7. Baranda L, *et al.* Severe and unresponsive HIV-associated alopecia areata successfully treated with thalidomide. *Acta Derm Venereol* 2005; **85:** 277–8.
8. Holmes A, *et al.* Thalidomide therapy for the treatment of hypertrophic herpes simplex virus-related genitalis in HIV-infected individuals. *Clin Infect Dis* 2007; **44:** e96–e99. Available at: http://www.journals.uchicago.edu/doi/abs/10.1086/517513 (accessed 18/01/08)
9. Reyes-Terán G, *et al.* Effects of thalidomide on HIV-associated wasting syndrome: a randomized, double-blind, placebo-controlled trial. *AIDS* 1996; **10:** 1501–7.
10. Little RF, *et al.* Activity of thalidomide in AIDS-related Kaposi's sarcoma. *J Clin Oncol* 2000; **18:** 2593–2602.

Inflammatory bowel disease. Small open-label studies[1-3] have shown efficacy of thalidomide in patients with refractory Crohn's disease (see under Inflammatory Bowel Disease, p.1697). In many of those patients already receiving corticosteroids the dosage could be reduced and in some corticosteroids could be stopped completely. Reduction of TNF-α and interleukin-12 by thalidomide may be responsible for its clinical effects in Crohn's disease.[4] Thalidomide has also been reported[5] to be of benefit in children and young adults with intractable inflammatory bowel disease (both Crohn's disease and ulcerative colitis).

1. Ehrenpreis ED, *et al.* Thalidomide therapy for patients with refractory Crohn's disease: an open-label trial. *Gastroenterology* 1999; **117:** 1271–7.
2. Vasiliauskas EA, *et al.* An open-label pilot study of low-dose thalidomide in chronically active, steroid-dependent Crohn's disease. *Gastroenterology* 1999; **117:** 1278–87.
3. Bariol C, *et al.* Early studies on the safety and efficacy of thalidomide for symptomatic inflammatory bowel disease. *J Gastroenterol Hepatol* 2002; **17:** 135–9.
4. Bauditz J, *et al.* Thalidomide reduces tumour necrosis factor α and interleukin 12 production in patients with chronic active Crohn's disease. *Gut* 2002; **50:** 196–200.
5. Lazzerini M, *et al.* Efficacy and safety of thalidomide in children and young adults with intractable inflammatory bowel disease: long-term results. *Aliment Pharmacol Ther* 2007; **25:** 419–27.

Kaposi's sarcoma. See under HIV-associated complications, above and under Malignant Neoplasms, below.

Lupus erythematosus. Thalidomide has been found to be of benefit in lupus erythematosus, including chronic discoid lupus erythematosus,[1,2] lupus erythematosus profundus,[3,4] SLE[5] (p.1513), and cutaneous lupus erythematosus.[6-11] The beneficial effect of thalidomide on cutaneous lupus erythematosus may be partly mediated through protection against UV-induced inflammation.[11]

1. Knop J, *et al.* Thalidomide in the treatment of sixty cases of chronic discoid lupus erythematosus. *Br J Dermatol* 1983; **108:** 461–6.
2. Brocard A, *et al.* Lupus érythémateux chronique: traitement par thalidomide. *Ann Dermatol Venereol* 2005; **132:** 853–6.
3. Burrows NP, *et al.* Lupus erythematosus profundus with partial C4 deficiency responding to thalidomide. *Br J Dermatol* 1991; **125:** 62–7.
4. Wienert S, *et al.* Facetten des Lupus erythematodes: Pannikulitis mit gutem Ansprechen auf Thalidomid. *J Dtsch Dermatol Ges* 2008; **6** 214–16.
5. Bessis D, *et al.* Thalidomide for systemic lupus erythematosus. *Lancet* 1992; **339:** 549–50.
6. Atra E, Sato EI. Treatment of the cutaneous lesions of systemic lupus erythematosus with thalidomide. *Clin Exp Rheumatol* 1993; **11:** 487–93.
7. Stevens RJ, *et al.* Thalidomide in the treatment of the cutaneous manifestations of lupus erythematosus: experience in sixteen consecutive patients. *Br J Rheumatol* 1997; **36:** 353–9.
8. Duong DJ, *et al.* American experience with low-dose thalidomide therapy for severe cutaneous lupus erythematosus. *Arch Dermatol* 1999; **135:** 1079–87.
9. Pelle MT, Werth VP. Thalidomide in cutaneous lupus erythematosus. *Am J Clin Dermatol* 2003; **4:** 379–87.
10. Cuadrado MJ, *et al.* Thalidomide for the treatment of resistant cutaneous lupus: efficacy and safety of different therapeutic regimens. *Am J Med* 2005; **118:** 246–50.
11. Cummins DL, Gaspari AA. Photoprotection by thalidomide in patients with chronic cutaneous and systemic lupus erythematosus: discordant effects on minimal erythema dose and sunburn cell formation. *Br J Dermatol* 2004; **151:** 458–64.

Malignant neoplasms. Thalidomide has shown benefit in the treatment of patients with relapsed advanced multiple myeloma[1-4] (p.658) and also in patients with newly diagnosed disease;[4-8] the response improves when given with dexamethasone. Thalidomide also improved response when added to the regimen of pegylated liposomal doxorubicin, vincristine, and decreased frequency dexamethasone in patients with relapsed-refractory or newly diagnosed multiple myeloma,[9] and when added to melphalan and prednisone in newly-diagnosed elderly patients.[10,11] Thalidomide has also been investigated as maintenance treatment after intensive chemotherapy supported with haematopoietic stem-cell transplantation in patients with newly diagnosed disease;[12,13] thalidomide improved the response rate and event-free survival in both studies, although no improvement in overall survival was seen in one.[12] Thalidomide has also been tried in the treatment of several non-plasma cell malignancies with variable results.[14] It has shown promise in patients with recurrent high-grade gliomas[15] (p.660) and is under investigation for non-AIDS-related Kaposi's sarcoma[16,17] (p.675), metastatic melanoma[18] (p.673), myelofibrosis with myeloid metaplasia,[19-21] and androgen-independent prostate cancer[22,23] (p.671). Thalidomide has shown some benefit in the treatment of cancer-related cachexia (p.2115) in patients with pancreatic cancer.[24]

1. Singhal S, *et al.* Antitumor activity of thalidomide in refractory multiple myeloma. *N Engl J Med* 1999; **341:** 1565–71.
2. Rajkumar SV, *et al.* Thalidomide in the treatment of relapsed multiple myeloma. *Mayo Clin Proc* 2000; **75:** 897–901.
3. Kumar S, *et al.* Response rate, durability of response, and survival after thalidomide therapy for relapsed multiple myeloma. *Mayo Clin Proc* 2003; **78:** 34–9.
4. Palumbo A, *et al.* Thalidomide for treatment of multiple myeloma: 10 years later. *Blood* 2008; **111:** 3968–77.
5. Rajkumar SV, *et al.* Combination therapy with thalidomide plus dexamethasone for newly diagnosed myeloma. *J Clin Oncol* 2002; **20:** 4319–23.
6. Weber D, *et al.* Thalidomide alone or with dexamethasone for previously untreated multiple myeloma. *J Clin Oncol* 2003; **21:** 16–19.
7. Rajkumar SV, *et al.* Phase III clinical trial of thalidomide plus dexamethasone compared with dexamethasone alone in newly diagnosed multiple myeloma: a clinical trial coordinated by the Eastern Cooperative Oncology Group. *J Clin Oncol*. 2006; **24:** 431–6.
8. Rajkumar SV, *et al.* Multicenter, randomized, double-blind, placebo-controlled study of thalidomide plus dexamethasone compared with dexamethasone as initial therapy for newly diagnosed multiple myeloma. *J Clin Oncol* 2008; **26:** 2171–7.
9. Hussein MA, *et al.* Phase 2 study of pegylated liposomal doxorubicin, vincristine, decreased-frequency dexamethasone, and thalidomide in newly diagnosed and relapsed-refractory multiple myeloma. *Mayo Clin Proc* 2006; **81:** 889–95.
10. Palumbo A, *et al.* Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomised controlled trial. *Lancet* 2006; **367:** 825–31.
11. Facon T, *et al.* Melphalan and prednisone plus thalidomide versus melphalan and prednisone alone or reduced-intensity autologous stem cell transplantation in elderly patients with multiple myeloma (IFM 99-06): a randomised trial. *Lancet* 2007; **370:** 1209–18.
12. Barlogie B, *et al.* Thalidomide and hematopoietic-cell transplantation for multiple myeloma. *N Engl J Med* 2006; **354:** 1021–30.
13. Attal M, *et al.* Maintenance therapy with thalidomide improves survival in patients with multiple myeloma. *Blood* 2006; **108:** 3289–94.
14. Kumar S, *et al.* Thalidomid: current role in the treatment of non-plasma cell malignancies. *J Clin Oncol* 2004; **22:** 2477–88. Correction. *ibid.*; 2973. [title]
15. Fine HA, *et al.* Phase II trial of the antiangiogenic agent thalidomide in patients with recurrent high-grade gliomas. *J Clin Oncol* 2000; **18:** 708–15.
16. Ben M'barek L, *et al.* A retrospective analysis of thalidomide therapy in non-HIV-related Kaposi's sarcoma. *Dermatology* 2007; **215:** 202–5.
17. Rubegni P, *et al.* Thalidomide in the treatment of Kaposi's sarcoma. *Dermatology* 2007; **215:** 240–4.
18. Danson S, *et al.* Randomized phase II study of temozolomide given every 8 hours or daily with either interferon alfa-2b or thalidomide in metastatic malignant melanoma. *J Clin Oncol* 2003; **21:** 2551–7.
19. Mesa RA, *et al.* Durable responses to thalidomide-based drug therapy for myelofibrosis with myeloid metaplasia. *Mayo Clin Proc* 2004; **79:** 883–9.
20. Marchetti M, *et al.* Low-dose thalidomide ameliorates cytopenias and splenomegaly in myelofibrosis with myeloid metaplasia: a phase II trial. *J Clin Oncol* 2004; **22:** 424–31.
21. Thomas DA, *et al.* Thalidomide therapy for myelofibrosis with myeloid metaplasia. *Cancer* 2006; **106:** 1974–84.
22. Figg WD. The 2005 Leon I. Goldberg Young Investigator Award Lecture: Development of thalidomide as an angiogenesis inhibitor for the treatment of androgen-independent prostate cancer. *Clin Pharmacol Ther* 2006; **79:** 1–8.
23. Cox MC, *et al.* The use of thalidomide in androgen-independent prostate cancer. *Urol Oncol* 2006; **24:** 246–9.
24. Gordon JN,*et al*. Thalidomide in the treatment of cancer cachexia: a randomised placebo controlled trial. *Gut* 2005; **54:** 540–5.

Mouth ulceration. See under Behçet's syndrome, above and under HIV-associated complications, above.

Oesophageal ulceration. Thalidomide has been shown to be of benefit in the treatment of idiopathic oesophageal ulcers in patients with AIDS (see under HIV-associated complications, above). Thalidomide has also been reported to have healed an oesophageal ulcer refractory to other treatments in an immunocompetent patient,[1] and in an immunocompromised patient after liver transplant.[2]

1. Ollivier S, *et al.* Idiopathic giant oesophageal ulcer in an immunocompetent patient: the efficacy of thalidomide treatment. *Gut* 1999; **45:** 463–4.
2. Atiq M, *et al.* Successful treatment with thalidomide in a liver transplant recipient with giant esophageal ulcers. *Liver Transpl* 2006; **12:** 987–8.

Rheumatic disorders. Beneficial responses to thalidomide have been reported in the treatment of refractory rheumatoid arthritis[1] and adult-onset Still's disease.[2] Thalidomide also improved symptoms in 2 children with systemic onset juvenile rheumatoid arthritis, in whom other therapy, including etanercept, had been ineffective.[3] Efficacy was also shown in a further 11 children with refractory disease who were able to reduce their use of prednisone.[4]

1. Gutiérrez-Rodríguez O, *et al.* Treatment of refractory rheumatoid arthritis—the thalidomide experience. *J Rheumatol* 1989; **16:** 158–63.
2. Stambe C, Wicks IP. TNFα and response of treatment-resistant adult-onset Still's disease to thalidomide. *Lancet* 1998; **352:** 544–5.
3. Lehman TJA, *et al.* Thalidomide therapy for recalcitrant systemic onset juvenile rheumatoid arthritis. *J Pediatr* 2002; **140:** 125–7.
4. Lehman TJ, *et al.* Thalidomide for severe systemic onset juvenile rheumatoid arthritis: a multicenter study. *J Pediatr* 2004; **145:** 856–7.

Sarcoidosis. Case reports[1-5] of thalidomide in the treatment of sarcoidosis suggest that it might be of benefit.

1. Carlesimo M, *et al.* Treatment of cutaneous and pulmonary sarcoidosis with thalidomide. *J Am Acad Dermatol* 1995; **32:** 866–9.
2. Baughman RP, *et al.* Thalidomide for chronic sarcoidosis. *Chest* 2002; **122:** 227–32.
3. Walter MC, *et al.* Successful treatment of muscle sarcoidosis with thalidomide. *Acta Myol* 2003; **22:** 22–5.
4. Nguyen YT, *et al.* Treatment of cutaneous sarcoidosis with thalidomide. *J Am Acad Dermatol* 2004; **50:** 235–41.
5. Hammond ER, *et al.* Thalidomide for acute treatment of neurosarcoidosis. *Spinal Cord* 2007; **45:** 802–3.

Skin disorders. Thalidomide has shown efficacy in several severe dermatological disorders refractory to conventional therapies.[1,2] A review[3] of studies of thalidomide in the treatment of severe type 2 (erythema nodosum leprosum) lepra reactions concluded that it is an effective alternative to corticosteroid therapy. It has also been investigated in other severe skin disorders and beneficial responses have been reported in erythema multiforme[4,5] (p.1580), pruritus associated with uraemia,[6] Langerhans-cell histiocytosis[7] (p.650), epidermolysis bullosa and its variants,[8-10] prurigo nodularis,[11,12] pyoderma gangrenosum[13,14] (p.1583), and Schnitzler's syndrome.[15]

1. Wu JJ, *et al.* Thalidomide: dermatological indications, mechanisms of action and side-effects. *Br J Dermatol* 2005; **153:** 254–73.
2. Faver IR, *et al.* Thalidomide for dermatology: a review of clinical uses and adverse effects. *Int J Dermatol* 2005; **44:** 61–7.
3. Walker SL, *et al.* The role of thalidomide in the management of erythema nodosum leprosum. *Lepr Rev* 2007; **78:** 197–215.
4. Bahmer FA, *et al.* Thalidomide treatment of recurrent erythema multiforme. *Acta Derm Venereol (Stockh)* 1982; **62:** 449–50.
5. Moisson YF, *et al.* Thalidomide for recurrent erythema multiforme. *Br J Dermatol* 1992; **126:** 92–3.
6. Silva SRB, *et al.* Thalidomide for the treatment of uremic pruritus: a crossover randomized double-blind trial. *Nephron* 1994; **67:** 270–3.
7. McClain KL, Kozinetz CA. A phase II trial using thalidomide for Langerhans cell histiocytosis. *Pediatr Blood Cancer* 2007; **48:** 44–9.
8. Goulden V, *et al.* Linear prurigo simulating dermatitis artefacta in dominant dystrophic epidermolysis bullosa. *Br J Dermatol* 1993; **129:** 443–6.
9. Ozanic Bulic S, *et al.* Thalidomide in the management of epidermolysis bullosa pruriginosa. *Br J Dermatol* 2005; **152:** 1332–4.
10. Strauss RM, *et al.* A child with laryngo-onychocutaneous syndrome partially responsive to treatment with thalidomide. *Br J Dermatol* 2006; **155:** 1283–6.
11. Ferrándiz C, *et al.* Sequential combined therapy with thalidomide and narrow-band (TL01) UVB in the treatment of prurigo nodularis. *Dermatology* 1997; **195:** 359–61.
12. Lan C-CE, *et al.* Treatment of idiopathic prurigo nodularis in Taiwanese patients with low-dose thalidomide. *J Dermatol* 2007; **34:** 237–42.
13. Federman GL, Federman DG. Recalcitrant pyoderma gangrenosum treated with thalidomide. *Mayo Clin Proc* 2000; **75:** 842–4.
14. Koca E, *et al.* Successful treatment of myelodysplastic syndrome-induced pyoderma gangrenosum. *Neth J Med* 2006; **64:** 422–4.
15. Worm M, Kolde G. Schnitzler's syndrome: successful treatment of two patients using thalidomide. *Br J Dermatol* 2003; **148:** 601–2.

Preparations

USP 31: Thalidomide Capsules.

Proprietary Preparations (details are given in Part 3)
India: Thalix; ***Mex.:*** Inmunoprin; Talizer; ***USA:*** Thalomid.

Thallium Acetate

Talio, acetato de; Thallous Acetate.

$C_2H_3O_2Tl$ = 263.4.

CAS — 7440-28-0 (thallium); 563-68-8 (thallium acetate); 7446-18-6 (thallium sulfate).

Adverse Effects

Thallium salts are toxic when inhaled, ingested, or absorbed through the skin. Symptoms of poisoning may appear within 12 to 24 hours of a single toxic dose and include severe abdominal pain, nausea and vomiting, diarrhoea, gastrointestinal haemorrhage, salivation, metallic taste, paralytic ileus, pancreatic damage, and in severe cases cardiovascular collapse, tremors, delirium, convulsions, paralysis, and coma, leading to death in 1 to 2 days. However, the acute reaction may subside, to be followed within about 10 days by the development of neurological effects including paraesthesia, myalgia, myopathy, motor neuropathy, and visual disturbances due to optic neuropathy, psychosis, delirium, convulsions, and other signs of encephalopathy, tachycardia, hypertension, skin eruptions, and hepatorenal injury. Recovery from neurological damage is slow and may be incomplete. Alopecia occurs within 15 to 20 days; stomatitis may also develop. Death may result from respiratory failure; patients are also predisposed for several weeks to cardiac arrhythmias and sudden death. Fatalities have occurred after ingestion of 1 g or less in adults, although the UK Poisons Information Service consider the usual lethal dose by ingestion to be in the range 3 to 10 g in adults.

Smaller repeated doses are also toxic, with symptoms appearing over several weeks. Constipation is a common feature of less severe poisoning.

Poisoning. References.
1. Moeschlin S. Thallium poisoning. *Clin Toxicol* 1980; **17:** 133–46.
2. Heyl T, Barlow RJ. Thallium poisoning: a dermatological perspective. *Br J Dermatol* 1989; **121:** 787–92.
3. Luckit J, *et al.* Thrombocytopenia associated with thallium poisoning. *Hum Exp Toxicol* 1990; **9:** 47–8.
4. Moore D, *et al.* Thallium poisoning. *BMJ* 1993; **306:** 1527–9.
5. Tabandeh H, Thompson GM. Visual function in thallium toxicity. *BMJ* 1993; **307:** 324.
6. Questel F, *et al.* Thallium-contaminated heroin. *Ann Intern Med* 1996; **124:** 616.
7. Tromme I, *et al.* Skin signs in the diagnosis of thallium poisoning. *Br J Dermatol* 1998; **138:** 321–5.
8. Hoffman RS. Thallium poisoning during pregnancy: a case report and comprehensive literature review. *J Toxicol Clin Toxicol* 2000; **38:** 767–75.
9. Misra UK, *et al.* Thallium poisoning: emphasis on early diagnosis and response to haemodialysis. *Postgrad Med J* 2003; **79:** 103–5.
10. Hoffman RS. Thallium toxicity and the role of Prussian blue in therapy. *Toxicol Rev* 2003; **22:** 29–40.
11. Thompson DF, Callen ED. Soluble or insoluble Prussian blue for radiocesium and thallium poisoning? *Ann Pharmacother* 2004; **38:** 1509–14.
12. Kuo H-C, *et al.* Acute painful neuropathy in thallium poisoning. *Neurology* 2005; **65:** 302–4.

Treatment of Adverse Effects

Gastric lavage should be considered if the patient presents within 1 hour of acute ingestion. Intensive supportive therapy is necessary.

Attempts have been made to increase the faecal and urinary excretion of thallium. A suspension of activated charcoal has been given to reduce intestinal absorption and enteric recycling. Prussian blue (p.1461) given orally as a drink or via a nasogastric tube is also used routinely. A purgative such as mannitol may be required with either activated charcoal or Prussian blue as constipation is common in severe thallium toxicity. Giving potassium chloride by mouth may mobilise thallium from the tissues but is hazardous, especially if given during the early stage as signs of poisoning may be aggravated. Traditional chelation therapy is not generally recommended for thallium poisoning.

Haemoperfusion, haemodialysis, or peritoneal dialysis have been reported to be effective in eliminating absorbed thallium, although clinical benefit is doubtful.

Uses and Administration

Thallium acetate was formerly used by mouth for depilation in ringworm and as an ingredient of depilatory creams but both systemic and local treatments have caused deaths, and it is no longer used for such purposes. It has also been used as a rodenticide and insecticide; thallium sulfate has been used similarly. The use of thallium salts is strictly regulated in many countries. However, use in industry could still constitute a hazard. Cases of malicious poisoning still occur occasionally.

Theobroma

Cacao or Cocoa Powder; Chocolate; Teobroma; Theobrom.

Pharmacopoeias. In *USNF*.

USNF 26 (Chocolate). A powder prepared from the roasted, cured kernels of the ripe seed of *Theobroma cacao* (Sterculiaceae).

Profile

Theobroma is used as a flavoured basis for tablets and lozenges. Theobroma oil (p.2033) is used as a basis for suppositories.

Breast feeding. The American Academy of Pediatrics[1] states that irritability or increased bowel activity have been reported in infants whose mothers ate excessive amounts of chocolate (16 ounces (about 450 g) or more daily).

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.* 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 08/07/04)

Preparations

USNF 26: Chocolate Syrup.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Asthmatee EF-EM-ES.

Theodrenaline Hydrochloride *(BANM, rINNM)* ⊗

H-8352; Hidrocloruro de teodrenalina; Noradrenaline Theophylline Hydrochloride; Théodrénaline, Chlorhydrate de; Theodrenalini Hydrochloridum. 7-[2-(3,4,β-Trihydroxyphenethylamino)ethyl]theophylline hydrochloride.

Теодреналина Гидрохлорид

$C_{17}H_{21}N_5O_5,HCl$ = 411.8.

CAS — 13460-98-5 (theodrenaline); 2572-61-4 (theodrenaline hydrochloride).

ATC — C01CA23.

ATC Vet — QC01CA23.

Profile

Theodrenaline is mainly used as the hydrochloride in preparations with cafedrine promoted for the treatment of hypotension.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Akrinor; ***Fr.:*** Praxinor; ***Ger.:*** Akrinor†; ***S.Afr.:*** Akrinor; ***Spain:*** Bifort†.

Thioctic Acid

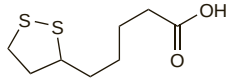
Acide thioctique; Acidum thiocticum; Alpha Lipoic Acid; Kwas tioktynowy; Kyselina thioktová; Lipoic Acid; α-Liponic Acid; Tióctico, ácido. 5-(1,2-Dithiolan-3-yl)valeric acid.

$C_8H_{14}O_2S_2$ = 206.3.

CAS — 62-46-4.

ATC — A16AX01.

ATC Vet — QA16AX01.



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

Ph. Eur. 6.2 (Thioctic Acid). A yellow, crystalline powder. M.p. about 61°. Very slightly soluble in water; very soluble in dimethylformamide; freely soluble in methyl alcohol. Protect from light.

USP 31 (Alpha Lipoic Acid). M.p. 60.0° to 62.0°.

Profile

Thioctic acid is used for its antoxidant effects in the treatment of diabetic neuropathy. It has been tried in the treatment of liver dysfunction and in subacute necrotising encephalopathy. Beneficial results have been claimed in amanitin poisoning after ingestion of the mushroom *Amanita phalloides*, but such use is controversial (see under Poisonous Mushrooms or Toadstools, p.2349). Ethylenediamine thioctate, sodium thioctate, thioctic acid amide (thioctamide), and trometamol thioctate have been used similarly.

Diabetic neuropathy. References[1-5] to the benefits of thioctic acid in diabetic neuropathy.

1. Ziegler D, *et al.* Effects of treatment with the antioxidant α-lipoic acid on cardiac autonomic neuropathy in NIDDM patients: a 4-month randomized controlled multicenter trial (DEKAN study). *Diabetes Care* 1997; **20:** 369–73.
2. Ziegler D, *et al.* Treatment of symptomatic diabetic polyneuropathy with the antioxidant α-lipoic acid: a 7-month multicenter randomized controlled trial (ALADIN III study). *Diabetes Care* 1999; **22:** 1296–1301.
3. Ametov AS, *et al.* The sensory symptoms of diabetic polyneuropathy are improved with α-lipoic acid: the SYDNEY trial. *Diabetes Care* 2003; **26:** 770–6. Correction. *ibid.*; 2227.
4. Ziegler D, *et al.* Treatment of symptomatic diabetic polyneuropathy with the antioxidant α-lipoic acid: a meta-analysis. *Diabet Med* 2004; **21:** 114–21.
5. Ziegler D, *et al.* Oral treatment with α-lipoic acid improves symptomatic diabetic polyneuropathy: the SYDNEY 2 trial. *Diabetes Care* 2006; **29:** 2365–70.

Pharmacokinetics. References.

1. Teichert J, *et al.* Pharmacokinetics of alpha-lipoic acid in subjects with severe kidney damage and end-stage renal disease. *J Clin Pharmacol* 2005; **45:** 313–28.

Preparations

USP 31: Alpha Lipoic Acid Capsules; Alpha Lipoic Acid Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Biletan; Ciagen; Neurotioct; Neutracol; Sigmus; Tioctan; ***Austria:*** Thioctacid; Tioctan; ***Cz.:*** Alpha-Lipon†; Thioctacid; Thiogamma; ***Ger.:*** Alpha-Lipogamma; Alpha-Lipon; alpha-Vibolex; Alphaflam; Azulipont†; Biomolipon; duralipon; espa-lipon†; Fenint†; Juthiac†; Neurium; Pleomix-Alpha†; Thioctacid; Thiogamma; Tromlipon; Verla-Lipon; Vitatrans; ***Hung.:*** Thioctacid; Thiogamma; ***Indon.:*** Alanox; Mecola Forte; ***Ital.:*** Tiobec Crema; ***Jpn:*** Tioctan†; ***Mex.:*** Thioctacid; ***Pol.:*** Neurex; Thiogamma; ***Rus.:*** Berlithion (Берлитион); Espa-Lipon (Эспа-липон); Thioctacid (Тиоктацид); Thiogamma (Тиогамма); ***Thai.:*** Lipoicin†.

Multi-ingredient: ***Arg.:*** Biletan Enzimatico; Carbogasol Digestivo; Co-Tioctan; Nervomax TB12; ***Canad.:*** Biotrim†; ***Hong Kong:*** Lipochol; ***India:*** Alcrin-M; ***Indon.:*** Alicron; Aptivium Liver Support; Mecola; Reliv; ***Ital.:*** Alfa Lip; Angiovein; Byodinoral; Depatox; Lipoacid Combi; Neuralfa; Neuroptic; Osteolip; Tiobec; Tiofort; ***Philipp.:*** Illumina; ***Port.:*** Lipoacid; Lipoacid Combi†; ***Spain:*** Policolinosil; ***Thai.:*** Lipochol.

Thiomucase

C-84-04; Chondroitinsulphatase; Tiomucasa.

Profile

Thiomucase is a mucopolysaccharidase with general properties similar to those of hyaluronidase, p.2321, but which also depolymerises chondroitin sulfate. It has been given to assist the diffusion of local anaesthetic injections.

Preparations

Proprietary Preparations (details are given in Part 3)

Spain: Thiocase.

Multi-ingredient: ***Braz.:*** Thiomucase.

Thiotriazoline

Tiotriazolin. Morpholine 5-methyl-1,2,4-triazoline-5-thioacetate.

Тиотриазолин

Profile

Thiotriazoline is reported to have anti-ischaemic, membrane stabilising, and antoxidant actions. It is used as a hepatoprotectant in various liver disorders and as a protectant in cardiovascular and cerebrovascular disorders. It is also used locally as an anti-inflammatory for wounds and lesions of the skin and mucous membranes and for vaginal or rectal inflammation.

Thiram *(USAN, rINN)*

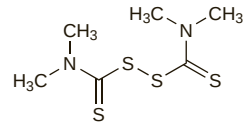
NSC-1771; SQ-1489; Thirame; Thiramum; Tiram; Tiramo; TMT; TMTD. Tetramethylthiuram disulphide.

Тирам

$C_6H_{12}N_2S_4$ = 240.4.

CAS — 137-26-8.

ATC — P03AA05.



Profile

Thiram, the methyl analogue of disulfiram (p.2296), has antibacterial and antifungal activity. It has been applied topically as an aerosol in the treatment of wounds and other skin disorders. It has been used as a fungicide in agriculture, and in industry as a rubber accelerator. Occupational exposure to thiram may cause irritation of mucous membranes and skin.

Thorium Dioxide

Thorium Oxide; Torio, dióxido de.

ThO_2 = 264.0.

CAS — 1314-20-1.

Profile

Colloidal solutions of thorium dioxide were formerly used as X-ray contrast media for examination of the liver and spleen, for arteriography, and occasionally for outlining the cerebral ventricles. Its elimination is very slow and incomplete. It accumulates in the reticuloendothelial system, especially in the liver and spleen. As it is radioactive (half-life: 1.41×10^{10} years), this accumulation is dangerous and there is strong evidence that the ensuing prolonged exposure to its radiation is a contributing factor in the development of malignant diseases and blood disorders often 20 to 30 years after its use.

Thuja

Tuya; White Cedar.

Profile

Thuja consists of the fresh leaves and twigs of *Thuja occidentalis* (Cupressaceae). It is included in some topical preparations for warts and in herbal antiseptic preparations. It is also used in herbal preparations for respiratory-tract disorders.

The oil distilled from the leaves and twigs is known as thuja oil or cedar leaf oil. It has been included in preparations for inhalation for the relief of respiratory-tract symptoms and for external use but is generally considered to be too toxic for internal use. Cedar leaf oil should be distinguished from cedar wood oil, obtained from *Juniperus virginiana* (see Red Cedar, p.2278).

Homoeopathy. Thuja has been used in homoeopathic medicines under the following names: Thuja occidentalis.

Preparations

Proprietary Preparations (details are given in Part 3)

Chile: Thujaderm.

Multi-ingredient: ***Austral.:*** Vicks Vaporub; ***Austria:*** Colda; Esberitox; Pe-Ce; ***Belg.:*** Aporil; Vicks Vaporub; ***Braz.:*** Calope†; Mentalol†; Vick Vaporub; ***Fr.:*** Item Alphacade; Item Alphazole; Item Lentes; Nitrol; Verrupan; Vicks Vaporub; ***Ger.:*** Esberitox N; ***Malaysia:*** Esberitox N; ***Pol.:*** Esberitox N; ***Port.:*** Alpha Cade; Alphacedre; Alphazole†; ***S.Afr.:*** Vicks Vaporub; ***Spain:*** Nitroina; ***Switz.:*** Esberitop; Vicks Vaporub N; ***Turk.:*** Kataljin; Vicks Vaporub; ***USA:*** Vicks Vaporub.

Thymalfasin *(USAN, rINN)*

Thymalfasine; Thymalfasinum; Thymosin α1; Timalfasina.

Тимальфазин

CAS — 62304-98-7; 69521-94-4.

Profile

Thymalfasin is a thymus hormone (p.2401) found in thymosin fraction 5 (a crude thymus gland extract) but now produced by synthesis. Thymalfasin is used alone or with interferon as an im-