sphincter of Oddi resulting in reflux of bile into the pancreas but the resulting pancreatitis is self-limited and