4. Richardson PG, *et al.* Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. *N Engl J Med* 2005; **352:** 2487–98.
5. O'Connor OA. Marked clinical activity of the proteasome inhibitor bortezomib in patients with follicular and mantle-cell lymphoma. *Clin Lymphoma Myeloma* 2005; **6:** 191–9.
6. Popat R, *et al.* Bortezomib for multiple myeloma. *Expert Opin Pharmacother* 2006; **7:** 1337–46.
7. Wang M, *et al.* Use of bortezomib in B-cell non-Hodgkin's lymphoma. *Expert Rev Anticancer Ther* 2006; **6:** 983–91.
8. NICE. Bortezomib monotherapy for relapsed multiple myeloma (issued October 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/TA129Guidance.pdf (accessed 23/05/08)

Preparations

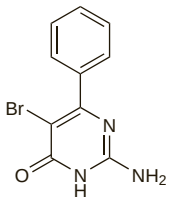
Proprietary Preparations (details are given in Part 3)
Arg.: Velcade; ***Austral.:*** Velcade; ***Belg.:*** Velcade; ***Canad.:*** Velcade; ***Chile:*** Velcade; ***Cz.:*** Velcade; ***Denm.:*** Velcade; ***Fin.:*** Velcade; ***Fr.:*** Velcade; ***Ger.:*** Velcade; ***Gr.:*** Velcade; ***Hong Kong:*** Velcade; ***Hung.:*** Velcade; ***Indon.:*** Velcade; ***Israel:*** Velcade; ***Ital.:*** Velcade; ***Malaysia:*** Velcade; ***Mex.:*** Velcade; ***Neth.:*** Velcade; ***Norw.:*** Velcade; ***NZ:*** Velcade; ***Philipp.:*** Velcade; ***Pol.:*** Velcade; ***Port.:*** Velcade; ***Rus.:*** Velcade (Велкейд); ***Singapore:*** Velcade; ***Spain:*** Velcade; ***Swed.:*** Velcade; ***Switz.:*** Velcade; ***Thai.:*** Velcade; ***UK:*** Velcade; ***USA:*** Velcade; ***Venez.:*** Velcade.

Bropirimine *(BAN, USAN, rINN)*

ABPP; Bropirimina; Bropiriminum; U-54461; U-54461S. 2-Amino-5-bromo-6-phenyl-4(3*H*)-pyrimidinone.

Бропиримин

$C_{10}H_8BrN_3O$ = 266.1.
CAS — 56741-95-8.



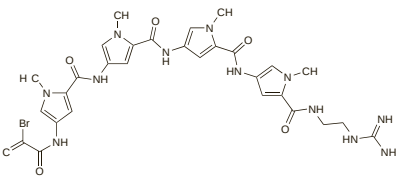
Profile
Bropirimine is reported to have immunomodulatory actions, possibly due to the induction of interferons. It has been investigated in the management of carcinoma in situ of the bladder (p.659).

Brostallicin *(rINN)*

Brostalicina; Brostallicine; Brostallicinum; PNU-166196 (hydrochloride). 4-(2-Bromoacrylamido)-*N*‴-(2-guanidinoethyl)-1,1′,-1″,1‴-tetramethyl-*N*,4′:*N*′,4″:*N*″,4‴-quater[pyrrole-2-carboxamide].

Бростальлицин

$C_{30}H_{35}BrN_{12}O_5$ = 723.6.
CAS — 203258-60-0.



Profile
Brostallicin is an antineoplastic that binds to DNA. It is under investigation for the treatment of soft-tissue sarcomas.

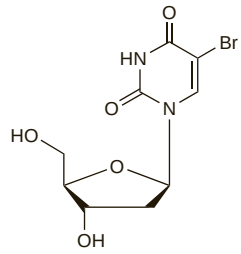
◊ References.
1. ten Tije AJ, *et al.* Phase I and pharmacokinetic study of brostallicin (PNU-166196), a new DNA minor-groove binder, administered intravenously every 3 weeks to adult patients with metastatic cancer. *Clin Cancer Res* 2003; **9:** 2957–64.
2. Broggini M, *et al.* Brostallicin: a new concept in minor groove DNA binder development. *Anticancer Drugs* 2004; **15:** 1–6.
3. Leahy M, *et al.* Brostallicin, an agent with potential activity in metastatic soft tissue sarcoma: a phase II study from the European Organisation for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. *Eur J Cancer* 2007; **43:** 308–15.

Broxuridine *(rINN)*

Bromodeoxyuridine; Broxuridina; Broxuridinum; BUDR; NSC-38297. 5-Bromo-2′-deoxyuridine; 5-Bromo-1-(2-deoxy-β-D-ribofuranosyl)pyrimidine-2,4(1*H*,3*H*)-dione.

Броксуридин

$C_9H_{11}BrN_2O_5$ = 307.1.
CAS — 59-14-3.



Profile
Broxuridine is a thymidine analogue which acts as a radiosensitiser to enhance the effects of radiotherapy. It is also reported to possess antiviral activity. A related compound brivudine (p.867) is used as an antiviral.

Broxuridine has been given by intra-arterial infusion, with radiotherapy and other antineoplastic agents, in the treatment of tumours of the brain, head, and neck. It has also been used diagnostically.

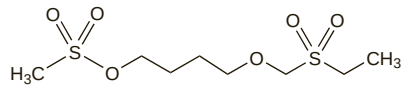
◊ References.
1. Freese A, *et al.* The application of 5-bromodeoxyuridine in the management of CNS tumors. *J Neurooncol* 1994; **20:** 81–95.
2. Phillips TL, *et al.* Results of a randomized comparison of radiotherapy and bromodeoxyuridine with radiotherapy alone for brain metastases: report of RTOG trial 89-05. *Int J Radiat Oncol Biol Phys* 1995; **33:** 339–48.
3. Prados MD, *et al.* Influence of bromodeoxyuridine radiosensitization on malignant glioma patient survival: a retrospective comparison of survival data from the Northern California Oncology Group (NCOG) and Radiation Therapy Oncology Group trials (RTOG) for glioblastoma multiforme and anaplastic astrocytoma. *Int J Radiat Oncol Biol Phys* 1998; **40:** 653–9.
4. Prados MD, *et al.* Phase III randomized study of radiotherapy plus procarbazine, lomustine, and vincristine with or without BUdR for treatment of anaplastic astrocytoma: final report of RTOG 9404. *Int J Radiat Oncol Biol Phys* 2004; **58:** 1147–52.

Busulfan *(BAN, rINN)*

Bussulfam; Busulfaani; Busulfanas; Busulfano; Busulfanum; Busulphan; Buszulfán; CB-2041; GT-41; Myelosan; NSC-750; WR-19508. Tetramethylene di(methanesulphonate); Butane-1,4-diol di(methanesulphonate).

Бусульфан

$C_6H_{14}O_6S_2$ = 246.3.
CAS — 55-98-1.
ATC — L01AB01.
ATC Vet — QL01AB01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Busulfan). A white or almost white, crystalline powder. Very slightly soluble in water and in alcohol; freely soluble in acetone and in acetonitrile. Store in airtight containers. Protect from light.
USP 31 (Busulfan). A white, crystalline powder. Very slightly soluble in water; slightly soluble in alcohol; soluble 1 in 45 of acetone. Store in airtight containers.

Adverse Effects and Treatment

For a general outline see Antineoplastics, p.635 and p.639.

The major adverse effect of busulfan with standard doses is bone-marrow depression, manifest as leucopenia, thrombocytopenia, and sometimes, anaemia. The nadir of the granulocyte count usually occurs after about 10 to 30 days with recovery occurring over up to 5 months, but busulfan has sometimes caused irreversible or extremely-prolonged bone-marrow depression.

Hyperpigmentation is common, and in a few cases after long-term therapy may be part of a syndrome simulating Addison's disease.

Rarely, progressive interstitial pulmonary fibrosis, known as 'busulfan lung', can occur on prolonged treatment. Gastrointestinal disturbances are rare at usual therapeutic doses but may be dose-limiting where high doses are given before bone marrow transplantation. Other rare adverse effects include dry skin and other skin reactions, liver damage, gynaecomastia, cataract formation, and, at high doses, CNS effects including convulsions.

Busulfan may result in impaired fertility and gonadal function. As with other alkylating agents, it is potentially carcinogenic, mutagenic, and teratogenic.

Effects on the bladder. Haemorrhagic cystitis occurred in a patient who had received prolonged therapy with busulfan.[1] High-dose busulfan used in conditioning regimens for haematopoietic stem cell transplantation may increase the risk of late-onset haemorrhagic cystitis.[2,3]

1. Pode D, *et al.* Busulfan-induced hemorrhagic cystitis. *J Urol (Baltimore)* 1983; **130:** 347–8.
2. Kondo M, *et al.* Late-onset hemorrhagic cystitis after hematopoietic stem cell transplantation in children. *Bone Marrow Transplant* 1998; **22:** 995–8.
3. Leung AYH, *et al.* Clinicopathological features and risk factors of clinically overt haemorrhagic cystitis complicating bone marrow transplantation. *Bone Marrow Transplant* 2002; **29:** 509–13.

Effects on the liver. Jaundice in the terminal phase of chronic myeloid leukaemia in a 31-year-old man was attributed to busulfan which had been taken for 6 years.[1] Busulfan toxicity involving the liver was also reported in a patient who had taken busulfan for 54 months,[2] while hepatitis possibly associated with busulfan therapy has also been described.[3] Dose-dependent veno-occlusive disease (VOD) has been reported in 20 to 40% of patients receiving high-dose busulfan before bone marrow transplantation.[4] Licensed product information from 1 manufacturer (*Pierre Fabre, UK*) states that previous radiotherapy, progenitor cell transplantation, or three cycles of chemotherapy or more, can increase the risk of hepatic VOD; another (*GSK*) lists concurrent use of multiple alkylating agents, or total doses of busulfan in excess of 16 mg/kg, as possible risk factors. A reduced incidence of hepatic VOD has been seen in those patients given high-dose busulfan and cyclophosphamide when the first dose of cyclophosphamide has been delayed for more than 24 hours after the last dose of busulfan.

1. Underwood JCE, *et al.* Jaundice after treatment of leukaemia with busulphan. *BMJ* 1971; **1:** 556–7.
2. Foadi MD, *et al.* Portal hypertension in a patient with chronic myeloid leukaemia. *Postgrad Med J* 1977; **53:** 267–9.
3. Morris L, Guthrie T. Busulfan-induced hepatitis. *Am J Gastroenterol* 1988; **83:** 682–3.
4. Hassan M. The role of busulfan in bone marrow transplantation. *Med Oncol* 1999; **16:** 166–76.

Effects on the nervous system. High-dose busulfan, used in conditioning regimens for bone marrow transplantation, has been associated with the development of convulsions,[1-4] both generalised[1,3,4] and myoclonic.[2,4] As a result, the use of prophylactic antiepileptic therapy has been suggested as a component of such regimens.[1,3,4] However, some do not consider the routine use of prophylactic antiepileptics justified,[5] and the potential for phenytoin to increase the metabolism of busulfan, thereby possibly decreasing its myeloablative efficacy, has been pointed out.[6] In addition, phenytoin plasma concentrations have been found to be subtherapeutic in patients who developed convulsions despite a standard prophylactic dose,[4] and the regimen was subsequently adjusted to take account of plasma concentrations. Clobazam has been suggested as an alternative to phenytoin for prophylaxis of busulfan-induced seizures.[7] Licensed product information from one manufacturer (*GSK, UK*) recommends the use of prophylactic anticonvulsants, and prefers a benzodiazepine to phenytoin. However, other manufacturers suggest use with phenytoin; *Otsuka* in the USA state that the recommended dose of their parenteral product is based on studies in which phenytoin was given, and that if other anticonvulsants are used exposure should be monitored, as a 15% increase in plasma-busulfan may be expected, with increased risk of toxicity.

1. Marcus RE, Goldman JM. Convulsions due to high-dose busulphan. *Lancet* 1984; **ii:** 1463.
2. Martell RW, *et al.* High-dose busulfan and myoclonic epilepsy. *Ann Intern Med* 1987; **106:** 173.
3. Sureda A, *et al.* High-dose busulfan and seizures. *Ann Intern Med* 1989; **111:** 543–4.
4. Grigg AP, *et al.* Busulphan and phenytoin. *Ann Intern Med* 1989; **111:** 1049–50. Correction. *ibid.*; **112:** 313.
5. Hugh-Jones K, Shaw PJ. No convulsions in children on high-dose busulphan. *Lancet* 1985; **i:** 220.
6. Fitzsimmons WE, *et al.* Anticonvulsants and busulfan. *Ann Intern Med* 1990; **112:** 552–3.
7. Schwarer AP, *et al.* Clobazam for seizure prophylaxis during busulfan chemotherapy. *Lancet* 1995; **346:** 1238.

Effects on the skin and hair. For the effect of radiotherapy in activating skin lesions in busulfan-treated patients, see under Precautions, below.

Permanent alopecia has been reported after use of busulfan.[1]

1. Tosti A, *et al.* Permanent alopecia after busulfan chemotherapy. *Br J Dermatol* 2005; **152:** 1056–8.

Precautions

For reference to the precautions necessary with antineoplastics, see p.641. Careful attention should be given to monitoring blood counts during therapy. This should be done at least weekly at the start of standard dose therapy. With high dose therapy blood counts should be monitored daily, as should liver function. Prophy-

lactic anticonvulsants should be used during high dose therapy (see Effects on the Nervous System, above).

Busulfan should be stopped if lung toxicity develops. The use of oxygen may exacerbate possible lung toxicity; if anaesthesia is required the concentration of oxygen should be minimised.

Handling. Busulfan is irritant; avoid contact with skin and mucous membranes.

Porphyria. Busulfan is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Radiotherapy. Severe cutaneous reactions occurred in patients given radiotherapy at least 30 days after combined chemotherapy with high-dose busulfan.[1]

It is possible that radiotherapy could worsen subclinical lung injury caused by busulfan.

1. Vassal G, *et al*. Radiosensitisation after busulphan. *Lancet* 1987; **i:** 571.

Interactions

For a general outline of antineoplastic drug interactions, see p.642. Phenytoin increases the clearance of busulfan (see Effects on the Nervous System, above).

Antifungals. Giving *itraconazole* with busulfan resulted in a decrease in the clearance of busulfan; *fluconazole* had no such effect.[1] Busulfan doses may need to be decreased if itraconazole is also given.

1. Buggia I, *et al*. Itraconazole can increase systemic exposure to busulfan in patients given bone marrow transplantation. *Anticancer Res* 1996; **16:** 2083–8.

Antineoplastics. When *tioguanine* was given with busulfan for chronic myeloid leukaemia, a number of cases of hepatic nodular regenerative hyperplasia, with abnormal liver function tests, portal hypertension, and oesophageal varices were noted. There were no cases in patients treated with busulfan alone, and the mechanism of this possible interaction is unclear.[1,2]

1. Key NS, *et al*. Oesophageal varices associated with busulfan-thioguanine combination therapy for chronic myeloid leukaemia. *Lancet* 1987; **ii:** 1050–2.
2. Shepherd PCA, *et al*. Thioguanine used in maintenance therapy of chronic myeloid leukaemia causes non-cirrhotic portal hypertension. *Br J Haematol* 1991; **79:** 185–92.

Antiprotozoals. In a study[1] of patients who received high-dose busulfan as part of a myeloablative regimen before stem cell transplantation, the use of *metronidazole* significantly increased plasma concentrations of busulfan and the degree of associated toxicity, including elevation of liver function tests, veno-occlusive disease, and mucositis.

1. Nilsson C, *et al*. The effect of metronidazole on busulfan pharmacokinetics in patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant* 2003; **31:** 429–35.

Pharmacokinetics

Busulfan is readily absorbed from the gastrointestinal tract and rapidly disappears from the blood with a half-life of 2 to 3 hours. It is extensively metabolised, and excreted in the urine almost entirely as sulfur-containing metabolites. It crosses the blood-brain barrier.

Metabolism. In a study of the pharmacokinetics of high-dose busulfan in 5 patients receiving 1 mg/kg orally every six hours for 4 days, the mean elimination half-life decreased from about 3.4 hours after the first dose to about 2.3 hours after the final dose, suggesting that busulfan may induce its own metabolism.[1]

1. Hassan M, *et al*. Pharmacokinetic and metabolic studies of high-dose busulphan in adults. *Eur J Clin Pharmacol* 1989; **36:** 525–30.

Therapeutic drug monitoring. A review concluded that therapeutic drug monitoring of busulfan would maximise engraftment and minimise toxicity and relapse in haematopoietic stem cell transplantation. In regimens using busulfan with cyclophosphamide, steady-state plasma concentrations of busulfan above 600 micrograms/litre appeared to favour engraftment.[1] A pharmacokinetic analysis found that in patients with graft rejections, busulfan trough concentrations were below 150 nanograms/mL; steady state concentrations also tended to be lower in this group but not significantly so.[2]

The bioavailability of oral busulfan is variable, particularly in children; intravenous conditioning regimens, adjusted on the basis of first-dose pharmacokinetics and therapeutic drug monitoring, have been used to overcome this problem.[3,4] A study found a significant correlation between busulfan concentration in plasma and saliva after oral dosing in children; busulfan saliva analysis may therefore be a useful, non-invasive alternative to plasma analysis.[5]

1. McCune JS, *et al*. Plasma concentration monitoring of busulfan: does it improve clinical outcome? *Clin Pharmacokinet* 2000; **39:** 155–65.
2. Chandy M, *et al*. Randomized trial of two different conditioning regimens for bone marrow transplantation in thalassemia—the role of busulfan pharmacokinetics in determining outcome. *Bone Marrow Transplant* 2005; **36:** 839–45.
3. Tran H, *et al*. Pharmacokinetics and individualized dose adjustment of intravenous busulfan in children with advanced hematologic malignancies undergoing allogeneic stem cell transplantation. *Biol Blood Marrow Transplant* 2004; **10:** 805–12.
4. Kletzel M, *et al*. Pharmacokinetics of a test dose of intravenous busulfan guide dose modifications to achieve an optimal area under the curve of a single daily dose of intravenous busulfan in children undergoing a reduced-intensity conditioning regimen with hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant* 2006; **12:** 472–9.
5. Rauh M, *et al*. Quantification of busulfan in saliva and plasma in haematopoietic stem cell transplantation in children : validation of liquid chromatography tandem mass spectrometry method. *Clin Pharmacokinet* 2006; **45:** 305–16.

Uses and Administration

Busulfan is an antineoplastic with a cell-cycle non-specific alkylating action unlike that of the nitrogen mustards, and having a selective depressant action on bone marrow. In small doses, it depresses granulocytopoiesis and to a lesser extent thrombocytopoiesis but has little effect on lymphocytes. With larger doses, severe bone-marrow depression eventually ensues.

Because of its selective action, busulfan has been used in the palliative treatment of chronic myeloid leukaemia (p.653). It provides symptomatic relief with a reduction in spleen size and a general feeling of well-being. The fall in leucocyte count is usually accompanied by a rise in the haemoglobin concentration. Permanent remission is not induced and resistance to its beneficial effects gradually develops.

Busulfan may be used in patients with polycythaemia vera (p.654) and in some patients with myelofibrosis and primary thrombocythaemia (p.654). It is also used at high doses as part of a conditioning regimen to prepare patients for bone marrow transplantation, a procedure discussed on p.1811 under Haematopoietic Stem Cell Transplantation.

The licensed initial oral dosage of busulfan in **chronic myeloid leukaemia** is 60 micrograms/kg daily, with a usual maximum single daily dose of 4 mg. This is continued until the white cell count has fallen to between 15 000 and 25 000 cells/mm^3 (typically 12 to 20 weeks). It should be stopped earlier if the platelet count falls below 100 000 cells/mm^3. Higher doses may be given if the response after 3 weeks is inadequate but this increases the risk of irreversible damage to the bone marrow and calls for special vigilance. Complete blood counts should be made at least every week and the trends followed closely; if haemorrhagic tendencies occur or there is a steep fall in the white cell count indicating severe bone-marrow depression, busulfan should be withdrawn until marrow function has returned.

Once an initial remission has been attained treatment is stopped and not resumed until the white cell count returns to 50 000 cells/mm^3. If this occurs within 3 months continuous maintenance treatment with a usual dose of 0.5 to 2 mg daily may be given.

In patients with **polycythaemia vera** the usual oral dose is 4 to 6 mg daily, continued for 4 to 6 weeks with careful monitoring of blood counts. Further courses are given when relapse occurs; alternatively, maintenance therapy may be given at half the dose required for induction. Doses of 2 to 4 mg daily have been given for **essential thrombocythaemia** or myelofibrosis.

In conditioning regimens for **bone marrow transplantation** busulfan has been given in usual doses of 3.5 to 4 mg/kg daily in divided doses for 4 days orally (total dose 14 to 16 mg/kg), with cyclophosphamide, for ablation of the recipient's bone marrow. When given by intravenous infusion in a regimen with phenytoin (see Effects on the Nervous System, above), a recommended dose is 3.2 mg/kg ideal body-weight daily for 4 days (total dose 12.8 mg/kg); actual body-weight is used for the calculation if it is less than the ideal weight. The daily dose is given as 4 infusions of 800 micrograms/kg at intervals of 6 hours; each dose should be diluted in sodium chloride 0.9% or glucose 5% to a final concentration of about 500 micrograms/mL, and given over 2 hours through a central venous catheter using an infusion pump. UK licensed product information states that cyclophosphamide dosing should not be started for at least 24 hours after the last dose of busulfan; US information permits use no sooner than 6 hours after the last busulfan dose.

In the UK, busulfan is licensed for use with cyclophosphamide or melphalan as a conditioning regimen prior to haematopoietic stem cell transplantation in children. The recommended dose for children up to 17 years of age is weight-based as follows:

- less than 9 kg: busulfan 1 mg/kg
- 9 to 16 kg: busulfan 1.2 mg/kg
- 16 to 23 kg: busulfan 1.1 mg/kg
- 23 to 34 kg: busulfan 950 micrograms/kg
- greater than 34 kg: busulfan 800 micrograms/kg

This dose is given every 6 hours over 4 days to a total of 16 doses, diluted and infused as for adults. Cyclophosphamide or melphalan should not be started for at least 24 hours after the last dose of busulfan.

◊ References.

1. Buggia I, *et al*. Busulfan. *Ann Pharmacother* 1994; **28:** 1055–62.
2. Socié G, *et al*. Busulfan plus cyclophosphamide compared with total-body irradiation plus cyclophosphamide before marrow transplantation for myeloid leukemia: long-term follow-up of 4 randomized studies. *Blood* 2001; **98:** 3569–74.
3. Ferry C, Socié G. Busulfan-cyclophosphamide versus total body irradiation-cyclophosphamide as preparative regimen before allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia: what have we learned? *Exp Hematol* 2003; **31:** 1182–6.

Preparations

BP 2008: Busulfan Tablets;
USP 31: Busulfan Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Myleran; ***Austral.:*** Myleran; ***Austria:*** Myleran; ***Belg.:*** Myleran; ***Braz.:*** Myleran; ***Canad.:*** Busulfex; Myleran; ***Chile:*** Myleran; ***Cz.:*** Busilvex; Myleran; ***Denm.:*** Busilvex; ***Fr.:*** Busilvex; Myleran; ***Ger.:*** Busilvex; Myleran; ***Gr.:*** Busilvex; Myleran; ***Hong Kong:*** Busulfex; Myleran; ***India:*** Myleran; ***Irl.:*** Myleran; ***Israel:*** Busulfex; Myleran; ***Ital.:*** Busilvex; Myleran; ***Malaysia:*** Myleran; ***Mex.:*** Myleran; ***Neth.:*** Busilvex; Myleran; ***Norw.:*** Busilvex; ***NZ:*** Myleran; ***Pol.:*** Busilvex; Myleran; ***Port.:*** Busilvex; Myleran; ***Rus.:*** Myleran (Милеран); ***S.Afr.:*** Myleran; ***Singapore:*** Myleran; ***Spain:*** Busilvex; ***Swed.:*** Busilvex; Myleran; ***Switz.:*** Busilvex; Myleran†; ***Thai.:*** Myleran; ***Turk.:*** Busulfex; Myleran; ***UK:*** Busilvex; Myleran; ***USA:*** Busulfex; Myleran.

Capecitabine *(BAN, USAN, rINN)*

Capecitabina; Capécitabine; Capecitabinum; Kapecitabin; Kapesitabiini; Kapesitabin; Ro-09-1978/000. Pentyl 1-(5-deoxy-β-D-ribofuranosyl)-5-fluoro-1,2-dihydro-2-oxo-4-pyrimidinecarbamate.

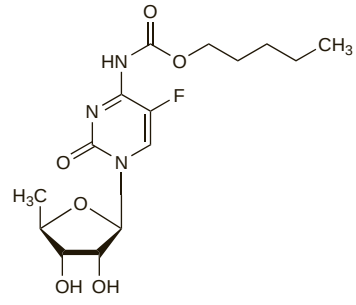
Капецитабин

$C_{15}H_{22}FN_3O_6$ = 359.4.

CAS — 154361-50-9; 158798-73-3.

ATC — L01BC06.

ATC Vet — QL01BC06.



Pharmacopoeias. In *US.*

USP 31 (Capecitabine). A white to off-white crystalline powder. Sparingly soluble in water; soluble in alcohol and in acetonitrile; freely soluble in methyl alcohol. Store in airtight containers at a temperature of 20° to 25°, excursions permitted between 15° and 30°.

Adverse Effects and Precautions

As for Fluorouracil, p.722. Diarrhoea (which may be severe), nausea and vomiting, abdominal pain, stomatitis, and palmar-plantar erythrodysesthesia syndrome (erythema and desquamation of hands and feet) occur commonly with capecitabine, and may be dose-limiting. Other common adverse effects include fatigue,