The ocular microfilarial load can be safely reduced by ivermectin[2,17] and early lesions of the anterior segment of the eye have improved.[17] A reduction in the incidence[18] and progression[19] of optic nerve damage has also been reported, but the effect on posterior segment disease is less certain.[20] A systematic review of 5 placebo-controlled studies, with data from 3810 individuals, found no statistically significant difference between ivermectin and placebo groups for preventing visual acuity loss.[21] Improvements in skin lesions have been reported.[22]

1. Basáñez MG, *et al.* Effect of single-dose ivermectin on Onchocerca volvulus: a systematic review and meta-analysis. *Lancet Infect Dis* 2008; **8:** 310–22.
2. Newland HS, *et al.* Effect of single-dose ivermectin therapy on human Onchocerca volvulus infection with onchocercal ocular involvement. *Br J Ophthalmol* 1988; **72:** 561–9.
3. Taylor HR, *et al.* Impact of mass treatment of onchocerciasis with ivermectin on the transmission of infection. *Science* 1990; **250:** 116–18.
4. Trpis M, *et al.* Effect of mass treatment of a human population with ivermectin on transmission of Onchocerca volvulus by Simulium yahense in Liberia, West Africa. *Am J Trop Med Hyg* 1990; **42:** 148–56.
5. Chavasse DC, *et al.* Low level ivermectin coverage and the transmission of onchocerciasis. *Trans R Soc Trop Med Hyg* 1995; **89:** 534–7.
6. Boussinesq M, *et al.* Onchocerca volvulus: striking decrease in transmission in the Vina valley (Cameroon) after eight annual large scale ivermectin treatments. *Trans R Soc Trop Med Hyg* 1997; **91:** 82–6.
7. Pond B. Distribution of ivermectin by health workers. *Lancet* 1990; **335:** 1539.
8. De Sole G, *et al.* Adverse reactions after large-scale treatment of onchocerciasis with ivermectin: combined results from eight community trials. *Bull WHO* 1989; **67:** 707–19.
9. Pacqué M, *et al.* Safety of and compliance with community-based ivermectin therapy. *Lancet* 1990; **335:** 1377–80.
10. Pacqué M, *et al.* Community-based treatment of onchocerciasis with ivermectin: safety, efficacy, and acceptability of yearly treatment. *J Infect Dis* 1991; **163:** 381–5.
11. Steel C, *et al.* Immunologic responses to repeated ivermectin treatment in patients with onchocerciasis. *J Infect Dis* 1991; **164:** 581–7.
12. Whitworth JAG, *et al.* A community trial of ivermectin for onchocerciasis in Sierra Leone: clinical and parasitological responses to four doses given at six-monthly interval. *Trans R Soc Trop Med Hyg* 1992; **86:** 277–80.
13. Greene BM, *et al.* A comparison of 6-, 12-, and 24-monthly dosing with ivermectin for treatment of onchocerciasis. *J Infect Dis* 1991; **163:** 376–80.
14. Gardon J,*et al.* Effects of standard and high doses of ivermectin on adult worms of Onchocerca volvulus: a randomised controlled trial. *Lancet* 2002; **360:** 203–10.
15. Kamgno J, *et al.* Adverse systemic reactions to treatment of onchocerciasis with ivermectin at normal and high doses given annually or three-monthly. *Trans R Soc Trop Med Hyg* 2004; **98:** 496–504.
16. Churchill DR, *et al.* A trial of a three-dose regimen of ivermectin for the treatment of patients with onchocerciasis in the UK. *Trans R Soc Trop Med Hyg* 1994; **88:** 242.
17. Dadzie KY, *et al.* Changes in ocular onchocerciasis after two rounds of community-based ivermectin treatment in a holo-endemic onchocerciasis focus. *Trans R Soc Trop Med Hyg* 1991; **85:** 267–71.
18. Abiose A, *et al.* Reduction in incidence of optic nerve disease with annual ivermectin to control onchocerciasis. *Lancet* 1993; **341:** 130–4.
19. Cousens SN, *et al.* Impact of annual dosing with ivermectin on progression of onchocercal visual field loss. *Bull WHO* 1997; **75:** 229–36.
20. Whitworth JAG, *et al.* Effects of repeated doses of ivermectin on ocular onchocerciasis: community-based trial in Sierra Lione. *Lancet* 1991; **338:** 1100–1103.
21. Ejere H, *et al.* Ivermectin for onchocercal eye disease (river blindness). Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2001 (accessed 29/07/07).
22. Pacqué M, *et al.* Improvements in severe onchocercal skin disease after a single dose of ivermectin. *Am J Med* 1991; **90:** 590–4.

Scabies and pediculosis. Scabies (p.2035) is usually treated with a topically applied acaricide. However, a single oral dose of ivermectin has been reported to be effective.[1,2] In a study of 11 patients with uncomplicated scabies, a single oral dose of ivermectin 200 micrograms/kg was effective in curing infection after 4 weeks. In a group of 11 patients, also infected with HIV, scabies was cured in 8 after 2 weeks.[1] Two of the remaining 3 patients received a second dose of ivermectin which cured the scabies infection by the fourth week. A single oral dose of ivermectin 150 micrograms/kg was partially effective in an outbreak of scabies in 1153 Tanzanian patients.[3] Crusted (Norwegian) scabies has also been reported to be effectively treated by a single oral dose of 12 mg of ivermectin in addition to topical application of 3% salicylic acid ointment in 2 patients; the treatment was effective in under one week.[2] A single oral dose of ivermectin 200 micrograms/kg was effective for crusted scabies in a 2-year-old infant who had contracted the disease following long-term corticosteroid use.[4]

Ivermectin has also been investigated[5] as a possible treatment for pediculosis (p.2034) although, again, topically applied insecticides are the usual method of control. A study *in vitro* and in *animals* showed that ivermectin killed nymphs and females of the human body louse (*Pediculus humanus humanus*). Ivermectin was known to be effective against other louse species that infect a range of *animals*.[6]

1. Meinking TL, *et al.* The treatment of scabies with ivermectin. *N Engl J Med* 1995; **333:** 26–30.
2. Aubin F, Humbert P. Ivermectin for crusted (Norwegian) scabies. *N Engl J Med* 1995; **332:** 612.
3. Leppard B, Naburi AE. The use of ivermectin in controlling an outbreak of scabies in a prison. *Br J Dermatol* 2000; **143:** 520–3.
4. Marlière V, *et al.* Crusted (Norwegian) scabies induced by use of topical corticosteroids and treated successfully with ivermectin. *J Pediatr* 1999; **135:** 122–4.
5. Foucault C, *et al.* Oral ivermectin in the treatment of body lice. *J Infect Dis* 2006; **193:** 474–6.
6. Mumcuoglu KY, *et al.* Systemic activity of ivermectin on the human body louse (Anoplura: Pediculidae). *J Med Entomol* 1990; **27:** 72–5.

Strongyloidiasis. Ivermectin is effective in the treatment of strongyloidiasis (p.138) and is considered by some authorities to be the drug of choice.

References.

1. Naquira C, *et al.* Ivermectin for human strongyloidiasis and other intestinal helminths. *Am J Trop Med Hyg* 1989; **40:** 304–9.
2. Wijesundera M de S, Sanmuganathan PS. Ivermectin therapy in chronic strongyloidiasis. *Trans R Soc Trop Med Hyg* 1992; **86:** 291.
3. Lyagoubi M, *et al.* Chronic persistent strongyloidiasis cured by ivermectin. *Trans R Soc Trop Med Hyg* 1992; **86:** 541.
4. Datry A, *et al.* Treatment of Strongyloides stercoralis infection with ivermectin compared with albendazole: results of an open study of 60 cases. *Trans R Soc Trop Med Hyg* 1994; **88:** 344–5.
5. Gann PH, *et al.* A randomized trial of single- and two-dose ivermectin versus thiabendazole for treatment of strongyloidiasis. *J Infect Dis* 1994; **169:** 1076–9.
6. Marti H, *et al.* A comparative trial of a single-dose ivermectin versus three days of albendazole for treatment of Strongyloides stercoralis and other soil-transmitted helminth infections in children. *Am J Trop Med Hyg* 1996; **55:** 477–81.
7. Igual-Adell R, *et al.* Efficacy and safety of ivermectin and thiabendazole in the treatment of strongyloidiasis. *Expert Opin Pharmacother* 2004; **5:** 2615–9.

Trichostrongyliasis. For mention of the use of ivermectin in *Trichostrongylus* infections, see p.139.

Preparations

USP 31: Ivermectin Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Dermopero; Securo; ***Austral.:*** Stromectol; ***Braz.:*** Ivermec†; Leverctin; Revectina; Vermectil; ***Fr.:*** Mectizan; Stromectol; ***Jpn:*** Stromectol; ***Mex.:*** Ivexterm; ***Neth.:*** Stromectol; ***NZ:*** Stromectol; ***USA:*** Mectizan; Stromectol.

Levamisole *(BAN, rINN)*

Levamisol; Lévamisole; Levamisoli; Levamisolum; Levamizol. (*S*)-2,3,5,6-Tetrahydro-6-phenylimidazo[2,1-*b*][1,3]thiazole.

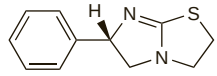
Левамизол

$C_{11}H_{12}N_2S$ = 204.3.

CAS — 14769-73-4.

ATC — P02CE01.

ATC Vet — QP52AE01.



Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.
Ph. Eur. 6.2 (Levamisole for Veterinary Use; Levamisole BP(Vet) 2008). A white or almost white powder. It exhibits polymorphism. Slightly soluble in water; freely soluble in alcohol and in methyl alcohol. Store in airtight containers. Protect from light.

Levamisole Hydrochloride *(BANM, USAN, rINNM)*

Cloridrato de Levamizol; Hidrocloruro de levamisol; ICI-59623; Lévamisole, chlorhydrate de; Levamisol-hydrochlorid; Levamisol-hydroklorid; Levamisoli hydrochloridum; Levamisolihydrokloridi; Levamizol-hidroklorid; Levamizolio hidrochloridas; Lewamizolu chlorowodorek; NSC-177023; R-12564; RP-20605; *l*-Tetramisole Hydrochloride; *l*-Tetramisole Hydrochloride.

Левамизола Гидрохлорид

$C_{11}H_{12}N_2S,HCl$ = 240.8.

CAS — 16595-80-5.

ATC — P02CE01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *US*, and *Viet.*
Ph. Eur. 6.2 (Levamisole Hydrochloride). A white to almost white crystalline powder. Freely soluble in water; soluble in alcohol; slightly soluble in dichloromethane. A 5% solution in water has a pH of 3.0 to 4.5. Protect from light.
USP 31 (Levamisole Hydrochloride). A white or almost white crystalline powder. Freely soluble in water; soluble in alcohol; slightly soluble in dichloromethane; practically insoluble in ether. pH of a 5% solution in water is between 3.0 and 4.5. Protect from light.

Adverse Effects

When given in single doses for the treatment of ascariasis or other worm infections, levamisole is generally well tolerated and adverse effects are usually limited to nausea, vomiting, diarrhoea, abdominal pain, dizziness, and headache.

When levamisole is used as an immunostimulant and given for longer periods, adverse effects are more frequent and diverse and, in common with other immunomodulators, may sometimes result from exacerbation of the primary underlying disease. Adverse effects associated especially with the more prolonged use of levamisole have included: hypersensitivity reactions such as fever, a flu-like syndrome, arthralgia, muscle pain, skin rashes, and cutaneous vasculitis; CNS effects including headache, insomnia, dizziness, and convulsions; haematological abnormalities such as agranulocytosis, leucopenia, and thrombocytopenia; and gastrointestinal disturbances, including an abnormal taste in the mouth.

Incidence of adverse effects. In a review[1] (by the manufacturers) of 46 controlled studies in which 2635 cancer patients received adjuvant levamisole treatment, most patients received levamisole on 3 consecutive days every 2 weeks (1102 patients) or on 2 consecutive days every week (1156 patients), usually in a daily dose of 150 mg. Levamisole caused several adverse effects, such as skin rash, nausea, vomiting, and a metallic or bitter taste in the mouth, which although troublesome were relatively trivial and often regressed during therapy or disappeared on cessation of therapy. A total of 38 patients developed agranulocytosis and of these 36 had received weekly treatment. Several contracted possible life-threatening infections and 2 died of septic shock.

1. Amery WK, Butterworth BS. Review/commentary: the dosage regimen of levamisole in cancer: is it related to efficacy and safety? *Int J Immunopharmacol* 1983; **5:** 1–9.

Effects on the endocrine system. Rechallenge confirmed that levamisole was responsible for inappropriate antidiuretic hormone syndrome in a patient receiving levamisole with fluorouracil.[1]

1. Tweedy CR, *et al.* Levamisole-induced syndrome of inappropriate antidiuretic hormone. *N Engl J Med* 1992; **326:** 1164.

Effects on the liver. Elevated aspartate aminotransferase concentrations in 2 of 11 patients given levamisole for recurrent pyoderma suggested liver toxicity, a very rarely occurring adverse effect.[1] In a later report, liver enzyme concentrations were raised in a 14-year-old boy treated with levamisole for minimal change nephrotic syndrome.[2]

1. Papageorgiou P, *et al.* Levamisole in chronic pyoderma. *J Clin Lab Immunol* 1982; **8:** 121–7.
2. Bulugahapitiya DTD. Liver toxicity in a nephrotic patient treated with levamisole. *Arch Dis Child* 1997; **76:** 289.

Effects on the nervous system. Reports[1,2] of inflammatory leukoencephalopathy were associated with the use of fluorouracil and levamisole in 4 patients being treated for adenocarcinoma of the colon. Active demyelination was demonstrated in 2 patients.[1] Clinical improvement occurred when chemotherapy was stopped; 3 patients were treated with corticosteroids.[1] A similar syndrome has been reported in a patient with a history of hepatitis C given levamisole alone.[3]

1. Hook CC, *et al.* Multifocal inflammatory leukoencephalopathy with 5-fluorouracil and levamisole. *Ann Neurol* 1992; **31:** 262–7.
2. Kimmel DW, Schutt AJ. Multifocal leukoencephalopathy: occurrence during 5-fluorouracil and levamisole therapy and resolution after discontinuation of chemotherapy. *Mayo Clin Proc* 1993; **68:** 363–5.
3. Lucia P, *et al.* Multifocal leucoencephalopathy induced by levamisole. *Lancet* 1996; **348:** 1450.

Precautions

The use of levamisole should be avoided in patients with pre-existing blood disorders. Patients given levamisole with fluorouracil should undergo appropriate monitoring of haematological and hepatic function.

Rheumatoid arthritis. The presence of HLA B27 in seropositive rheumatoid arthritis is an important predisposing factor to the development of agranulocytosis with levamisole; it is recommended that the use of levamisole in this group should be avoided.[1]

1. Mielants H, Veys EM. A study of the hematological side effects of levamisole in rheumatoid arthritis with recommendations. *J Rheumatol* 1978; **5** (suppl 4): 77–83.

Sjögren's syndrome. The appearance of adverse effects in 9 of 10 patients with rheumatoid arthritis and Sjögren's syndrome while being treated with levamisole led to abandonment of the study.[1] Levamisole should be given with caution, if at all, to patients with Sjögren's syndrome.

1. Balint G, *et al.* Sjögren's syndrome: a contraindication to levamisole treatment? *BMJ* 1977; **2:** 1386–7.

Interactions

Alcohol. US licensed product information states that levamisole can produce a disulfiram-like reaction with *alcohol.*

Anticoagulants. For an increase in the activity of *warfarin* when given with levamisole and fluorouracil, see Interactions, Levamisole, under Warfarin, p.1431.

Antiepileptics. For increased *phenytoin* concentrations when given with levamisole and fluorouracil, see Interactions, Antineoplastics, under Phenytoin, p.499.

Pharmacokinetics

Levamisole is rapidly absorbed from the gastrointestinal tract. Maximum plasma concentrations are attained within 1.5 to 2 hours. It is extensively metabolised in the liver. The plasma half-life for levamisole is 3 to 4 hours and for the metabolites is 16 hours. It is excreted mainly in the urine as metabolites and a small proportion in the faeces. About 70% of a dose is excreted in the urine over 3 days, with about 5% as unchanged levamisole.

◊ References.

1. Luyckx M, *et al.* Pharmacokinetics of levamisole in healthy subjects and cancer patients. *Eur J Drug Metab Pharmacokinet* 1982; **7:** 247–54.
2. Kouassi E, *et al.* Novel assay and pharmacokinetics of levamisole and p-hydroxylevamisole in human plasma and urine. *Biopharm Drug Dispos* 1986; **7:** 71–89.

Uses and Administration

Levamisole hydrochloride is the active laevo-isomer of tetramisole hydrochloride. It is used as an anthelmintic and as an adjuvant in malignant disease. It has also been tried in several conditions where its stimulant effect on the depressed immune response might be useful.

Levamisole is active against intestinal nematode worms and appears to act by paralysing susceptible worms which are subsequently eliminated from the intestines. In particular, levamisole is effective in the treatment of ascariasis (p.134). It is also used in hookworm infections (p.136).

Doses of levamisole hydrochloride are expressed in terms of the equivalent amount of levamisole. Levamisole hydrochloride 1.18 g is equivalent to about 1 g of levamisole. The usual adult dose in ascariasis is 150 mg of levamisole orally as a single dose; children have been given 3 mg/kg as a single dose. For the hookworm infection ancylostomiasis or for mixed ascariasis-hookworm infections, both adults and children may be given 2.5 mg/kg as a single dose, repeated after 7 days in cases of severe hookworm infection.

Levamisole influences host defences by modulating cell-mediated immune responses; it restores depressed T-cell functions and has been described as an immunostimulant, although stimulation above normal levels does not seem to occur. It has been tried in many disorders, including bacterial and viral infections and rheumatic disorders, although in these conditions results have not been encouraging.

Levamisole has also been used as an adjunct in patients with malignant disease, although it is not clear that any response is due to its action on the immune system. Adjuvant treatment with levamisole and fluorouracil has been given to reduce recurrence after resection of adenocarcinoma of the colon with regional lymph node involvement (but see Malignant Neoplasms, below).

◊ Reviews.

1. Amery WKP, Bruynseels JPJM. Levamisole, the story and the lessons. *Int J Immunopharmacol* 1992; **14:** 481–6.
2. Scheinfeld N, *et al.* Levamisole in dermatology : a review. *Am J Clin Dermatol* 2004; **5:** 97–104.

Malignant neoplasms. Levamisole has been tried in the adjuvant treatment of various malignant neoplasms[1,2] with conflicting results. Based on the results of early adjuvant trials,[3-5] levamisole was used as standard therapy to modulate fluorouracil in patients with colorectal cancer (p.665), particularly in the USA. However, whether levamisole actually added to the beneficial effect of adjuvant fluorouracil was unclear. Adjuvant levamisole alone was no more effective than placebo in 1 study,[6] and more recent trials have indicated that levamisole is no more effective than placebo when added to fluorouracil,[7] or to fluorouracil plus folinic acid.[8]

1. Spreafico F. Use of levamisole in cancer patients. *Drugs* 1980; **20:** 105–16.
2. Amery WK, Butterworth BS. Review/commentary: the dosage regimen of levamisole in cancer: is it related to efficacy and safety? *Int J Immunopharmacol* 1983; **5:** 1–9.
3. Laurie JA, *et al.* Surgical adjuvant therapy of large-bowel carcinoma: an evaluation of levamisole and the combination of levamisole and fluorouracil: the North Central Cancer Treatment Group and the Mayo Clinic. *J Clin Oncol* 1989; **7:** 1447–56.
4. Moertel CG, *et al.* Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *N Engl J Med* 1990; **322:** 352–8.
5. Moertel CG, *et al.* Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. *Ann Intern Med* 1995; **122:** 321–6.
6. Chlebowski RT, *et al.* Long-term survival following levamisole or placebo adjuvant treatment of colorectal cancer: a Western Cancer Study Group trial. *Oncology* 1988; **45:** 141–3.
7. QUASAR Collaborative Group. Comparison of fluorouracil with additional levamisole, higher-dose folinic acid, or both, as adjuvant chemotherapy for colorectal cancer: a randomised trial. *Lancet* 2000; **355:** 1588–96.
8. Wolmark N, *et al.* Clinical trial to assess the relative efficacy of fluorouracil and leucovorin, fluorouracil and levamisole, and fluorouracil, leucovorin, and levamisole in patients with Dukes' B and C carcinoma of the colon: results from National Surgical Adjuvant Breast and Bowel Project C-04. *J Clin Oncol* 1999; **17:** 3553–9.

Mansonella infections. Levamisole is one of the drugs that has been suggested for the treatment of *Mansonella* infections (p.137). There have been reports[1,2] of response when given with mebendazole.

1. Maertens K, Wery M. Effect of mebendazole and levamisole on Onchocerca volvulus and Dipetalonema perstans. *Trans R Soc Trop Med Hyg* 1975; **69:** 359–60.
2. Bernberg HC, *et al.* The combined treatment with levamisole and mebendazole for a perstans-like filarial infection in Rhodesia. *Trans R Soc Trop Med Hyg* 1979; **73:** 233–4.

Mouth ulceration. Levamisole might be beneficial in severe mouth ulceration (p.1700) but is limited by its adverse effects. A review[1] of its use in recurrent aphthous stomatitis indicated that beneficial results have been reported with levamisole in open studies, but results of double-blind studies have been conflicting. Nevertheless, there have been patients with severe recurrent aphthous stomatitis refractory to all other modes of treatment who have responded to levamisole. Dosage has been with 150 mg daily in divided doses given for 3 days at the first sign of ulceration, followed by 11 days without treatment, repeated as necessary.

1. Miller MF. Use of levamisole in recurrent aphthous stomatitis. *Drugs* 1980; **20:** 131–6.

Renal disorders. In a randomised double-blind study, children with frequently relapsing corticosteroid-sensitive and corticosteroid-dependent nephrotic syndrome were given placebo or levamisole 2.5 mg/kg on alternate days and steroid therapy was gradually withdrawn.[1] Of 31 children being treated with levamisole, 14 were still in remission 112 days after the start of the study compared with 4 of 30 receiving placebo. There have been subsequent reports of adjunctive use in children with nephrotic syndrome,[2-6] but its place in therapy remains to be established. For a discussion of the treatment of glomerular kidney disorders, including the nephrotic syndrome, see p.1504.

1. British Association for Paediatric Nephrology. Levamisole for corticosteroid-dependent nephrotic syndrome in childhood. *Lancet* 1991; **337:** 1555–7.
2. Donia AF, *et al.* Levamisole: adjunctive therapy in steroid dependent minimal change nephrotic children. *Pediatr Nephrol* 2002; **17:** 355–8.
3. Fu LS, *et al.* Levamisole in steroid-sensitive nephrotic syndrome children with frequent relapses and/or steroid dependency: comparison of daily and every-other-day usage. *Nephron Clin Pract* 2004; **97:** c137–c141.
4. Sümegi V, *et al.* Long-term effects of levamisole treatment in childhood nephrotic syndrome. *Pediatr Nephrol* 2004; **19:** 1354–60.
5. Al-Saran K, *et al.* Experience with levamisole in frequently relapsing, steroid-dependent nephrotic syndrome. *Pediatr Nephrol* 2006; **21:** 201–5.
6. Boyer O, *et al.* Short- and long-term efficacy of levamisole as adjunctive therapy in childhood nephrotic syndrome. *Pediatr Nephrol* 2008; **23:** 575–80.

Vitiligo. In a study[1] involving 36 patients with limited slow-spreading vitiligo, response to levamisole treatment occurred in 34 within 2 to 4 months. Patients received 150 mg of oral levamisole daily on 2 consecutive days each week. Patients who were additionally treated with topical fluocinolone or clobetasol had higher rates of repigmentation. A later controlled study[2] involving 43 patients reported less benefit.

The usual treatment of vitiligo is discussed under Pigmentation Disorders, p.1582.

1. Pasricha JS, Khera V. Effect of prolonged treatment with levamisole on vitiligo with limited and slow-spreading disease. *Int J Dermatol* 1994; **33:** 584–7.
2. Agarwal S, *et al.* A randomized placebo-controlled double-blind study of levamisole in the treatment of limited and slowly spreading vitiligo. *Br J Dermatol* 2005; **153:** 163–6.

Preparations

USP 31: Levamisole Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Levam; Meglum; ***Austral.:*** Ergamisol†; ***Belg.:*** Ergamisol†; ***Braz.:*** Ascaridil; ***Canad.:*** Ergamisol†; ***Cz.:*** Decaris†; ***Ger.:*** Ergamisol†; ***Gr.:*** Ergamisol; ***Hong Kong:*** Decaris; ***Hung.:*** Decaris; ***India:*** Levomol; Vermisol; Vizole; ***Indon.:*** Askamex; ***Irl.:*** Ketrax†; ***Israel:*** Ergamisol; ***Mex.:*** Decaris; ***Neth.:*** Ergamisol†; ***Rus.:*** Decaris (Декарис); ***S.Afr.:*** Ergamisol; ***Turk.:*** Paraks; Sitraks; ***UK:*** Ketrax†; ***USA:*** Ergamisol†; ***Venez.:*** Decaris†.

Male Fern

Aspidium; Farnwurzel; Felce Maschio; Feto Macho; Filix Mas; Fougère Mâle; Helecho macho; Rhizoma Filicis Maris.

Щитовник Мужской

Pharmacopoeias. In *Chin.*

Profile

Male fern consists of the rhizome, frond-bases, and apical bud of *Dryopteris filix-mas* agg. (Polypodiaceae), collected late in the autumn, divested of the roots and dead portions and carefully dried, retaining the internal green colour. It contains not less than 1.5% of filicin. During storage the green colour of the interior gradually disappears, often after a lapse of 6 months, and such material is unfit for medicinal use.

Filicin is the mixture of ether-soluble substances obtained from male fern. Its activity is chiefly due to flavaspidic acid, a phloroglucinol derivative.

Male fern has anthelmintic properties and was formerly used as male fern extract (aspidium oleoresin) for the expulsion of tapeworms. However, male fern is highly toxic and has been superseded by other drugs.

Adverse effects include headache, nausea and vomiting, severe abdominal cramp, diarrhoea, dyspnoea, albuminuria, hyperbilirubinaemia, dizziness, tremors, convulsions, visual disturbances including blindness (possibly permanent), stimulation of uterine muscle, coma, respiratory failure, bradycardia, and cardiac failure. Fatalities have occurred.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austria:*** Digestodoron; ***Ger.:*** Digestodoron; ***S.Afr.:*** Digestodoron.

Mebendazole *(BAN, USAN, rINN)*

Mebendatsoli; Mebendazol; Mebendazolas; Mébendazole; Mebendazolum; R-17635. Methyl 5-benzoyl-1*H*-benzimidazol-2-ylcarbamate.

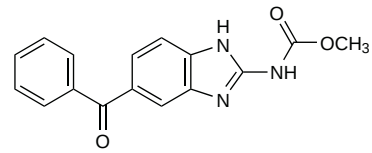
Мебендазол

$C_{16}H_{13}N_3O_3$ = 295.3.

CAS — 31431-39-7.

ATC — P02CA01.

ATC Vet — QP52AC09.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *US*, and *Viet.*
Ph. Eur. 6.2 (Mebendazole). A white or almost white powder. It shows polymorphism. Practically insoluble in water, in alcohol, and in dichloromethane. Protect from light.
USP 31 (Mebendazole). A white to slightly yellow, almost odourless, powder. Practically insoluble in water, in alcohol, in chloroform, in ether, and in dilute mineral acids; freely soluble in formic acid.

Adverse Effects

Since mebendazole is poorly absorbed from the gastrointestinal tract at the usual therapeutic doses, adverse effects have generally been restricted to gastrointestinal disturbances, such as transient abdominal pain and diarrhoea, and have tended to occur in patients being treated for heavy intestinal infection. Headache and dizziness have been reported. Adverse effects have been reported more frequently with the high doses tried in echinococcosis and have included allergic reactions, raised liver enzyme values, alopecia, and bone marrow depression.

Incidence of adverse effects. In the first phase[1] of WHO-coordinated multicentre studies on the treatment of echinococcosis (hydatid disease) involving *Echinococcus granulosus* or *E. multilocularis*, the most frequent adverse effects in the 139 patients given *high-dose* mebendazole, generally for 3 months, were reduced leucocyte count (25 patients), gastrointestinal symptoms (22), and raised serum-transaminase values (22). Other adverse effects were allergic conditions such as fever and skin reactions (4), CNS symptoms including headache (6), and loss of hair (7). Seven patients stopped treatment because of adverse effects.

The second phase of studies[2] compared albendazole with mebendazole in more prolonged high-dosage schedules for cystic *E. granulosus* infection. Adverse effects were similar to those reported with the first phase. However, in the first phase the allergic consequences of the 14 ruptured lung cysts and the 4 ruptured