Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Debrisan†; ***Ger.:*** Debrisorb†; ***Hong Kong:*** Debrisan†; ***Hung.:*** Crupodex†; ***Irl.:*** Debrisan†; ***Ital.:*** Debrisan; ***Mex.:*** Debrisan†; ***Pol.:*** Acudex; ***S.Afr.:*** Debrisan; ***UK:*** Debrisan†; ***USA:*** Debrisan.

Multi-ingredient: ***UK:*** Zuidex; ***USA:*** Deflux.

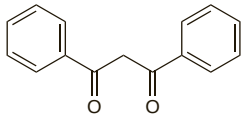
Dibenzoylmethane

Dibenzoilmetano. 1,3-Diphenyl-1,3-propanedione.

Дибензоилметан

$C_{15}H_{12}O_2$ = 224.3.

CAS — 120-46-7.



Profile

Dibenzoylmethane is a sunscreen (p.1576) with actions similar to those of avobenzone (p.1589). It is effective against UVA light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

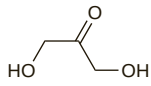
Dihydroxyacetone

DHA; Dihidroxiacetona; Ketotriose. 1,3-Dihydroxypropan-2-one.

Дигидроксиацетон

$C_3H_6O_3$ = 90.08.

CAS — 96-26-4.



NOTE. DHA is also used as a synonym for docosahexaenoic acid (p.1362).

Pharmacopoeias. In *US.*

USP 31 (Dihydroxyacetone). A white to off-white crystalline powder. The monomeric form is freely soluble in water, in alcohol, and in ether; the dimeric form is freely soluble in water, soluble in alcohol, and sparingly soluble in ether. A 5% solution in water has a pH between 4.0 and 6.0. Store at a temperature of 8° to 15° in airtight containers.

Adverse Effects and Precautions

Skin irritation from dihydroxyacetone occurs rarely; rashes and allergic dermatitis have been reported. Contact with eyes, abraded skin, and clothing should be avoided.

Uses and Administration

Application to the skin of preparations containing dihydroxyacetone slowly produces a brown coloration similar to that caused by exposure to the sun, probably due to a reaction with the amino acids of the skin.

A single application may give rise to a patchy appearance; progressive darkening of the skin results from repeated use until a point is reached when the maximum effect is achieved. If the treatment is stopped the colour starts to fade after about 2 days and disappears completely within 8 to 14 days as the external epidermal cells are lost by normal attrition.

Preparations usually contain 5% of dihydroxyacetone and have been used to camouflage vitiligo (see Pigmentation Disorders, p.1582) or to produce an artificial suntan. Some preparations include sunscreens since the pigmentation produced gives no protection against sunburn.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Autohelios†; Eurocolor Sin Sol; Ikx Autobronceante; Leche Autobronceadora†; Lelco sin Sol; ***Austral.:*** Le Tan Fast Extra Dark†; Le Tan Fast Self Tan†; Vitadye; ***Braz.:*** Autohelios; ***Chile:*** Fotoprotectores; Leche Autobronceadora Cara Y Cuerpo; Neutrogena Bronceador; ROC Minesol Bronze; Sans Soleil Skin Ceuticals†; ***Malaysia:*** Vitadye†; ***Mex.:*** Dermacrom; ***USA:*** Chromelin Complexion Blender.

Multi-ingredient: ***Arg.:*** Fotosol Ultra Autobronceante; Polysianes Autobronceante; ***Austral.:*** Le Tan Fast Plus†; ***Braz.:*** Sunmax Autobronzeador; ***UK:*** ViTicolor; ***USA:*** QT.

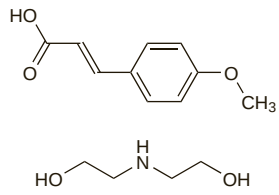
Diolamine Methoxycinnamate

Diolamine *p*-Methoxycinnamate *(pINNM)*; DEA-Methoxycinnamate; Diethanolamine Methoxycinnamate; Diolamina metoxicinnamato; Diolamine Méthoxycinnamate; Diolaminum Metoxicinnamatum. *p*-Methoxycinnamic acid compound with 2,2′-iminodiethanol (1:1).

Диоламин Метоксисинамат

$C_{10}H_{10}O_3.C_4H_{11}NO_2$ = 283.3.

CAS — 56265-46-4.



Profile

Diolamine methoxycinnamate, a compounded substituted cinnamate, is a sunscreen (p.1576) with actions similar to those of octinoxate (p.1608). It is effective against UVB light (for definitions, see p.1580).

Preparations

Proprietary Preparations some preparations are listed in Part 3.

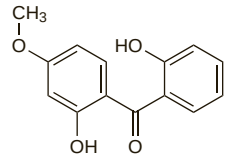
Dioxybenzone *(USAN, rINN)*

Benzofenon-8; Benzophenone-8; Dioxibenzona; Dioxybenzonum; NSC-56769. 2,2′-Dihydroxy-4-methoxybenzophenone.

Диоксибензон

$C_{14}H_{12}O_4$ = 244.2.

CAS — 131-53-3.



Pharmacopoeias. In *US.*

USP 31 (Dioxybenzone). A yellow powder. Practically insoluble in water; freely soluble in alcohol and in toluene. Store in airtight containers. Protect from light.

Profile

Dioxybenzone, a substituted benzophenone, is a sunscreen (p.1576) with actions similar to those of oxybenzone (p.1608). It is effective against UVB and some UVA light (for definitions, see p.1580).

Preparations

USP 31: Dioxybenzone and Oxybenzone Cream.

Proprietary Preparations some preparations are listed in Part 3.

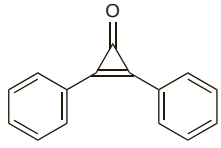
Diphencyprone

Difenciprona. 2,3-Diphenylcyclopropenone-1.

Дифенципрон

$C_{15}H_{10}O$ = 206.2.

CAS — 886-38-4.



Profile

Diphencyprone has been applied as a contact sensitiser for the treatment of alopecia. It has also been tried in warts.

Adverse effects. Diphencyprone is considered to lack serious adverse effects but some patients may not be able to tolerate the induced hypersensitivity reaction. There have been reports of generalised urticaria and dermographism, sometimes severe, following the use of diphencyprone.[1-5] In another case, a severe reaction of urticaria and dermographism, which lasted several months, occurred after the initial sensitisation dose.[6] Allergy to diphencyprone has been reported in medical and nursing staff in spite of taking protective precautions during its application.[7] A patient who received diphencyprone treatment for warts developed a widespread pruritic rash and palpitations due to ventricular extrasystoles.[1] Vitiligo has also been reported in patients treated with diphencyprone[8-10] and it has been suggested that this might be due to unmasking of subclinical vitiligo.[8,9] Erythema multiforme-like eruptions have been associated with the topical application of diphencyprone.[11,12]

1. Lane PR, Hogan DJ. Diphencyprone. *J Am Acad Dermatol* 1988; **19:** 364–5.
2. Tosti A, *et al.* Contact urticaria during topical immunotherapy. *Contact Dermatitis* 1989; **21:** 196–7.
3. Skrebova N, *et al.* Severe dermographism after topical therapy with diphenylcyclopropenone for alopecia universalis. *Contact Dermatitis* 2000; **42:** 212–15.
4. Francomano M, Seidenari S. Urticaria after topical immunotherapy with diphenylcyclopropenone. *Contact Dermatitis* 2002; **47:** 310–11.
5. Short KA, Higgins EM. Urticaria as a side-effect of diphencyprone therapy for resistant viral warts. *Br J Dermatol* 2005; **152:** 583–5.
6. Alam M, *et al.* Severe urticarial reaction to diphenylcyclopropenone therapy for alopecia areata. *J Am Acad Dermatol* 1999; **40:** 110–12.
7. Shah M, *et al.* Hazards in the use of diphencyprone. *Br J Dermatol* 1996; **134:** 1153.
8. Hatzis J, *et al.* Vitiligo as a reaction to topical treatment with diphencyprone. *Dermatologica* 1988; **177:** 146–8.
9. Duhra P, Foulds IS. Persistent vitiligo induced by diphencyprone. *Br J Dermatol* 1990; **123:** 415–16.
10. Henderson CA, Ilchyshyn A. Vitiligo complicating diphencyprone sensitization therapy for alopecia universalis. *Br J Dermatol* 1995; **133:** 496–7.
11. Perret CM, *et al.* Erythema multiforme-like eruptions: a rare side effect of topical immunotherapy with diphenylcyclopropenone. *Dermatologica* 1990; **180:** 5–7.
12. Oh C-W, *et al.* Bullous erythema multiforme following topical diphenylcyclopropenone application. *Contact Dermatitis* 1998; **38:** 220–1.

Alopecia. Diphencyprone has been used as a contact sensitiser in the treatment of various forms of alopecia (p.1577) including areata, totalis, and universalis. Case series reports generally describe treatment of adults, but some groups have also included adolescents and children, and some have reported solely on treatment in children.[1,2]

Initial sensitisation is usually achieved by applying a 2% solution of diphencyprone in acetone to a small area of scalp, which may be repeated if necessary beneath plastic occlusion if adequate sensitisation is not produced. Thereafter, weaker concentrations are applied once weekly and gradually increased in strength to produce erythema and pruritus for 36 to 48 hours post-therapy. Concentrations that have been used vary between reports and the first treatment application may be as dilute as 0.00001%, with further applications gradually increased to up to 2%. Only one side of the scalp is treated until the optimum concentration is found, in order to prevent a widespread adverse reaction. Once hair regrowth has started on the treated side the applications may be extended to the entire scalp.[1-8] As well as erythema and pruritus, patients usually experience transient eczema and regional lymph node swelling.[2,5,7,8]

Hair regrowth may not start for several months,[4,6,8] and the required duration of therapy can vary considerably; at least 8 months of treatment may be required,[3,6] and up to 12 months[1,2] or more[4,6] has been reported. Not all patients will respond to treatment and reported response rates vary, although these have probably been influenced by the different definitions used for complete, partial, and no response. Overall, however, regrowth of hair can occur in up to about 70% of patients, with around half of these having complete regrowth.[1,4,6-8] Some reports have attempted to determine which factors might be associated with clinical response to diphencyprone. There is disagreement between studies but some possible unfavourable prognostic factors include extensive involvement,[4,6,8] younger age at onset,[8] longer disease duration before treatment,[5,7] and a history of atopic eczema.[4,7] The need for high diphencyprone concentrations and prolonged therapy have also been associated with a less favourable outcome.[8]

Despite these rates of response a significant number of patients will relapse, either during or after stopping treatment, and retreatment may be considered.[4,6,7] The time to relapse can be variable. Remission in a small group of complete responders ranged from 1 month to 2 years after stopping therapy.[4] Another group of patients who achieved total regrowth of hair were able to stop treatment with diphencyprone for a mean of 15 months without relapse[9] while a further group maintained satisfactory hair growth for a mean follow-up period of 19.8 months.[5]

1. MacDonald Hull S, *et al.* Alopecia areata in children: response to treatment with diphencyprone. *Br J Dermatol* 1991; **125:** 164–8.
2. Schuttelaar M-L, *et al.* Alopecia areata in children: treatment with diphencyprone. *Br J Dermatol* 1996; **135:** 581–5.
3. MacDonald Hull S, Cunliffe WJ. Successful treatment of alopecia areata using the contact allergen diphencyprone. *Br J Dermatol* 1991; **124:** 212–13.
4. Hoting E, Boehm A. Therapy of alopecia areata with diphencyprone. *Br J Dermatol* 1992; **127:** 625–9.
5. Gordon PM, *et al.* Topical diphencyprone for alopecia areata: evaluation of 48 cases after 30 months' follow-up. *Br J Dermatol* 1996; **134:** 869–71.

6. Pericin M, Trüeb RM. Topical immunotherapy of severe alopecia areata with diphenylcyclopropenone: evaluation of 68 cases. *Dermatology* 1998; **196:** 418–21.
7. Cotellessa C, *et al.* The use of topical diphenylcyclopropenone for the treatment of extensive alopecia areata. *J Am Acad Dermatol* 2001; **44:** 73–6.
8. Wiseman MC, *et al.* Predictive model for immunotherapy of alopecia areata with diphencyprone. *Arch Dermatol* 2001; **137:** 1063–8.
9. van der Steen PHM, *et al.* Topical immunotherapy for alopecia areata: re-evaluation of 139 cases after an additional follow-up period of 19 months. *Dermatology* 1992; **184:** 198–201.

Warts. Diphencyprone has been tried in the treatment of recalcitrant warts. The successful treatment of digital or plantar warts in 42 of 60 patients has been described.[1] The patients were initially sensitised with a 2% topical solution of diphencyprone in acetone, then the warts treated every 1 to 4 weeks with solutions ranging from 0.01 to 6%. In another series,[2] diphencyprone in a paraffin ointment was effective in the clearance of palmar, plantar, palmoplantar, and periungual warts in 135 of 154 patients. A concentration of diphencyprone 2% was used for the initial sensitisation, and concentrations of 0.5 to 4% were used for treatment once every 3 weeks. After initial sensitisation with diphencyprone 2% in acetone, a preparation of diphencyprone with salicylic acid in white soft paraffin applied every night as tolerated was reported to be successful in 44 of 50 patients treated for palmoplantar warts.[3] The concentration of diphencyprone in the ointment ranged from 0.01 to 0.2%, and the concentration of salicylic acid was 15%.

1. Buckley DA, *et al.* Recalcitrant viral warts treated by diphencyprone immunotherapy. *Br J Dermatol* 1999; **141:** 292–6.
2. Upitis JA, Krol A. The use of diphenylcyclopropenone in the treatment of recalcitrant warts. *J Cutan Med Surg* 2002; **6:** 214–17.
3. Armour K, Orchard D. Treatment of palmoplantar warts with a diphencyprone and salicylic acid ointment. *Australas J Dermatol* 2006; **47:** 182–5.

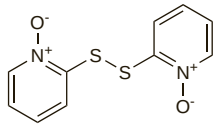
Dipyrithione *(USAN, rINN)*

Bispiriyon; Bispyrithione; Dipiritiona; Dipyrithionum; OMDS; Piriyon Disülfit; Pyrithione Disulfide. 2,2′-Dithiodipyridine 1,1′-dioxide.

Дипиритион

$C_{10}H_8N_2O_2S_2$ = 252.3.

CAS — 3696-28-4.



Profile

Dipyrithione is reported to have antibacterial and antifungal properties and is included in preparations for the treatment of dandruff.

Preparations

Proprietary Preparations (details are given in Part 3)

Turk.: Perkapil.

Multi-ingredient: ***Canad.:*** Dan-Tar Plus; Polytar AF; ***Switz.:*** Crimanex.

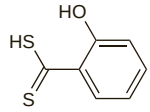
Dithiosalicylic Acid

Ditiosalicílico, ácido. 2-Hydroxybenzenecarbodithioic acid.

Дитиосалициловая Кислота

$C_7H_6OS_2$ = 170.3.

CAS — 527-89-9.



Profile

Dithiosalicylic acid has been used in multi-ingredient preparations used topically for the treatment of acne and seborrhoeic dermatitis.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Ital.:*** Sacnel.

Dithranol *(BAN, rINN)*

Anthralin; Antralin; Dioxyanthranol; Dithranolum; Ditranol; Ditranoli; Ditranolis. 1,8-Dihydroxyanthrone; 1,8-Dihydroxy-9(10*H*)-anthracenone.

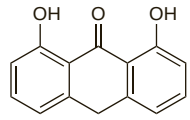
Дитранол

$C_{14}H_{10}O_3$ = 226.2.

CAS — 1143-38-0 (dithranol); 16203-97-7 (dithranol triacetate).

ATC — D05AC01.

ATC Vet — QD05AC01.



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

Ph. Eur. 6.2 (Dithranol). A yellow or brownish-yellow, crystalline powder. Practically insoluble in water; slightly soluble in alcohol; sparingly soluble in acetone; soluble in dichloromethane; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Anthralin). A yellowish-brown, odourless, crystalline powder. Insoluble in water; slightly soluble in alcohol, in ether, and in glacial acetic acid; soluble in acetone, in chloroform, in benzene, and in solutions of alkali hydroxides. The filtrate from a suspension in water is neutral to litmus. Store at a temperature of 8° to 15° in airtight containers. Protect from light.

Stability. The stability of dithranol has been studied in a number of bases and vehicles.[1-4] The weaker preparations of dithranol may be less stable.[1,3,4] Salicylic acid is included in dithranol preparations as an antoxidant and its inclusion in pastes also containing zinc oxide prevents their discoloration due to the inactivation of dithranol by zinc oxide.[5] However, zinc oxide or starch can be omitted from dithranol pastes without loss of effectiveness provided stiffness is maintained.[5] Addition of ascorbic or oxalic acid may improve dithranol's stability in '*Unguentum Merck*' but salicylic acid appears to be ineffective.[1] The effect of salicylic acid on the instability of dithranol in yellow soft paraffin is variable[1,2] and its inclusion has been questioned as it can be irritant and percutaneous absorption can be significant.[1] Dithranol is relatively stable in white soft paraffin.[1]

The application of any type of heat and contact with metal spatulas should be avoided during the manufacture of dithranol pastes[6] and if milling facilities are not available dithranol can be incorporated into Lassar's paste by dissolving it first in chloroform.[5]

1. Green PG, *et al.* The stability of dithranol in various bases. *Br J Dermatol* 1985; **113** (suppl 29): 26.
2. Lee RLH. Stability of dithranol (anthralin) in various vehicles. *Aust J Hosp Pharm* 1987; **17:** 254–8.
3. Hiller C, *et al.* How stable is dithranol? An investigation into the degradation of different dithranol formulations. *Pharm Pract* 1995; **5:** 428–31.
4. Thoma K, Holzmann C. Stabilization of dithranol in topical formulations. *Acta Pharm Hung* 1998; **68:** 313–21.
5. Comaish S, *et al.* Factors affecting the clearance of psoriasis with dithranol (anthralin). *Br J Dermatol* 1971; **84:** 282–9.
6. *PSGB Lab Report P/79/1* 1979.

Adverse Effects and Precautions

Dithranol may cause a burning sensation especially on perilesional skin. Patients with fair skin may be more sensitive than those with dark skin. It is irritant to the eyes and mucous membranes. Use on the face, skin flexures, and genitals should be avoided. Hands should be washed after use.

Dithranol should not be used for acute or pustular psoriasis or on inflamed skin. It stains skin, hair, some fabrics, plastics, and enamel. Staining of bathroom ware may be less of a problem with creams than ointments. Stains on skin and hair slowly disappear on cessation of treatment.

Handling. Dithranol is a powerful irritant and should be kept away from the eyes and tender parts of the skin.

Uses and Administration

Dithranol is used in the treatment of subacute and chronic psoriasis, usually in one of two ways.

Conventional treatment is commonly started with an ointment or paste containing 0.1% dithranol (0.05% in very fair patients) applied for a few hours; the strength is gradually increased as necessary to 0.5%, occasionally to 1%, and the duration of contact extended to overnight periods or longer. The preparation is sparingly and accurately applied to the lesions only. If, on initial treatment, lesions spread or excessive irritation occurs, the concentration of dithranol or the frequency of application should be reduced; if necessary, treatment should be stopped. After each treatment period the patient should bathe or shower to remove any residual dithranol.

For *short-contact therapy* dithranol is usually applied in a soft basis to the lesions for up to 60 minutes daily, before being washed off. As with conventional treatment the strength used is gradually increased from 0.1 to 2% but strengths up to 5% have been used. Surrounding unaffected skin may be protected by white soft paraffin.

Treatment for psoriasis should be continued until the skin is entirely clear. Intermittent courses may be needed to maintain the response. Treatment schedules often involve coal tar and UV irradiation (preferably UVB) before the application of dithranol (see below). Salicylic acid is included in many topical preparations of dithranol.

A cream containing dithranol triacetate has been used similarly to dithranol in conventional treatment of psoriasis.

Alopecia. Dithranol cream (0.5 to 1%) applied for 20 to 60 minutes to the scalp and then washed off, has been found to be of benefit in the treatment of alopecia areata (p.1577). However, at least 6 months of treatment may be required for a cosmetically acceptable result.[1] The response rate has, however, been difficult to evaluate because of the small number of reports, and although it has been widely prescribed for limited patchy alopecia areata, some guidelines conclude that there is no convincing evidence of efficacy.[2]

1. Meidan VM, Touitou E. Treatments for androgenetic alopecia and alopecia areata: current options and future prospects. *Drugs* 2001; **61:** 53–69.
2. MacDonald Hull SP, *et al.* British Association of Dermatologists. Guidelines for the management of alopecia areata. *Br J Dermatol* 2003; **149:** 692–9. Also available at: http://www.bad.org.uk/healthcare/guidelines/Alopecia_Areata.pdf (accessed 27/09/07)

Psoriasis. Dithranol used alone or with coal tar, (with or without ultraviolet light), continues to be one of the drugs of first-line treatment for psoriasis (p.1583). It is particularly suited to the treatment of stable chronic plaque psoriasis but unlike coal tar, is irritant to healthy skin and care is required to ensure that it is only applied to lesions. Treatment with dithranol is therefore more feasible when the plaques are large, or few in number. Use with coal tar may help to reduce the irritant effects of dithranol without affecting efficacy. Traditional treatment with dithranol is time consuming and more suitable for use on hospital inpatients. Dithranol formulated in stiff preparations such as Lassar's paste to minimise spreading to perilesional skin is left on overnight covered with a suitable dressing and washed off the next day. Treatment is usually started with a concentration of 0.1% (0.05% in fair-skinned patients) and gradually increased according to the response and irritation produced. Cream formulations may be less effective but are more suitable for domestic use. Short-contact therapy in which concentrations of up to 5% of dithranol are applied daily for up to 1 hour is more suitable for use on an outpatient basis and there appears to be little reduction in efficacy; irritation and staining may also be reduced.

Dithranol is also used with UVB phototherapy and there have been many modifications of the original Ingram's regimen in which dithranol is applied after bathing in a tar bath and exposure to ultraviolet light. Inpatient stays of up to 3 weeks may be required but long periods of remission can be obtained.

Reviews.

1. Mahrle G. Dithranol. *Clin Dermatol* 1997; **15:** 723–37.

Preparations

BP 2008: Dithranol Cream; Dithranol Ointment; Dithranol Paste;
USP 31: Anthralin Cream; Anthralin Ointment.

Proprietary Preparations (details are given in Part 3)

Austral.: Dithrocream†; Micanol†; ***Austria:*** Micanol; ***Belg.:*** Micanol†; ***Canad.:*** Anthraforte; Anthranol; Anthrascalp; Micanol†; ***Denm.:*** Micanol†; ***Fin.:*** Micanol†; ***Ger.:*** Micanol; ***Hong Kong:*** Micanol†; ***India:*** Psorinol; ***Indon.:*** Anthramed; ***Irl.:*** Dithrocream; Micanol†; ***Israel:*** Dithrocream; Micanol; ***Ital.:*** Psoriderm; Timicolid†; ***Neth.:*** Psoricreme; Psoristick; ***Norw.:*** Micanol; ***NZ:*** Micanol; ***Port.:*** Micanol; ***S.Afr.:*** Anthranol; ***Spain:*** Micanol; ***Swed.:*** Micanol; ***Thai.:*** Micanol†; ***UK:*** Dithrocream; Micanol; ***USA:*** Anthra-Derm†; Dritho-Scalp; Drithocreme†; Psoriatec.

Multi-ingredient: ***Austral.:*** Dithrasal; ***Fr.:*** Anaxeryl; ***Ger.:*** Psoradexan; Psoralon MT; ***Hong Kong:*** Dithrasal; ***India:*** Derobin Skin; ***Singapore:*** Dithrasal; ***Spain:*** Lapices Epiderm Metadier; ***Turk.:*** Psoraks; ***UK:*** Psorin.