Profile

Voclosporin is an analogue of ciclosporin (p.1822) that is under investigation for the treatment of uveitis, psoriasis, and for the prevention of rejection in organ transplantation.

◊ References.

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3. Papp K, *et al.* Efficacy of ISA247 in plaque psoriasis: a randomised, multicentre, double-blind, placebo-controlled phase III study. *Lancet* 2008; **371:** 1337–42.

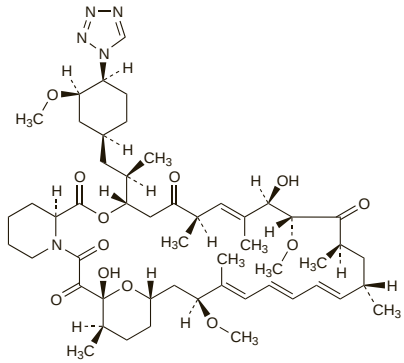
Zotarolimus *(USAN, rINN)*

ABT-578; Zotarolimusum. (3*S*,6*R*,7*E*,9*R*,10*R*,12*R*,14*S*,15*E*,17*E*,19*E*,21*S*,23*S*,26*R*,27*R*,34a*S*)-9,27-Dihydroxy-10,21-dimethoxy-3-{(2*R*)-1-[(1*S*,3*R*,4*S*)-3-methoxy-4-(1*H*-tetrazol-1-yl)cyclohexyl]propan-2-yl}-6,8,12,14,20,26-hexamethyl-3,4,9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34a-octadecahydro-5*H*-23,27-epoxypyrido[2,1-*c*][1,4]oxaazahentriacontine-1,5,11,28,29(6*H*,31*H*)-pentone.

Зотаролимус

$C_{52}H_{79}N_5O_{12}$ = 966.2.

CAS — 221877-54-9.



Profile

Zotarolimus is an analogue of sirolimus (p.1841) that is used in the form of a drug-eluting stent to reduce the risk of restenosis after percutaneous coronary stenting.

Reperfusion and revascularisation procedures. References to the use of zotarolimus-eluting stents.

1. Burke SE, *et al.* Zotarolimus (ABT-578) eluting stents. *Adv Drug Deliv Rev* 2006; **58:** 437–46.
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4. Korovesis S, *et al.* Subacute thrombosis following implantation of zotarolimus-eluting stent. *Hellenic J Cardiol* 2006; **47:** 310–2.
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6. Chen Y-W, *et al.* Zotarolimus, a novel sirolimus analogue with potent anti-proliferative activity on coronary smooth muscle cells and reduced potential for systemic immunosuppression. *J Cardiovasc Pharmacol* 2007; **49:** 228–35.
7. Gershlick A, *et al.* ENDEAVOR Investigators. Zotarolimus-eluting stents in patients with native coronary artery disease: clinical and angiographic outcomes in 1,317 patients. *Am J Cardiol* 2007; **100** (suppl 2): S45–S55.
8. Meredith IT, *et al.* Four-year clinical follow-up after implantation of the endeavor zotarolimus-eluting stent: ENDEAVOR I, the first-in-human study. *Am J Cardiol* 2007; **100** (suppl 2): S56–S61.
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management of acute or chronic pain associated with a well-defined anatomical site, especially when the pain is unresponsive to or not adequately controlled by conventional therapy. The route of administration and method used depend on the site to be blocked but may include peripheral nerve block, autonomic nerve blocks such as sympathetic nerve blocks and coeliac plexus block, and central nerve blocks such as epidural (including caudal) and spinal block. **Local anaesthetics** are used when a temporary effect is required. **Neurolytics** such as phenol or alcohol or freezing of the nerve (cryoanalgesia) produce more prolonged block, but even so the effects may last no more than a few months, and the variable and non-selective neural damage produced correlates poorly with pain relief; some consider the risk of complications to outweigh the benefits obtained.[1]

The use of nerve blocks in the *management of cancer* (p.5) has declined following the refinement of the use of conventional analgesics. Some consider that their value may be limited to patients with a life expectancy of 3 months or less[2] and that the main benefit of nerve blocks in cancer is to produce maximum pain relief rapidly. However, others consider that chemical and thermal neurolysis can provide long-term control of severe cancer pain without a substantial incidence of adverse effects.[3] Neurolytic blocks may be of particular value in cancer pain syndromes involving the viscera or the torso, but are rarely applicable in the management of extremity pain.[4] Neuropathic pain is rarely helped by somatic neural block and may even be aggravated,[1] but block of the splanchnic nerves or coeliac plexus with alcohol or phenol is reputed to be effective in relieving severe intractable pain caused by cancer of the pancreas, stomach, small intestine, gallbladder, or other abdominal viscera, especially when the cancer has not spread to the parietal peritoneum.[5]

Similar neurolytic blocks preceded by a local anaesthetic have also been used in patients with *severe intractable pain* of chronic pancreatitis, postcholecystectomy syndrome, or other chronic abdominal visceral diseases unrelieved by medical or surgical therapy.

Central nerve blocks using local anaesthetics with or without **opioids** are used for the *management of acute pain* such as labour pain (p.7) and postoperative pain (p.4) including that in children (p.3); they are also sometimes used for cancer pain.[1,6]

Sympathetic nerve blocks using repeated injections of local anaesthetics or neurolytics have been used for sympathetically maintained pain. Intravenous regional sympathetic block is an alternative when a single limb is involved;[1] guanethidine is one of the drugs that has been used.[7]

Injections of local anaesthetics with or without **corticosteroids** are often used for blocks of localised painful joints. Nerve blocks are also used to block localised painful trigger areas[8] such as postoperative or post-traumatic neuroma formation and for focal muscle pain.

For the role of nerve blocks in the management of low back pain, see p.7.

1. Hanks GW, Justins DM. Cancer pain: management. *Lancet* 1992; **339:** 1031–6.
2. WHO. Cancer pain relief and palliative care: report of a WHO expert committee. *WHO Tech Rep Ser 804*, 1990. Also available at: http://libdoc.who.int/trs/WHO_TRS_804.pdf (accessed 11/08/08)
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5. Bonica JJ. Management of pain with regional analgesia. *Postgrad Med J* 1984; **60:** 897–904.
6. Hunt R, Massolino J. Spinal bupivacaine for the pain of cancer. *Med J Aust* 1989; **150:** 350.
7. Hannington-Kiff JG. Relief of causalgia in limbs by regional intravenous guanethidine. *BMJ* 1979; **2:** 367–8.
8. Foley KM. The treatment of cancer pain. *N Engl J Med* 1985; **313:** 84–95.

Postherpetic neuralgia. For the role of local anaesthetics in the management of postherpetic neuralgia, see p.9.

Premature ejaculation. A cream containing lidocaine 2.5% and prilocaine 2.5% has been applied topically to the penis for a desensitising effect in the management of premature ejaculation (p.2181). The cream is usually applied to the penis and covered with a condom for a period of time, then washed off before sexual intercourse. It has been reported to increase intravaginal ejaculatory latency time compared with a placebo cream,[1] and a study[2] of different application times found 20 minutes to be the optimum. Longer application times were associated with erection loss because of numbness of the penis, and delayed ejaculation. Decreased vaginal sensitivity in female partners, from residual anaesthetic, has also been reported.[1]

1. Busato W, Galindo CC. Topical anaesthetic use for treating premature ejaculation: a double-blind, randomized, placebo-controlled study. *BJU Int* 2004; **93:** 1018–21.
2. Atikeler MK, *et al*. Optimum usage of prilocaine-lidocaine cream in premature ejaculation. *Andrologia* 2002; **34:** 356–9.

Soft-tissue rheumatism. For the adjunctive use of local anaesthetics in the management of soft-tissue rheumatism, see p.13.

Spasticity. The management of spasticity (p.1887) involves physiotherapy and the use of antispastic drugs. Other approaches to treatment include nerve blocks with local anaesthetics; these can improve spasticity but should generally only be used when further muscle relaxation would not increase disability.

Stuttering. Local anaesthetics have been tried in the treatment of stuttering (p.1001).

Local Anaesthetic Techniques

Local anaesthetics are used in several techniques. In order of increasing level of anaesthesia they are: surface or topical anaesthesia; infiltration anaesthesia; and regional nerve block, including peripheral nerve block, sympathetic nerve block, and central nerve block which includes epidural and spinal (intrathecal or subarachnoid) block. Local anaesthetics may also be given intravenously for regional anaesthesia in the extremities.

Infiltration anaesthesia

Infiltration anaesthesia is produced by injection of a local anaesthetic such as lidocaine or bupivacaine directly into and around the field of operation without attempting to identify individual nerves. The drug used should not be absorbed too rapidly otherwise the anaesthesia will wear off too quickly for practical use; some local anaesthetics require the addition of a vasoconstrictor in low concentrations, which can increase the duration of infiltration anaesthesia and reduce peak plasma concentrations of the local anaesthetic. Infiltration anaesthesia is extensively used in dentistry.

Anaesthesia of small areas by infiltration techniques requires a relatively large amount of local anaesthetic, which is not a problem for minor surgery but would be for more extensive areas that required anaesthesia. The amount of local anaesthetic used can be reduced and the duration of anaesthesia increased by blocking specific nerves that innervate the area. This may be carried out at several levels. In *field block* anaesthesia subcutaneous injection of a local anaesthetic close to the nerves around the area to be anaesthetised blocks sensory nerve paths. This is a form of infiltration anaesthesia, but the technique requires less drug for a given area to be anaesthetised.

Intravenous regional anaesthesia

Intravenous regional anaesthesia (Bier's block) involves injection of a dilute solution of local anaesthetic into a suitable limb vein after exsanguination and application of a tourniquet, in order to produce anaesthesia distal to it. Arterial flow must remain occluded for at least 20 minutes after injection and adrenaline should not be used. Intravenous regional anaesthesia may be used for short procedures where postoperative pain is not marked, such as manipulation of fractures and minor surgical procedures to the limbs. Although a safe procedure when performed correctly, complications have arisen; there have been fatalities associated with the use of bupivacaine, and prilocaine is the drug of choice. Facilities for resuscitation should be available.

Regional nerve block

Regional nerve block anaesthesia involves specific blocks at the levels of major nerves or spinal roots, and may include peripheral nerve block, sympathetic nerve block, and central nerve block including epidural and spinal block. For a discussion of the use of nerve blocks in the management of pain, see Nerve Blocks, above.

Central nerve block. Central nerve block includes epidural and spinal block.

Epidural block (also referred to as *extradural* or *peridural block*) is widely used to provide analgesia or anaesthesia in surgical and obstetric procedures. It involves injecting a local anaesthetic such as lidocaine, bupivacaine, or ropivacaine, alone or with a small dose of an opioid analgesic into the epidural space in the lumbar, sacral (*caudal block*), thoracic, or cervical regions. Introduction of a cannula into the epidural space enables prolonged analgesia or anaesthesia (epidural anaesthesia) to be provided through the use of 'top-up' doses or continuous infusion of the drugs. A vasoconstrictor is sometimes added to reduce systemic exposure to the local anaesthetic. A test dose at the intended injection site is recommended before starting epidural anaesthesia to ensure that the main dose is not accidentally injected intravascularly or into the subarachnoid space.

Spinal block (also referred to as *subarachnoid* or *intrathecal block*) is produced by injecting a solution of a suitable drug such as bupivacaine within the spinal subarachnoid space, causing temporary paralysis of the nerves with which it comes into contact. It may be used, for example, to produce spinal anaesthesia in surgical procedures on the lower body. Vasoconstrictors have been added to prolong the duration of the block but the effect is not always clinically useful and there is a danger of restricting the blood supply to the spinal cord; therefore this practice is not recommended. The somatic level at which anaesthesia occurs depends on many factors including the specific gravity or baricity of the anaesthetic solution used and the positioning of the patient.

For the adverse effects of and precautions for central block, see above.

Peripheral nerve block. Peripheral nerve block anaesthesia involves injection into or around a peripheral nerve or plexus supplying the part to be anaesthetised; motor fibres may be blocked as well as sensory fibres. *Brachial plexus block* is widely used for procedures involving the arm; lower limb blocks are less simple although *sciatic* and *femoral blocks* may be combined to permit surgery below the knee. Other peripheral nerve blocks such as those for the head and neck, or *intercostal* or *paravertebral blocks* for local anaesthesia of the trunk, are mostly highly specialised techniques. Lidocaine, prilocaine, bupivacaine, or ropivacaine have all been widely used for peripheral nerve blocks. Adrenaline is often added as a vasoconstrictor.

Pudendal block (usually with prilocaine) may be useful in obstetrics before forceps delivery, but as mentioned under Labour Pain on p.7, the technique of *paracervical local anaesthetic block* has largely fallen out of favour because of the high incidence of serious adverse effects on the fetus.

Sympathetic nerve block. Sympathetic nerve block such as *stellate ganglion blockade* and *lumbar sympathectomy* is used in the management of a range of painful conditions and vascular diseases (see under Complex Regional Pain Syndrome on p.6). Temporary block is obtained using local anaesthetics such as lidocaine or bupivacaine but permanent block may be produced with use of neurolytic agents such as phenol (see Pain, p.1657) or alcohol (see Pain, p.1627).

Surface anaesthesia

Surface or topical anaesthesia blocks the sensory nerve endings in the skin or mucous membranes. Many local anaesthetics are effective surface anaesthetics, a notable exception being procaine. Penetration of intact skin by most local anaesthetics is poor whereas absorption through mucous membranes may be rapid. However, reliable percutaneous anaesthesia can be achieved by application of a eutectic mixture of lidocaine and prilocaine to intact skin (see under Surface Anaesthesia in Lidocaine, p.1866). Eutectic mixtures may be of value in providing surface anaesthesia for a number of minor medical or surgical procedures. Tetracaine also provides reliable percutaneous anaesthesia. Other methods of dermal delivery of local anaesthetics include a transdermal patch of lidocaine (either alone or with tetracaine), an iontophoretic drug delivery system incorporating lidocaine and adrenaline. Anaesthesia of the skin and subcutaneous tissues is also discussed under Infiltration Anaesthesia, above.

There are a number of special uses of topical anaesthesia including anaesthetising the cornea during ophthalmological procedures and the throat and larynx before intubation and bronchoscopy. Absorption from the respiratory tract is rapid and care is essential to avoid giving a toxic dose. Great care is also necessary when using local anaesthetics to anaesthetise the urethra; if trauma has occurred, rapid absorption of the drug may occur and give rise to serious adverse effects.

Local anaesthetics have been included in topical preparations to relieve the pain of haemorrhoids (p.1697) but good evidence of their efficacy is lacking. Similar uses include pain relief in pruritus ani and anal fissure. Excessive application of local anaesthetics to the rectal mucosa should be avoided as absorption can occur; use for periods of no longer than a few days is recommended to prevent sensitisation of the anal skin. Local anaesthetics are sometimes included in topical preparations for the relief of pruritus (p.1582). However, they are only marginally effective and can very occasionally cause sensitisation. The use of local anaesthetics in rubefacient and topical analgesic preparations is mentioned on p.5.

Amylocaine Hydrochloride *(BANM)*

Amilocaína, hidrocloruro de; Amyleinii Chloridum; Amylocain. Hydrochlor.; Chlorhydrate d'Amyléine. 1-(Dimethylaminomethyl)-1-methylpropyl benzoate hydrochloride.

$C_{14}H_{21}NO_2$,HCl = 271.8.

CAS — 532-59-2 (amylocaine hydrochloride); 644-26-8 (amylocaine hydrochloride).

Profile

Amylocaine, a benzoic acid ester, is a local anaesthetic (p.1850) used mainly as the hydrochloride in a range of preparations for application to the skin or mucous membranes. It has also been used in preparations for the relief of painful anorectal conditions and has been included in oral mixtures for the relief of coughs.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Dolodent.

Multi-ingredient: ***Belg.:*** Dentophar; Odonto-Baby; Rectovasol; ***Braz.:*** Fonergin; Hemodotti; ***Cz.:*** Avenoc; ***Fr.:*** Collustan†; Elenol; Parkipan†; Pulmoll; ***Hong Kong:*** Frazoline; ***Ital.:*** Dentinale; Proctosedyl; ***Spain:*** Hemodren Compuesto†; ***Thai.:*** Bacal; Basina; Biochin†; Izac†; Medcin; Mybacin.
