Peyronie's disease. Beneficial effects have been reported with colchicine in men with Peyronie's disease. Small studies show colchicine to be most effective in reducing pain during penile erection.[1] A combination of vitamin E and colchicine has also been suggested as an alternative in early disease.[2]

1. Kadioğlu A, *et al.* Treatment of Peyronie's disease with oral colchicine: long-term results and predictive parameters of successful outcome. *Int J Impot Res* 2000; **12:** 169–75.
2. Prieto Castro RM, *et al.* Combined treatment with vitamin E and colchicine in the early stages of Peyronie's disease. *BJU Int* 2003; **91:** 522–4.

Primary biliary cirrhosis. Primary biliary cirrhosis (p.2408) is a chronic progressive liver disease with no specific treatment, and in general drug therapy has been poor or largely ineffective. Reviewers have noted[1-3] that several studies have been conducted with colchicine, and, although biochemical parameters were improved, a beneficial effect on clinical symptoms or liver histology was not found. A comparative study of colchicine and methotrexate showed that while both drugs improved biochemical test results and symptoms, the response to methotrexate was greater.[4] Some consider that combination therapy with colchicine, methotrexate, and ursodeoxycholic acid may be more promising than monotherapy.[2]

1. Heathcote EJ. Evidence-based therapy of primary biliary cirrhosis. *Eur J Gastroenterol Hepatol* 1999; **11:** 607–15.
2. Holtmeier J, Leuschner U. Medical treatment of primary biliary cirrhosis and primary sclerosing cholangitis. *Digestion* 2001; **64:** 137–50.
3. Gong Y, Gluud C. Colchicine for primary biliary cirrhosis. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2004 (accessed 27/04/05).
4. Kaplan MM, *et al.* A prospective trial of colchicine and methotrexate in the treatment of primary biliary cirrhosis. *Gastroenterology* 1999; **117:** 1173–80.

Pyoderma gangrenosum. Pyoderma gangrenosum (p.1583) associated with inflammatory bowel disease has been successfully treated with colchicine in 2 patients.[1,2] Colchicine was also of benefit in 3 patients with pyoderma associated with familial Mediterranean fever.[3] Other isolated reports include the use of low-dose colchicine in idiopathic pyoderma gangrenosum.[4]

1. Paolini O, *et al.* Treatment of pyoderma gangrenosum with colchicine. *Lancet* 1995; **345:** 1057–8.
2. Rampal P, *et al.* Colchicine in pyoderma gangrenosum. *Lancet* 1998; **351:** 1134–5.
3. Lugassy G, Ronnen M. Severe pyoderma associated with familial Mediterranean fever: favourable response to colchicine in three patients. *Am J Med Sci* 1992; **304:** 29–31.
4. Kontochristopoulos GJ, *et al.* Treatment of pyoderma gangrenosum with low-dose colchicine. *Dermatology* 2004; **209:** 233–6.

Preparations

BP 2008: Colchicine Tablets;
USP 31: Colchicine Injection; Colchicine Tablets; Probenecid and Colchicine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Xuric; ***Austral.:*** Colgout; Lengout; ***Braz.:*** Cixin; Colchin; Colchis; ***Hong Kong:*** Colcina; Colgout; CP-Colchi; ***Hung.:*** Colchicum-Dispert; ***India:*** Goutnil; ***Indon.:*** Recolfar; ***Malaysia:*** Goutnil†; ***Mex.:*** Colchiquim; Sixol; Ticolcin; ***NZ:*** Colgout; ***Thai.:*** Cochic; Colchily; Colcine; Goutichine; Prochic; Tolchicine; ***Turk.:*** Colchicum-Dispert; Kolsin.

Multi-ingredient: ***Arg.:*** Artrex; Colpuril; Xuric-A; ***Fr.:*** Colchimax; ***Mex.:*** Butayonacol; ***Spain:*** Colchimax; ***USA:*** ColBenemid.

Colchicum

Colchico; Colchique.

Безвременник

Profile

Colchicum, the dried ripe seeds or dried corm of the meadow saffron, *Colchicum autumnale*, contains colchicine (p.556) and has been used similarly for the prophylaxis and relief of acute gout.

It is also included in several herbal preparations.

Homoeopathy. Colchicum has been used in homoeopathic medicines under the following names: Colchicinum; Colchicum autumnale; Colchicum, tuber; Colch. at.

Poisoning. *Colchicum autumnale* is quite similar to a species of garlic *Allium ursinum*, especially in leaf appearance, and both plants grow in the same areas at the same time of year. There are reports of colchicine poisoning, some of them fatal, after accidental ingestion of *C. autumnale*.[1-6] Colchicine poisoning should be considered in patients with gastroenterocolitis after a wild plant meal.

1. Brnčić N, *et al.* Accidental plant poisoning with Colchicum autumnale: report of two cases. *Croat Med J* 2001; **42:** 673–5.
2. Sannohe S, *et al.* Colchicine poisoning resulting from accidental ingestion of meadow saffron (Colchicum autumnale). *J Forensic Sci* 2002; **47:** 1391–6.
3. Gabrscek L, *et al.* Accidental poisoning with autumn crocus. *J Toxicol Clin Toxicol* 2004; **42:** 85–8.
4. Brvar M, *et al.* Case report: fatal poisoning with Colchicum autumnale. *Crit Care* 2004; **8:** R56–R59.
5. Brvar M, *et al.* Acute poisoning with autumn crocus (Colchicum autumnale L.). *Wien Klin Wochenschr* 2004; **116:** 205–8.
6. Sundov Z, *et al.* Fatal colchicine poisoning by accidental ingestion of meadow saffron-case report. *Forensic Sci Int* 2005; **149:** 253–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Colchysat.

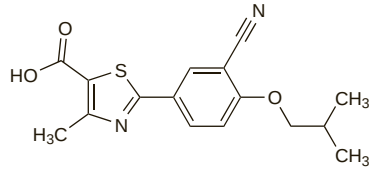
Multi-ingredient: ***Ger.:*** Unguentum lymphaticum; ***Venez.:*** Linfoderm.

Febuxostat *(USAN, rINN)*

Febuxostatum; TMX-67. 2-[3-Cyano-4-(2-methylpropoxy)phenyl]-4-methylthiazole-5-carboxylic acid.

Фебуксостат

$C_{16}H_{16}N_2O_3S$ = 316.4.
CAS — 144060-53-7.
ATC — M04AA03.
ATC Vet — QM04AA03.



Profile

Febuxostat is a non-purine, selective inhibitor of xanthine oxidase, and is under investigation for the treatment of hyperuricaemia in patients with chronic gout.

◊ References.

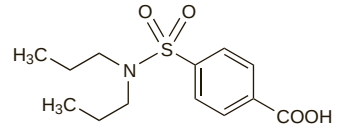
1. Mayer MD, *et al.* Pharmacokinetics and pharmacodynamics of febuxostat, a new non-purine selective inhibitor of xanthine oxidase in subjects with renal impairment. *Am J Ther* 2005; **12:** 22–34.
2. Schumacher HR. Febuxostat: a non-purine, selective inhibitor of xanthine oxidase for the management of hyperuricaemia in patients with gout. *Expert Opin Invest Drugs* 2005; **14:** 893–903.
3. Becker MA, *et al.* Febuxostat compared with allopurinol in patients with hyperuricemia and gout. *N Engl J Med* 2005; **353:** 2450–61. Correction. *ibid.* 2006; **354:** 1533.
4. Khosravan R, *et al.* The effect of mild and moderate hepatic impairment on pharmacokinetics, pharmacodynamics, and safety of febuxostat, a novel nonpurine selective inhibitor of xanthine oxidase. *J Clin Pharmacol* 2006; **46:** 88–102.
5. Khosravan R, *et al.* Pharmacokinetics, pharmacodynamics and safety of febuxostat, a non-purine selective inhibitor of xanthine oxidase, in a dose escalation study in healthy subjects. *Clin Pharmacokinet* 2006; **45:** 821–41.
6. Bruce SP. Febuxostat: a selective xanthine oxidase inhibitor for the treatment of hyperuricemia and gout. *Ann Pharmacother* 2006; **40:** 2187–94.

Probenecid *(BAN, rINN)* ⊗

Probenecidas; Probénécide; Probenecidum; Probenesid; Probenesidi. 4-(Dipropylsulphamoyl)benzoic acid.

Пробенецид

$C_{13}H_{19}NO_4S$ = 285.4.
CAS — 57-66-9.
ATC — M04AB01.
ATC Vet — QM04AB01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Probenecid). A white or almost white crystalline powder or small crystals. Practically insoluble in water; sparingly soluble in dehydrated alcohol; soluble in acetone.
USP 31 (Probenecid). A white or practically white, fine, practically odourless, crystalline powder. Practically insoluble in water and in dilute acids; soluble in alcohol, in acetone, in chloroform, and in dilute alkali.

Adverse Effects and Treatment

Probenecid may cause nausea, vomiting, anorexia, headache, sore gums, flushing, alopecia, dizziness, anaemia, and urinary frequency. Hypersensitivity reactions, with fever, dermatitis, pruritus, urticaria, and, rarely, anaphylaxis, and Stevens-Johnson syndrome have occurred. There have been reports of leucopenia, hepatic necrosis, nephrotic syndrome, and aplastic anaemia. Haemolytic anaemia has also occurred, and may be associated with G6PD deficiency.

When used in chronic gout, and particularly during the first few months of therapy, probenecid may precipitate acute attacks. Uric acid renal calculi, with or without haematuria, costovertebral pain and renal colic may occur.

In massive overdosage probenecid causes stimulation of the CNS, with convulsions and death from respiratory failure. Severe overdosage should be managed by lavage and symptomatic treatment.

Precautions

Probenecid therapy should not be started during an acute attack of gout; however treatment is usually continued when acute attacks occur in patients already receiving the drug, and the acute attack is treated separately. Probenecid is also unsuitable for the control of hyperuricaemia secondary to cancer or cancer chemotherapy. Probenecid should not be given to patients with a history of uric acid renal calculi or blood disorders. It should be used with caution in patients with a history of peptic ulceration. Probenecid should not be used as an antibacterial adjunct in patients with known renal impairment, and it is ineffective in gout in patients with severe renal impairment.

To reduce the risk of uric acid renal calculi in patients with gout an adequate fluid intake (2 to 3 litres daily) is required, and, if necessary, especially during the first few months of treatment, sodium bicarbonate or potassium citrate may be given to render the urine alkaline.

A reducing substance has been found in the urine of some patients taking probenecid, and may give false positive results with some tests for glucose in the urine. Probenecid reduces the excretion of some iodinated contrast media and may interfere with laboratory tests by decreasing the excretion of aminohippuric acid, phenolsulfonphthalein, and sulfobromophthalein.

Abuse. It has been alleged that some athletes using banned anabolic steroids have taken probenecid in an attempt to inhibit the urinary excretion of steroid metabolites in order to avoid detection by urine screening tests.[1]

1. Anonymous. Does probenecid mask steroid use? *Pharm J* 1987; **239:** 299.

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

Interactions

The dose of probenecid may need to be increased if patients are also given drugs, such as diuretics or pyrazinamide, that increase the blood concentration of uric acid. Salicylates, including aspirin, and probenecid are mutually antagonistic and should not be given together.

Probenecid may also affect many other drugs. By inhibiting renal tubular secretion, it has the potential to increase the toxicity and/or to enhance the therapeutic efficacy of drugs excreted by that route. In some instances a reduction in dose is essential to counteract an increase in toxicity, as is the case with methotrexate. Some combinations, such as that with ketorolac, should be avoided. Conversely, probenecid may be given with some antibacterials such as the penicillins and cephalosporins to increase their effects.

Altered excretion may also increase serum concentrations of other antibacterials (aminosalicylic acid, conjugated sulfonamides, dapsone, meropenem, some quinolones, rifampicin), some antivirals (aciclovir, ganciclovir, zalcitabine, zidovudine, and possibly famciclovir), some benzodiazepines (adinazolam, lorazepam, and nitrazepam), some ACE inhibitors (captopril and enalapril), some NSAIDs (diflunisal, indometacin, ketoprofen, meclofenamate, naproxen), paracetamol, and sulfonylurea hypoglycaemic drugs. The clinical significance of such interactions is not entirely clear although the possibility of the need for a reduction in dosage of these drugs should be borne in mind.

It has been reported that patients receiving probenecid require lower doses of thiopental for induction of anaesthesia. Probenecid may increase the speed of induction of anaesthesia with midazolam.