Preparations

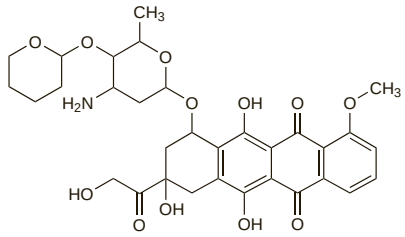
Proprietary Preparations (details are given in Part 3)
Fr.: Vercyte; ***Ital.:*** Vercite.

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

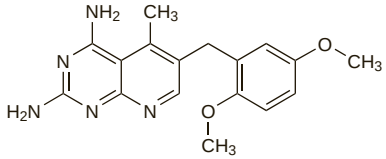
Proprietary Preparations (details are given in Part 3)
Cz.: Pinorubin†; ***Fr.:*** Theprubicine.

Piritrexim Isetionate *(rINNM)*

BW-301U (piritrexim); Isetionato de piritrexima; NSC-351521; Piritrexim Isethionate *(USAN)*; Piritreximе, 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.

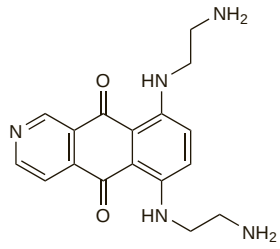
1. Khorsand M, *et al.* Phase II trial of oral piritrexim in advanced, previously treated transitional cell cancer of bladder. *Invest New Drugs* 1997; **15:** 157–63.
2. Roth BJ, *et al.* Piritrexim in advanced, refractory carcinoma of the urothelium (E3896): a phase II trial of the Eastern Cooperative 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.

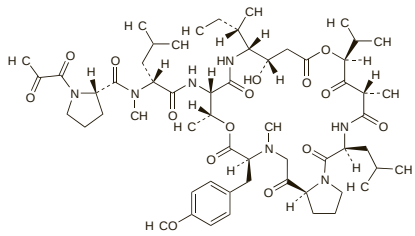
1. Borchmann P, Schnell R. The role of pixantrone in the treatment of non-Hodgkin's lymphoma. *Expert Opin Invest Drugs* 2005; **14:** 1055–61.

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-