posed to the correct wavelength of light the drug produces toxic oxygen radicals that destroy cell membranes and thereby kill the tumour cells. Vascular damage and immune-mediated injury may also occur.[2,3] Tumour cells must have an adequate supply of oxygen to be sensitive to photodynamic therapy,[2] and as light penetration is usually limited, early or superficial malignant lesions respond best to therapy.[1,2] Photodynamic therapy has been tried in skin, gastrointestinal, head and neck, bladder, gynaecological, pancreatic, pulmonary, and various intraperitoneal malignancies[2-11] It is also used for the treatment of Barrett's oesophagus[11-13] and for the treatment of age-related macular degeneration (p.785); it has been tried for other ocular disorders.[14] There is also an interesting report of cytotoxicity against leukaemic cells *in vitro* when exposure to porfimer sodium was combined with ultrasound.[5]

The main adverse effect of photosensitisers such as porfimer is photosensitivity lasting 4 to 8 weeks; patients should be advised to avoid sunlight during this period and therapy is best delayed until the darker winter months if possible.[1] Newer photosensitisers are being developed to show increased tissue penetration and less prolonged photosensitivity.[2] The natural haem precursor 5-aminolevulinic acid (p.679) has the advantage that photosensitivity lasts only a few hours.

1. Bown SG. New techniques in laser therapy. *BMJ* 1998; **316:** 754–7.
2. Hsi RA, *et al.* Photodynamic therapy in the treatment of cancer: current state of the art. *Drugs* 1999; **57:** 725–34.
3. Ost D, *et al.* Photodynamic therapy in lung cancer. *Oncology* 2000; **14:** 379–86.
4. Wilson JHP, *et al.* Photodynamic therapy for gastrointestinal tumors. *Scand J Gastroenterol* 1991; **26** (suppl 188): 20–5.
5. Tachibana K, *et al.* Eliminating adult T-cell leukaemia cells with ultrasound. *Lancet* 1997; **349:** 325.
6. Walther MM. The role of photodynamic therapy in the treatment of recurrent superficial bladder cancer. *Urol Clin North Am* 2000; **27:** 163–70.
7. Metz JM, Friedberg JS. Endobronchial photodynamic therapy for the treatment of lung cancer. *Chest Surg Clin North Am* 2001; **11:** 829–39.
8. Biel MA. Photodynamic therapy in head and neck cancer. *Curr Oncol Rep* 2002; **4:** 87–96.
9. Moghissi K. Role of bronchoscopic photodynamic therapy in lung cancer management. *Curr Opin Pulm Med* 2004; **10:** 256–60.
10. Bown SG, *et al.* Photodynamic therapy for cancer of the pancreas. *Gut* 2002; **50:** 549–57.
11. Brown SB, *et al.* The present and future role of photodynamic therapy in cancer treatment. *Lancet Oncol* 2004; **5:** 497–508.
12. Wolfsen HC, *et al.* Photodynamic therapy for dysplastic Barrett esophagus and early esophageal adenocarcinoma. *Mayo Clin Proc* 2002; **77:** 1176–81.
13. Kelty CJ, *et al.* Photodynamic therapy for Barrett's esophagus: a review. *Dis Esophagus* 2002; **15:** 137–44.
14. Sivaprasad S, Hykin P. The role of photodynamic therapy in ophthalmology. *Br J Hosp Med* 2006; **67:** 647–50.

Preparations

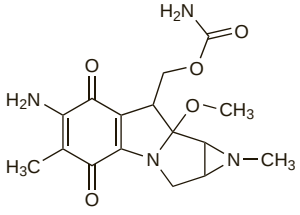
Proprietary Preparations (details are given in Part 3)
Canad.: Photofrin; ***Cz.:*** Photobarr; ***Fr.:*** Photobarr; ***Ger.:*** Photofrin; ***Gr.:*** Photofrin; ***Hung.:*** Photofrin; ***Israel:*** Photofrin; ***Neth.:*** Photobarr; Photofrin; ***Port.:*** Photobarr; Photofrin; ***USA:*** Photofrin.

Porfiromycin *(BAN, USAN, rINN)*

Methyl Mitomycin; NSC-56410; Porfiromicina; Porfiromycine; Porfiromycinum; U-14743. 6-Amino-1,1a,2,8,8a,8b-hexahydro-8-(hydroxymethyl)-8a-methoxy-1,5-dimethylazirino[2′,3′:3,4]-pyrrolo[1,2-*a*]-indole-4,7-dione carbamate ester.

Порфиромицин

$C_{16}H_{20}N_4O_5$ = 348.4.
CAS — 801-52-5.



Profile
Porfiromycin is an antibiotic antineoplastic structurally related to mitomycin (p.752). It is being studied as a radiosensitiser in the management of malignant neoplasms of the head and neck.

◊ References.

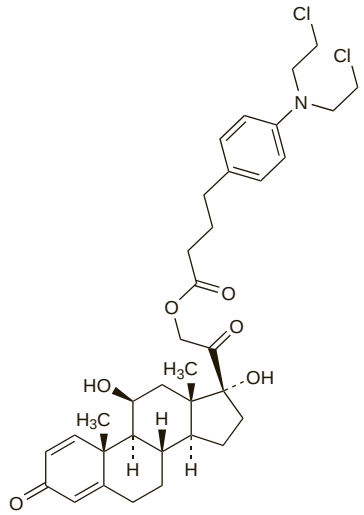
1. Haffty BG, *et al.* Bioreductive alkylating agent porfiromycin in combination with radiation therapy for the management of squamous cell carcinoma of the head and neck. *Radiat Oncol Invest* 1997; **5:** 235–45.
2. Haffty BG, *et al.* Concurrent chemo-radiotherapy with mitomycin C compared with porfiromycin in squamous cell cancer of the head and neck: final results of a randomized clinical trial. *Int J Radiat Oncol Biol Phys* 2005; **61:** 119–28.

Prednimustine *(USAN, rINN)*

Leo-1031; NSC-134087; Prednimustiini; Prednimustin; Prednimustina; Prednimustinum. 11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione 21-(4-{4-[bis(2-chloroethyl)amino]phenyl}butyrate).

Преднимустин

$C_{35}H_{45}Cl_2NO_6$ = 646.6.
CAS — 29069-24-7.
ATC — L01AA08.
ATC Vet — QL01AA08.



Profile
Prednimustine is the prednisolone ester of chlorambucil, (p.696) and has been given orally in the treatment of various malignant diseases.

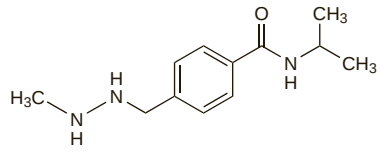
Procarbazine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de procarbazina; Ibenzmethyzin Hydrochloride; NSC-77213; Procarbazine, Chlorhydrate de; Procarbazini Hydrochloridum; Ro-4-6467/1. *N*-Isopropyl-α-(2-methylhydrazino)-*p*-toluamide hydrochloride.

Прокарбазина Гидрохлорид

$C_{12}H_{19}N_3O$,HCl = 257.8.
CAS — 671-16-9 (procarbazine); 366-70-1 (procarbazine hydrochloride).
ATC — L01XB01.
ATC Vet — QL01XB01.



(procarbazine)

Pharmacopoeias. In *Chin.*, *Int.*, *Jpn*, and *US*.
USP 31 (Procarbazine Hydrochloride). Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

For general discussions see Antineoplastics, p.635, p.639, and p.641.

The most common adverse effects associated with procarbazine are gastrointestinal disturbances such as anorexia, nausea and vomiting (although patients may soon become tolerant), and bone-marrow depression. Leucopenia and thrombocytopenia may be delayed with a nadir at about 4 weeks after a dose, and recovery usually within 6 weeks. Anaemia, haemolysis, and bleeding tendencies have been reported.

Neurotoxicity is also common, with central effects such as somnolence, depression, nervousness or confusion, headache, hallucinations, and dizziness, and peripheral neuropathies including paraesthesias and decreased reflexes. Lethargy, ataxia, and sleep disorders have also occurred, and tremors, convulsions, and coma have been reported.

Other adverse effects reported include fever and myalgia, pulmonary fibrosis or pneumonitis, haematuria, urinary frequency, skin reactions including dermatitis, pruritus, and hyperpigmentation, tachycardia, orthostatic hypotension, ocular defects, infertility, and hepatic impairment.

Procarbazine is a carcinogen, mutagen, and teratogen.

Procarbazine should be used with caution in patients with hepatic or renal impairment, and is contra-indicated if impairment is severe. The haematological status of the patient should be determined at least every 3 or 4 days and hepatic and renal function determined weekly. Care is also advisable in patients with phaeochromocytoma, epilepsy, or cardiovascular or cerebrovascular disease. Treatment should be interrupted if allergic skin reactions occur.

Handling and disposal. *Urine* produced for up to 48 hours after a dose of procarbazine should be handled wearing protective clothing.[1]

1. Harris J, Dodds LJ. Handling waste from patients receiving cytotoxic drugs. *Pharm J* 1985; **235:** 289–91.

Interactions

For a general outline of antineoplastic drug interactions, see p.642. Procarbazine is a weak MAOI and the possibility of reactions with other drugs and food, although very rare, must be borne in mind—for details of MAOI reactions see p.417. Procarbazine may enhance the sedative effects of other CNS depressants. A disulfiram-like reaction has been reported with alcohol and the effects of antihypertensive agents may be enhanced.

Antiepileptics. Use with enzyme-inducing antiepileptics is associated with an increased risk of hypersensitivity reactions to procarbazine, possibly through a reactive intermediate generated by induction of the cytochrome P450 isoenzyme CYP3A subfamily.[1] Non-enzyme-inducing antiepileptics might be more appropriate in patients with brain tumours in whom procarbazine therapy is anticipated.

1. Lehmann DF, *et al.* Anticonvulsant usage is associated with an increased risk of procarbazine hypersensitivity reactions in patients with brain tumors. *Clin Pharmacol Ther* 1997; **62:** 225–9.

Pharmacokinetics

Procarbazine is readily absorbed from the gastrointestinal tract. It crosses the blood-brain barrier and diffuses into the CSF. A plasma half-life of about 10 minutes has been reported. Procarbazine is rapidly metabolised (mainly in liver and kidneys) and only about 5% is excreted unchanged in the urine. The remainder is oxidised to *N*-isopropylterephthalamic acid and excreted in the urine, up to about 70% of a dose being excreted in 24 hours. Some of the drug is excreted as carbon dioxide and methane via the lungs. During oxidative breakdown in the body hydrogen peroxide is formed which may account for some of the drug's actions.

Uses and Administration

Procarbazine hydrochloride is a methylhydrazine derivative whose antineoplastic effect, although not fully understood, may resemble that of the alkylating agents; it appears to inhibit protein and nucleic acid synthesis and suppress mitosis. It does not exhibit cross-resistance with other cytotoxic drugs.

Its main use is the treatment of Hodgkin's disease (p.655) when it is usually given with other drugs, as in the MOPP regimen (with chlormethine, vincristine, and prednisone) and its variants. Procarbazine has also been used in the treatment of other lymphomas (p.656) and in some other malignant neoplasms including tumours of the brain (p.660).

Doses of procarbazine hydrochloride are calculated in terms of procarbazine; procarbazine hydrochloride 116 mg is equivalent to about 100 mg of procarbazine. In many of the combination regimens it has been given orally to adults and children in doses of the equivalent