Pentostatin *(BAN, USAN, rINN)*

CI-825; Covidarabine; Co-vidarabine; Deoxycoformycin; 2′-Deoxycoformycin; NSC-218321; PD-81565; Pentostatina; Pentostatine; Pentostatinum. (*R*)-3-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol; 1,2-Dideoxy-1-[(*R*)-3,6,7,8-tetrahydro-8-hydroxyimidazo[4,5-*d*][1,3]-diazepin-3-yl]-D-*erythro*-pentofuranose.

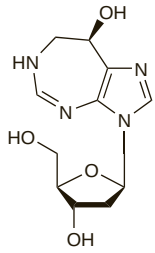
Пентостатин

$C_{11}H_{16}N_4O_4$ = 268.3.

CAS — 53910-25-1.

ATC — L01XX08.

ATC Vet — QL01XX08.



Adverse Effects and Precautions

The most common adverse effects in patients receiving pentostatin include myelosuppression (and in particular suppression of CD4+ lymphocyte subset), headache, abdominal pain, fever and chills, gastrointestinal disturbances (notably diarrhoea and nausea and vomiting), hypersensitivity reactions, and hepatotoxicity. Central neurotoxicity may be manifest as tiredness, anxiety, depression, sleep disturbances, and paraesthesias: treatment should be withheld or stopped in such patients. Impaired renal function and pulmonary toxicity (cough, dyspnoea, and pneumonia) may occur. Severe toxicity in early studies, affecting mainly the CNS, kidneys, liver, and lungs, was associated with the use of doses higher than those currently recommended and produced some fatalities.

Other adverse effects reported with pentostatin include dry skin and rashes (sometimes severe and worsening with continued treatment), pruritus, conjunctivitis, alopecia, arthralgia and myalgia, peripheral oedema, thrombophlebitis, and cardiovascular disorders including arrhythmias, angina pectoris, and heart failure.

Pentostatin should not be given to patients with impaired renal function, or in active infection. It is teratogenic in *animals* and potentially genotoxic: it is therefore contra-indicated in pregnancy and men receiving pentostatin should not father children for 6 months after therapy.

Interactions

Pentostatin should not be given with fludarabine, as the combination may increase pulmonary toxicity. A similar increase in toxicity is expected when pentostatin is used with vidarabine.

Use of pentostatin with carmustine, etoposide and high-dose cyclophosphamide, has produced acute pulmonary oedema and hypotension, leading to death. Pentostatin should therefore not be given with high-dose cyclophosphamide.

Allopurinol. Fatal acute necrotising arteritis developed in a patient given pentostatin and allopurinol.[1] Although the hypersensitivity vasculitis may have been due to allopurinol alone there is circumstantial evidence to suggest that pentostatin may predispose patients to drug hypersensitivity and it may be wise to avoid this combination, and to observe pentostatin-treated patients closely for allergic manifestations.

1. Steinmetz JC, *et al.* Hypersensitivity vasculitis associated with 2-deoxycoformycin and allopurinol therapy. *Am J Med* 1989; **86:** 498–9.

Pharmacokinetics

After intravenous injection, pentostatin has an elimination half-life of about 6 hours. Approximately 90% of a dose is excreted in the urine as unchanged drug and metabolites. Pentostatin crosses the blood-brain barrier and can be measured in the CSF.

Uses and Administration

Pentostatin is a potent inhibitor of the enzyme adenosine deaminase and probably exerts its cytotoxic actions through the interruption of normal purine metabolism and DNA synthesis. Lymphocytes are particularly sensitive to its actions.

Pentostatin is used as a single agent in the treatment of hairy-cell leukaemia (p.654), in usual doses of 4 mg/m^2 every other week. The dose is given as an intravenous bolus injection, or as an infusion over 20 to 30 minutes. Hydration with 500 mL to 1 litre of glucose 5% in sodium chloride 0.18 or 0.9%, or equivalent, is recommended beforehand; a further 500 mL of the hydration solution should be infused once the drug has been given.

Pentostatin has been tried in cutaneous T-cell lymphomas (see Mycosis Fungoides, p.657) and histiocytic syndromes (p.650). It is also under investigation in some other lymphoid malignancies, including chronic lymphocytic leukaemia (p.653) and non-Hodgkin's lymphomas (p.656) and for the management of chronic graft-versus-host disease following haematopoietic stem cell transplantation (p.1811).

◊ References.

1. Grever MR, *et al.* Pentostatin in the treatment of hairy-cell leukemia. *Best Pract Res Clin Haematol* 2003; **16:** 91–9.
2. Drapkin R, *et al.* Results of a phase II multicenter trial of pentostatin and rituximab in patients with low grade B-cell non-Hodgkin's lymphoma: an effective and minimally toxic regimen. *Clin Lymphoma* 2003; **4:** 169–75.
3. Tsimberidou AM, *et al.* Phase II study of pentostatin in advanced T-cell lymphoid malignancies: update of an MD Anderson Cancer Center series. *Cancer* 2004; **100:** 342–9.
4. Tsiara SN, *et al.* Treatment of resistant/relapsing chronic lymphocytic leukemia with a combination regimen containing deoxycoformycin and rituximab. *Acta Haematol (Basel)* 2004; **111:** 185–8.
5. Dillman RO. Pentostatin (Nipent) in the treatment of chronic lymphocyte leukemia and hairy cell leukemia. *Expert Rev Anticancer Ther* 2004; **4:** 27–36.
6. Higman M, *et al.* Pentostatin—pharmacology, immunology, and clinical effects in graft-versus-host disease. *Expert Opin Pharmacother* 2004; **5:** 2605–13.

Preparations

Proprietary Preparations (details are given in Part 3)
Canad.: Nipent†; ***Fr.:*** Nipent; ***Ger.:*** Nipent; ***Gr.:*** Nipent; ***Ital.:*** Nipent; ***Neth.:*** Nipent; ***Port.:*** Nipent; ***Spain:*** Nipent; ***UK:*** Nipent; ***USA:*** Nipent.

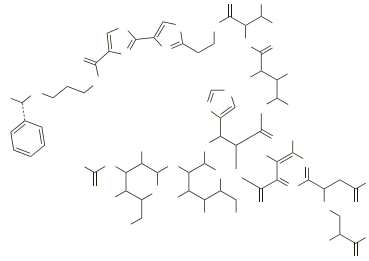
Peplomycin Sulfate *(USAN, rINNM)*

NK-631; Pepleomycin Sulphate; Peplomycin Sulphate; Péplomycine, Sulfate de; Peplomycini Sulfas; Sulfato de peplomicina. N^1-{3-[(*S*)-(α-Methylbenzyl)amino]propyl}bleomycinamide sulphate.

Пепломицина Сульфат

$C_{61}H_{88}N_{18}O_{21}S_2,H_2SO_4$ = 1571.7.

CAS — 68247-85-8 (peplomycin); 70384-29-1 (peplomycin sulfate).



(peplomycin)

Pharmacopoeias. In *Jpn.*

Profile

Peplomycin is an antineoplastic derived from bleomycin (see p.687) and with similar properties. It has been given as the sulfate in the treatment of a variety of malignant neoplasms, including lymphomas and tumours of the head and neck, breast, cervix, lung, prostate, and skin.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Pepleo.

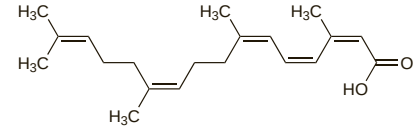
Peretinoin *(rINN)*

Ácido poliprénico; E-5166; Pérétinoin; Peretinoína; Peretinoinum; Polyprenic Acid; Polyprenoic Acid. (*all-E*)-3,7,11,15-Tetramethyl-2,4,6,10,14-hexadecapentaenoic acid.

Перетиноин; Полипреноевая Кислота

$C_{20}H_{30}O_2$ = 302.5.

CAS — 81485-25-8.



Profile

Peretinoin is a retinoid that has been tried in psoriasis and keratoderma and is being studied in the treatment of liver cancers.

◊ References.

1. Muto Y, *et al.* Prevention of second primary tumors by an acyclic retinoid, polyprenoic acid, in patients with hepatocellular carcinoma. *N Engl J Med* 1996; **334:** 1561–7.
2. Muto Y, *et al.* Prevention of second primary tumors by an acyclic retinoid in patients with hepatocellular carcinoma. *N Engl J Med* 1999; **340:** 1046–7.
3. Takai K, *et al.* Prevention of second primary tumors by an acyclic retinoid in patients with hepatocellular carcinoma: updated analysis of the long-term follow-up data. *Intervirology* 2005; **48:** 39–45.

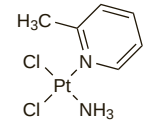
Picoplatin *(BAN, USAN, rINN)*

AMD-473; NX-473; Picoplatine; Picoplatino; Picoplatinum; ZD-0473. *cis*-Amminedichloro(2-methylpyridine)platinum(II).

Пикоплатин

$C_6H_{10}Cl_2N_2Pt$ = 376.1.

CAS — 181630-15-9.



Profile

Picoplatin is a platinum derivative that is under investigation as an intravenous antineoplastic for the treatment of small-cell lung cancer. It is also under investigation for the treatment of colorectal cancer and prostate cancer. An oral dosage form is also being developed.

Pipobroman *(USAN, pINN)*

A-8103; NSC-25154; Pipobromán; Pipobromanum. 1,4-Bis(3-bromopropionyl)piperazine.

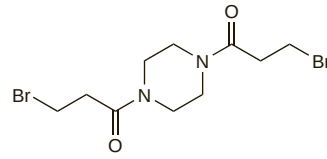
Пипоброман

$C_{10}H_{16}Br_2N_2O_2$ = 356.1.

CAS — 54-91-1.

ATC — L01AX02.

ATC Vet — QL01AX02.



Profile

Pipobroman is an antineoplastic which appears to act by alkylation. It may be used in the treatment of polycythaemia vera (p.654), in patients requiring myelosuppressive therapy, and in refractory chronic myeloid leukaemia (p.653).

The usual initial dose for polycythaemia vera is 1 mg/kg daily, given orally, and increased to 3 mg/kg, if necessary, according to response. Maintenance dosage is 100 to 200 micrograms/kg daily.

The main adverse effect is moderate bone-marrow depression, which may develop 4 weeks or more from starting treatment. Anaemia may be marked at higher doses and is usually accompanied by leucopenia. Thrombocytopenia and haemolysis have occurred. In the initial stages of treatment, white cell and platelet counts should be determined on alternate days and complete blood counts once or twice weekly. Dosage should be stopped if the white cell or platelet counts fall below acceptable levels (see also Bone-marrow Depression, p.639).

Preparations

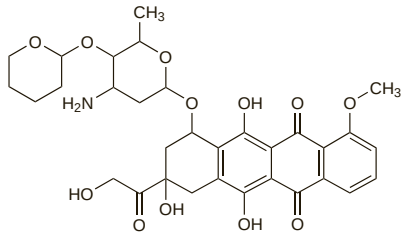
Proprietary Preparations (details are given in Part 3)
Fr.: Vercyte; ***Ital.:*** Vercite.

Pirarubicin *(rINN)*

Pirarubicina; Pirarubicine; Pirarubicinum; 1609-RB; Tepirubicin; THP-ADM; THP-doxorubicin. (8*S*,10*S*)-10-{[3-Amino-2,3,6-trideoxy-4-*O*-(2*R*-tetrahydro-2*H*-pyran-2-yl)-α-L-*lyxo*-hexopyranosyl]oxy}-8-glycoloyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-5,12-naphthacenedione.

Пирарубицин

$C_{32}H_{37}NO_{12}$ = 627.6.
CAS — 72496-41-4.
ATC — L01DB08.
ATC Vet — QL01DB08.



Pharmacopoeias. In *Jpn.*

Profile

Pirarubicin is an antineoplastic anthracycline antibiotic that is a structural analogue of doxorubicin (p.712), and has similar properties. It is used in the management of breast cancer and has also been tried in other solid neoplasms, acute leukaemias and lymphomas.

Pirarubicin is formulated as the hydrochloride but doses are in terms of the base. A usual dose of 25 to 50 mg/m^2 every 3 to 4 weeks has been recommended in breast cancer, but other dosage regimens have been used. Doses may be given by intravenous injection over 5 to 10 minutes into a rapidly-flowing intravenous infusion of glucose 5%. Patients should undergo regular blood counts and monitoring of cardiac function: at cumulative doses above 600 mg/m^2 ventricular ejection fraction should be checked before each course. Pirarubicin has also been given by the intra-arterial and intravesical routes.

Preparations

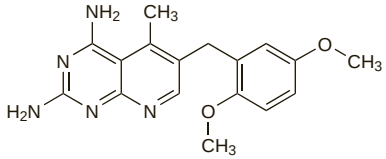
Proprietary Preparations (details are given in Part 3)
Cz.: Pinorubin†; ***Fr.:*** Theprubicine.

Piritrexim Isetionate *(rINNM)*

BW-301U (piritrexim); Isetionato de piritrexima; NSC-351521; Piritrexim Isethionate *(USAN)*; Piritrexime, Isétionate de; Piritreximi Isetionas. 2,4-Diamino-6-(2,5-dimethoxybenzyl)-5-methylpyrido[2,3-*d*]pyrimidine mono(2-hydroxyethanesulphonate).

Пиритрексима Изетионат

$C_{17}H_{19}N_5O_2,C_2H_6O_4S$ = 451.5.
CAS — 72732-56-0 (piritrexim); 79483-69-5 (piritrexim isetionate).



(piritrexim)

Profile

Piritrexim is a folate antagonist with general properties similar to those of methotrexate (p.745). It has been tried by mouth for its antineoplastic properties, and has also been used (as the isetionate) for the treatment of opportunistic infections in immunosuppressed patients. Myelosuppression, gastrointestinal disturbances, and hepatotoxicity have been reported.

Piritrexim isetionate has also been investigated for severe psoriasis.

◊ References.

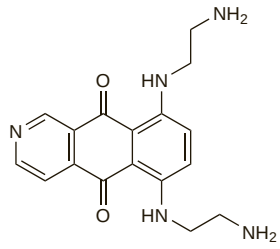
1. Khorsand M, *et al.* Phase II trial of oral piritrexim in advanced, previously treated transitional cell cancer of bladder. *Invest New Drugs* 1997; **15:** 157–63.
2. Roth BJ, *et al.* Piritrexim in advanced, refractory carcinoma of the urothelium (E3896): a phase II trial of the Eastern Cooperative Oncology Group. *Invest New Drugs* 2002; **20:** 425–9.
3. Huie M, *et al.* Phase I study of piritrexim and gemcitabine in patients with advanced solid tumors. *Am J Clin Oncol* 2005; **28:** 613–17.
4. Lassiter LK, *et al.* Phase II open-label study of oral piritrexim in patients with advanced carcinoma of the urothelium who have experienced failure with standard chemotherapy. *Clin Genitourin Cancer* 2008; **6:** 31–5.

Pixantrone *(BAN, USAN, rINN)*

BBR-2778; Pixantrona; Pixantronum. 6,9-Bis[(2-aminoethyl)amino]benzo[*g*]isoquinoline-5,10-dione.

Пиксантрон

$C_{17}H_{19}N_5O_2$ = 325.4.
CAS — 144510-96-3 (pixantrone); 144675-97-8 (pixantrone maleate);.



Profile

Pixantrone is an anthracycline antineoplastic that is under investigation for the treatment of non-Hodgkin's lymphoma.

◊ References.

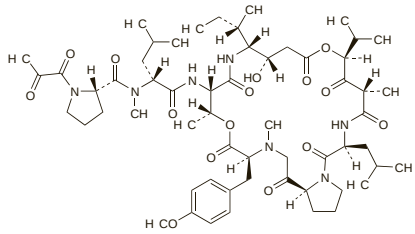
1. Borchmann P, Schnell R. The role of pixantrone in the treatment of non-Hodgkin's lymphoma. *Expert Opin Invest Drugs* 2005; **14:** 1055–61.

Plitidepsin *(BAN, rINN)*

Aplidine; Dehydrodidemnin B; Plitidepsina; Plitidepsine; Plitidepsinum. 3,6-Anhydro(*N*-{(2*S*,4*S*)-4-[(3*S*,4*R*,5*S*)-3-hydroxy-4-{[*N*-(2-oxopropanoyl)-L-prolyl-*N*-methyl-D-leucyl-L-threonyl]amino}-5-methylheptanoyloxy]-2,5-dimethyl-3-oxohexanoyl}-L-leucyl-L-prolyl-*N*,*O*-dimethyl-L-tyrosine).

Плитидепсин

$C_{57}H_{87}N_7O_{15}$ = 1110.3.
CAS — 137219-37-5.



Profile

Plitidepsin is an antineoplastic isolated from the marine tunicate *Aplidium albicans*. It is under investigation in the treatment of acute lymphoblastic leukaemia, multiple myeloma, and solid tumours.

◊ References.

1. Faivre S, *et al.* Phase I and pharmacokinetic study of aplidine, a new marine cyclodepsipeptide in patients with advanced malignancies. *J Clin Oncol* 2005; **23:** 7871–80.
2. Maroun JA, *et al.* Phase I study of Aplidine in a daily×5 one-hour infusion every 3 weeks in patients with solid tumors refractory to standard therapy. A National Cancer Institute of Canada Clinical Trials Group study: NCIC CTG IND 115. *Ann Oncol* 2006; **17:** 1371–8.
3. Izquierdo MA, *et al.* Phase I clinical and pharmacokinetic study of plitidepsin as a 1-hour weekly intravenous infusion in patients with advanced solid tumors. *Clin Cancer Res* 2008; **14:** 3105–12.
4. Peschel C, *et al.* Phase II study of plitidepsin in pretreated patients with locally advanced or metastatic non-small cell lung cancer. *Lung Cancer* 2008; **60:** 374–80.

Porfimer Sodium *(BAN, USAN, rINN)*

CL-184116; Dihaematoporphyrin Ether; Porfimeerinatrium; Porfimère Sodique; Porfimernatrium; Porfímero sódico; Porfimerum Natricum.

Порфимер Натрий
CAS — 87806-31-3.
ATC — L01XD01.
ATC Vet — QL01XD01.

Adverse Effects and Precautions

Photosensitivity occurs in all patients treated with porfimer sodium. This effect is likely to be prolonged, and patients should avoid sunlight or bright indoor light for at least 30 days. However, exposure to ambient indoor light is encouraged, as it allows gradual inactivation of any remaining drug. Other reported adverse effects include local inflammation, chest pain, respiratory insufficiency or distress (including dyspnoea), abdominal pain, dysphagia, constipation, nausea and vomiting, fever, tachycardia and atrial fibrillation, pleural effusion, mucositis, and anaemia due to tumour bleeding. Pneumonia and bronchitis may occur. Anxiety and insomnia have also been reported. Photodynamic therapy with porfimer sodium is contra-indicated in patients with severe hepatic impairment, oesophageal fistulae, erosion of major blood vessels, or severe acute respiratory distress. Sufficient time should be allowed between photodynamic therapy and radiotherapy to allow inflammatory reactions from either treatment to subside.

Porphyria. The use of porfimer sodium is contra-indicated in patients with porphyria.

Interactions

Use of porfimer sodium with other drugs causing photosensitivity should be avoided as the reaction may be increased.

Pharmacokinetics

Porfimer sodium is distributed and eliminated slowly after intravenous injection, with plasma elimination half-life reported to be between 11 and 28 days. *In vitro* studies indicate that plasma protein binding is about 90%. Excretion occurs primarily via the faeces.

Uses and Administration

Porfimer sodium is a haematoporphyrin derivative that reportedly accumulates in malignant tissue on injection. It is then activated by laser light to release oxygen radicals within malignant cells, producing cytotoxicity. Porfimer sodium is used as a photosensitiser in the photodynamic therapy of non-small cell lung cancer (p.668), oesophageal cancer (p.664), and superficial bladder cancer (p.659). It is also used for the treatment of dysplasia associated with Barrett's oesophagus (see Gastro-oesophageal Reflux Disease, p.1696), and has been investigated in various other neoplasms, including tumours of the gastrointestinal tract and cervix.

Porfimer sodium should be reconstituted with glucose 5% to a final concentration of 2.5 mg/mL. It is given by slow intravenous injection at a dose of 2 mg/kg. This is followed, 40 to 50 hours later, by activation using a laser tuned to a wavelength of 630 nanometres and delivered to the area of the tumour using a fibre optic guide. Residual tumour may subsequently be debrided surgically. A second laser treatment may be given 96 to 120 hours after the original injection. A maximum of 3 courses of photodynamic therapy may be used, with each injection separated by a minimum of 30 days for oesophageal and endobronchial tumours, and a minimum of 90 days for dysplasia in Barrett's oesophagus. However, in the treatment of superficial bladder cancer, only one dose of drug and light is given due to an increased risk of bladder contracture, and no surgical debridement is performed.

Photodynamic therapy. Photodynamic therapy probably has the greatest potential of the various forms of light-activated treatment.[1] Photosensitising drugs are given intravenously, orally, or topically, and are selectively retained by tumour cells. When ex-