2. Health Canada. Valdecoxib (Bextra): severe cutaneous reactions. *Can Adverse React News* 2004; **14** (1): 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v14n1-eng.pdf (accessed 29/08/08)
3. EMEA. EMEA public statement on valdecoxib (Bextra/Valdyn) and parecoxib sodium (Dynastat/Rayzon): cardiovascular risks in coronary artery bypass graft (CABG) surgery and serious adverse skin reactions (issued 15th December, 2004). Available at: http://www.emea.europa.eu/pdfs/human/press/pus/20480204en.pdf (accessed 29/08/08)

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Bextra†; ***Braz.:*** Bextra†; ***Canad.:*** Bextra†; ***Chile:*** Bextra†; ***Cz.:*** Bextra†; ***Fin.:*** Bextra†; ***Fr.:*** Bextra†; ***Ger.:*** Bextra†; ***Gr.:*** Bextra†; ***Hong Kong:*** Bextra†; ***India:*** Bioval†; Valdiff†; Valdixx†; Valdone†; Valus†; Vorth†; ***Indon.:*** Bextra†; ***Irl.:*** Bextra†; ***Malaysia:*** Bextra†; ***Neth.:*** Kudeq†; ***Norw.:*** Bextra†; ***NZ:*** Bextra†; ***Port.:*** Bextra†; ***S.Afr.:*** Bextra†; ***Singapore:*** Bextra†; ***Swed.:*** Bextra†; ***Switz.:*** Bextra†; ***Thai.:*** Bextra†; ***UK:*** Bextra†; ***USA:*** Bextra†; ***Venez.:*** Bextra†.

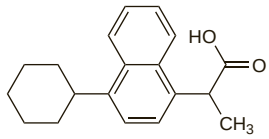
Multi-ingredient: ***India:*** Valus Insta†; Valus-XT†; Vectra-P†; Vorth Insta†; Vorth-XT†.

Vedaprofen *(BAN, USAN, rINN)*

CERM-10202; PM-150; Vedaprofeeni; Védaprofène; Vedaprofeno; Vedaprofenum. (±)-4-Cyclohexyl-α-methyl-1-naphthaleneacetic acid.

Ведапрофен

$C_{19}H_{22}O_2$ = 282.4.
CAS — 71109-09-6.
ATC Vet — QM01AE90.



Profile

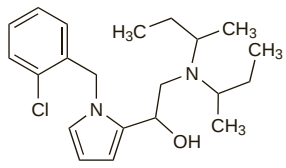
Vedaprofen, a propionic acid derivative, is an NSAID used in veterinary medicine for the treatment of inflammation and pain.

Viminol Hydroxybenzoate *(rINNM)*

Diviminol Hydroxybenzoate; Hidroxibenzoato de viminol; Viminol, Hydroxybenzoate de; Viminoli Hydroxybenzoas; Z-424 (viminol). 1-[1-(2-Chlorobenzyl)pyrrol-2-yl]-2-(di-*sec*-butyl)aminoethanol 4-hydroxybenzoate.

Виминола Гидроксибензоат

$C_{21}H_{31}ClN_2O,C_7H_6O_3$ = 501.1.
CAS — 21363-18-8 (viminol); 21466-60-4 (viminol hydroxybenzoate); 23784-10-3 (viminol hydroxybenzoate).
ATC — N02BG05.
ATC Vet — QN02BG05.



(viminol)

Profile

Viminol hydroxybenzoate has analgesic and antipyretic properties. The equivalent of 400 mg of viminol has been given daily in divided doses by mouth.

Preparations

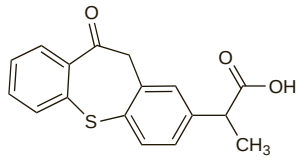
Proprietary Preparations (details are given in Part 3)
Braz.: Dividol; ***Ital.:*** Dividol.

Zaltoprofen *(rINN)*

CN-100; Zaltoprofène; Zaltoprofeno; Zaltoprofenum; ZC-102. (±)-10,11-Dihydro-α-methyl-10-oxodibenzo[*b,f*]thiepin-2-acetic acid.

Зальтопрофен

$C_{17}H_{14}O_3S$ = 298.4.
CAS — 89482-00-8.



Pharmacopoeias. In *Jpn*.

Profile

Zaltoprofen is an NSAID (p.96) that has been given in an oral dose of 80 mg three times daily for pain and musculoskeletal and joint disorders.

◊ References.
1. Ishizaki T, *et al.* Pharmacokinetic profile of a new nonsteroidal anti-inflammatory agent, CN-100, in humans. *Drug Invest* 1991; **3:** 1–7.
2. Hatori M, Kokubun S. The long-term efficacy and tolerability of the new anti-inflammatory agent zaltoprofen in rheumatoid arthritis. *Curr Med Res Opin* 1998; **14:** 79–87.
3. Hase K, *et al.* The effect of zaltoprofen on physiotherapy for limited shoulder movement in breast cancer patients: a single-blinded before-after trial. *Arch Phys Med Rehabil* 2006; **87:** 1618–22.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Soleton.

Ziconotide *(USAN, rINN)*

CI-1009; ω-Conotoxin M VIIA; SNX-111; Ziconotida; Ziconotidum. L-Cysteinyl-L-lysylglycyl-L-lysylglycl-L-alanyl-L-lysyl-L-cysteinyl-L-seryl-L-arginyl-L-leucyl-L-methionyl-L-tyrosyl-L-α-aspartyl-L-cysteinyl-L-cysteinyl-L-threonylglycyl-L-seryl-L-cysteinyl-L-arginyl-L-serylglycyl-L-lysyl-L-cysteinamide cyclic(1→16),(8→20),(15→25)-tris(disulfide).

Зиконотид

$C_{102}H_{172}N_{36}O_{32}S_7$ = 2639.1.
CAS — 107452-89-1.
ATC — N02BG08.
ATC Vet — QN02BG08.

Ziconotide Acetate *(rINNM)*

Acetato de ziconotida; Ziconotide, Acétate de; Ziconotidi Acetas.

Зиконотида Ацетат

$C_{102}H_{172}N_{36}O_{32}S_7$, $C_2H_4O_2$ = 2699.2.
ATC — N02BG08.
ATC Vet — QN02BG08.

Adverse Effects and Precautions

The most common adverse effects reported with ziconotide have included dizziness, nausea and vomiting, nystagmus, abnormal gait, blurred vision, headache, elevated creatine kinase levels, and asthenia. Cognitive impairment, particularly confusion and impaired memory, is also very common, and typically develops after several weeks of treatment. Severe CNS symptoms such as hallucinations, paranoid reactions, speech disorders, aphasia, and decreased alertness may occur but convulsions, stroke, delirium, encephalopathy, and coma have been reported less commonly. Creatine kinase may be elevated, and monitoring of blood concentrations is recommended, but clinical myopathy or rhabdomyolysis is uncommon. Ziconotide may cause or exacerbate depression. Patients with a history of psychosis should not be treated with ziconotide.

◊ References.
1. Penn RD, Paice JA. Adverse effects associated with the intrathecal administration of ziconotide. *Pain* 2000; **85:** 291–6.

Uses and Administration

Ziconotide is a synthetic form of a peptide derived from the venom of the cone shell *Conus magus* (a sea snail). It is reported to be a neurone-specific calcium-channel blocker. Ziconotide is given as a continuous intrathecal infusion in the management of severe chronic pain in patients who are intolerant of or refractory to more conventional treatments (see Choice of Analgesic, p.2).

Ziconotide is given intrathecally as the acetate; doses may be expressed in terms of the base or the acetate. In the EU, the initial dose (expressed in terms of the base) is 2.4 micrograms daily adjusted according to response, in increments of up to 2.4 micrograms, to a maximum daily dose of 21.6 micrograms. Licensed product information recommends that the interval between dose increases is at least 2 days. In the USA, the initial dose (expressed in terms of the acetate) should be no more than 2.4 micrograms daily, adjusted according to response. Dose increases of up to 2.4 micrograms two or three times a week are permitted, over a period of at least 3 weeks, up to a maximum daily dose of 19.2 micrograms.

Ziconotide has been tried in other conditions such as head trauma.

◊ References.
1. Verweij BH, *et al.* Mitochondrial dysfunction after experimental and human brain injury and its possible reversal with a selective N-type calcium channel antagonist (SNX-111). *Neurol Res* 1997; **19:** 334–9.
2. Jain KK. An evaluation of intrathecal ziconotide for the treatment of chronic pain. *Expert Opin Invest Drugs* 2000; **9:** 2403–10.
3. Wermeling D, *et al.* Pharmacokinetics and pharmacodynamics of intrathecal ziconotide in chronic pain patients. *J Clin Pharmacol* 2003; **43:** 624–36.
4. Staats PS, *et al.* Intrathecal ziconotide in the treatment of refractory pain in patients with cancer or AIDS: a randomized controlled trial. *JAMA* 2004; **291:** 63–70.
5. Wermeling DP. Ziconotide, an intrathecally administered N-type calcium channel antagonist for the treatment of chronic pain. *Pharmacotherapy* 2005; **25:** 1084–94.
6. Rauck RL, *et al.* A randomized, double-blind, placebo-controlled study of intrathecal ziconotide in adults with severe chronic pain. *J Pain Symptom Manage* 2006; **31:** 393–406.
7. Lynch SS, *et al.* Intrathecal ziconotide for refractory chronic pain. *Ann Pharmacother* 2006; **40:** 1293–1300.
8. Wermeling DP, Berger JR. Ziconotide infusion for severe chronic pain: case series of patients with neuropathic pain. *Pharmacotherapy* 2006; **26:** 395–402.
9. Lyseng-Williamson KA, Perry C. Ziconotide. *CNS Drugs* 2006; **20:** 331–8.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Prialt; ***Fr.:*** Prialt; ***Neth.:*** Prialt; ***Port.:*** Prialt; ***UK:*** Prialt; ***USA:*** Prialt.

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2. Gardiner CH, Schantz PM. Mammomonogamus infection in a human: report of a case. *Am J Trop Med Hyg* 1983; **32:** 995–7.
3. Leers WD, *et al.* Syngamosis, an unusual cause of asthma: the first reported case in Canada. *Can Med Assoc J* 1985; **132:** 269–70.
4. Nosanchuk JS, *et al.* Case report of and description of parasite in Mammomonogamus laryngeus (human syngamosis) infection. *J Clin Microbiol* 1995; **33:** 998–1000.
5. Turner P, *et al.* A case of human syngamosis. *Travel Med Infect Dis* 2003; **1:** 231–3.
6. Castaño JC, *et al.* Reporte del primer caso humano de infección parasitaria por Mammomonogamus laryngeus en Colombia. *Biomedica* 2006; **26:** 337–41.

Taeniasis

Taeniasis is an infection of the intestine with beef tapeworm, *Taenia saginata*, or pork tapeworm, *T. solium*, acquired through ingestion of contaminated raw or undercooked meat. The larval form of *T. solium* can cause the systemic infection cysticercosis (see above).

Infection with the adult worm usually produces symptoms only when the worm reaches a size that can cause obstruction or related problems. Segments of the worm containing eggs may be excreted in the faeces so maintaining the cycle of reproduction. Treatment is with a single dose of praziquantel,[1] which has the advantage of also being active, in higher doses, against the larval form of *T. solium*. Niclosamide is also effective but is only active against adult worms.

1. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.

Toxocariasis

Toxocariasis[1] is infection with the larval form of *Toxocara canis* or, less commonly, *T. cati*. The adult worms live in the intestines of dogs and cats respectively, and man becomes infected when eggs excreted in animal faeces are ingested. Once ingested the eggs hatch and the larvae migrate from the intestine to other organs, most commonly the liver, lung, and eye. Most infections are asymptomatic but two clinical syndromes, ocular larva migrans and visceral larva migrans, can occur, usually in children.

Ocular larva migrans occurs when larvae invade the eye causing a granuloma which may impair vision and can cause blindness. There is no specific treatment.[2] Anthelmintics such as albendazole or tiabendazole, corticosteroids, ocular surgery, and laser photocoagulation have been used but assessment of their efficacy is difficult because of the variable natural course of the disease.

The clinical symptoms of visceral larva migrans depend upon the organs involved but commonly include cough, wheezing, fever, and hepatomegaly. Encephalitis and seizures may occur and there is usually eosinophilia. Acute infection normally resolves without treatment.[3] However, severe or prolonged infections may be treated with albendazole;[4] mebendazole or tiabendazole have also been used.[1,4]

1. Despommier D. Toxocariasis: clinical aspects, epidemiology, medical ecology, and molecular aspects. *Clin Microbiol Rev* 2003; **16:** 265–72.
2. Shields JA. Ocular toxocariasis: a review. *Surv Ophthalmol* 1984; **28:** 361–81.
3. Gillespie SH. Human toxocariasis. *Commun Dis Rep* 1993; **3:** R140–R143.
4. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.

Trichinosis

Trichinosis (trichinellosis) is an infection caused by *Trichinella spiralis*. Man becomes infected through ingestion of raw or undercooked meat, usually pork, containing infective larvae. The larvae mature into adult worms in the small intestine and the mature females deposit larvae which migrate in the blood to skeletal muscle and sometimes to the myocardium. Symptoms usually occur only in heavy infections. Invasion of the intestines by the maturing adult worms can cause diarrhoea, abdominal pain, and vomiting followed about a week later by hypersensitivity reactions to the migrating larvae. These may include eosinophilia, fever, muscle pain, periorbital oedema and, more rarely, encephalitis, myocarditis, or pneumonia which may be fatal.

All patients with confirmed or suspected infection should be treated to prevent the continued production of larvae. Albendazole or mebendazole are considered to be the anthelmintics of choice. A corticosteroid should be given for severe hypersensitivity reactions.[1]

1. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.

Trichostrongyliasis

Trichostrongyliasis is an infection of the small intestine caused by *Trichostrongylus* spp. including *T. colubriformis*. *Trichostrongylus* spp. are normally parasites of herbivores, but infections in man have been found. They have a similar life cycle to *Ancylostoma duodenale* (see Hookworm Infections, above). Pyrantel embonate, albendazole, or mebendazole are recommended for the treatment of trichostrongyliasis.[1] Successful treatment with ivermectin has occurred in areas where widespread use of benzimidazole carbamate derivatives in grazing animals has led to resistance to these drugs.[2]

1. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
2. Ralph A, *et al.* Abdominal pain and eosinophilia in suburban goat keepers. *Med J Aust* 2006; **184:** 467–9. Correction. *ibid.*; **185:** 49. [title]

Trichuriasis

Trichuriasis is an infection of the large intestine with *Trichuris trichiura*, sometimes known as whipworm. Distribution is worldwide, but most infections occur in the tropics and subtropics. Eggs are excreted in the faeces and can remain viable in the soil for extended periods. Under optimum conditions the eggs become infective in about 2 to 4 weeks. After ingestion, larvae are released from the eggs and develop within the wall of the small intestine for about 3 to 10 days, before migrating to the lumen of the large intestine where they remain attached to the mucosal lining. Eggs are detectable in the faeces about 1 to 3 months after infection. Trichuriasis is often asymptomatic, but heavy infection can result in anaemia, diarrhoea, and rectal prolapse.

Treatment is with a benzimidazole carbamate derivative such as albendazole or mebendazole[1-3] and such broad-spectrum therapy can be useful if the patient is suffering from a mixed intestinal nematode infection. Ivermectin[2] and nitazoxanide[4] are alternatives. However, a systematic review[3] considered the treatment of trichuriasis to be unsatisfactory with current drugs.

1. Bethony J, *et al.* Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. *Lancet* 2006; **367:** 1521–32.
2. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
3. Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. *JAMA* 2008; **299:** 1937–48.
4. Juan JO, *et al.* Comparative clinical studies of nitazoxanide, albendazole and praziquantel in the treatment of ascariasis, trichuriasis and hymenolepiasis in children from Peru. *Trans R Soc Trop Med Hyg* 2002; **96:** 193–6.

Abamectin *(USAN, rINN)*

Abamectina; Abamectine; Abamectinum; MK-0936. A mixture of abamectin component B_{1a} and abamectin component B_{1b}.

Абамектин

CAS — 65195-55-3 (component B_{1a}); 65195-56-4 (component B_{1b}).

ATC Vet — QP54AA02.

Profile

Abamectin is an avermectin anthelmintic used in veterinary medicine for nematode infections. It is also used as a systemic veterinary ectoparasiticide.

Albendazole *(BAN, USAN, rINN)*

Albendatsoli; Albendazol; Albendazolas; Albendazolum; SKF-62979. Methyl 5-propylthio-1*H*-benzimidazol-2-ylcarbamate.

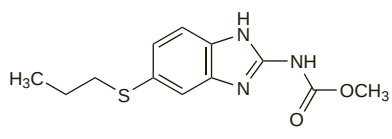
Альбендазол

$C_{12}H_{15}N_3O_2S$ = 265.3.

CAS — 54965-21-8.

ATC — P02CA03.

ATC Vet — QP52AC11.



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

Ph. Eur. 6.2 (Albendazole). A white to faintly yellowish powder. Practically insoluble in water and in alcohol; very slightly soluble in dichloromethane; freely soluble in anhydrous formic acid. Protect from light.

USP 31 (Albendazole). A white to faintly yellowish powder. Practically insoluble in water and in alcohol; very slightly soluble in ether and in dichloromethane; freely soluble in anhydrous formic acid. Store in airtight containers.

Adverse Effects and Precautions

As for Mebendazole, p.148.

Incidence of adverse effects. Although generally well-tolerated, the following adverse reactions were reported in the first phase of WHO-coordinated studies[1] involving 30 patients given *high-dose* therapy with albendazole for the treatment of cystic echinococcosis (hydatid disease): raised serum-transaminase levels (2 patients), reduced leucocyte counts (1), gastrointestinal symptoms (1), allergic conditions (1), and loss of hair (1). Treatment was stopped in a further patient with alveolar echinococcosis because of depressed bone-marrow activity. In the second phase of these studies,[2] of 109 patients given albendazole for cystic echinococcosis, 20 had adverse effects; similar findings were reported with mebendazole. The range of effects with albendazole was: elevation of transaminases (5 patients), abdominal pain and other gastrointestinal symptoms (7), severe headache (4), loss of hair (2), leucopenia (2), fever and fatigue (1), thrombocytopenia (1), and urticaria and itching (1). Albendazole had to be withdrawn in 5 patients because of adverse effects, although in 3 the withdrawal was only temporary.

1. Davis A, *et al.* Multicentre clinical trials of benzimidazolecarbamates in human echinococcosis. *Bull WHO* 1986; **64:** 383–8.
2. Davis A, *et al.* Multicentre clinical trials of benzimidazolecarbamates in human cystic echinococcosis (phase 2). *Bull WHO* 1989; **67:** 503–8.

Effects on growth. A multiple-dose regimen of albendazole in children with asymptomatic trichuriasis has been reported to be associated with impaired growth in those with low levels of infection.[1] However it was considered that this should not prevent the use of single doses in mass treatment programmes.[2]

1. Forrester JE, *et al.* Randomised trial of albendazole and pyrantel in symptomless trichuriasis in children. *Lancet* 1998; **352:** 1103–8.
2. Winstanley P. Albendazole for mass treatment of asymptomatic trichuris infections. *Lancet* 1998; **352:** 1080–1.

Effects on the liver. In a series of 40 patients given albendazole for echinococcosis, 7 developed abnormalities in liver function tests during therapy.[1] Six had a hepatocellular type of abnormality attributable to albendazole; the seventh had cholestatic jaundice which was probably not due to albendazole. See also Incidence of Adverse Effects, above for reports of raised serum-transaminase levels.

Albendazole should only be used in the treatment of echinococcosis if there is constant medical supervision with regular monitoring of serum-transaminase concentrations and of leucocyte and platelet counts. Patients with liver damage should be treated with reduced doses of benzimidazole carbamates, if at all.[2]

1. Morris DL, Smith PG. Albendazole in hydatid disease—hepatocellular toxicity. *Trans R Soc Trop Med Hyg* 1987; **81:** 343–4.
2. Davis A, *et al.* Multicentre clinical trials of benzimidazolecarbamates in human cystic echinococcosis (phase 2). *Bull WHO* 1989; **67:** 503–8.

Pregnancy. Albendazole is teratogenic in some *animals* and there are no adequate and well controlled studies in human pregnancy. Albendazole is therefore usually contra-indicated during pregnancy and licensed product information cautions against becoming pregnant while taking albendazole or within one month of completing treatment.

Interactions

Anthelmintics. The plasma concentration of albendazole sulfoxide has been increased by *praziquantel*,[1] although the practical consequences of this were considered uncertain.

1. Homeida M, *et al.* Pharmacokinetic interaction between praziquantel and albendazole in Sudanese men. *Ann Trop Med Parasitol* 1994; **88:** 551–9.

Antiepileptics. *Phenytoin*, *carbamazepine*, and *phenobarbital* appear to induce the oxidative metabolism of albendazole via the cytochrome P450 isoenzyme CYP3A by roughly the same extent, resulting in significantly reduced concentrations of albendazole sulfoxide. This interaction is likely to be clinically significant when albendazole is used to treat systemic worm infections, and increased doses of albendazole would be needed.[1] The interaction is probably not clinically significant when albendazole is used for intestinal worm infections.

1. Lanchote VL, *et al.* Pharmacokinetic interaction between albendazole sulfoxide enantiomers and antiepileptic drugs in patients with neurocysticercosis. *Ther Drug Monit* 2002; **24:** 338–45.

Corticosteroids. Plasma concentrations of the active metabolite of albendazole (albendazole sulfoxide) were reported to be raised by about 50% in a study in 8 patients receiving *dexamethasone*.[1]

1. Jung H, *et al.* Dexamethasone increases plasma levels of albendazole. *J Neurol* 1990; **237:** 279–80.