Austria: Exorex; ***Braz.:*** Ionil-T Plus†; Tarflex; Theratar; ***Canad.:*** Balnetar; Doak-Oil; Estar†; Mazon Medicated Soap; Neutrogena T/Gel; Neutrogena T/Gel Therapeutic; Pentrax; Spectro Tar†; Targel; Tersa-Tar; ***Chile:*** DHS Tar Gel; Neutrogena Shampoo Neutar; Psorigel†; Tarmed; Tigel IRM; ***Cz.:*** Delatar; Teer-Linola-Fett N†; ***Denm.:*** Basotar†; ***Fr.:*** Caditar; ***Ger.:*** Basiter†; Berniter; Hoepixin Bad N†; Lorinden Teersalbe; Tarmed; Teer-Linola-Fett; ***Gr.:*** Exorex; Ionil; Tarmed; ***Hong Kong:*** Pinetarsol; Zetar; ***Irl.:*** Alphosyl†; Exorex; Pentrax; Psoriderm; ***Israel:*** Alphosyl 2 in 1; Denorex†; T/Gel; ***Ital.:*** Konor; Shampoo SDE Tar†; ***Malaysia:*** Pin-Xol; Pinetarsol; ***Mex.:*** Ionil-T Plus; Shampoo Tersa-Tar†; Tarmed; ***Neth.:*** Exorex; ***Norw.:*** Soraderm†; ***NZ:*** Pinetarsol; Psorigel†; ***Pol.:*** Delatar; Freederm Tar; Polytar; ***Port.:*** Neutar; Tarmed; ***Rus.:*** Freederm Tar (Фридерм Деготь); ***S.Afr.:*** Alphosyl; Denorex; Exarex†; Linotar; ***Singapore:*** Pinetarsol; ***Spain:*** Alfitar; Alphosyl; Piroxgel; Psoriasdin; Tar Isdin Champu; Tarmed; Tejel; ***UK:*** Alphosyl 2 in 1; Carbo-Dome; Clinitar; Exorex; Pentrax; Pinetarsol; Psoriderm; T/Gel; ***USA:*** Balnetar; Creamy Tar; DHS Tar; Estar†; Fototar; Ionil-T Plus; MG217 Medicated; Neutrogena T/Gel; Oxipor VHC; PC-Tar; Pentrax; Polytar; Psorigel†; Taraphilic; Tegrin; Tera-Gel; Zetar; ***Venez.:*** Alma-Tar†.

Multi-ingredient: ***Arg.:*** Acnetrol; Adop-Tar†; Aeroseb; Champuacid; Cicatrol; Confor-Tar†; Cremsor N; Domtisona†; Eurocoal; Farm-X; Hyaluron; Ingemet; Ionil-T; Laurinol Plus; Medic†; Mencogrin; Mencogrin AP; Oilalfo; Sequals G; Sorsis; Sorsis Beta; ***Austral.:*** Alphosyl; Eczema Cream; Egopsoryl TA; ER Cream†; Fongitar; Hamilton Pine Tar with Menthol; Ionil-T; Neutrogena T/Sal†; Pinetarsol; Polytar; Psor-Asist; Sebitar; Tarband†; ***Austria:*** Alphosyl; Alpicort; Locacorten Tar; ***Belg.:*** Locacortene Tar†; ***Braz.:*** Hebrin; Ionil-T; Polytar; Xarope Sao Joao†; ***Canad.:*** Boil Ease†; Dan-Tar Plus; Denorex Medicated; Mazon Medicated Cream; Mazon Medicated Shampoo; Medi-Dan; Multi-Tar Plus; Oxipor; P & S Plus; Polytar; Polytar AF; Sebcur/T; Sebutone†; SJ Liniment; Spectro Tar†; Sterex; Sterex Plus; Tardan; Targel SA; X-Seb T; X-Seb T Plus; X-Tar; ***Chile:*** Denorex Herbal†; Ionil-T; Tarytar†; ***Cz.:*** Locacorten Tar†; Polytar; Polytar AF; Suspensio Visnevski cum Pice Liquida Herbacos; ***Fr.:*** Alphosyl†; Cystel Shampooing Antiseborrheique†; Epiphane†; Item Alphacade; Laccoderme a l'huile de cade; Node DS; Node K; Node P; Novophane; Novophane S; Phytolithe†; Psocortene; Sebosquam; Squaphane; Squaphane E; Squaphane Masque-Creme; Squaphane P; Squaphane S; ***Ger.:*** Lorinden T†; Psorigerb N†; ***Hong Kong:*** 2-4-2†; Cocois†; Egopsoryl TA; Fongitar; Ionil-T; Locacorten Tar†; Multi-Tar; Polytar; Polytar Emollient; Sebitar; ***Hung.:*** Aknefug-liquid N†; Polytar; Polytar AF; ***India:*** Derobin Skin; Ionax T; ***Indon.:*** Polytar; ***Irl.:*** Alphosyl HC†; Capasal; Cocois; Denorex; Gelcotar†; Ionil-T†; Polytar; Polytar Emollient†; Pragmatar; ***Israel:*** Alphosyl HC†; Alphosyl†; Capasal; CT Ointment†; CT Pommade†; CT Shampoo†; Polytar; Topicorten-Tar; ***Ital.:*** Alphosyle†; Balta-Crin Tar†; Rivescal Tar; ***Malaysia:*** Cocois†; Egopsoryl TA; Mentar; Polytar; Sebitar; ***Mex.:*** Antaderm; Dariseb; Dealan; Dermoscalp; Ionil-T; Jabon del Tio Nacho; Polytar; Sebryl; Sebryl Plus; Sebstopp; Shampoo del Tio Nacho; ***Neth.:*** Denorex; ***NZ:*** Coco-Scalp; Cocois†; Egopsoryl TA; Fongitar†; Ionil-T; Polytar; Polytar Emollient; Polytar Plus; Sebitar; ***Philipp.:*** Fongitar; Ionil-T; Polytar; ***Pol.:*** Cocois; Polytar AF; Psorisan; ***Port.:*** Alpha Cade; Banholeum Composto; Betacade†; Edoltar†; Fongitar; Polytar; Sucadermil; ***S.Afr.:*** Alphosyl; Fongitar; Haarlemensis; Oxipor VHC; Polytar; SB Universal Ointment; ***Singapore:*** Denorex†; Egopsoryl TA; Fongitar; Ionil-T; Polytar; Sebitar; ***Spain:*** Alphosyl; Bazalin; Emolytar; Ionil Champu; Ionil†; Polytar; Quinortar†; Tar Isdin Plus†; Zincation Plus; ***Swed.:*** Alphosyl†; ***Switz.:*** Alphosyl†; ***Thai.:*** Fongitar; Ionil-T†; Polytar; ***Turk.:*** Kadolin; Wilkinson; ***UK:*** Alphosyl HC; Capasal; Cocois; Polytar AF; Polytar Emollient; Polytar Liquid; Polytar Plus; Pragmatar†; Psorin; Sebco; Snowfire; Varicose Ointment; ***USA:*** Boil Ease; Ionil-T; Medotar; Neutrogena T/Sal; Sal-Oil-T; Sebex-T; SLT†; Tarlene; Tarsum; X-Seb T; X-Seb T Plus; ***Venez.:*** Vitar†.

Tazarotene *(BAN, USAN, rINN)*

AGN-190168; Tatsaroteeni; Tazaroten; Tazarotène; Tazaroteno; Tazarotenum. Ethyl 6-[(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate.

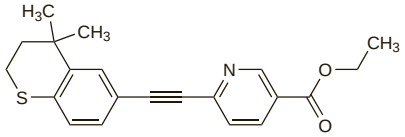
Тазаротен

$C_{21}H_{21}NO_2S$ = 351.5.

CAS — 118292-40-3.

ATC — D05AX05.

ATC Vet — QD05AX05.



Adverse Effects and Precautions

As for Tretinoin, p.1618.

Systemic absorption from tazarotene applied topically is low, and the most frequent adverse effects are on the skin; the incidence of adverse events appears to be concentration related.

Animal studies have indicated that tazarotene is fetotoxic and teratogenic, and licensed product information recommends that tazarotene should not be used during pregnancy or in women planning a pregnancy. Similarly, tazarotene should not be used, or used with caution, during breast feeding, as *animal* data indicate that it may be distributed into breast milk.

Effects on the skin. A 57-year-old man with diabetes and recalcitrant psoriasis on the trunk and limbs developed acute dermatitis[1] in the genital area 2 weeks after starting treatment with topical tazarotene 0.1%. The affected areas became ulcerated over the next few days. It was suspected that accidental contact with the tazarotene that had been applied to the truncal psoriasis was responsible. Pyogenic granuloma has been associated with topical tazarotene and other retinoids given orally or applied topically (see Effects on the Skin, Hair, and Nails, under Isotretinoin, p.1601).

1. Wollina U. Genital ulcers in a psoriasis patient using topical tazarotene. *Br J Dermatol* 1998; **138:** 713–14.

Uses and Administration

Tazarotene is a retinoid used for the topical treatment of mild to moderate acne and plaque psoriasis, and to treat signs of photoageing. Tazarotene is a prodrug that is de-esterified in the skin to its active form, tazarotenic acid. The mode of action is unknown but it appears to modulate cell proliferation and differentiation.

In the treatment of **psoriasis**, tazarotene 0.05% cream or gel is used initially and increased to 0.1% if necessary. It is applied once daily in the evening. In the UK tazarotene is licensed for use in patients with psoriasis affecting up to 10% of the body-surface; in the USA, it may be used on psoriasis involving up to 20% of the body-surface.

In the treatment of **acne**, tazarotene is applied as a 0.1% gel or cream once daily in the evening.

There may be exacerbation of acne during early treatment or of psoriasis at any time during treatment. The treatment period is usually up to 12 weeks, although tazarotene has been used for up to 12 months in the treatment of psoriasis.

A 0.1% cream is used in the topical treatment of certain signs of **photoageing** (facial fine wrinkling, mottled hypo- and hyperpigmentation, and benign facial lentigines). It is applied once daily at bedtime to lightly cover the entire face.

◊ Reviews.

1. Foster RH, *et al.* Tazarotene. *Drugs* 1998; **55:** 705–11.
2. Tang-Liu DD-S, *et al.* Clinical pharmacokinetics and drug metabolism of tazarotene: a novel topical treatment for acne and psoriasis. *Clin Pharmacokinet* 1999; **37:** 273–87.
3. Guenther LC. Optimizing treatment with topical tazarotene. *Am J Clin Dermatol* 2003; **4:** 197–202.

Malignant neoplasms. There has been some interest in the use of topical tazarotene in the treatment of neoplasms affecting the skin. Preliminary studies have reported some lesion regression or clearance in basal cell[1] and squamous cell carcinomas[2] (p.673), and mycosis fungoides[3] (p.657).

1. Bianchi L, *et al.* Topical treatment of basal cell carcinoma with tazarotene: a clinicopathological study on a large series of cases. *Br J Dermatol* 2004; **151:** 148–56.
2. Bardazzi F, *et al.* A pilot study on the use of topical tazarotene to treat squamous cell carcinoma in situ. *J Am Acad Dermatol* 2005; **52:** 1102–4.
3. Apisarnthanarax N, *et al.* Tazarotene 0.1% gel for refractory mycosis fungoides lesions: an open-label pilot study. *J Am Acad Dermatol* 2004; **50:** 600–607.

Skin disorders. Tazarotene is used for the topical treatment of mild to moderate acne[1,2] (p.1577) and plaque psoriasis[3,4] (p.1583); benefit has also been reported for psoriasis of the nails.[5,6] Improvement has been reported too in keratinisation disorders such as Darier's disease[7,8] (p.1578) and congenital ichthyosis[9-11] (p.1580). Topical tazarotene can also improve some signs of photoageing (p.1581), including fine wrinkling, mottled hyperpigmentation, and lentigines (liver spots).[12-14]

1. Leyden JJ. Meta-analysis of topical tazarotene in the treatment of mild to moderate acne. *Cutis* 2004; **74** (4 suppl): 9–15.
2. Shalita AR, *et al.* Effects of tazarotene 0.1% cream in the treatment of facial acne vulgaris: pooled results from two multicenter, double-blind, randomized, vehicle-controlled, parallel-group trials. *Clin Ther* 2004; **26:** 1865–73.
3. Weinstein GD, *et al.* Tazarotene cream in the treatment of psoriasis: two multicenter, double-blind, randomized, vehicle-controlled studies of the safety and efficacy of tazarotene creams 0.05% and 0.1% applied once daily for 12 weeks. *J Am Acad Dermatol* 2003; **48:** 760–7.
4. Dando TM, Wellington K. Topical tazarotene: a review of its use in the treatment of plaque psoriasis. *Am J Clin Dermatol* 2005; **6:** 255–72.
5. Scher RK, *et al.* Tazarotene 0.1% gel in the treatment of fingernail psoriasis: a double-blind, randomized, vehicle-controlled study. *Cutis* 2001; **68:** 355–8.
6. Bianchi L, *et al.* Tazarotene 0.1% gel for psoriasis of the fingernails and toenails: an open, prospective study. *Br J Dermatol* 2003; **149:** 207–9.
7. Oster-Schmidt C. The treatment of Darier's disease with topical tazarotene. *Br J Dermatol* 1999; **141:** 603–4.
8. Brazzelli V, *et al.* Linear Darier's disease successfully treated with 0.1% tazarotene gel "short-contact" therapy. *Eur J Dermatol* 2006; **16:** 59–61.
9. Hofmann B, *et al.* Effect of topical tazarotene in the treatment of congenital ichthyosis. *Br J Dermatol* 1999; **141:** 642–6.
10. Marulli GC, *et al.* Type I lamellar ichthyosis improved by tazarotene 0.1% gel. *Clin Exp Dermatol* 2003; **28:** 391–3.
11. Kundu RV, *et al.* Lamellar ichthyosis treated with tazarotene 0.1% gel. *J Am Acad Dermatol* 2006; **55** (suppl 5): S94–S95.
12. Phillips TJ, *et al.* Efficacy of 0.1% tazarotene cream for the treatment of photodamage: a 12-month multicenter, randomized trial. *Arch Dermatol* 2002; **138:** 1486–93.
13. Machtinger LA, *et al.* Histological effects of tazarotene 0.1% cream vs. vehicle on photodamaged skin: a 6-month, multicentre, double-blind, randomized, vehicle-controlled study in patients with photodamaged facial skin. *Br J Dermatol* 2004; **151:** 1245–52.
14. Kang S, *et al.* A multicenter, randomized, double-blind trial of tazarotene 0.1% cream in the treatment of photodamage. *J Am Acad Dermatol* 2005; **52:** 268–74.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Zorac; ***Belg.:*** Zorac; ***Braz.:*** Zorac†; ***Canad.:*** Tazorac; ***Cz.:*** Tazorac; ***Fin.:*** Zorac†; ***Fr.:*** Zorac; ***Ger.:*** Zorac; ***Gr.:*** Zorac; ***India:*** La Tez; Tazret†; ***Irl.:*** Zorac; ***Israel:*** Zorac; ***Ital.:*** Zorac; ***Mex.:*** Suretin; ***Pol.:*** Zorac; ***S.Afr.:*** Zorak; ***Spain:*** Zorac; ***Swed.:*** Zorac†; ***Switz.:*** Zorac; ***UK:*** Zorac; ***USA:*** Avage; Tazorac.

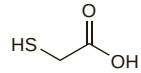
Thioglycollic Acid

Kwas tioglikolowy; Tioglicólico, ácido. Mercaptoacetic acid.

Тиогликолевая Кислота

$C_2H_4O_2S$ = 92.12.

CAS — 68-11-1.



Calcium Thioglycollate

Calcium Mercaptoacetate; Tioglicolato cálcico. Calcium mercaptoacetate trihydrate.

Тиогликолят Кальция

$C_2H_2CaO_2S,3H_2O$ = 184.2.

CAS — 814-71-1.

Profile

Thioglycollic acid is used, usually as the calcium salt, in depilatory preparations. Thioglycollates are also used in hair waving or straightening products with potassium bromate as the neutraliser. There have been reports of skin reactions associated with the use of thioglycollates.

Tioxolone *(BAN, rINN)*

OL-110; Thioxolone; Tioksolon; Tioksoloni; Tioxolon; Tioxolona; Tioxolonum. 6-Hydroxy-1,3-benzoxathiol-2-one; .

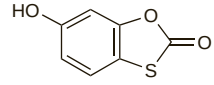
Тиоксолон

$C_7H_4O_3S$ = 168.2.

CAS — 4991-65-5.

ATC — D10AB03.

ATC Vet — QD10AB03.



Pharmacopoeias. In *Pol.*

Profile

Tioxolone has astringent and keratolytic effects, and has been used topically in the treatment of various skin and scalp disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Ger.:*** Loscon†.

Titanium Dioxide

CI Pigment White 6; Colour Index No. 77891; E171; Oxid titaničitý; Titaanidioksidi; Titandioxid; Titán-dioxid; Titane, dioxyde de; Titanii dioxidum; Titanio, dióxido de; Titanium Oxide; Titano dioksidas; Titanyum Dioksit; Tytanu(IV) tlenek.

Двуокись Титана; Диоксид Титана

TiO_2 = 79.87.

CAS — 13463-67-7.

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

Ph. Eur. 6.2 (Titanium Dioxide). A white or almost white powder. Practically insoluble in water; it does not dissolve in dilute mineral acids but dissolves slowly in hot concentrated sulfuric acid.

USP 31 (Titanium Dioxide). A white odourless powder. Insoluble in water, in hydrochloric acid, in nitric acid, and in 2N sulfuric acid; dissolves in hot sulfuric acid and in hydrofluoric acid; it is rendered soluble by fusion with potassium bisulfate or with alkali hydroxides or carbonates. A 10% suspension in water is neutral to litmus.

Profile
Titanium dioxide has an action on the skin similar to that of zinc oxide (p.1621) and has similar uses. Titanium peroxide and titanium salicylate are used with titanium dioxide for nappy rash. Titanium dioxide reflects ultraviolet light and is used as a physical sunscreen (p.1576). It is also an ingredient of some cosmetics. It is used to pigment and opacify hard gelatin capsules and tablet coatings and as a delustring agent for regenerated cellulose and other man-made fibres. Specially purified grades may be used in food colours.

Preparations
BP 2008: Titanium Ointment.

Proprietary Preparations numerous preparations are listed in Part 3.

Trafermin *(USAN, rINN)*

CAB-2001; Trafermina; Trafermine; Traferminum. 2-155-Basic fibroblast growth factor (human clone λKB7/λHFL1 precursor reduced).

Трафермин

CAS — 131094-16-1.

Profile
Trafermin is a human recombinant basic fibroblast growth factor (b-FGF) that promotes tissue granulation and the formation of new blood vessels. It is used as a topical liquid spray for the treatment of burns and intractable skin ulcers.

◊ References.

1. Robson MC, *et al.* Sequential cytokine therapy for pressure ulcers: clinical and mechanistic response. *Ann Surg* 2000; **231:** 600–11.
2. Payne WG, *et al.* Long-term outcome study of growth factor-treated pressure ulcers. *Am J Surg* 2001; **181:** 81–6.
3. Ichioka S, *et al.* The positive experience of using a growth factor product on deep wounds with exposed bone. *J Wound Care* 2005; **14:** 105–9.
4. Motomura H, *et al.* Aggressive conservative therapy for refractory ulcer with diabetes and/or arteriosclerosis. *J Dermatol* 2006; **33:** 353–9.

Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Fiblast.

Tretinoin *(BAN, USAN, rINN)*

Ácido retinoico; NSC-122758; Retinoic Acid; Tretinoiini; Tretinoína; Tretinoinas; Trétinoïne; Tretinoinum; Tretynoina; Vitamin A Acid; Vitamina A ácida. *all-trans*-Retinoic acid; 15-Apo-β-caroten-15-oic acid; 3,7-Dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-*all-trans*-tetraenoic acid.

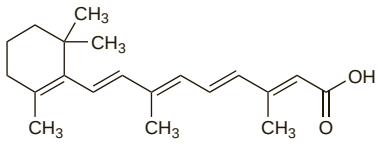
Третиноин

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

CAS — 302-79-4.

ATC — D10AD01; L01XX14.

ATC Vet — QD10AD01; QL01XX14.



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

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

USP 31 (Tretinoin). A yellow to light-orange crystalline powder. Insoluble in water; slightly soluble in alcohol and in chloroform. Store in airtight containers, preferably under an atmosphere of an inert gas. Protect from light.

Adverse Effects
Tretinoin is a skin irritant. Topical application may cause transitory stinging and a feeling of warmth, and in normal use it produces some erythema, dryness, pruritus, and peeling similar to that of mild sunburn. Sensitive individuals may experience oedema, blistering, and crusting of the skin. Excessive application can cause severe erythema, peeling, and discomfort with no increase in efficacy. Photosensitivity may occur. Temporary hypopigmentation and hyperpigmentation have been reported.

Oral doses of tretinoin may produce similar adverse effects to those of isotretinoin (see p.1599). Adverse cardiovascular effects have also been reported; the most common were arrhythmias, flushing, hypotension, hypertension, and heart failure. Less common events were cardiac arrest, myocardial infarction, cardiomegaly, heart murmur, ischaemia, stroke, myocarditis, pericarditis, pulmonary hypertension, and secondary cardiomyopathy. A potentially life-threatening 'retinoic acid syndrome' (see below) has been described after oral use.

Carcinogenicity. Studies in *mice* suggested that tretinoin could enhance photocarcinogenesis.[1] However, other studies refuted this[2] and evidence indicates that topical tretinoin is not carcinogenic in humans.

1. Epstein JH. Chemicals and photocarcinogenesis. *Australas J Dermatol* 1977; **18:** 57–61.
2. Epstein JH. All-trans-retinoic acid and cutaneous cancers. *J Am Acad Dermatol* 1986; **15:** 772–8.

Effects on the blood. Transient and asymptomatic thrombocytosis has been reported with the use of oral tretinoin, see under Isotretinoin, p.1599.

Effects on the cardiovascular system. Tretinoin given for induction remission rapidly improves the coagulopathy associated with acute promyelocytic leukaemia, but there are associated reports of arterial and venous thromboembolism. In a number of cases the combination of tretinoin with an antifibrinolytic drug such as tranexamic acid may have increased the risk of thrombosis.[1-3] In other cases,[2,4] thrombosis occurred in the absence of tranexamic acid and appeared to be related to the retinoic acid syndrome (below). An assessment of 124 patients, including 11 who developed thrombosis, found that the expression of particular phenotypic and genotypic features of leukaemic cells may indicate an increased risk of thrombotic events in patients given tretinoin.[5]

For reports associated with other retinoids, see under Isotretinoin, p.1600.

1. Brown JE, *et al.* All-trans retinoic acid (ATRA) and tranexamic acid: a potentially fatal combination in acute promyelocytic leukaemia. *Br J Haematol* 2000; **110:** 1010–12.
2. Goldschmidt N, *et al.* Extensive splenic infarction, deep vein thrombosis and pulmonary emboli complicating induction therapy with all-trans-retinoic acid (ATRA) for acute promyelocytic leukemia. *Leuk Lymphoma* 2003; **44:** 1433–7.
3. Levin M-D, *et al.* Acute renal cortex necrosis caused by arterial thrombosis during treatment for acute promyelocytic leukemia. *Haematologica* 2003; **88:** ECR21. Available at: http://www.haematologica.org/cgi/reprint/88/6/ECR21.pdf (accessed 28/07/08)
4. Torromeo C, *et al.* Intraventricular thrombosis during all-trans retinoic acid treatment in acute promyelocytic leukemia. *Leukemia* 2001; **15:** 1311–13.
5. Breccia M, *et al.* Occurrence of thrombotic events in acute promyelocytic leukemia correlates with consistent immunophenotypic and molecular features. *Leukemia* 2007; **21:** 79–83.

Effects on the eyes. Papilloedema, retinal haemorrhage and visual changes as a result of benign intracranial hypertension have been associated with oral tretinoin;[1] children appear to be particularly sensitive. For further information about oral retinoids, including tretinoin, causing benign intracranial hypertension, see Effects on the Eyes under Isotretinoin, p.1600.

1. Mahmoud HH, *et al.* Tretinoin toxicity in children with acute promyelocytic leukaemia. *Lancet* 1993; **342:** 1394–5.

Effects on the musculoskeletal system. For reports of myositis occurring in patients receiving oral tretinoin, see under Isotretinoin, p.1600.

Effects on the nervous system. Neurotoxicity (ataxia, dysarthria, and headache) has been reported in a woman with liver impairment using topical tretinoin 0.025% for acne.[1]

1. Bernstein AL, Leventhal-Rochon JL. Neurotoxicity related to the use of topical tretinoin (Retin-A). *Ann Intern Med* 1996; **124:** 227–8.

Effects on the skin. Painful scrotal ulcers, often accompanied by fever, have occurred in men receiving oral tretinoin for acute promyelocytic leukaemia.[1-5] The appearance of the ulcers ranged from days 9 to 30 of the tretinoin course and improved after it was stopped (either at complete remission or because of the ulceration or other adverse effects). Management of the ulcers often included an intravenous or topical corticosteroid and in some cases an antibacterial ointment. Genital ulcers have also been reported in 2 women;[3] an 8-year-old girl developed ulcers 5 days after finishing a course of tretinoin.[6]

Sweet's syndrome (acute febrile neutrophilic dermatosis) has been reported in at least 12 patients treated with oral tretinoin for acute promyelocytic leukaemia.[7] In some cases there was also systemic involvement affecting muscle, kidneys, and lungs, and in a few cases patients also had retinoic acid syndrome (below). Most patients responded to systemic corticosteroid treatment and in some cases the course of tretinoin therapy could be continued as a result. There has also been a report[8] of Sweet's syndrome with myalgia and arthralgia in a child treated with oral tretinoin for acute myeloid leukaemia.

Details of other skin reactions to oral and topical retinoids, including tretinoin, are described under Isotretinoin, p.1601.

1. Mori A, *et al.* Scrotal ulcer occurring in patients with acute promyelocytic leukemia during treatment with all-trans retinoic acid. *Oncol Rep* 1999; **6:** 55–8.
2. Charles KS, *et al.* Scrotal ulceration during all-trans retinoic (ATRA) therapy for acute promyelocytic leukaemia. *Clin Lab Haematol* 2000; **22:** 171–4.
3. Fukuno K, *et al.* Genital ulcers during treatment with ALL-trans retinoic acid for acute promyelocytic leukemia. *Leuk Lymphoma* 2003; **44:** 2009–13.
4. Gettinger S, *et al.* Scrotal ulceration during all-trans-retinoic acid therapy for acute promyelocytic leukemia. *J Clin Oncol* 2004; **22:** 4648–9.
5. Shimizu D, *et al.* Scrotal ulcers arising during treatment with all-trans retinoic acid for acute promyelocytic leukemia. *Intern Med* 2005; **44:** 480–3.
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Retinoic acid syndrome. A syndrome consisting primarily of fever and respiratory distress developed in 9 of 35 patients between 2 and 21 days after starting induction therapy with oral tretinoin for suspected acute promyelocytic leukaemia.[1] Other symptoms included weight gain, oedema of the lower extremities, pleural or pericardial effusions, and episodic hypotension. Symptoms were life-threatening in 5 patients, 3 of whom subsequently died of multi-system failure. Leucocytosis was frequently, although not invariably, associated with development of the syndrome. Experience showed that early treatment with high-dose corticosteroids should be given to these patients irrespective of the leucocyte count. There have also been a few reports of thrombosis occurring with the retinoic acid syndrome (see Effects on the Cardiovascular System, above).

Reviews[2,3] of this syndrome, known as the 'retinoic acid syndrome', reported that it occurs in about 25% of patients with acute promyelocytic leukaemia treated with tretinoin and that the median time to onset is 10 to 12 days after the start of treatment; the severity of the syndrome varies greatly. A high leucocyte count at diagnosis or a rapidly-increasing count on initiation of therapy appears to increase the likelihood of the syndrome occurring. Close monitoring of leucocyte counts and clinical signs is recommended; high-dose intravenous corticosteroids, and possibly antineoplastic drugs, should be given if symptoms appear or the leucocyte count increases rapidly.

A similar syndrome has been reported in patients with acute promyelocytic leukaemia treated with arsenic trioxide (see p.2260). A capillary leak syndrome, similar to retinoic acid syndrome, has also been described with acitretin (see p.1586).

1. Frankel SR, *et al.* The "retinoic acid syndrome" in acute promyelocytic leukemia. *Ann Intern Med* 1992; **117:** 292–6.
2. Fenaux P, De Botton S. Retinoic acid syndrome: recognition, prevention and management. *Drug Safety* 1998; **18:** 273–9.
3. Larson RS, Tallman MS. Retinoic acid syndrome: manifestations, pathogenesis, and treatment. *Best Pract Res Clin Haematol* 2003; **16:** 453–61.

Vasculitic syndromes. For a report of vasculitis associated with oral tretinoin, see under Isotretinoin, p.1601.

Precautions
Contact of tretinoin with the eyes, mouth, or other mucous surfaces should be avoided. It should not be applied to eczematous, sunburnt, or abraded skin and the effects of other topical treatment, especially with keratolytics, should be allowed to subside before topical use of tretinoin. Exposure to UV light and excessive exposure to sunlight should be avoided.

Absorption does not seem to occur to any great extent with topical use. Nevertheless, because of teratogenicity in *animal* studies and isolated cases of congenital abnormalities (see below), licensed product information suggests that the use of topical tretinoin should be avoided during pregnancy. It is not known whether tretinoin is distributed into breast milk, and it should therefore be used topically with caution in breast-feeding mothers.

When tretinoin is given by mouth the precautions described under isotretinoin (see p.1601) should be adopted. Oral tretinoin is contra-indicated in pregnancy and in breast-feeding mothers.

Pregnancy. Although there have been isolated reports[1-4] of congenital abnormalities in infants born to mothers who used tretinoin topically before and during pregnancy, studies involving a