tion,[3,10] gastrointestinal effects,[2-4,10,11] and flushing.[2-4,10,11] There has been a report of exanthema in a patient receiving dimethyl fumarate for lichen planus.[12]

1. van Loenen AC, *et al.* Fumaarzuurtherapie: van fictie tot werkelijkheid? *Pharm Weekbl* 1989; **124:** 894–900.
2. Kolbach DN, Nieboer C. Fumaric acid therapy in psoriasis: a long-term retrospective study on the effect of fumaric acid combination (FAC-EC) therapy and dimethyl-fumaric acid ester (DMFAE) monotherapy. *Br J Dermatol* 1990; **123:** 534–5.
3. Nugteren-Huying WM, *et al.* Fumaric acid therapy for psoriasis: a randomized, double-blind, placebo-controlled study. *J Am Acad Dermatol* 1990; **22:** 311–12.
4. Altmeyer PJ, *et al.* Antipsoriatic effect of fumaric acid derivatives: results of a multicenter double-blind study in 100 patients. *J Am Acad Dermatol* 1994; **30:** 977–81.
5. Mrowietz U, *et al.* Treatment of severe psoriasis with fumaric acid esters: scientific background and guidelines for therapeutic use. *Br J Dermatol* 1999; **141:** 424–9.
6. Ständer H, *et al.* Efficacy of fumaric acid ester monotherapy in psoriasis pustulosa palmoplantaris. *Br J Dermatol* 2003; **149:** 220–2.
7. Anonymous. Fumaric acid derivatives and nephrotoxicity. *WHO Drug Inf* 1990; **4:** 28.
8. Hoefnagel JJ, *et al.* Long-term safety aspects of systemic therapy with fumaric acid esters in severe psoriasis. *Br J Dermatol* 2003; **149:** 363–9.
9. Harries MJ, *et al.* Fumaric acid esters for severe psoriasis: a retrospective review of 58 cases. *Br J Dermatol* 2005; **153:** 549–51.
10. Nieboer C, *et al.* Systemic therapy with fumaric acid derivates: new possibilities in the treatment of psoriasis. *J Am Acad Dermatol* 1989; **20:** 601–8.
11. Mrowietz U, *et al.* Treatment of psoriasis with fumaric acid esters: results of a prospective multicentre study. *Br J Dermatol* 1998; **138:** 456–60.
12. Guenther CH, *et al.* Macular exanthema due to fumaric acid esters. *Ann Pharmacother* 2003; **37:** 234–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ingepsor; ***Ger.:*** Psoriasis-Solution†; Psoriasis-Tabletten†.

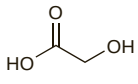
Multi-ingredient: ***Arg.:*** Noqueral†; ***Austral.:*** Pro-PS†; ***Ger.:*** Fumaderm; Psoriasis-Bad†; Psoriasis-Salbe S†.

Glycolic Acid

Glicólico, ácido; Hydroxyacetic Acid. Hydroxyethanoic acid.

Гидроксиуксусная Кислота; Гликолевая Кислота

$C_2H_4O_3$ = 76.05.
CAS — 79-14-1.



Profile

Glycolic acid is an alpha hydroxy organic acid that has been used in topical preparations for hyperpigmentation (see Pigmentation Disorders, p.1582) and photodamaged skin (see Photoageing, p.1581).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Alfabase 8; Geloforte†; Glicoisdin; Gligel; Lactrime†; Lipomax†; Loxidil; Vansame G; ***Canad.:*** Reversa; ***Chile:*** Alastik†; Neosolets; Teen Derm†; ***Hong Kong:*** Glyderm; ***Indon.:*** Exfoliac; Glycare; ***Ital.:*** Neostrata; Revitalizing†; ***Malaysia:*** Glyderm†; ***Mex.:*** Glicoderm; Glicolic; Nova Derm; ***Philipp.:*** Teranex; ***Singapore:*** Glyderm; Sunsense Anti-Ageing; ***Venez.:*** Glyco-A†; Teen Derm†.

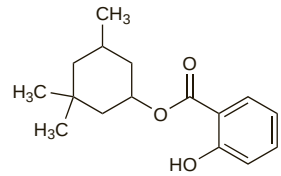
Multi-ingredient: ***Arg.:*** Cellskinlab C + AHA; Controlacne; Diacneal; Effalpha†; Hidroskin; Hydragenic†; Keracnyl; Melacler†; Negacne; Neoquin; Neoquin Forte; Neostrata; Neostrata Gel Despigmentante; Purasoft; Revital; Vansame GS; Vansame Plus; ***Austral.:*** Neostrata; ***Braz.:*** Glyquin; ***Canad.:*** Biobase-G; Dilusol AHA†; Glyquin XM; Neostrata; NeoStrata Blemish Spot Gel; NeoStrata Daytime; NeoStrata HQ; Reversa UV; Viquin Forte†; ***Chile:*** Alastik†; D 4†; Diacneal; Neostrata; Neutrogena Healthy Skin; Neutrogena Limpiadora; Primacy C+AHA†; Ureadin Forte; ***Fr.:*** Alpha 5 DS†; Aniospray 29; Body Peel; Cleanance K; Correcteur Anti-Taches; Cosmodex Uniwhite†; Day Peel; Hyfac soin keratolytique†; Item Alphakeptol; Kelual DS; Keracnyl; Keracnyl eau nettoyante; Keracnyl stop bouton; Kertyol-S; Night Peel; Photakne†; Seborheane; ***Hong Kong:*** Glyquin; ***Indon.:*** Exfoliac; Interquin Plus; ***Ital.:*** Acnesan†; Biophase Shampoo; Lightening; Neoceuticals Spot Treatment; Phytic Acid; Same-Seb Beta; Sebacnol†; ***Mex.:*** Nova Derm; ***Port.:*** Bioclin Sebo Care; Ureadin; Ureadin Forte; ***Singapore:*** Glyquin; Glyquin XM; Percutalfa; ***USA:*** Glyquin XM; ***Venez.:*** Diacneal; Photoderm AKN.

Homosalate *(USAN, rINN)*

Homomenthyl Salicylate; Homosalato; Homosalatum. 3,3,5-Trimethylcyclohexyl salicylate.

Гомосалат

$C_{16}H_{22}O_3$ = 262.3.
CAS — 118-56-9.



NOTE. Eusolex HMS and Neo-Heliopan HMS are trade names that have been used for homosalate.

Pharmacopoeias. In *US.*
USP 31 (Homosalate). Store in airtight containers.

Profile

Homosalate, a substituted salicylate, is a sunscreen (p.1576) with actions similar to those of octisalate (p.1608). It is effective against UVB light (for definitions, see p.1580).

Preparations

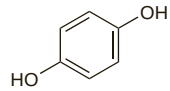
Proprietary Preparations numerous preparations are listed in Part 3.

Hydroquinone

Hidrokinon; Hidroquinona; Hydrochinon; Hydrochinonum; Quinol. 1,4-Benzenediol.

Гидрохинон

$C_6H_6O_2$ = 110.1.
CAS — 123-31-9.
ATC — D11AX11.
ATC Vet — QD11AX11.



NOTE. Do not confuse with Hydroquinine (p.2322).

Pharmacopoeias. In *US.*
USP 31 (Hydroquinone). Fine white needles which darken on exposure to light and air. Soluble 1 in 17 of water, 1 in 4 of alcohol, 1 in 51 of chloroform, and 1 in 16.5 of ether. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

Topical hydroquinone may cause transient erythema and a mild burning sensation. Occasionally hypersensitivity has occurred and US licensed product information recommends skin testing before use. Hydroquinone should not be applied to abraded or sunburnt skin. It should not be used to bleach eyelashes or eyebrows and contact with the eyes should be avoided as it may produce staining and corneal opacities. High concentrations or prolonged use may produce a blue-black hyperpigmentation (ochronosis) or pigmented colloid milium. The systemic effects of hydroquinone and their treatment are similar to those of phenol (see p.1656) but tremors and convulsions may also occur.

Carcinogenicity. There is some evidence from *animal* studies that hydroquinone might be carcinogenic (see Effects on the Skin, below).

Effects on the liver. Toxic hepatitis in a radiographer was attributed to occupational exposure to hydroquinone fumes from the developing medium used in the darkroom.[1] However, it has been pointed out[2] that hydroquinone is not volatile under normal conditions of use and that surveillance of 879 people engaged in the manufacture and use of hydroquinone from 1942 to 1990 found no association between toxic hepatitis and hydroquinone exposure.

1. Nowak AK, *et al.* Darkroom hepatitis after exposure to hydroquinone. *Lancet* 1995; **345:** 1187.
2. O'Donaghue JL, *et al.* Hydroquinone and hepatitis. *Lancet* 1995; **346:** 1427–8.

Effects on the skin. The incidence of exogenous ochronosis (blue-black hyperpigmentation) in a survey of black South African patients was found to be 15% in males and 42% in females with 69% of affected individuals admitting to using hydroquinone-containing preparations.[1] This was considered to be more consistent with a toxic effect of a drug with a low therapeutic index, rather than an idiosyncratic reaction. The data revealed that even preparations with hydroquinone 2% or less with a sunscreen produced ochronosis. Ochronosis usually became apparent after about 6 months of use and, once established, was probably irreversible. Patients may initially use skin lighteners for cosmetic purposes but once ochronosis develops they may fall into the 'skin lightener trap' as they use other hydroquinone preparations to remove the disfigurement.[1] Treatment of exogenous ochronosis is based on stopping the use of hydroquinone, but it may take years for any improvement to be apparent. There are a few reports of benefit from topical tretinoin, dermabrasion, and laser therapy, but these are far from established therapies.[2] Reversible brown discoloration of the nails has also been reported after the use of skin lighteners containing hydroquinone.[3-5]

In addition to the risk of ochronosis it has been suggested that, based on *animal* studies, long-term use of hydroquinone might be carcinogenic.[6] In the USA, preparations containing up to 2% hydroquinone may be sold without prescription, but in 2006, based on data regarding potential carcinogenicity and reports of ochronosis, the FDA proposed to reclassify these products as drugs and make them available by prescription only.[7] In Europe the use of hydroquinone in cosmetic preparations for skin lightening is already banned, but it is still available for prescription as a medicine.[6]

1. Hardwick N, *et al.* Exogenous ochronosis: an epidemiological study. *Br J Dermatol* 1989; **120:** 229–38.
2. Levin CY, Maibach H. Exogenous ochronosis: an update on clinical features, causative agents and treatment options. *Am J Clin Dermatol* 2001; **2:** 213–17.
3. Mann RJ, Harman RRM. Nail staining due to hydroquinone skin-lightening creams. *Br J Dermatol* 1983; **108:** 363–5.
4. Ozluer SM, Muir J. Nail staining from hydroquinone cream. *Australas J Dermatol* 2000; **41:** 255–6.
5. Parlak AH, *et al.* Discolouration of the fingernails from using hydroquinone skin-lightening cream. *J Cosmet Dermatol* 2003; **2:** 199–201.
6. Kooyers TJ, Westerhof W. Toxicology and health risks of hydroquinone in skin lightening formulations. *J Eur Acad Dermatol Venereol* 2006; **20:** 777–80.
7. FDA. Skin bleaching drug products for over-the-counter human use: proposed rule. *Fed Regist* 2006; **71:** 51146–55. Available at: http://a257.g.akamaitech.net/7/257/2422/01jan20061800/edocket.access.gpo.gov/2006/pdf/E6-14263.pdf (accessed 27/09/07)

Uses and Administration

Hydroquinone increases melanin excretion from melanocytes and may also prevent its production. Hydroquinone is used topically as a depigmenting agent for the skin in hyperpigmentation conditions (p.1582) such as chloasma (melasma), freckles, and lentigines (liver spots). Concentrations of 2 to 4% are commonly used; higher concentrations may be very irritant and increase the risk of ochronosis. It may be several weeks before any effect is apparent but depigmentation may last for 2 to 6 months after stopping. Application of hydroquinone should stop if there is no improvement after 2 months. Hydroquinone should be applied twice daily only to intact skin which should be protected from sunlight to reduce repigmentation. A preparation containing hydroquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01% may be applied once daily at night in the treatment of chloasma (melasma). Hydroquinone preparations often include a sunscreen or a sunblocking basis.

Hydroquinone is also used as an antoxidant in topical preparations and in photographic developers.

Preparations

USP 31: Hydroquinone Cream; Hydroquinone Topical Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Claripel; ***Braz.:*** Claripel; Solaquin; ***Canad.:*** African Gold†; Banishing Cream; Eldopaque; Eldoquin; Esoterica Regular; Esoterica Unscented; Lustra; Nadinola†; NeoStrata Canada HQ Plus; Porcelana Nighttime Formula†; Ultraquin Plain; ***Chile:*** Etnoderm; Unitone 4; ***Hong Kong:*** Derma-Rx Lightener; Eldopaque; Eldoquin; Solaquin; ***Indon.:*** Bioquin; Mediquin; Melanox; Melaskin; Pigmet; Pylaquin; Qutifar; Vitaquin; ***Israel:*** Esomed; ***Malaysia:*** Eldopaque; Eldoquin; ***Mex.:*** Crema Blanca; Eldopaque; Eldoquin; Hidroquin; Melanex; Quinoret Forte; ***NZ:*** Eldoquin; ***Singapore:*** Eldopaque; Eldoquin; Polyquin; Solaquin; ***Spain:*** Hidroquilaude; Licostrata; Melanasa; Nadona; Pigmentasa; ***Thai.:*** Clariderm; ***Turk.:*** Expigment; ***UK:*** Eldopaque; Eldoquin; Solaquin; ***USA:*** Aclaro; Claripel; Eldopaque; Eldoquin; EpiQuin; Esoterica Regular; Lustra; Solaquin; ***Venez.:*** Pharquinon†.

Multi-ingredient: ***Arg.:*** Melacler†; Melasmax; Neoceuticals Crema Despigmentante de Dia†; Neoquin; Neoquin Forte; Neostrata Gel Despigmentante; Solaquin Forte; Tri-Luma; ***Austral.:*** Superfade; ***Braz.:*** Glyquin; Tri-Luma; Vitacid Plus; ***Canad.:*** Esoterica; Glyquin XM; Lustra-AF; NeoStrata Canada HQ Plus; NeoStrata HQ; Porcelana Daytime Formula†; Solaquin Forte†; Ultraquin; Viquin Forte†; ***Chile:*** Alastik†; Clasifel; D 4†; Neostrata; Tri-Luma; Trio-D†; ***Ger.:*** Pigmanorm; ***Hong Kong:*** Glyquin; Superfade; Tri-Luma; ***India:*** Melalite 15; ***Indon.:*** Hidrogel; Interquin; Interquin Plus; Nu-Derm Sunblock; ***Malaysia:*** Solaquin Forte; Tri-Luma; ***Mex.:*** Clasifel; Nova Derm; Quinoret; Solaquin; Tri-Luma; ***Philipp.:*** Tri-Luma; ***Singapore:*** Glyquin; Glyquin XM; Tri-Luma; ***Switz.:*** Pigmanorm; ***Thai.:*** Tri-Luma; ***Turk.:*** Metamorfoz; ***USA:*** Esoterica Facial and Sunscreen; Glyquin XM; Solaquin Forte; Tri-Luma; ***Venez.:*** Tri-Luma.

Ichthammol *(BAN)*

Ammonii Bituminosulfonas; Ammonii Sulfogyrodalas; Ammonio Sulfoittiolato; Ammonium Bithiolicum; Ammonium Bitumenosulfonicum; Ammonium Bituminosulphonate; Ammonium Ichthosulphonate; Ammonium Sulfobituminosum; Ammonium Sulpho-Ichthyolate; Amonowy sulfobituminian; Bithiolate Ammonique; Bithyol; Bitiol; Bitiolato amónico; Bitomol; Bituminol; Ichtammol; Ichtamolis; Ichthammolum; Ichthamol; Ichthosulphol; Ichthyol; Ichthyolammonium; Ictamol; Ictiolsulfonato amónico; Ihtamol; Iktammol; Iktammoli; Sulfobituminato amónico; Sulfoictiolato amónico.

Ихтаммол; Ихтиол

CAS — 8029-68-3.

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

Ph. Eur. 6.2 (Ichthammol). A dense blackish-brown liquid. It is obtained by distillation of certain bituminous schists, sulfonation of the distillate, and neutralisation of the product with ammonia. It contains not less than 4.5% and not more than 7.0% of total ammonia, not less than 10.5% of organically combined sulfur, calculated with reference to the dried substance, and not more than 20% of the total sulfur in the form of sulfates.

Miscible with water and with glycerol; slightly soluble in alcohol, in fatty oils, and in liquid paraffin; forms homogeneous mixtures with wool fat and soft paraffin.

USP 31 (Ichthammol). A reddish-brown to brownish-black viscous fluid with a strong characteristic empyreumatic odour. It is obtained by the destructive distillation of a bituminous schist, sulfonation of the distillate, and neutralisation of the product with ammonia. It yields not less than 10.0% of total sulfur and not less than 2.5% of ammonia. Miscible with water, with glycerol, and with fixed oils and fats. Partially soluble in alcohol and in ether.

Incompatibility. Ichthammol is incompatible with wool alcohols.

Profile

Ichthammol has slight bacteriostatic properties and is used in a wide range of topical preparations, for a variety of skin disorders; it has also been used in suppositories for anorectal disorders. Ichthammol is often used with zinc oxide in medicated bandages for chronic lichenified eczema (p.1579). Ichthammol may be slightly irritant to the skin and there have been rare reports of hypersensitivity.

Light Ammonium Bituminosulfonate (Ammoniumbituminosulfonat Hell) is produced from the light distillate fraction of shale oil.

Ammoniumsulfobitol, an ammonium bituminosulfonate similar to ichthammol but with a low sulfur content, was commercially available as Tumenol Ammonium.

Preparations

BP 2008: Zinc and Ichthammol Cream;
USP 31: Ichthammol Ointment.

Proprietary Preparations (details are given in Part 3)

Austral.: Egoderm; ***Austria:*** Ichtho-Bad; Ichtholan; Ichtopur; ***Belg.:*** Bithiol; Poudre Velours; ***Cz.:*** Ichtoxyl; ***Fr.:*** Gelictar†; ***Ger.:*** Ichtho-Bad; Ichtholan; Ichtholan spezial; Ichthyol; Thiobitum; ***Neth.:*** Daroderm Trekzalf; Trekzalf; ***Switz.:*** Ichtho-Bad; Ichtholan; ***Turk.:*** Ihtiyol; Pomat Ichthyole; Pommade Ichthyole.

Multi-ingredient: ***Arg.:*** Cicatrina; ***Austral.:*** Egoderm; Icthaband†; ***Austria:*** Aknemycin compositum; Delta-Hadensa; Hadensa; Ichth-Oestren; Inotyol; ***Belg.:*** Antipiol; Inotyol; ***Canad.:*** Boil Ease†; ***Cz.:*** Pityol; Saloxyl; ***Denm.:*** Inotyol; ***Fin.:*** Hadensa; ***Fr.:*** Anaxeryl; Gelictar Fort; Inotyol†; Node DS; Novophane S; Oxythyol; Phytheol; Phytolithe†; Provictol†; Selegel; Squaphane Masque-Creme; ***Ger.:*** Aknemycin; ***Hong Kong:*** Acnederm; Egoderm; ***Israel:*** Aknemycin; Inotyol; ***Ital.:*** Antiemorroidali; Dermatar; Ichthopaste; Inotyol†; Tricoderm F; ***Malaysia:*** Acnederm†; Egoderm; ***Norw.:*** Inotyol; ***NZ:*** Acnederm†; Egoderm; ***Pol.:*** Neo-Tormentil; Tormentile Forte; Tormentiol; ***Port.:*** Efluvium Anti-caspa; Efluvium Anti-seborreico; Oleoban Composto†; Pansebase Composto; Secpel Composto; ***Rus.:*** Bethiol (Бетиол); ***S.Afr.:*** Antipeol; ***Singapore:*** Egoderm; ***Spain:*** Hadensa; Ictiomen; Lamnotyl†; ***Swed.:*** Inotyol; ***Switz.:*** Aknemycin; Bain extra-doux dermatologique; Epithelial†; Furodermal; Leucen; Radix; Riccovitan†; ***Turk.:*** Hedensa; ***UK:*** Antipeol; Ichthopaste; Icthaband; St James Balm; ***USA:*** Boil Ease; Boyol Salve; Medicone Derma†; ***Venez.:*** Node DS.

Ictasol *(USAN)*

Ichtasol; Ichthyol-Natrium Hell; Light Sodium Bituminosulphonate; Natrium Sulfobituminosum Decoloratum; Sulfobituminato sódico; Sulfobituminato sódico decolorado.

$C_{28}H_{36}Na_2O_6S_3$ = 610.8.

CAS — 12542-33-5; 1340-06-3.

ATC — D10BX01.

ATC Vet — QD10BX01.

Profile

Ictasol is a sodium bituminosulfonate produced from the light distillate fraction of shale oil. Sodium bituminosulfonate is obtained by the destructive distillation of certain bituminous schists, sulfonation of the distillate, and neutralisation of the product with sodium hydroxide.

Ictasol has similar properties to ichthammol (above) and is used in a wide range of preparations for a variety of skin disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Crino Cordes; Ichthraletten; Lavichthol; ***Ger.:*** Aknichthol Creme; Crino Cordes N†; Dermichthol†; Ichthoderm; Ichtholan T; Ichthosin; Ichthraletten; Leukichtan; Solutio Cordes.

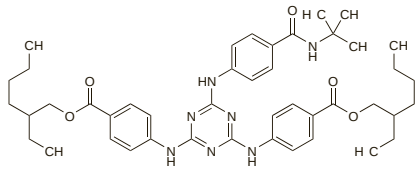
Multi-ingredient: ***Arg.:*** Selegel; ***Austria:*** Aknichthol; Ichthalgan forte; Ichtho-Bellol; Ichtho-Cortin; Leukichtan; ***Chile:*** Ichtyosoft†; ***Fr.:*** I-Soft†; Ichtyosoft†; Sebosquam; ***Ger.:*** Aknederm Neu; Aknichthol N; Ichthalgan†; Ichtho-Bellol compositum S†; Ichtho-Bellol†; Ichthocortin; Ichthoseptal; Pelvichthol N; ***Switz.:*** Aknichthol N.

Iscotrizinol *(USAN)*

Diethylhexyl Butamido Triazone; Diethylhexylbutamido Triazone; Dioctylbutamidotriazone. Bis(2-ethylhexyl) 4,4′-[(6-{[4-(*tert*-butylcarbamoyl)phenyl]amino}-1,3,5-triazine-2,4-diyl)diimino]dibenzoate.

$C_{44}H_{59}N_7O_5$ = 766.0.

CAS — 154702-15-5.



NOTE. Uvasorb HEB is a trade name that has been used for iscotrizinol.

Profile

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

Preparations

Proprietary Preparations some preparations are listed in Part 3.

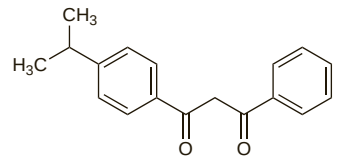
Isopropyldibenzoylmethane

Isopropildibenzoilmetano. 1-[4-(1-Methylethyl)phenyl]-3-phenyl-1,3-propanedione.

Изопропилдибензоилметан

$C_{18}H_{18}O_2$ = 266.3.

CAS — 63250-25-9.



Profile

Isopropyldibenzoylmethane, a substituted 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.

Isotretinoin *(BAN, USAN, rINN)*

Isotretinoiini; Isotretinoína; Isotrétinoïne; Isotretinoinum; Izotretinoin; Izotretinoinas; Izotretynoina; 13-*cis*-Retinoic Acid; Ro-4-3780. (13*Z*)-15-Apo-β-caroten-15-oic acid; (2*Z*,4*E*,6*E*,8*E*)-3,7-Dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetraenoic acid.

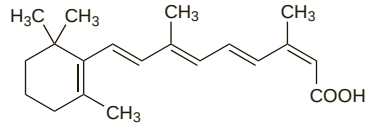
Изотретиноин

$C_{20}H_{28}O_2$ = 300.4.

CAS — 4759-48-2.

ATC — D10AD04; D10BA01.

ATC Vet — QD10AD04; QD10BA01.



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

Ph. Eur. 6.2 (Isotretinoin). A yellow or light orange, crystalline powder. Practically insoluble in water; slightly soluble in alcohol; soluble in dichloromethane. It is sensitive to air, heat, and light, especially in solution. Store in airtight containers at a temperature not exceeding 25°. Protect from light. It is recommended that the contents of an opened container be used as soon as possible and that any unused part be protected by an atmosphere of an inert gas.

USP 31 (Isotretinoin). Yellow crystals. Practically insoluble in water; sparingly soluble in alcohol, in isopropyl alcohol, and in macrogol 400; soluble in chloroform. Store in airtight containers under an atmosphere of an inert gas. Protect from light.

Adverse Effects

The adverse effects of isotretinoin and other oral retinoids are similar to those of vitamin A (see p.1971) and are generally reversible and dose-related. The most common are dryness of the mucous membranes and skin, which can often progress to cheilitis, epistaxis, conjunctivitis, localised exfoliation including palmoplantar exfoliation, pruritus, erythematous rash, and skin fragility. Less common effects have included hair thinning (occasionally irreversible), hirsutism, photosensitivity, changes in skin pigmentation, paronychia, nail dystrophy, pyogenic granuloma, and increased sweating. Acne can be exacerbated at the beginning of isotretinoin treatment, and there are very rare reports of acne fulminans occurring. Less common adverse effects on the eyes include corneal opacities, visual disturbances such as blurred vision and colour vision disorders, impaired night vision that may persist, photophobia, and keratitis. Papilloedema, visual disturbances, headache, and nausea and vomiting can be signs and symptoms of benign intracranial hypertension. Arthralgia, myalgia, and back pain are commonly reported, and there have been rare reports of arthritis, osteoporosis, and tendinitis. Hyperostosis and calcinosis have also occurred, particularly in patients treated with high doses of isotretinoin over long periods for keratinisation disorders. Premature closure of the epiphyses has occurred in children treated with isotretinoin. Elevation of serum triglycerides is common, and pancreatitis has occurred in patients with high concentrations; cholesterol concentrations may also be increased. Increases in hepatic enzymes, erythrocyte sedimentation rate, and blood glucose can also occur. Alterations in haematological measures are common; there have also been reports of anaemia, thrombocytopenia, and neutropenia, and very rare reports of agranulocytosis. Other effects that have been reported rarely include gastrointestinal symptoms, hepatitis, hearing impairment, drowsiness, seizures, vasculitis, and hypersensitivity reactions including anaphylaxis. Mood changes, psychotic symptoms, depression, and suicidal behaviour have occurred in patients treated with oral isotretinoin. There may also be an association with skin infections and an inflammatory bowel syndrome.

Isotretinoin and other retinoids are teratogenic.

When isotretinoin is applied topically the adverse effects are similar to those of tretinoin (see p.1618).

◊ General references.

1. Mills CM, Marks R. Adverse reactions to oral retinoids: an update. *Drug Safety* 1993; **9:** 280–90.
2. Keefe M. Adverse reactions profile: retinoids. *Prescribers' J* 1995; **35:** 71–6.
3. McLane J. Analysis of common side effects of isotretinoin. *J Am Acad Dermatol* 2001; **45:** S188–S194.
4. British Association of Dermatologists. Advice on the safe introduction and continued use of isotretinoin in acne (2003). Available at: http://www.bad.org.uk/healthcare/guidelines/acne.asp (accessed 27/09/07)
5. Charakida A, *et al.* Safety and side effects of the acne drug, oral isotretinoin. *Expert Opin Drug Saf* 2004; **3:** 119–29.
6. Goldsmith LA, *et al.* American Academy of Dermatology consensus conference on the safe and optimal use of isotretinoin: summary and recommendations. *J Am Acad Dermatol* 2004; **50:** 900–906. Correction. *ibid.*; **51:** 348. [dose]

Effects on the blood. Serious adverse effects on the blood have been reported rarely with oral retinoids, and are thought to be idiosyncratic in nature. There have been reports of thrombocytopenia in patients taking isotretinoin[1] and etretinate.[2,3] A few cases of agranulocytosis have involved isotretinoin[4] and acitretin.[5] In contrast, there are also reports of transient and asymptomatic thrombocytosis associated with isotretinoin[6] and tretinoin.[7,8] Leucocytosis is often associated with the retinoic acid syndrome caused by tretinoin (p.1618).

1. Moeller KE, Touma SC. Prolonged thrombocytopenia associated with isotretinoin. *Ann Pharmacother* 2003; **37:** 1622–4.
2. Naldi L, *et al.* Etretinate therapy and thrombocytopenia. *Br J Dermatol* 1991; **124:** 395.