Polygynax; Polyoph; Terramycin with Polymyxin B; ***Hung.:*** Oftalmotrim†; Otosporin; Polyspor; ***India:*** Chlormixin; Dexosyn Plus; Neosporin; Neosporin-H; Ocupol; Ocupol-D; ***Indon.:*** Inmatrol; Isotic Enpigi; Isotic Neolysson; Isotic Nepafrin; Kenetrol; Kloramixin; Kloramixin D; Maxitrol; Nelicort; Neocortic; Neofen; Neosyd; Oregan; Osatrol; Otolin; Otopain; Otopraf; Otozambon; Polidemisin; Polifrisin; Terramycin Poly; Ximex Optixitrol; ***Irl.:*** Maxitrol; Neosporin†; Otosporin; Polyfax; ***Israel:*** Auricularum; Bamyxin; Desoren; Dex-Otic; Maxitrol; Phenimixin; Tarocidin; Tarocidin D; Terramycin; ***Ital.:*** Anauran; Cicatrene; Mixotone; Otosporin†; Rinojet SF†; ***Malaysia:*** Bacitracin-N; Maxitrol; Oftalmotrim; Pocin G; Pocin H; Terramycin; ***Mex.:*** Alosol; Biodexan; Biofrin; Biotriamin; Cortisporin; Dexsul; Hidropolicin; Maxitrol; Neobacigrin; Neosporin; Nicobio†; Polixin; Poly-Micron; Rinadex Compuesto; Septilisin; Sulned; Synalar N; Synalar O; Synalar Oftalmico; Terramicina; Tribiot; ***Neth.:*** Maxitrol; Otosporin; Panotile; Polyspectran G†; Polytrim; Synalar Bi-Otic†; Terra-Cortril Gel Steraject met polymyxine-B†; Terra-Cortril met polymyxine-B; ***Norw.:*** Maxitrol; Terra-Cortril Polymyxin B; Terramycin Polymyxin B; ***NZ:*** Maxitrol; ***Philipp.:*** Aplosyn-Otic; BNP Ointment; Cortisporin; Hydrospor; Isonep; Isonep H; Maxirap; Maxitrol; Maxoptic; Neosporin; Novasorin; Postop; Postotic; Predmycin-P; Statrol; Synalar Otic; Syntemax; Terramycin; Terramycin Plus; Trimycin; Trimycin-H; ***Pol.:*** Atecortin; Dexadent; Maxitrol; Multibiotic; Neotopic; Tribiotic; ***Port.:*** Conjunctilone; Conjunctilone-S; Oftalmotrim; Otosporin; Polisulfade; Polydexa; ***Rus.:*** Anauran (Анауран); Maxitrol (Макситрол); Polydexa (Полидекса); Polydexa with Phenylephrine (Полидекса С Фенилефрином); Polygynax (Полижинакс); ***S.Afr.:*** Maxitrol; Neosporin†; Otosporin; Polysporin; Polytrim†; Terra-Cortril; Terramycin; ***Singapore:*** Maxitrol; Polybamycin; Polydexa; Polygynax; Predmycin-P†; Terramycin; ***Spain:*** Bacisporin; Blastoestimulina; Creanolona; Dermisone Tri Antibiotic; Liquipom Dexa Antib; Maxitrol; Neocones; Oftalmotrim; Oftalmotrim Dexa†; Oftalmowell; Otix; Otosporin; Panotile; Phonal; Poly Pred; Pomada Antibiotica; Synalar Nasal; Synalar Otico; Terra-Cortril; Terramicina; Tivitis; Tulgrasum Antibiotico; Vinciseptil Otico; ***Swed.:*** Isopto Biotic†; Terracortril med polymyxin B; Terramycin Polymyxin B; ***Switz.:*** Baneopol; Maxitrol; Mycinopred; Neosporin; Otosporin; Panotile; Polydexa; Spersapolymyxin; Terracortril†; ***Thai.:*** Banocin; Maxitrol; My-B; Neosporin†; Opsacin†; Otosamthong; Otosporin†; Polyoph; Predmycin†; Primoptic†; Spersapolymyxin; Terramycin; Terrasil†; Xanalin; ***Turk.:*** Cebemyxine; Geotril; Heksa; Neosporin; Oftalmotrim; Polimisin; Polycilline; Polytrim; Sekamisin; Terramycin; ***UK:*** Gregoderm†; Maxitrol; Neosporin; Otosporin; Polyfax; Polytrim†; ***USA:*** Ak-Poly-Bac; Ak-Spore; Ak-Trol†; Betadine First Aid Antibiotics + Moisturizer; Betadine Plus First Aid Antibiotics & Pain Reliever; Cortatrigen; Cortimycin; Cortisporin; Dexacidin†; Dexacine†; Dexasporin; Ear-Eze; Lanabiotic†; LazerSporin-C; Maxitrol; Mycitracin†; Neocin; Neopolydex; Neosporin; Neosporin + Pain Relief; Neosporin GU; Neosporin†; Neotricin HC; Opticair†; Ocu-Spor-B; Ocu-Spor-G; Ocu-Trol; Ocutricin; Otic-Care; OtiTricin; Otobiotic; Otocort; Otomycin-HPN; Otosporin; Pediotic; Poly-Dex; Poly-Pred; Polycin-B; Polymycin; Polysporin†; Polytracin; Polytrim; Spectrocin Plus†; Terak; Terramycin with Polymyxin B; Tri-Biozene; UAD-Otic; ***Venez.:*** Dermabiotic; Maxicort; Maxitrol; Neo-Synalar†; Ofterra; Otocort; Poli-Otico; Terramicina con Polimixina B.

## Pristinamycin *(BAN, rINN)*

Pristinamicina; Pristinamycine; Pristinamycinum; RP-7293.

Пристинамицин

*CAS — 270076-60-3.*
*ATC — J01FG01.*
*ATC Vet — QJ01FG01.*

### Profile

Pristinamycin is a streptogramin antibacterial produced by the growth of *Streptomyces pristina spiralis*, with actions and uses similar to those of virginiamycin (p.361). It is given orally in the treatment of susceptible infections, particularly staphylococcal infections, in a dose of 2 to 4 g daily in divided doses.

◊ Pristinamycin is a naturally occurring mixture of two synergistic components, pristinamycin I which is a macrolide, and pristinamycin II which is a depsipeptide.[1] It has been available for many years as an oral antistaphylococcal drug, and also acts against streptococci. It is effective against strains showing resistance to erythromycin; resistance to pristinamycin is rare,[2,3] although resistance in staphylococci has been reported in the past.[4,5] It is effective against meticillin-resistant *Staphylococcus aureus* (MRSA)[6,7] but its usefulness in severe infection is limited by its poor solubility, which prevents development of an intravenous formulation. Oral pristinamycin has been shown to be as effective as standard therapy with intravenous then oral penicillin in the treatment of erysipelas.[8]

Mixtures of water-soluble derivatives of pristinamycins I and II, such as quinupristin/dalfopristin (p.322), are in clinical use or under investigation.


1. Hamilton-Miller JMT. From foreign pharmacopoeias: 'new' antibiotics from old? *J Antimicrob Chemother* 1991; **27:** 702–5.
2. Weber P. Streptococcus pneumoniae: absence d'émergence de résistance à la pristinamycine. *Pathol Biol (Paris)* 2001; **49:** 840–5.
3. Leclercq R, *et al.* Activité in vitro de la pristinamycine vis-à-vis des staphylocoques isolés dans les hôpitaux français en 1999-2000. *Pathol Biol (Paris)* 2003; **51:** 400–4.
4. Loncle V, *et al.* Analysis of pristinamycin-resistant Staphylococcus epidermidis isolates responsible for an outbreak in a Parisian hospital. *Antimicrob Agents Chemother* 1993; **37:** 2159–65.
5. Allignet J, *et al.* Distribution of genes encoding resistance to streptogramin A and related compounds among staphylococci resistant to these antibiotics. *Antimicrob Agents Chemother* 1996; **40:** 2523–8.
6. Dancer SJ, *et al.* Oral streptogramins in the management of patients with methicillin-resistant Staphylococcus aureus (MRSA) infections. *J Antimicrob Chemother* 2003; **51:** 731–5.
7. Ng J, Gosbell IB. Successful oral pristinamycin therapy for osteoarticular infections due to methicillin-resistant Staphylococcus aureus (MRSA) and other Staphylococcus spp. *J Antimicrob Chemother* 2005; **55:** 1008–12.
8. Bernard P, *et al.* Oral pristinamycin versus standard penicillin regimen to treat erysipelas in adults: randomised, non-inferiority, open trial. *BMJ* 2002; **325:** 864–6.


### Preparations

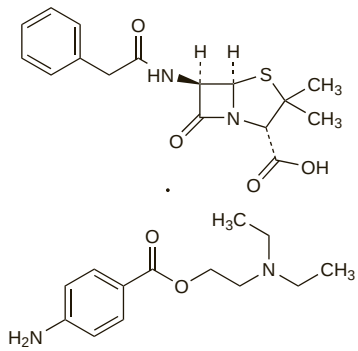
**Proprietary Preparations** (details are given in Part 3)
***Fr.:*** Pyostacine; ***Israel:*** Pyostacine.

## Procaine Benzylpenicillin *(BAN, rINNM)*

Bensylpenicillinprokain; Bentsyylipenisilliinprokaiini; Benzilpenicilinas prokainas; Benzilpenicillin-prokain; Benzylopenicylina prokainowa; Benzylpenicillin Novocaine; Benzylpénicilline Procaïne; Benzylpenicillinum procainum; Penicillin G Procaine; Procaína bencilpenicilina; Procaïne Benzylpénicilline; Procaine Penicillin G; Procaini Benzylpenicillinum; Procainum Benzylpenicillinum; Prokain Benzilpenisilin; Prokain Penisilin G; Prokain-benzylpenicilin. 2-(4-Aminobenzoyloxy)ethyldiethylammonium (6*R*)-6-(2-phenylacetamido)penicillanate monohydrate.

Прокаин Бензилпенициллин

$C_{13}H_{20}N_2O_2,C_{16}H_{18}N_2O_4S,H_2O$ = 588.7.
*CAS — 54-35-3 (anhydrous procaine benzylpenicillin); 6130-64-9 (procaine benzylpenicillin monohydrate).*
*ATC — J01CE09.*
*ATC Vet — QJ01CE09; QJ51CE09.*



**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, and *US.*
**Ph. Eur. 6.2** (Benzylpenicillin, Procaine). A white or almost white, crystalline powder. Slightly soluble in water; sparingly soluble in alcohol. A 0.33% solution in water has a pH of 5.0 to 7.5. Store in airtight containers.
**USP 31** (Penicillin G Procaine). White crystals or white, very fine, microcrystalline powder, odourless or practically odourless. Slightly soluble in water; soluble in alcohol and in chloroform. It is rapidly inactivated by acids, by alkali hydroxides, and by oxidising agents. pH of a saturated solution in water is between 5.0 and 7.5.

### Adverse Effects and Precautions

As for Benzylpenicillin, p.213.

Procaine benzylpenicillin should not be given to patients known to be hypersensitive to either of its components. Procaine benzylpenicillin should not be injected intravascularly since ischaemic reactions may occur.

Severe, usually transient, reactions with symptoms of severe anxiety and agitation, confusion, psychotic reactions including visual and auditory hallucinations, seizures, tachycardia and hypertension, cyanosis, and a sensation of impending death have occasionally been reported with procaine benzylpenicillin and may be due to accidental intravascular injection. Since similar reactions have also occurred with other depot penicillin preparations that do not contain procaine, its presence is unlikely to be the major cause of such reactions, but may be a contributory factor, especially after injection of high doses. These reactions have been termed non-allergic, pseudoallergic, pseudoanaphylactic, or Hoigné's syndrome; the term 'embolic-toxic reaction' has also been proposed.

### Interactions

As for Benzylpenicillin, p.214.

### Pharmacokinetics

When procaine benzylpenicillin is given by intramuscular injection, it forms a depot from which it is slowly released and hydrolysed to benzylpenicillin. Peak plasma concentrations are produced in 1 to 4 hours, and effective concentrations of benzylpenicillin are usually maintained for 12 to 24 hours. However, plasma concentrations are lower than those after an equivalent dose of benzylpenicillin potassium or sodium.

Distribution into the CSF is reported to be poor.

### Uses and Administration

Procaine benzylpenicillin has the same antimicrobial action as benzylpenicillin (p.214) to which it is hydrolysed gradually following deep intramuscular injection. This results in a prolonged effect, but because of the relatively low blood concentrations produced, its use should be restricted to infections caused by microorganisms that are highly sensitive to penicillin. Procaine benzylpenicillin should not be used as the sole treatment for severe acute infections, or when bacteraemia is present.

Procaine benzylpenicillin is used mainly in the treatment of syphilis; other indications have included pneumonia (in children in developing countries), and Whipple's disease. For details of these infections and their treatment, see under Choice of Antibacterial, p.162.

*Administration and dosage.* Doses of procaine benzylpenicillin may sometimes be expressed in terms of equivalent units of benzylpenicillin. Procaine benzylpenicillin 600 mg is equivalent to about 360 mg of benzylpenicillin (600 000 units). Procaine benzylpenicillin is given by deep intramuscular injection in usual doses of 0.6 to 1.2 g daily.

Patients with syphilis are given procaine benzylpenicillin 1.2 g daily for 10 to 14 days; infants up to 2 years of age with congenital syphilis may be given 50 mg/kg daily. Treatment may be continued for 3 weeks in patients with late syphilis.

Procaine benzylpenicillin is also used in combined preparations with other penicillins, including benzylpenicillin and benzathine benzylpenicillin.

### Preparations

***USP 31:*** Penicillin G Benzathine and Penicillin G Procaine Injectable Suspension; Penicillin G Procaine for Injectable Suspension; Penicillin G Procaine Injectable Suspension.

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Mudapenil†; Penicil Dermol†; ***Austral.:*** Cilicaine Syringe; ***Cz.:*** Pendepon Compositum; ***Ger.:*** Jenacillin O†; ***Hung.:*** Retardillin; ***Mex.:*** Benzotripen; Farmabep; Promizol; Sodilin; Unicil 3/1; Unicil 6:3:3; ***NZ:*** Cilicaine; ***S.Afr.:*** Bio-Cillin; Novocillin†; Procillin; ***Spain:*** Aquicilina; Farmaproina; ***Turk.:*** Benzapen 6.3.3; Deposilin 6.3.3; Devapen; Iecilline; Penadur 6.3.3; Penkain-K; Procillin; ***USA:*** Crysticillin; ***Venez.:*** Pebencil†; Pronapen; Silcopen†.

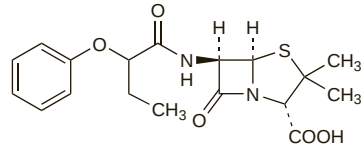
**Multi-ingredient:** ***Austria:*** Fortepen; Retarpen compositum; ***Braz.:*** Benapen; Benzapen G; Despacilina; Drenovac†; Expectovac†; Ginurovac†; Linfocilin†; Odontovac†; Ortocilin†; Pencil 400; Penkaron; Wycillin; ***Chile:*** Karbasalin†; ***Ger.:*** Bipensaar; Jenacillin A†; Retacillin compositum; ***Hong Kong:*** Penicillin G Procaine Fortified; ***Hung.:*** Promptcillin Forte; ***India:*** Bistrepen; ***Ital.:*** Tri-Wycillina†; ***Mex.:*** Bencelin Combinado; Benzanil Compuesto; Benzetacil Combinado; Hidrocilina; Lugaxil; Pecivax; Pendiben Compuesto; Penicil; Penipot; Penisodina; Penprocilina; Procilin; Respicil; Robencaxil; Suipen; ***Neth.:*** Penidural D/F†; ***Port.:*** Atralcilina; Lentocilin; Penadur 6.3.3†; ***Rus.:*** Bicillin-3 (Бициллин-3); Bicillin-5 (Бициллин-5); ***S.Afr.:*** Penilente Forte†; Ultracillin; ***Spain:*** Aquicilina D A; Benzetacil Compuesta; Cepacilina 633; ***USA:*** Bicillin C-R; ***Venez.:*** Benzetacil 3-3; Benzetacil 6-3-3.

## Propicillin Potassium *(BANM, pINNM)*

Kalii Propicillinum; Potassium α-Phenoxypropylpenicillin; Propicilina potásica; Propicilline Potassique; Propicillinum Kalicum. A mixture of the D(+)- and L(−)-isomers of potassium (6*R*)-6-(2-phenoxybutyramido)penicillanate.

Калия Пропициллин

$C_{18}H_{21}KN_2O_5S$ = 416.5.
*CAS — 551-27-9 (propicillin); 1245-44-9 (propicillin potassium).*
*ATC — J01CE03.*
*ATC Vet — QJ01CE03.*



*(propicillin)*

### Profile
Propicillin is a phenoxypenicillin with actions and uses similar to those of phenoxymethylpenicillin (p.314). Propicillin potassium is given orally for the treatment of susceptible mild to moderate infections in a usual dose of 700 mg three times daily.

### Preparations
**Proprietary Preparations** (details are given in Part 3)
***Ger.:*** Baycillin.

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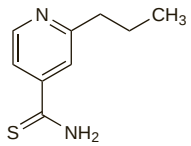
## Protionamide *(BAN, rINN)*
Prothionamide; Protionamid; Protionamida; Protionamidi; Protionamidum; RP-9778; TH-1321. 2-Propylpyridine-4-carbothioamide.

Протионамид
$C_9H_{12}N_2S$ = 180.3.
*CAS — 14222-60-7.*
*ATC — J04AD01.*
*ATC Vet — QJ04AD01.*



**Pharmacopoeias.** In *Chin.*, *Int.*, and *Jpn.*

### Adverse Effects, Precautions, and Antimicrobial Action
As for Ethionamide, p.275.

### Pharmacokinetics
Protionamide is readily absorbed from the gastrointestinal tract and produces peak plasma concentrations about 2 hours after an oral dose. It is widely distributed throughout body tissues and fluids, including the CSF. Protionamide is metabolised to the active sulfoxide and other inactive metabolites and less than 1% of a dose appears in the urine as unchanged drug.

### Uses and Administration
Protionamide is a thioamide derivative considered to be interchangeable with ethionamide (p.276) and is used as a second-line drug in the treatment of multidrug-resistant tuberculosis (p.196). It has also been used, as a substitute for clofazimine, in regimens for the treatment of leprosy (p.176) but less toxic alternatives are now preferred. Complete cross-resistance occurs between the two drugs. Protionamide has been given orally in doses similar to those used for ethionamide. It has also been given as rectal suppositories; protionamide hydrochloride has been given intravenously. Like ethionamide, it has generally been replaced by less toxic antimycobacterials.

### Preparations
**Proprietary Preparations** (details are given in Part 3)
***Ger.:*** ektebin; Peteha; ***Hong Kong:*** Peteha; ***India:*** Prothicid; ***Turk.:*** Promid; Tionamid.

**Multi-ingredient:** ***Austria:*** Isoprodian; ***Ger.:*** Isoprodian†; Peteha†; ***Rus.:*** Protiocomb (Протиокомб).

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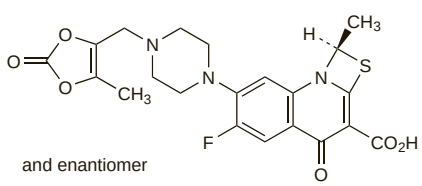
## Prulifloxacin *(rINN)*
NM-441; Prulifloxacine; Prulifloxacino; Prulifloxacinum. (±)-7-{4-[(*Z*)-2,3-Dihydroxy-2-butenyl]-1-piperazinyl}-6-fluoro-1-methyl-4-oxo-1*H*,4*H*-[1,3]thiazeto[3,2-*a*]quinoline-3-carboxylic acid cyclic carbonate.

Прулифлоксацин
$C_{21}H_{20}FN_3O_6S$ = 461.5.
*CAS — 123447-62-1.*
*ATC — J01MA17.*
*ATC Vet — QJ01MA17.*



and enantiomer

### Profile
Prulifloxacin is the prodrug of ulifloxacin, a fluoroquinolone antibacterial. It is given for the treatment of susceptible infections in a usual oral dose of 600 mg daily.

◊ Reviews.


1. Keam SJ, Perry CM. Prulifloxacin. *Drugs* 2004; **64:** 2221–34.
2. Prats G, *et al.* Prulifloxacin: a new antibacterial fluoroquinolone. *Expert Rev Anti Infect Ther* 2006; **4:** 27–41.


### Preparations
**Proprietary Preparations** (details are given in Part 3)
***Cz.:*** Unidrox; ***Gr.:*** Glimbax; Prixina; ***Ital.:*** Chinoplus; Keraflox; Unidrox; ***Port.:*** Keraflox; Oliflox.

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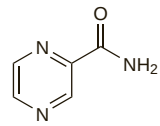
# Pyrazinamide *(BAN, rINN)*
Pirazinamid; Pirazinamida; Pirazinamidas; Pirazynamid; Pyratsiinamidi; Pyrazinamid; Pyrazinamidum; Pyrazinoic Acid Amide. Pyrazine-2-carboxamide.

Пиразинамид
$C_5H_5N_3O$ = 123.1.
*CAS — 98-96-4.*
*ATC — J04AK01.*
*ATC Vet — QJ04AK01.*



**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet*.
**Ph. Eur. 6.2** (Pyrazinamide). A white or almost white, crystalline powder. Sparingly soluble in water, slightly soluble in alcohol and in dichloromethane.
**USP 31** (Pyrazinamide). A white to practically white, odourless or practically odourless, crystalline powder. Soluble 1 in 67 of water, 1 in 175 of dehydrated alcohol, 1 in 135 of chloroform, 1 in 1000 of ether, and 1 in 72 of methyl alcohol; slightly soluble in alcohol.

## Adverse Effects and Treatment
Hepatotoxicity is the most serious adverse effect of pyrazinamide therapy and its frequency appears to be dose related. However, in currently recommended doses, when given with isoniazid and rifampicin, the incidence of hepatitis has been reported to be less than 3%. Patients may have a transient increase in liver enzyme values; more seriously hepatomegaly, splenomegaly, and jaundice may develop and on rare occasions death has occurred.

Hyperuricaemia commonly occurs and may lead to attacks of gout.

Other adverse effects are anorexia, nausea, vomiting, aggravation of peptic ulcer, arthralgia, malaise, fever, sideroblastic anaemia, thrombocytopenia, and dysuria. Photosensitivity, pellagra, and skin rashes have been reported on rare occasions.

**Effects on the cardiovascular system.** Acute hypertension was associated with pyrazinamide in a previously normotensive woman.[1]


1. Goldberg J, *et al.* Acute hypertension as an adverse effect of pyrazinamide *JAMA* 1997; **277:** 1356.


**Effects on the liver.** The risk of hepatitis with antituberculous regimens containing pyrazinamide may be lower than suggested by early studies, in which large doses were used, often for long periods. The incidence of hepatitis in studies[1] of short-course regimens containing pyrazinamide has ranged from 0.2% in Africa, to 0.6% in Hong Kong, to 2.8% in Singapore. These and later studies[2-4] have shown that hepatotoxicity is not increased when pyrazinamide is added to the initial phase of short-term chemotherapy containing rifampicin and isoniazid. Nevertheless, a report[5] of 4 cases of fulminant hepatic failure in patients given triple therapy with the potentially hepatotoxic drugs rifampicin, isoniazid, and pyrazinamide (1 patient also received ethambutol) highlighted the importance of strict liver function monitoring and this was reinforced by others. The Joint Tuberculosis Committee of the British Thoracic Society has produced recommendations[6] for initial measurement of liver function in all patients and regular monitoring in patients with pre-existing liver disease, as well as the response to deteriorating liver function; prompt re-introduction of appropriate antituberculosis therapy is recommended once normal liver function is restored. Similar guidelines have been produced for the USA.[7,8] For further information on hepatotoxicity caused by antituberculous drugs see Effects on the Liver, under Isoniazid, p.288.

The incidence of severe hepatotoxicity was found to be lower in patients receiving isoniazid, rifampicin, and pyrazinamide for initial treatment of active disease, than in those receiving rifampicin and pyrazinamide for 2 months for latent tuberculosis infection. For further information on hepatotoxicity caused by rifampicin and pyrazinamide see Effects on the Liver, under Rifampicin, p.326.


1. Girling DJ. The role of pyrazinamide in primary chemotherapy for pulmonary tuberculosis. *Tubercle* 1984; **65:** 1–4.
2. Parthasarathy R, *et al.* Hepatic toxicity in South Indian patients during treatment of tuberculosis with short-course regimens containing isoniazid, rifampicin and pyrazinamide. *Tubercle* 1986; **67:** 99–108.
3. Combs DL, *et al.* USPHS tuberculosis short-course chemotherapy trial 21: effectiveness, toxicity, and acceptability: the report of final results. *Ann Intern Med* 1990; **112:** 397–406.
4. le Bourgeois M, *et al.* Good tolerance of pyrazinamide in children with pulmonary tuberculosis. *Arch Dis Child* 1989; **64:** 177–8.
5. Mitchell I, *et al.* Anti-tuberculous therapy and acute liver failure. *Lancet* 1995; **345:** 555–6.
6. Joint Tuberculosis Committee of the British Thoracic Society. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. *Thorax* 1998; **53:** 536–48. [Although these guidelines were replaced by ones issued by NICE in 2006 the latter do not *"explain tuberculosis or its treatment in detail"* and therefore reference to the earlier guidelines has been retained] Also available at: http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Tuberculosis/Guidelines/Chemotherapy.pdf (accessed 29/07/08)
7. American Thoracic Society, CDC, and the Infectious Diseases Society of America. Treatment of tuberculosis. *MMWR* 2003; **52** (RR-11): 1–77. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf (accessed 03/10/07) Correction. *ibid.* 2005; **53:** 1203. [dose]
8. Saukkonen JJ, *et al.* American Thoracic Society. An official ATS statement: hepatotoxicity of antituberculosis therapy. *Am J Respir Crit Care Med* 2006; **174:** 935–52. Also available at: http://www.thoracic.org/sections/publications/statements/resources/hepatotoxicity-of-antituberculosis-therapy.pdf (accessed 05/10/07)


**Effects on the nervous system.** Convulsions that developed in a 2-year-old child receiving antituberculous therapy appeared to be due to pyrazinamide, given in a dose of 250 mg daily.[1]


1. Herlevsen P, *et al.* Convulsions after treatment with pyrazinamide. *Tubercle* 1987; **68:** 145–6.


**Hyperuricaemia.** Hyperuricaemia during therapy with pyrazinamide may be due to inhibition of uric acid excretion by pyrazinoic acid, the main metabolite of pyrazinamide.[1]

In a large multicentre study,[2] the incidence of elevated serum concentrations of uric acid for patients receiving rifampicin, isoniazid, and pyrazinamide was 52.2% at 8 weeks while the incidence for patients receiving rifampicin and isoniazid was 5.4%. Arthralgia was reported in 6 of 617 patients receiving rifampicin, isoniazid, and pyrazinamide, but in none of 445 patients receiving rifampicin and isoniazid.

Slight increases in plasma concentrations of uric acid occurred in 9 of 43 children after one month's treatment with rifampicin, isoniazid, ethambutol, and pyrazinamide. Arthralgias and gout did not occur. Uric acid concentrations were normal on completion of treatment with pyrazinamide.[3] Some studies[4] have suggested a relationship between elevated serum uric acid levels and arthralgia, but this has not been confirmed.[5]


1. Ellard GA, Haslam RM. Observations on the reduction of the renal elimination of urate in man caused by the administration of pyrazinamide. *Tubercle* 1976; **57:** 97–103.
2. Combs DL, *et al.* USPHS tuberculosis short-course chemotherapy trial 21: effectiveness, toxicity, and acceptability: the report of final results. *Ann Intern Med* 1990; **112:** 397–406.
3. le Bourgeois M, *et al.* Good tolerance of pyrazinamide in children with pulmonary tuberculosis. *Arch Dis Child* 1989; **64:** 177–8.
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**Pellagra.** Pellagra, probably due to pyrazinamide, developed in a 26-year-old woman receiving antituberculous therapy.[1] Symptoms regressed, despite continued therapy, on giving nicotinamide.


1. Jørgensen J. Pellagra probably due to pyrazinamide: development during combined chemotherapy of tuberculosis. *Int J Dermatol* 1983; **22:** 44–5.


## Precautions
Pyrazinamide should be used with caution in patients with liver disorders and is contra-indicated in established chronic or severe liver disease. In patients with liver disorders, liver function should be assessed before and regularly during treatment. The British Thoracic Society has recommended that pyrazinamide treatment should be suspended if serum aminotransferase concentrations are elevated to 5 times the normal upper limit or if the bilirubin concentration rises. They allow cautious sequential re-introduction of antimycobacterial drugs once liver function has returned to normal: first isoniazid, then rifampicin, and then pyrazinamide. WHO recommends that pyrazinamide not be reintroduced if the hepatitis produced a clinical jaundice.

Pyrazinamide should not be given to patients with acute gout or hyperuricaemia and should be used with