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.

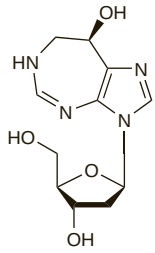
Пентостатин

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

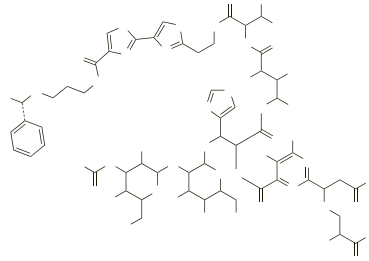
Peplomycin Sulfate *(USAN, rINNM)*

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.

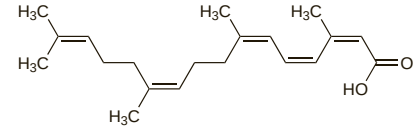
Peretinoin *(rINN)*

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.

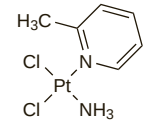
Picoplatin *(BAN, USAN, rINN)*

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.

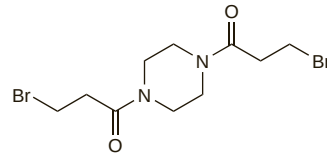
Пипоброман

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