2. Albazzaz MK, *et al.* Alveolitis and haemolytic anaemia induced by azapropazone. *BMJ* 1986; **293:** 1537–8.
3. Montgomery RD, Babb RG. Alveolitis and haemolytic anaemia induced by azapropazone. *BMJ* 1987; **294:** 375.

Effects on the gastrointestinal tract. In a review[1] of the relative safety of 7 oral NSAIDs, the UK CSM commented that azapropazone was associated with the highest risk of gastrointestinal reactions in both epidemiological studies and an analysis of spontaneous reporting of adverse reactions. Although it appeared that some patients over 60 years of age had received doses exceeding those recommended for this age group, it was considered that even when this was taken into account a marked difference remained between gastrointestinal reactions for azapropazone compared with other NSAIDs.

The CSM recommended that azapropazone should be restricted to use in rheumatoid arthritis, ankylosing spondylitis, and acute gout and only when other NSAIDs have been ineffective. Its use in patients with a history of peptic ulceration was contra-indicated. It was also recommended that when used in patients over 60 years of age for rheumatoid arthritis or ankylosing spondylitis the dose should be restricted to a maximum of 600 mg daily.

Azapropazone has been withdrawn in many countries including the UK.

1. CSM/MCA. Relative safety of oral non-aspirin NSAIDs. *Current Problems* 1994; **20:** 9–11. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015615&RevisionSelectionMethod=LatestReleased (accessed 01/11/07)

Effects on the skin. Of 917 reports of adverse reactions associated with azapropazone forwarded to the WHO Collaborating Centre for International Drug Monitoring[1] before September 1984, 190 (21%) were of photosensitivity. Of 154 reports of photosensitivity evaluated a causal relationship to use of azapropazone was considered certain in 6, probable in 138, and possible in 10. In May 1994 the UK CSM stated[2] that since 1976 they had received 464 reports of photosensitivity reactions associated with azapropazone and commented that, when corrected for prescription volume, reporting of this reaction was 50 times greater than with other commonly prescribed NSAIDs. They recommended that patients should be advised to avoid direct exposure to sunlight or to use sunblock preparations.

1. Olsson S, *et al.* Photosensitivity during treatment with azapropazone. *BMJ* 1985; **291:** 939.
2. CSM/MCA. Photosensitivity associated with azapropazone (Rheumox). *Current Problems* 1994; **20:** 6. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015616&RevisionSelectionMethod=LatestReleased (accessed 01/11/07)

Porphyria. Azapropazone is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Preparations

BP 2008: Azapropazone Capsules; Azapropazone Tablets.

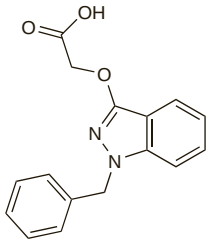
Proprietary Preparations (details are given in Part 3)
Arg.: Debelex†; ***Austria:*** Prolixan†; ***Gr.:*** Prolixan†; ***Hung.:*** Prolixan†; ***Irl.:*** Rheumox†; ***Port.:*** Prolixan†; ***S.Afr.:*** Rheumox; ***Turk.:*** Prodisan; ***UK:*** Rheumox†.

Bendazac *(BAN, USAN, rINN)*

AF-983; Bendazaco; Bendazacum; Bindazac. (1-Benzyl-1*H*-indazol-3-yloxy)acetic acid.

Бендазак

$C_{16}H_{14}N_2O_3$ = 282.3.
CAS — 20187-55-7.
ATC — M02AA11; S01BC07.
ATC Vet — QM02AA11; QS01BC07.



Bendazac Lysine *(BANM, rINNM)*

AF-1934; Bendazac lisina; Bendazacum Lysinum. L-Lysine-(1-benzyl-1*H*-indazol-3-yloxy)acetic acid.

Бендазак Лизин

$C_{22}H_{28}N_4O_5$ = 428.5.
CAS — 81919-14-4.
ATC — S01BC07.
ATC Vet — QS01BC07.

Pharmacopoeias. In *Chin.*

Profile

Bendazac is an NSAID (p.96) structurally related to indometacin (p.66). It has been used topically in preparations containing 1 or 3% for the treatment of various inflammatory skin disorders.

Bendazac lysine has been used in the management of cataract, eye drops containing 0.5% being instilled three times daily.

Hepatotoxicity has been reported.

◊ References.

1. Balfour JA, Clissold SP. Bendazac lysine: a review of its pharmacological properties and therapeutic potential in the management of cataracts. *Drugs* 1990; **39:** 575–96.
2. Prieto de Paula JM, *et al.* Hepatotoxicidad por bendazaco: análisis de 16 casos. *Rev Clin Esp* 1995; **195:** 387–9.

Preparations

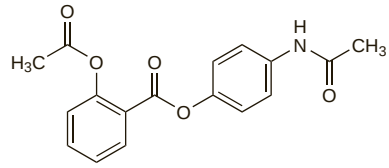
Proprietary Preparations (details are given in Part 3)
Austria: Versus; ***Gr.:*** Versalba; ***Ital.:*** Bendalina; Versus; ***Philipp.:*** Bendalina; ***Port.:*** Bendalina; ***Venez.:*** Bendalina.

Benorilate *(BAN, rINN)*

Benorilaatti; Benorilat; Bénorilate; Benorilato; Benorilatum; Benorylate; FAW-76; Fenasprate; Win-11450. 4-Acetamidophenyl *O*-acetylsalicylate.

Бенорилат

$C_{17}H_{15}NO_5$ = 313.3.
CAS — 5003-48-5.
ATC — N02BA10.
ATC Vet — QN02BA10.



Pharmacopoeias. In *Br.* and *Chin.*
BP 2008 (Benorilate). A white or almost white, odourless or almost odourless, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol and in methyl alcohol; soluble in acetone and in chloroform.

Profile

Benorilate is an aspirin-paracetamol ester with analgesic, anti-inflammatory, and antipyretic properties. After absorption, it is rapidly metabolised to salicylate and paracetamol. It has been used orally in the treatment of mild to moderate pain (see Choice of Analgesic, p.2) and fever (p.10). It has also been used in osteoarthritis, rheumatoid arthritis, and soft-tissue rheumatism.

When an overdose of benorilate is suspected, it has been suggested that plasma concentrations of both salicylate and paracetamol should be measured since a normal plasma-paracetamol concentration cannot necessarily be assumed from a normal plasma-salicylate measurement.

◊ References.

1. Aylward M. Toxicity of benorylate. *BMJ* 1973; **2:** 118.
2. Symon DNK, *et al.* Fatal paracetamol poisoning from benorylate therapy in child with cystic fibrosis. *Lancet* 1982; **ii:** 1153–4.

Preparations

BP 2008: Benorilate Oral Suspension; Benorilate Tablets.

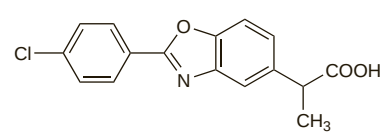
Proprietary Preparations (details are given in Part 3)
Belg.: Duvium†; ***Fr.:*** Salipran†; ***Irl.:*** Benoral†; ***Switz.:*** Duvium†; ***UK:*** Benoral†.

Benoxaprofen *(BAN, USAN, rINN)*

Benoksaprofeeni; Bénoxaprofène; Benoxaprofeno; Benoxaprofenum; Compound 90459; LRCL-3794. 2-[2-(4-Chlorophenyl)benzoxazol-5-yl]propionic acid.

Беноксапрофен

$C_{16}H_{12}ClNO_3$ = 301.7.
CAS — 51234-28-7.
ATC — M01AE06.
ATC Vet — QM01AE06.



Profile

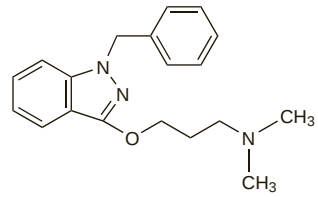
Benoxaprofen is an NSAID (p.96) structurally related to ibuprofen (p.64). It was formerly given orally in rheumatoid arthritis and osteoarthritis but because of reports of adverse reactions and fatalities the manufacturers halted worldwide marketing of the preparation known as *Opren* in the early 1980s. Adverse effects that have occurred with benoxaprofen include skin disorders, notably photosensitivity reactions but also erythema multiforme and the Stevens-Johnson syndrome, onycholysis and other nail disorders, gastrointestinal disturbances including peptic ulceration and bleeding, blood disorders such as thrombocytopenia, cholestatic jaundice and other liver or biliary disorders, and renal failure.

Benzydamine Hydrochloride *(BANM, USAN, rINNM)*

AF-864; Benzidamin Hidroklorür; Benzindamine Hydrochloride; Benzydamine, Chlorhydrate de; Benzydamini Hydrochloridum; Benzydaminy chlorowodorek; Hidrocloruro de bencidamina. 3-(1-Benzyl-1*H*-indazol-3-yloxy)-*NN*-dimethylpropylamine hydrochloride.

Бензидамина Гидрохлорид

$C_{19}H_{23}N_3O$,HCl = 345.9.
CAS — 642-72-8 (benzydamine); 132-69-4 (benzydamine hydrochloride).
ATC — A01AD02; G02CC03; M01AX07; M02AA05.
ATC Vet — QA01AD02; QG02CC03; QM01AX07; QM02AA05.



(benzydamine)

Pharmacopoeias. In *Br.* and *Pol.*
BP 2008 (Benzydamine Hydrochloride). A white crystalline powder. Very soluble in water; freely soluble in alcohol and in chloroform; practically insoluble in ether. A 10% solution in water has a pH of 4.0 to 5.5.

Adverse Effects

After topical application to the skin local reactions such as erythema or rash may occur and photosensitivity has been reported. After use as mouth and throat preparations, numbness or stinging sensations of the oral mucosa have been reported; hypersensitivity reactions including urticaria, photosensitivity, and bronchospasm may also occur rarely.

Effects on the kidneys. A 57-year-old woman who had used 400 g of a topical cream containing benzydamine hydrochloride 3% over a period of 4 months was found to have raised plasma concentrations of creatinine and urea consistent with a substantial reduction in glomerular filtration rate.[1]

1. O'Callaghan CA, *et al.* Renal disease and use of topical non-steroidal anti-inflammatory drugs. *BMJ* 1994; **308:** 110–11.

Effects on the skin. Photoallergic contact dermatitis developed on the hands of a 65-year-old woman after the use of a genital wash containing benzydamine 0.1% for several years.[1] The lesions disappeared once the patient stopped using the solution.

1. Lasa Elgezua O, *et al.* Photoallergic hand eczema due to benzydamine. *Eur J Dermatol* 2004; **14:** 69–70.

Overdose. A 6-year old girl had hallucinations[1] after receiving 500 mg of benzydamine orally; it had been intended as a vaginal douche for pruritus vulvae; recovery was spontaneous.

1. Gómez-López L, *et al.* Acute overdose due to benzydamine. *Hum Exp Toxicol* 1999; **18:** 471–3.

Uses and Administration

Benzydamine hydrochloride is an NSAID (p.99). It is used topically on the skin in concentrations of 3 to 5% in painful musculoskeletal and soft-tissue disorders. Benzydamine hydrochloride is also used as a mouthwash or spray in concentrations of 0.15% for the relief of inflammatory conditions of the mouth and throat. It has been given orally or rectally for the relief of painful and inflammatory conditions, and as a topical solution for vaginal irrigation.

Benzydamine salicylate (benzasal) has been used topically on the skin as a 6% cream or spray.

Mouth disorders. Results of a randomised placebo-controlled study in patients undergoing radiotherapy for oropharyngeal cancer indicated that benzydamine as an oral rinse was effective in reducing the area and severity of mucositis.[1] Benzydamine is also used locally for the management of mouth ulcers (p.1700) although an early study[2] found it no more useful than placebo.

1. Epstein JB, *et al.* Benzydamine HCl for prophylaxis of radiation-induced oral mucositis: results from a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Cancer* 2001; **92:** 875–85.
2. Matthews RW, *et al.* Clinical evaluation of benzydamine, chlorhexidine, and placebo mouthwashes in the management of recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol* 1987; **63:** 189–91.