

Pharmacokinetics

♦ Work in vitro and in animals¹ suggests that although there is some absorption of benzoyl peroxide after topical application, any absorbed drug appears to be metabolised in the skin to benzoic acid and rapidly excreted in the urine.

1. Yeung D, *et al.* Benzoyl peroxide: percutaneous penetration and metabolic disposition II: effect of concentration. *J Am Acad Dermatol* 1983; **9**: 920-4.

Uses and Administration

Benzoyl peroxide has mild keratolytic properties. Its antimicrobial action is probably due to its oxidising effect and activity has been reported against *Staphylococcus epidermidis* and *Propionibacterium acnes*. It is used mainly in the treatment of acne (below), applied once or twice daily in topical preparations usually containing 2.5 to 10%, sometimes with other antimicrobials. For use in young children, see below. It has been used similarly in the treatment of fungal skin infections (p.521), such as tinea pedis although other drugs are usually preferred. A 20% lotion has been applied every 8 to 12 hours in the treatment of decubitus or stasis ulcers. Strengths are expressed as anhydrous benzoyl peroxide although it is used in a hydrous form for safety (see Pharmacopoeias, above).

Benzoyl peroxide is also used as a bleaching agent in the food industry and as a catalyst in the plastics industry.

Acne. Benzoyl peroxide applied topically in concentrations of up to 10% is probably the most widely used first-line drug in the management of mild acne (p.1577). Early studies in animals found benzoyl peroxide to be sebosuppressive¹ but later studies demonstrated that sebum excretion rises during the first few months of treatment,^{2,3} probably due to the comedolytic action of benzoyl peroxide, and remains at a stable level thereafter. Benzoyl peroxide has been shown to have a significant inhibitory effect on skin microflora, with reductions in surface and follicular micro-organisms within 48 hours of beginning treatment, but clinical improvement took several more days to appear.⁴ The combined use of benzoyl peroxide with topical clindamycin or erythromycin can inhibit the development of antibacterial resistance and bring about clinical improvement when resistance already exists.⁵

1. Gloor M, *et al.* Cytokinetic studies on the sebo-suppressive effect of drugs using the example of benzoyl peroxide. *Arch Dermatol Res* 1980; **267**: 97-9.
2. Cunliffe WJ, *et al.* Topical benzoyl peroxide increases the sebum excretion rate in patients with acne. *Br J Dermatol* 1983; **109**: 577-9.
3. Pierard-Franchimont C, *et al.* Topical benzoyl peroxide increases the sebum excretion rate. *Br J Dermatol* 1984; **110**: 506.
4. Bojar RA, *et al.* The short-term treatment of acne vulgaris with benzoyl peroxide: effects on the surface and follicular cutaneous microflora. *Br J Dermatol* 1995; **132**: 204-8.
5. Taylor GA, Shalita AR. Benzoyl peroxide-based combination therapies for acne vulgaris: a comparative review. *Am J Clin Dermatol* 2004; **5**: 261-5.

Administration in children. Benzoyl peroxide has been used topically in the treatment of neonatal and infantile acne, applied once or twice daily starting with lower strength preparations of 2.5%.

Preparations

BP 2008: Benzoyl Peroxide Cream; Benzoyl Peroxide Gel; Benzoyl Peroxide Lotion; Potassium Hydroxyquinoline Sulphate and Benzoyl Peroxide Cream; **USP 31:** Benzoyl Peroxide Gel; Benzoyl Peroxide Lotion; Erythromycin and Benzoyl Peroxide Topical Gel.

Proprietary Preparations (details are given in Part 3)

Arg: Acneap; Acnesan; Benzihex; Cildan B; Eclaran; Ecnagel PB; Paracne; PB Gel; Solugel; Tiltis; Vixiderm E; **Austral:** Benzac; Brevoxyl; Clearasil Ultra; Neutrogena Acne Mask†; Oxy; PanOxyl†; **Austria:** Akneroxid; Benzac; Brevoxyl; PanOxyl; Scherogel; **Belg:** Akneroxid; Benzac; Brevoxyl; Pangel; **Braz:** Acnase; Benzac AC; PanOxyl; Solugel; **Canad:** Acetoxyl; Benzoxyl; Benzac; Benzagel†; Clean & Clear Continuous Control; Clean & Clear Persa Gel; Clearasil B.P. Plus; Dermacne†; Dermoxyl†; Desquam-X; Neo Strata Astringent Acne Treatment†; Neo Strata Blemish Spot†; Neutrogena Acne Mask†; Neutrogena On The Spot Acne Treatment†; Oxy; Oxyderm; PanOxyl; Solugel; **Chile:** Benzac; Pansulfox; Peroxiben Plus; Pirobac; Solugel; **Cz:** Aknecide†; Aknefug-oxid†; Akneroxid; Antopart†; Basiron AC; Eclaran; Innoxiant†; Oxy; **Fin:** Basiron; Brevoxyl; **Fr:** Brevoxyl; Cutacnyl; Eclaran; Efficace; Pannogel; PanOxyl; **Ger:** Aknederm Oxid†; Aknefug-oxid; Akneroxid; Benzaknen; Benzoyt; Benzperox; Brevoxyl; Cordes BPO; Dercome; Klinoxid; Marduk; PanOxyl; Sanoxit; Scherogel†; **Gr:** Benzac-V; Brevoxyl; **Hong Kong:** Acnacyl†; Acneclear; Benzac AC; Brevoxyl; Oxy; PanOxyl; **Hung:** Acne-Med†; Aknefug-oxid; Akneroxid; Lubexyl; **India:** Benzac AC; Persol; **Indon:** Benzolac; Pimplex; **Irl:** Acnecide; Brevoxyl; PanOxyl; **Israel:** Acne Derm; Acne Mask†; Benzac AC; Clearax Cover Up; Oxy; Oxy Sensitive; PanOxyl; **Ital:** Benoxid; Benzac; PanOxyl; Reloxyl; **Malaysia:** Akneroxid; Benzac AC; Brevoxyl; PanOxyl; **Mex:** Akeprul; Benzoxyl; Benzac AC; Benzaderm; Oxy†; Solugel; **Neth:** Akneroxid; Benzac; Clearamed†; Oxy; Tendox; **Norw:** Basiron; Brevoxyl; PanOxyl; **NZ:** Benzac; Brevoxyl; Clearasil Ultra; PanOxyl; **Philipp:** Benzoxyl; Benzac AC; Brevoxyl; PanOxyl; Ultra Clearasil; **Pol:** Akneroxid; Benzacne; Benzapur; Brevoxyl; Clearasil Ultra†; Lubexyl; **Port:** Benacne; Benzoxyl; Benzac; Eclaran; Lutsimed; PanOxyl; Peroxiben; **Rus:** Basiron (Базирон); **S.Afr:** Benzoxyl; Benzac AC; Brevoxyl; Clearasil Benzoyl P; Dry & Clear; PanOxyl;

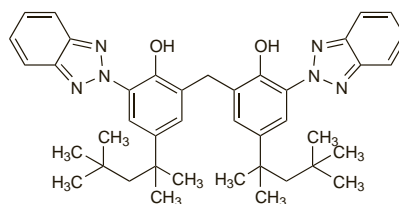
Singapore: Acnacyl†; Akneroxid; Benzac; Brevoxyl; PanOxyl; **Spain:** Benzoxyl; Acneclear; PanOxyl; Peroxace; Peroxiben; Solucel; Stop-Epimilla Normaderm; **Swed:** Basiron; Bexid†; Brevoxyl; Stioxy†; **Switz:** Acnefuge†; Akneroxid; Aknex; Basiron†; Benzac; Efficace†; Lubexyl; PanOxyl†; **Thai:** Acnacyl†; Benzac; Brevoxyl; PanOxyl; **Turk:** Aknefug BP; Aksil; Benzac AC; **UK:** Acnecide; Brevoxyl; Oxy; PanOxyl; **USA:** Acne Clear; Ambi 10; Benzac; Benzoyl; Brevoxyl; Clearasil; Clinac BPO; Del Aqua; Desquam; Forstex; NeoBenz; Oxy; PanOxyl; Triax; Zaclir; **Venez:** Acnec; Benzoxyl†; Benzac AC; Ecuaderm; PanOxyl†; Solugel†.

Multi-ingredient Arg: Acnepas E; Benzamycin†; Clindacur; Clindoxyl; CP-Acne; Dermaclean; Duo Clindacin; Erimicin; Kitane PB†; Pentoclave Comb†; Perclin; Peroximinica; **Austral:** Duac; **Austria:** Acne Plus; Clindoxyl; **Belg:** Acneplus; Benzamycin; **Braz:** Acnase; Akirol†; Benzac Eritromicina†; Clindoxyl; **Canad:** Benzadlin; Benzamycin; Clindoxyl; **Chile:** Benzac Plus; Benzamycin†; Erimicin; Indoxyl; Kina; **Cz:** Duac; **Fr:** Epiduo; **Ger:** Acne Plus; **Gr:** Benzamycin†; Indoxyl; **Hong Kong:** Benzamycin; Duac; **India:** Persol Forte; **Indon:** Benzolac C†; Feldixid; **Irl:** Benzamycin; Duac; Quinoderm; **Israel:** Benzamycin; **Ital:** Acnidazil; Delta 80; Delta 80 Plus; Katoxy; **Mex:** Benzac Plus; Benzadlin; Benzamycin; Clindapack; Indoxyl; **Neth:** Acnecare; Acnecure†; Acnidazil†; Duac; **NZ:** Duac; **Philipp:** Acne Plus; **Pol:** Duac; **Port:** Duac; Zacne; **S.Afr:** Acneclear; Acnidazil; Benzamycin†; Quinoderm; **Singapore:** Benzamycin; **Spain:** Duac; **Swed:** Duac; **Switz:** Acne Creme Plus; **Turk:** Benzamycin; **UK:** Benzamycin†; Duac Once Daily; Quinoderm; **USA:** Benzadlin; Benzamycin; Duac; Sulfoxy†; Vanoxide-HC; Zacare Kit; Zoderm.

Bisotrizole (USAN, rINN)

Bisotrizol; Bisotrizolum; FAT-75634; MBBT; Methylene Bis-Benzotriazolyl Tetramethylbutylphenol. 2,2'-Methylenbis[6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol].

БизОТРИЗОЛ
C₄₁H₅₀N₆O₂ = 658.9.
CAS — 103597-45-1.



NOTE. Tinosorb M is a trade name that has been used for bisotrizole.

Pharmacopoeias. In *US*.

USP 31 (Bisotrizole). Store at a temperature of 20° to 25°, excursions permitted between 15° and 30°.

Profile

Bisotrizole is used as a sunscreen (p.1576). It is effective against UVB and UVA light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

Calamine

Calamina; Calamin; Prepared Calamine.

Каламин

Pharmacopoeias. In *Br*, *Chin*, *Int*, and *US*.

BP 2008 (Calamine). It is a basic zinc carbonate coloured with ferric oxide. It is an amorphous, impalpable, pink or reddish-brown powder, the colour depending on the variety and amount of ferric oxide present and the process by which it is incorporated. Practically insoluble in water; it dissolves with effervescence in hydrochloric acid.

USP 31 (Calamine). It is zinc oxide with a small proportion of ferric oxide. A pink, odourless, fine powder. Insoluble in water; practically completely soluble in mineral acids.

Profile

Calamine has mild astringent and antipruritic actions and is used as a dusting powder, cream, lotion, or ointment in a variety of skin conditions although its value is uncertain.

Preparations

BP 2008: Aqueous Calamine Cream; Calamine and Coal Tar Ointment; Calamine Lotion; Calamine Ointment;

USP 31: Calamine Topical Suspension; Phenolated Calamine Topical Suspension.

Proprietary Preparations (details are given in Part 3)

Braz: Calaphyl†; Duclamina; **Spain:** Talquistina.

Multi-ingredient Arg: Acuaderm; Caladryl; Calcusan; Dermithan; Irricutan; Northalim; Pinklot; Piracalamina; Prunipelen†; Prunisedan; Prunisedan Rosa; Urtikalma; **Austral:** Animine; Calaband; Calamine Lotion; Dermalefe Plus; Quinaband†; **Belg:** Caladryl; **Braz:** Caladerm†; Caladryl; Calamed; Calamina; Calamyn; Dermamina; Dermidryl†; Solardril Composito; **Canad:** Aveeno Anti-Itch; Caladryl; Calamine Antihistamine; **Chile:** Ivarest; Prunice; **Fr:** Gel de Calamine; Prunice; **Hong Kong:** Cadramine-V; Caladryl; Calamine-D†; **India:** Caladryl; Siloderm; **Indon:** Caladine; Caladryl; Calame; Calarex; Minos; Regata; **Irl:** Benadryl; RBC; Vasogen; **Israe:** Baby Paste + Chamomile; Calamine Lotion; Calatrim cum Sulphur†; Calatrim†; **Ital:** Maviplu†; **Malaysia:** Dermoplex; Calamine; Twinkle Calamine; **Mex:** Caladryl; Dermocare; Procaric; **NZ:** Am-O-Lin; Lacto Calamine†; **Philipp:** Caladryl; Calmoseptine; **Port:** Benaderma com Calamina; Benaderma Pruridemase†; Caladryl; Pruridemase†; Solip†; **S.Afr:**

Biohist; Caladryl; Calasthetic; Histamed; Lacto Calamine†; **Singapore:** Acne Clear; **Thai:** Ancamin†; Cadryl; Cadramine; Caladerm†; Caladryl; Calanol; Calapro; Hista; Lanol; M-D; **Turk:** Caladryl; Diyenil; Kalmosan; Tanol; **UK:** Calaband; Lacto Calamine; Quinaband†; RBC; Swarm; Vasogen; **USA:** Caladryl; Calamine; Dome-Paste; Ivarest; RA Lotion; **Venez:** Boro-canfor; Caladryl†; Calaminol; Calaminol Simple†; Calasyl Original; Micofeet.

Calcipotriol (BAN, rINN)

Calcipotriene (USAN); Calcipotriolum; Calcipotriol; Kalcypotriol; Kalsipotriol; Kalsipotrioli; MC-903. (5Z,7E,22E,24S)-24-Cyclopropyl-9,10-secochole-5,7,10(19),22-tetraene-1 α ,3 β ,24-triol.

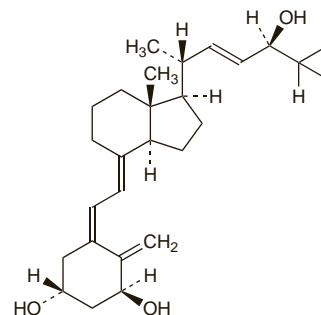
КальЦИПОТРИОЛ

C₂₇H₄₀O₃ = 412.6.

CAS — 112828-00-9; 112965-21-6.

ATC — D05AX02.

ATC Vet — QD05AX02.



Pharmacopoeias. In *Eur* (see p.vii), which also includes the monohydrate.

Ph. Eur. 6.2 (Calcipotriol, Anhydrous; Calcipotriolum Anhydricum). A white or almost white, crystalline powder. It is sensitive to heat and light. A reversible isomerisation to pre-calcipotriol takes place in solution, depending on temperature and time. The activity is due to both compounds. Practically insoluble in water; freely soluble in alcohol; slightly soluble in dichloromethane. Store in airtight containers at a temperature of -20° or below. Protect from light.

Ph. Eur. 6.2 (Calcipotriol Monohydrate; Calcipotriolum Monohydricum). A white or almost white, crystalline powder. It is sensitive to light. A reversible isomerisation to pre-calcipotriol takes place in solution, depending on temperature and time. The activity is due to both compounds. Practically insoluble in water; freely soluble in alcohol; slightly soluble in dichloromethane. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

The most frequent adverse effect associated with calcipotriol is skin irritation and it should not therefore be applied to the facial area. Symptoms may include burning, itching, erythema, and dry skin, but stopping therapy is seldom necessary. Aggravation of psoriasis may occur. Hypercalcaemia has occurred during treatment with calcipotriol and although rapidly reversible on withdrawal, it should not be used in patients with disorders of calcium metabolism. Other rare adverse effects may include skin atrophy, hyperpigmentation, and photosensitivity. Patients should limit or avoid excessive exposure to both natural and artificial sunlight, because animal studies have suggested that topical calcipotriol may enhance the effect of UV radiation to induce skin tumours.

Effects on calcium homeostasis. Calcipotriol is a vitamin D derivative and therefore has the potential to cause hypercalcaemia and hypercalciuria. Up to December 1993, when about 150 000 patients in the UK had been treated with calcipotriol, the UK CSM had received 6 reports of hypercalcaemia and 2 of hypercalciuria.¹ Three of the patients with hypercalcaemia either had used doses in excess of the recommended maximum (see Uses and Administration, below) or had pustular or exfoliative psoriasis. Hypercalcaemia and hypercalciuria were reversible on withdrawal of calcipotriol. A study² investigating the effect of calcipotriol on urine calcium excretion found that use of the maximum recommended dose for 4 weeks produced increased urine calcium excretion, and the authors suggested that patients requiring the maximum dose of calcipotriol should be monitored for hypercalciuria before and during treatment. A review³ of the effects of vitamin D analogues on calcium homeostasis concluded that patients with unstable psoriasis are at particular risk of

The symbol † denotes a preparation not locally marketed