that may contribute to its analgesic activity. Tramadol is used for moderate to severe pain.

Tramadol hydrochloride is given by mouth, intravenously, or rectally as a suppository. The intramuscular route has also been used. It may also be given by infusion or as part of a patient-controlled analgesia system.

Usual oral doses are 50 to 100 mg every 4 to 6 hours. Tramadol hydrochloride may also be given orally as a modified-release preparation once or twice daily. The total oral daily dosage should not exceed 400 mg. Preparations containing tramadol hydrochloride with other analgesics such as paracetamol are also used.

A dose of 50 to 100 mg may be given every 4 to 6 hours by intramuscular or intravenous injection over 2 to 3 minutes, or by intravenous infusion. For the treatment of postoperative pain, the initial dose is 100 mg followed by 50 mg every 10 to 20 minutes if necessary to a total maximum (including the initial dose) of 250 mg in the first hour. Thereafter, doses are 50 to 100 mg every 4 to 6 hours up to a total daily dose of 600 mg.

Usual rectal doses by suppository are 100 mg up to 4 times daily.

For details of doses in children and in patients with hepatic or renal impairment, see below.

◊ References.

1. Scott LJ, Perry CM. Tramadol: a review of its use in perioperative pain. *Drugs* 2000; **60:** 139–76.
2. McClellan K, Scott LJ. Tramadol/paracetamol. *Drugs* 2003; **63:** 1079–86. Correction. *ibid.*; 1636.
3. Bennett RM, *et al.* Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. *Am J Med* 2003; **114:** 537–45.
4. Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet* 2004; **43:** 879–923.
5. Leppert W, Luczak J. The role of tramadol in cancer pain treatment—a review. *Support Care Cancer* 2005; **13:** 5–17.
6. Close BR. Tramadol: does it have a role in emergency medicine? *Emerg Med Australas* 2005; **17:** 73–83.
7. Cepeda MS, *et al.* Tramadol for osteoarthritis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 26/06/08).
8. Hollingshead J, *et al.* Tramadol for neuropathic pain. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 26/06/08).
9. Keating GM. Tramadol sustained-release capsules. *Drugs* 2006; **66:** 223–30.
10. Hair PI, *et al.* Tramadol extended-release tablets. *Drugs* 2006; **66:** 2017–27.
11. Lee EY, *et al.* Tramadol 37.5-mg/acetaminophen 325-mg combination tablets added to regular therapy for rheumatoid arthritis pain: a 1-week, randomized, double-blind, placebo-controlled trial. *Clin Ther* 2006; **28:** 2052–60.
12. Freeman R, *et al.* Randomized study of tramadol/acetaminophen versus placebo in painful diabetic peripheral neuropathy. *Curr Med Res Opin* 2007; **23:** 147–61.

Administration in children. In the UK, tramadol hydrochloride is licensed for the management of moderate to severe pain in children 12 years of age and older; usual adult doses may be given (see above). However, in some other European countries it is licensed in younger children although the age range permitted can vary: for example, in *France*, a usual dose in those aged 3 years and over is 1 to 2 mg/kg orally, which may be repeated 3 or 4 times daily, whereas in *Germany*, similar doses are permitted in children as young as 1 year old. Tramadol has also been given parenterally to children in doses similar to those used orally.

Some references on the use of tramadol in children.

1. Finkel JC, *et al.* An evaluation of the efficacy and tolerability of oral tramadol hydrochloride tablets for the treatment of postsurgical pain in children. *Anesth Analg* 2002; **94:** 1469–73.
2. Demiraran Y, *et al.* A comparison of the postoperative analgesic efficacy of single-dose epidural tramadol versus morphine in children. *Br J Anaesth* 2005; **95:** 510–13.
3. Bozkurt P. Use of tramadol in children. *Paediatr Anaesth* 2005; **15:** 1041–7.
4. Chu Y-C, *et al.* Intraoperative administration of tramadol for postoperative nurse-controlled analgesia resulted in earlier awakening and less sedation than morphine in children after cardiac surgery. *Anesth Analg* 2006; **102:** 1668–73.

Administration in hepatic or renal impairment. A dosage interval of 12 hours is recommended for tramadol usage in severe hepatic impairment. The dosage interval should also be increased to 12 hours in patients with a creatinine clearance (CC) less than 30 mL/minute; in the USA licensed product information suggests that the maximum oral dose should not exceed 200 mg daily in these patients. Tramadol should not be given to patients with more severe renal impairment (CC less than 10 mL/minute).

Preparations

BP 2008: Tramadol Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Adamon†; Calmador; Nobligan; Trama-Klosidol; Tramal; Tramalan†; ***Austral.:*** Tramahexal; Tramal; Tramedo; Zydol; ***Austria:*** Adamon; Contramal; Cromatodol; Dolol; Lanalget; Nycodol; Tradolan; Tramabene; Tramadolor; Tramal; Tramamed; Tramastad; Tramundal; Tramundin; ***Belg.:*** Contramal; Doctramado; Dolzam; Tradonal; Tramium; ***Braz.:*** Anangor; Dorless; Sensitram; Sylador; Timasen†; Trabilin; Tramadon; Tramal; Tramaliv; Zamadol; ***Chile:*** Manol; Minidol; Timarol; Tramal; Zodol; ***Cz.:*** Mabron; Noax Uno; Protradon; Trabar†; Tradef; Tradonal†; Tralgit; Tramabene; Tramagit; Tramal; Tramundin; ***Denm.:*** Dolol; Mandolgin; Nobligan; Tadol; Tradolan; ***Fin.:*** Tradolan; Tramadin; Tramagetic; Tramal; Trambo; ***Fr.:*** Biodalgic; Contramal; Monocrixo; Orozamudol; Takadol; Topalgic; Trasedal†; Zamudol; Zumalgic; ***Ger.:*** Amadol; Jutadol; T-long; Tial; Tradol†; Trama; Trama-Dorsch†; Tramabeta; Tramadoc; Tramadolor; Tramadura; Tramagetic†; Tramagit; Tramal; Tramundin; Travex One; ***Gr.:*** Tramal; ***Hong Kong:*** Acugesic; Mabron; Sefmal; Tradonal†; Tramal; Tramo; ***Hung.:*** Adamon; Contramal; Ralgen; Tramadolor; Tramalgic; ***India:*** Contramal; Tramacip; Tramazac; TRD-Contin; Urgendol; ***Indon.:*** Andalpha; Bellatram; Camigesik; Contram; Dolana; Dolgesik; Dolocap; Forgesic; Kamadol; Katrasic; Nonalges; Nufapotram; Orasic; Pinorec; Radol; Simatral; Tradosik; Tradyl; Tragesik; Tramal; Trasik; Traumasik; Trunal; Tugesal; Zumatram; ***Irl.:*** Biodol; By-Madol; Tradol; Tramake; Tramapine; Tramex; Xymel; Zamadol; Zydol; ***Israel:*** Trabar; Tramadex; Tramal; ***Ital.:*** Adamon; Contramal; Fortradol; Fraxidol; Prontalgin; Tradonal; Traflash; Tralodie; Tramalin; ***Malaysia:*** Acugesic; Analab; Mabron; Pengesic; Sefmal; Tracidol; Tramada; Tramal†; Tramundin; ***Mex.:*** Durodor; Nobligan; Prontofort; Tradol; Tralic; Tramed; Trexol; Veldrol; ***Neth.:*** Doltard; Theradol; Tradonal; Tramagetic; Tramal; Tramelene; ***Norw.:*** Nobligan; Tradolan; Tramagetic; ***NZ:*** Tramal; Tramedo; Zytram; ***Philipp.:*** Dolmal; Dolotral; Dolpaz; Milador; Pengesic; Peptrad; Siverol; TDL; Tolma; Tradonal; Tramal; Tramkor; Tramundin; Unitral; ***Pol.:*** Poltram; Tramahexal; Tramal; Tramcod; Tramundin; ***Port.:*** Dolpar; Gelotralib; Nobligan; Paxilfar; Tramal; Tramy; Travex; Zydol; Zytram; ***Rus.:*** Mabron (Маброн); Sintradon (Синтрадон); Tramal (Трамал); ***S.Afr.:*** Dolotram; Tramahexal; Tramal; Tramazac; ***Singapore:*** Mabron; Pengesic; Sefmal; Tradol†; Tramal; Tramium; ***Spain:*** Adolonta; Ceparidin; Dolodol; Sofrodol; Tioner; Tradonal; Tralgiol; Zytram; ***Swed.:*** Nobligan; Tiparol; Tradolan; ***Switz.:*** Dolotramine; Ecodolor; Tramal; Tramkor; Tramundin; ***Thai.:*** Amanda; Ammitram; Anadol; Analab; Mabron†; Madol; Madola; Millidol; Paindol†; Pharmadol; Rofy; Sefmal; Tamolan; Tracine; Tradolgesic; Tradonal; Tramadil; Tramal; Tramamed; Tramax; Tramoda; Trosic; Volcidol-S; ***Turk.:*** Contramal; Tramadolor; ***UK:*** Dromadol; Larapam; Mabron; Nobligan; Tradorec; Tramake; Tramulief; Zamadol; Zeridame; Zydol; ***USA:*** Ultram; ***Venez.:*** Tramal.

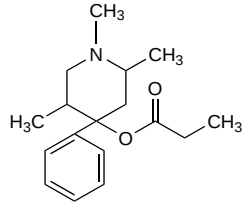
Multi-ingredient: ***Arg.:*** Calmador Plus; Tramacet; ***Austria:*** Zaldiar; ***Belg.:*** Zaldiar; ***Braz.:*** Ultracet; ***Canad.:*** Tramacet; ***Chile:*** Cronus; Minidol Plus; Zafin; Zaldiar; ***Cz.:*** Zaldiar; ***Fr.:*** Ixprim; Zaldiar; ***Ger.:*** Zaldiar; ***Hong Kong:*** Ultracet; ***India:*** Tolydol; Tramacip Plus; Ultrazac; ***Malaysia:*** Ultracet; ***Mex.:*** Gammadol; Sinergix; Tramacet; Zaldiar; ***Neth.:*** Tilalgin; Zaldiar; ***Philipp.:*** Dolcet; ***Pol.:*** Zaldiar; ***Port.:*** Tilalgin; Zaldiar; ***Rus.:*** Zaldiar (Залдиар); ***S.Afr.:*** Tramacet; ***Singapore:*** Ultracet; ***Spain:*** Pazital; Pontalsic; Zaldiar; ***Switz.:*** Zaldiar; ***Thai.:*** Ultracet; ***UK:*** Tramacet; ***USA:*** Ultracet; ***Venez.:*** Ultracet; Zaldiar.

Trimeperidine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de trimeperidina; Promedol (trimeperidine); Promedolum (trimeperidine); Trimépéridine, Chlorhydrate de; Trimeperidini Hydrochloridum. 1,2,5-Trimethyl-4-phenyl-4-piperidyl propionate hydrochloride.

Тримеперидина Гидрохлорид

$C_{17}H_{25}NO_2$,HCl = 311.8.
CAS — 64-39-1 (trimeperidine); 125-80-4 (trimeperidine hydrochloride).



(trimeperidine)

Profile

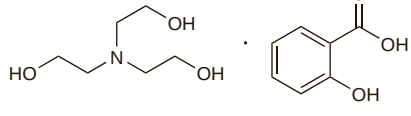
Trimeperidine hydrochloride is an opioid analgesic (p.101) with actions and uses similar to those of pethidine (p.113).

Trolamine Salicylate *(pINNM)*

Salicilato de trietanolamina; Triethanolamine Salicylate; Trolamine, Salicylate de; Trolamini Salicylas.

Троламина Салицилат

$C_{13}H_{21}NO_6$ = 287.3.
CAS — 2174-16-5.



Pharmacopoeias. In *US*.
USP 31 (Trolamine Salicylate). A compounded mixture of trolamine and salicylic acid in propylene glycol. pH of a 5% solution in water is between 6.5 and 7.5. Store in airtight containers in a cool place.

Profile

Trolamine salicylate is a salicylic acid derivative used similarly to methyl salicylate (p.85) in topical rubefacient preparations in a concentration of 10 to 20% for the relief of muscular and rheumatic pain. It has also been used as a sunscreen.

Percutaneous absorption. In contrast to methyl salicylate, which undergoes considerable absorption and produces high subcutaneous and dermal concentrations of salicylic acid after application to intact skin, concentrations of salicylic acid after topical application of trolamine salicylate were substantially lower in tissue[1] and undetectable in serum.[2]

1. Cross SE, *et al.* Is there tissue penetration after application of topical salicylate formulations? *Lancet* 1997; **350:** 636.
2. Morra P, *et al.* Serum concentrations of salicylic acid following topically applied salicylate derivatives. *Ann Pharmacother* 1996; **30:** 935–40.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Geniol Flex†; ***Austral.:*** Dencorub Arthritis; Goanna Arthritis Cream; Metsal AR Analgesic; ***Canad.:*** Antiphlogistine Rub A-535 No Odour; Aspercreme; Bengay No Odor; Myoflex; ***Mex.:*** Myoflex; ***Singapore:*** Metsal AR Analgesic; ***Spain:*** Bexidermil; ***USA:*** Analgesia Creme; Aspercreme; Coppertone Tan Magnifier; Flex-Power Performance Sports; Mobisyl; Myoflex; Sportscreme; Tropical Blend Tan Magnifier.

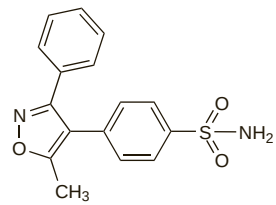
Multi-ingredient: ***Arg.:*** Duo Minoxi†; ***Canad.:*** Myoflex Extra Strength Ice.

Valdecoxib *(BAN, USAN, rINN)*

SC-65872; Valdécoxib; Valdecoxibum; Valdekoksib. *p*-(5-Methyl-3-phenyl-4-isoxazolyl)benzenesulfonamide.

Вальдекоксиб

$C_{16}H_{14}N_2O_3S$ = 314.4.
CAS — 181695-72-7.
ATC — M01AH03.
ATC Vet — QM01AH03.



Profile

Valdecoxib is an NSAID (p.96) reported to be a selective inhibitor of cyclo-oxygenase-2 (COX-2). It was given orally in the treatment of osteoarthritis and rheumatoid arthritis, and for the pain of dysmenorrhoea. The risk of serious skin reactions with valdecoxib, in addition to its cardiovascular adverse effects (see below), prompted its general withdrawal worldwide in April 2005.

Effects on the cardiovascular system. The short-term use of parecoxib and valdecoxib after coronary artery bypass graft surgery has been associated with an increased risk of adverse effects such as myocardial infarction, deep-vein thrombosis, pulmonary embolism, and stroke.[1] When compared with patients in the placebo group, the risk of such effects was almost 4 times greater in those who had received intravenous parecoxib for 3 days followed by oral valdecoxib for the next 7 days. Those patients who received oral valdecoxib only for 7 days postoperatively had a non-significant increase in risk for adverse cardiovascular effects.

The adverse cardiovascular effects associated with valdecoxib treatment were one of the reasons the drug was generally withdrawn in April 2005.

1. Nussmeier NA, *et al.* Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery. *N Engl J Med* 2005; **352:** 1081–91.

Effects on the skin. Toxic epidermal necrolysis developed in a patient who took valdecoxib for 8 days, despite stopping the drug at the first signs of a rash and starting treatment with oral prednisolone;[1] the patient had a history of hypersensitivity to sulfonamides. Health Canada[2] noted in January 2004 that it had received 5 reports of serious cutaneous adverse reactions associated with valdecoxib over less than 1 year from marketing of the drug in December 2002. However, none of these were erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis although such reactions had been reported to other regulatory authorities. In December 2004, the EMEA[3] stated that it had received reports of all 3 reactions, as well as exfoliative dermatitis; most of them had occurred within the first 2 weeks of starting treatment and the incidence rate appeared greater for valdecoxib than other selective COX-2 inhibitors. The EMEA also noted that use of parecoxib (a prodrug of valdecoxib, see p.111) had been associated with erythema multiforme.

The increased risk of serious skin reactions with valdecoxib treatment was one of the reasons the drug was generally withdrawn in April 2005.

1. Glasser DL, Burroughs SH. Valdecoxib-induced toxic epidermal necrolysis in a patient allergic to sulfa drugs. *Pharmacotherapy* 2003; **23:** 551–3.

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†.

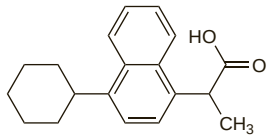
Multi-ingredient: ***India:*** Valus Insta†; Valus-XT†; Vectra-P†; Vorth Insta†; Vorth-XT†.

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

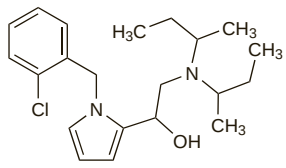
Vedaprofen, a propionic acid derivative, is an NSAID used in veterinary medicine for the treatment of inflammation and pain.

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

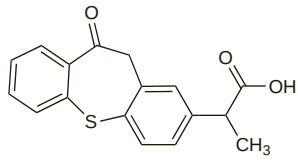
Proprietary Preparations (details are given in Part 3)
Braz.: Dividol; ***Ital.:*** Dividol.

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.
