Pharmacokinetics

◊ Work *in vitro* and in *animals*[1] 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 sebosuppressive[1] 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.: Acnepas; Acnesan; Benzihex; Clidan B; Eclaran; Ecnagel PB; Paracne; PB Gel; Solugel; Tiltis; Vixiderm E; ***Austral.:*** Benzac; Brevoxyl; Clearasil Ultra; Neutrogena Acne Mask†; Oxy; PanOxyl; ***Austria:*** Akneroxid; Benzaknen; Brevoxyl; PanOxyl; Scherogel; ***Belg.:*** Akneroxid; Benzac; Brevoxyl; Pangel; ***Braz.:*** Acnase; Benzac AC; PanOxyl; Solugel; ***Canad.:*** Acetoxyl; Benoxyl; Benzac; Benzagel†; Clean & Clear Continuous Control; Clean & Clear Persa Gel; Clearasil B.P. Plus; Dermance†; 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; Antopar†; Basiron AC; Eclaran; Inoxitan†; Oxy; ***Fin.:*** Basiron; Brevoxyl; ***Fr.:*** Brevoxyl; Cutacnyl; Eclaran; Effacne; Pannogel; PanOxyl; ***Ger.:*** Aknederm Oxid†; Aknefug-oxid; Akneroxid; Benzaknen; Benzoyt; Benzperox; Brevoxyl; Cordes BPO; Dercome; Klinoxid; Marduk; PanOxyl; Sanoxit; Scherogel†; ***Gr.:*** Benzac-W; 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; Clearex Cover Up; Oxy; Oxy Sensitive; PanOxyl; ***Ital.:*** Benoxid; Benzac; PanOxyl; Reloxyl; ***Malaysia:*** Akneroxid; Benzac AC; Brevoxyl; PanOxyl; ***Mex.:*** Akeprul; Benoxyl; Benzac AC; Benzaderm; Oxy†; Solugel; ***Neth.:*** Akneroxid; Benzac; Clearamed†; Oxy; Tendox; ***Norw.:*** Basiron; Brevoxyl; PanOxyl; ***NZ:*** Benzac; Brevoxyl; Clearasil Ultra; PanOxyl; ***Philipp.:*** Benoxyl; Benzac AC; Brevoxyl; PanOxyl; Ultra Clearasil; ***Pol.:*** Akneroxid; Benzacne; Benzapur; Brevoxyl; Clearasil Ultra†; Lubexyl; ***Port.:*** Benacne; Benoxygel; Benzac; Eclaran; Lutsimed; PanOxyl; Peroxiben; ***Rus.:*** Basiron (Базирон); ***S.Afr.:*** Benoxyl; Benzac AC; Brevoxyl; Clearasil Benzoyl P; Dry & Clear; PanOxyl; ***Singapore:*** Acnacyl†; Akneroxid; Benzac; Brevoxyl; PanOxyl; ***Spain:*** Benoxygel; Oxiderma; PanOxyl; Peroxacne; Peroxiben; Solucel; Stop Espinilla Normaderm; ***Swed.:*** Basiron; Bexid†; Brevoxyl; Stioxyl†; ***Switz.:*** Acnefuge†; Akneroxid; Aknex; Basiron†; Benzac; Effacne†; Lubexyl; PanOxyl†; ***Thai.:*** Acnexyl†; Benzac; Brevoxyl; PanOxyl; ***Turk.:*** Aknefug BP; Aksil; Benzac AC; ***UK:*** Acnecide; Brevoxyl; Oxy; PanOxyl; ***USA:*** Acne Clear; Ambi 10; Benzac; Benziq; Brevoxyl; Clearasil; Clinac BPO; Del Aqua; Desquam; Fostex; NeoBenz; Oxy; PanOxyl; Triaz; Zaclir; ***Venez.:*** Acnex; Benoxyl†; Benzac AC; Ecuaderm; PanOxyl†; Solugel†.

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

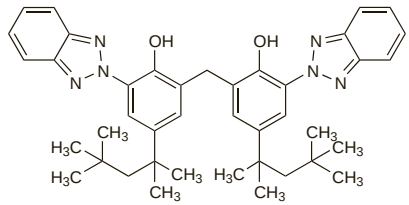
Bisoctrizole *(USAN, rINN)*

Bisoctrizol; Bisoctrizolum; FAT-75634; MBBT; Methylene Bis-Benzotriazolyl Tetramethylbutylphenol. 2,2′-Methylenebis[6-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol].

Бизоктризол

$C_{41}H_{50}N_6O_2$ = 658.9.

CAS — 103597-45-1.



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

Pharmacopoeias. In *US*.
USP 31 (Bisoctrizole). Store at a temperature of 20° to 25°, excursions permitted between 15° and 30°.

Profile

Bisoctrizole 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; Kalamin; 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†; Ducilamina; ***Spain:*** Talquistina.

Multi-ingredient: ***Arg.:*** Acuaderm; Caladryl; Calcusan; Dermithan; Irricutan; Northicalm; Pinklot; Piracalamina; Pruripelen†; Prurisedan; Prurisedan Rosa; Urtikalma; ***Austral.:*** Animine; Calaband; Calamine Lotion; Dermalife Plus; Quinaband†; ***Belg.:*** Caladryl; ***Braz.:*** Caladerm†; Caladryl; Calamed; Calamina; Calamyn; Dermamina; Dermdryl†; Solardril Composto; ***Canad.:*** Aveeno Anti-Itch; Caladryl; Calamine Antihistamine; ***Chile:*** Ivarest; Pruriced; ***Fr.:*** Gel de Calamine; Pruriced; ***Hong Kong:*** Cadramine-V; Caladryl; Calamine-D†; ***India:*** Caladryl; Siloderm; ***Indon.:*** Caladine; Caladryl; Calamec; Calarex; Minos; Regata; ***Irl.:*** Benadryl; RBC; Vasogen; ***Israel:*** Baby Paste + Chamomile; Calamine Lotion; Calatrim cum Sulphur†; Calatrim†; ***Ital.:*** Mavipiu†; ***Malaysia:*** Dermoplex Calamine; Twinkle Calamine; ***Mex.:*** Caladryl; Dermocare; Procicar; ***NZ:*** Am-O-Lin; Lacto Calamine†; ***Philipp.:*** Caladryl; Calmoseptine; ***Port.:*** Benaderma com Calamina; Benaderma Pruridermase†; Caladryl; Pruridermase†; Solpic†; ***S.Afr.:*** Biohist; Caladryl; Calasthetic; Histamed; Lacto Calamine†; ***Singapore:*** Acne Clear; ***Thai.:*** Ancamin†; Cadinyl; Cadramine; Caladerm†; Caladryl; Calanol; Calapro; Hista; Lanol; M-D; ***Turk.:*** Caladryl; Diyenil; Kalmosan; Tanol; ***UK:*** Calaband; Lacto Calamine; Quinaband†; RBC; Swarm; Vasogen; ***USA:*** Caladryl; Calamycin; Dome-Paste; Ivarest; RA Lotion; ***Venez.:*** Borocanfor; Caladryl†; Calaminol; Calaminol Simple†; Calasyl Original; Micofeet.

Calcipotriol *(BAN, rINN)*

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

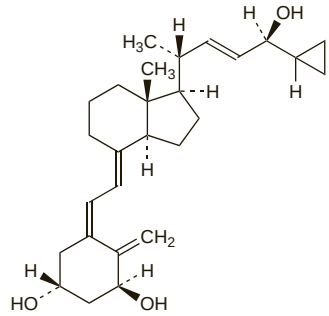
Кальципотриол

$C_{27}H_{40}O_3$ = 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 homoeostasis. 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 study[2] 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 review[3] of the effects of vitamin D analogues on calcium homoeostasis concluded that patients with unstable psoriasis are at particular risk of

toxicity from calcipotriol and that measurement of urine calcium excretion is a more sensitive indicator of toxicity than serum-calcium concentrations.

1. Committee on Safety of Medicines/Medicines Control Agency. Dovonex ointment (calcipotriol). *Current Problems* 1994; **20:** 3. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024457&RevisionSelectionMethod=LatestReleased (accessed 27/09/07)
2. Berth-Jones J, *et al.* Urine calcium excretion during treatment of psoriasis with topical calcipotriol. *Br J Dermatol* 1993; **129:** 411–14.
3. Bourke JF, *et al.* Vitamin D analogues in psoriasis: effects on systemic calcium homeostasis. *Br J Dermatol* 1996; **135:** 347–54.

Hyperpigmentation. Hyperpigmentation occurred at the site of calcipotriol application in 2 patients after use with PUVA-bath therapy (a topical psoralen with UVA irradiation) for psoriasis.[1] The effect persisted for at least 4 months in these patients. Hyperpigmentation of psoriatic plaques was also reported in a patient treated with topical calcipotriol and UVB phototherapy.[2] Abnormal lentiginous pigmentation of psoriatic plaques occurred in a patient treated with topical calcipotriol for psoriasis, which had worsened during chemotherapy for melanoma, and was still present 2 years after stopping chemotherapy and calcipotriol.[3] The authors also noted that melanoma can cause pigment changes and may have played a role in this case.

There has been some interest in the hyperpigmentary effects of calcipotriol for the possible treatment of vitiligo (see Skin Disorders, below).

1. Gläser R, *et al.* Hyperpigmentation due to topical calcipotriol and photochemotherapy in two psoriatic patients. *Br J Dermatol* 1998; **139:** 148–51.
2. Rütter A, Schwarz T. Ausgeprägte Hyperpigmentierung in psoriatischen Plaques als Folge einer Kombinationsbehandlung mit UVB-311 nm und Calcipotriol. *Hautarzt* 2000; **51:** 431–3.
3. Oláh J, *et al.* Pigment anomaly caused by calcipotriol in a subject with melanoma. *J Eur Acad Dermatol Venereol* 2004; **18:** 113–15.

Uses and Administration

Calcipotriol is a vitamin D_3 derivative. *In vitro* it appears to induce differentiation and to suppress proliferation of keratinocytes.

Calcipotriol is used in a cream or ointment for the management of plaque psoriasis and as a solution in the management of scalp psoriasis; the concentration of calcipotriol used is 0.005%. Applications should be made once or twice daily. No more than 100 g of cream or ointment, or 60 mL of scalp solution, should be applied in one week. If both are used, the limit is 60 g of cream or ointment with 30 mL of scalp solution, or 30 g of cream or ointment with 60 mL of scalp solution.

For the use of calcipotriol in children, see below.

Administration in children. Topical calcipotriol may be used in the management of plaque psoriasis in children. In the UK, the cream or ointment (0.005%) may be applied twice daily. The maximum applied in one week should be 50 g in children aged 6 to 12 years, and 75 g in children more than 12 years of age. The *BNFC* also suggests that under specialist supervision the scalp solution (0.005%) may be applied twice daily to children aged 6 years and over for the treatment of scalp psoriasis; no more than 30 mL of the solution should be applied in one week to those aged 6 to 12 years, with older children receiving a maximum of 45 mL in one week. When preparations are used together, the *BNFC* recommends a maximum total calcipotriol dose of 2.5 mg in any one week for children aged 6 to 12 years (e.g. 20 mL of the scalp solution with 30 g of the cream or ointment); in older children, the maximum is 3.75 mg in any one week (e.g. 30 mL of the scalp solution with 45 g of the cream or ointment). In the UK, the scalp solution is not licensed for use in children and the cream and ointment are not licensed for use in children under 6 years; however, safety and efficacy have been reported in small 8-week studies that have included children as young as 2 years old.[1-3] There are also a few case reports of topical calcipotriol use in infants with psoriasis, aged 3 months[4] and 6 months.[5]

1. Darley CR, *et al.* Safety and efficacy of calcipotriol ointment (Dovonex) in treating children with psoriasis vulgaris. *Br J Dermatol* 1996; **135:** 390–3.
2. Oranje AP, *et al.* Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol* 1997; **36:** 203–8.
3. Patrizi A, *et al.* Topical calcipotriol in childhood psoriasis. *Acta Derm Venereol* 1999; **79:** 477.
4. Travis LB, Silverberg NB. Psoriasis in infancy: therapy with calcipotriene ointment. *Cutis* 2001; **68:** 341–4.
5. Choi YJ, *et al.* Infantile psoriasis: successful treatment with topical calcipotriol. *Pediatr Dermatol* 2000; **17:** 242–4.

Skin disorders. Topical drugs are the treatment of first choice for *chronic plaque psoriasis* (p.1583). Calcipotriol, dithranol, and coal tar are commonly used for mild to moderate forms of the disorder. Calcipotriol inhibits cell proliferation and increases cell differentiation by binding to vitamin D receptors, thus inhibiting epidermal growth and returning some normality to the skin's structure. It is also possible that calcipotriol affects immunological and inflammatory processes in the skin.[1] Topical calcipotriol has been shown to be effective in mild to moderate chronic plaque psoriasis; it is at least as effective as dithranol, coal tar, and corticosteroids, and has been reported to be superior in a number of studies.[1,2] Calcipotriol is also more cosmetically acceptable than dithranol, which can stain, and coal tar, which can have an unpleasant smell. Benefits have been maintained with long-term use, and repeat courses are effective for the management of relapse. Although there are fewer studies in children, calcipotriol has been reported to be safe and effective in studies including children aged 2 to 15 years[1] (see also Administration in Children, above). Calcipotriol, applied as a topical solution, is also effective for *scalp psoriasis*.[3] When solutions of calcipotriol and betamethasone were compared for mild to moderate scalp psoriasis,[4] calcipotriol produced a satisfactory response, but betamethasone was more effective and was associated with less irritation of the scalp and face. Similar results were reported in a study comparing calcipotriol with clobetasol propionate in moderate to severe scalp psoriasis.[5] In a study of patients with *nail psoriasis* about half received benefit from calcipotriol ointment over a 3 to 5 month treatment period.[6] This result was similar to that found for patients treated with betamethasone and salicylic acid ointment.

Use of calcipotriol with other antipsoriatic drugs may be beneficial. The combination of calcipotriol with a topical corticosteroid is more effective than monotherapy with either of these.[1,7,8] Treatment for up to 4 weeks is usually effective and may be followed by maintenance calcipotriol monotherapy.[9] Topical calcipotriol with systemic therapies has also been tried. There is evidence that the response to oral ciclosporin or acitretin can be improved,[1] as can the response to phototherapy (UVB) or photochemotherapy (PUVA).[1,10] Combination therapy may also reduce the cumulative dose of acitretin, UVB, or PUVA required to achieve clearance or marked improvement of psoriasis, potentially reducing the risk of long-term adverse effects from these treatments.[1,10,11] However, because of the potential for the vehicle of topical calcipotriol preparations to block UV irradiation, they should be applied at least 2 hours before irradiation.[12] Despite promising reports from combination therapy using topical calcipotriol with systemic treatment, phototherapy, or photochemotherapy, a systematic review[13] found that although there can be a measurable additive effect, it may not be clinically significant in patients' own assessments.

A 2-week course of high-dose calcipotriol (up to 360 g of 0.005% ointment weekly) has been used for inpatient treatment of extensive psoriasis, followed by the usual recommended dose (up to 100 g weekly) for residual psoriasis.[14] Asymptomatic hypercalcaemia and hypercalciuria occurred in some patients, and the authors suggested that the monitoring of calcium homoeostasis is mandatory with this regimen (see also Effects on Calcium Homoeostasis, above). Relapse occurred in most patients within one year.

Beneficial results with calcipotriol have also been reported in small numbers of patients with various skin disorders[15] including *acrodermatitis continua of Hallopeau*, *confluent and reticulated papillomatosis*, *congenital ichthyosis*, *inflammatory linear verrucous epidermal nevus*, *lichen amyloidosis*, *morphea or linear scleroderma*, *pityriasis rubra pilaris*, *prurigo nodularis*, and *seborrhoeic dermatitis*. A small open study[16] has indicated that topical calcipotriol may be effective in the treatment of oral *leucoplakia* (see under Bleomycin, p.688). It has also been tried, alone or with UVA or UVB, or a topical corticosteroid, in the treatment of *vitiligo*[17-21] (see Pigmentation Disorders, p.1582), but results have been mixed.

1. Scott LJ, *et al.* Calcipotriol ointment: a review of its use in the management of psoriasis. *Am J Clin Dermatol* 2001; **2:** 95–120.
2. Ashcroft DM, *et al.* Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. *BMJ* 2000; **320:** 963–7.
3. Thaçi D, *et al.* Calcipotriol solution for the treatment of scalp psoriasis: evaluation of efficacy, safety and acceptance in 3,396 patients. *Dermatology* 2001; **203:** 153–6.
4. Klaber MR, *et al.* Comparative effects of calcipotriol solution (50 micrograms/mL) and betamethasone 17-valerate solution (1 mg/mL) in the treatment of scalp psoriasis. *Br J Dermatol* 1994; **131:** 678–83.
5. Reygagne P, *et al.* Clobetasol propionate shampoo 0.05% and calcipotriol solution 0.005%: a randomized comparison of efficacy and safety in subjects with scalp psoriasis. *J Dermatol Treat* 2005; **16:** 31–6.
6. Tosti A, *et al.* Calcipotriol ointment in nail psoriasis: a controlled double-blind comparison with betamethasone dipropionate and salicylic acid. *Br J Dermatol* 1998; **139:** 655–9.
7. Fenton C, Plosker GL. Calcipotriol/betamethasone dipropionate: a review of its use in the treatment of psoriasis vulgaris. *Am J Clin Dermatol* 2004; **5:** 463–78.
8. Kragballe K, van de Kerkhof PCM. Consistency of data in six phase III clinical studies of a two-compound product containing calcipotriol and betamethasone dipropionate ointment for the treatment of psoriasis. *J Eur Acad Dermatol Venereol* 2006; **20:** 39–44.
9. White S, *et al.* Use of calcipotriene cream (Dovonex cream) following acute treatment of psoriasis vulgaris with the calcipotriene/betamethasone dipropionate two-compound product (Taclonex): a randomized, parallel-group clinical trial. *Am J Clin Dermatol* 2006; **7:** 177–84.
10. Torras H, *et al.* A combination therapy of calcipotriol cream and PUVA reduces the UVA dose and improves the response of psoriasis vulgaris. *J Dermatol Treat* 2004; **15:** 98–103.
11. Woo WK, McKenna KE. Combination TL01 ultraviolet B phototherapy and topical calcipotriol for psoriasis: a prospective randomized placebo-controlled clinical trial. *Br J Dermatol* 2003; **149:** 146–50.
12. De Rie MA, *et al.* Calcipotriol ointment and cream or their vehicles applied immediately before irradiation inhibit ultraviolet B-induced erythema. *Br J Dermatol* 2000; **142:** 1160–5.
13. Ashcroft DM, *et al.* Combination regimens of topical calcipotriene in chronic plaque psoriasis: systematic review of efficacy and tolerability. *Arch Dermatol* 2000; **136:** 1536–43.
14. Bleiker TO, *et al.* Long-term outcome of severe chronic plaque psoriasis following treatment with high-dose topical calcipotriol. *Br J Dermatol* 1998; **139:** 285–6.
15. Holm EA, Jemec GBE. The therapeutic potential of calcipotriol in diseases other than psoriasis. *Int J Dermatol* 2002; **41:** 38–43.
16. Femiano F, *et al.* Oral leukoplakia: open trial of topical therapy with calcipotriol compared with tretinoin. *Int J Oral Maxillofac Surg* 2001; **30:** 402–6.
17. Ameen M, *et al.* Topical calcipotriol as monotherapy and in combination with psoralen plus ultraviolet A in the treatment of vitiligo. *Br J Dermatol* 2001; **145:** 476–9.
18. Chiaverini C, *et al.* Treatment of vitiligo by topical calcipotriol. *J Eur Acad Dermatol Venereol* 2002; **16:** 137–8.
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21. Arca E, *et al.* Narrow-band ultraviolet B as monotherapy and in combination with topical calcipotriol in the treatment of vitiligo. *J Dermatol* 2006; **33:** 338–43.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Daivonex; Dermocal†; ***Austral.:*** Daivonex; ***Austria:*** Psorcutan; ***Belg.:*** Daivonex; ***Braz.:*** Daivonex; ***Canad.:*** Dovonex; ***Chile:*** Daivonex; ***Cz.:*** Daivonex; Psorcutan†; ***Denm.:*** Daivonex; ***Fin.:*** Daivonex; ***Fr.:*** Daivonex; ***Ger.:*** Daivonex; Psorcutan; ***Gr.:*** Cipocal; Dovonex; F-Psorin; Psoraffect; ***Hong Kong:*** Daivonex; ***Hung.:*** Daivonex; ***India:*** Daivonex; ***Indon.:*** Daivonex; ***Irl.:*** Dovonex; ***Israel:*** Daivonex; ***Ital.:*** Daivonex; Psorcutan; ***Jpn:*** Dovonex; ***Malaysia:*** Daivobet; Daivonex; ***Mex.:*** Daivonex; Eukadar; ***Neth.:*** Daivonex; ***Norw.:*** Daivonex; ***NZ:*** Daivonex; ***Philipp.:*** Daivonex; ***Pol.:*** Daivonex; ***Port.:*** Daivonex; ***Rus.:*** Daivonex (Дайвонекс); ***S.Afr.:*** Dovonex; ***Singapore:*** Daivonex; ***Spain:*** Daivonex; ***Swed.:*** Daivonex; ***Switz.:*** Daivonex; ***Thai.:*** Daivonex; ***Turk.:*** Psorcutan; ***UK:*** Dovonex; ***USA:*** Dovonex; ***Venez.:*** Daivonex†.

Multi-ingredient: ***Austral.:*** Daivobet; ***Austria:*** Psorcutan Beta; ***Belg.:*** Dovobet; ***Braz.:*** Daivobet; ***Canad.:*** Dovobet; ***Cz.:*** Daivobet; ***Denm.:*** Daivobet; ***Fin.:*** Daivobet; ***Fr.:*** Daivobet; ***Ger.:*** Daivobet; Psorcutan Beta; ***Gr.:*** Dovobet; ***Hong Kong:*** Daivobet; ***Hung.:*** Daivobet; ***Indon.:*** Daivobet; ***Irl.:*** Dovobet; ***Israel:*** Daivobet; ***Ital.:*** Dovobet; Token; ***Mex.:*** Daivobet; ***Neth.:*** Dovobet; ***Norw.:*** Daivobet; ***NZ:*** Daivobet; ***Philipp.:*** Daivobet; ***Pol.:*** Daivobet; ***Port.:*** Daivobet; ***Rus.:*** Daivobet (Дайвобет); ***Singapore:*** Daivobet; ***Spain:*** Daivobet; ***Swed.:*** Daivobet; ***Switz.:*** Daivobet; ***Thai.:*** Daivobet; ***UK:*** Dovobet; ***USA:*** Taclonex.

Centella

Azijinės centelės žolė; Ázsiai gázlófű; Centellae asiaticae herba; Herba Centellae; Hidrocótilo; Hydrocotyle; Indian Pennywort; Nat' centely asijské; Rohtosammakonputki; Sallatsspikblad.

Центелла Азиатская (*Centella asiatica*)

CAS — 18449-41-7 (madecassic acid); 464-92-6 (asiatic acid); 16830-15-2 (asiaticoside).

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).

Ph. Eur. 6.2 (Centella). The dried, fragmented aerial parts of *Centella asiatica*. It contains not less than 6% of total triterpenoid derivatives, expressed as asiaticoside, calculated with reference to dried drug. Protect from light.

Profile

Centella contains madecassic acid, asiatic acid, and asiaticoside. It has been used topically and orally in the management of wounds, ulcers, and keloid scars.

The names gotu kola, gotu cola, and gota kola are used for *Centella asiatica* (=*Hydrocotyle asiatica*) in herbal medicine. Centella is also used in homoeopathic medicine.

Adverse effects. Contact dermatitis has been reported with the topical use of centella.[1] There is also a report of 3 cases of hepatotoxicity associated with ingestion of centella, all presenting with jaundice, painful hepatomegaly, and granulomatous hepatitis with areas of necrosis.[2]

1. Gonzalo Garijo MA, *et al.* Allergic contact dermatitis due to Centella asiatica: a new case. *Allergol Immunopathol (Madr)* 1996; **24:** 132–4.
2. Jorge OA, Jorge AD. Hepatotoxicity associated with the ingestion of Centella asiatica. *Rev Esp Enferm Dig* 2005; **97:** 115–24.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Gotu Kola†; Pertusan†; Remiderm†; ***Austria:*** Madecassol; ***Belg.:*** Madecassol; ***Braz.:*** Centelax; Centella-Vit; ***Chile:*** Celulase; Celulase Plus; Centabel; Escar T; Madecassol; ***Fr.:*** Madecassol; ***Gr.:*** Madecassol; ***Hong Kong:*** Madecassol; ***Indon.:*** Fitocassol; Lanakeloid; Madecassol; ***Ital.:*** Centellase; ***Malaysia:*** Lanakeloid; ***Mex.:*** Madecassol; ***Port.:*** Madecassol; ***Singapore:*** Centellase; Centica; ***Spain:*** Blastoestimulina; ***Thai.:*** Madecassol†; ***Turk.:*** Madecassol; ***Venez.:*** Litonate; Madecassol; Triffadiane†.

Multi-ingredient: ***Arg.:*** Celu-Atlas; Centella Asiatica Compuesta; Centella Asiatica Diates; Centella Asiatica Vital; Centella Incaico; Centella Queen Complex; Centella Queen Reductora; Centellacrom; Centellase de Centella Queen; Centellase Gel; Clevosan; Enlinea†; Estri-Atlas; Garcinol Max; Ginal Cent; Ginkan; Herbaccion Celfin; Lidersoft†; Linfol Cicatrizante; Lociherp Liposomas Antiage; Lociherp Liposomas Vitaminado; Mailen; Moragen; Nio Marine; No-Gras; Ovumix; Pentol; Redudiet; Septigyn; Vagicural Plus; Venoful; VNS 45; ***Austral.:*** Extralife Leg-Care; ***Braz.:*** Composto Anticelulitico†; Composto Emagrecedor†; Derm'attive 10†; Emagrevit†;