Histiocytic syndromes. The value of systemic chemotherapy in patients with Langerhans-cell histiocytosis (p.650) is uncertain; however, it is certainly widely used in extensive disease, vinblastine being one of the drugs often employed.[1,2]

1. The French Langerhans' Cell Histiocytosis Study Group. A multicentre retrospective survey of Langerhans' cell histiocytosis: 348 cases observed between 1983 and 1993. *Arch Dis Child* 1996; **75:** 17–24.
2. Gadner H, *et al.* A randomized trial of treatment for multisystem Langerhans' cell histiocytosis. *J Pediatr* 2001; **138:** 728–34. Correction. *ibid.*; **139:** 170.

Malignant neoplasms. Vinblastine plays an important role in the ABVD regimen in patients with Hodgkin's disease (p.655). It also formed part of the effective, if toxic, PVB regimen used to treat germ cell (ovarian or testicular) cancer, p.670 and p.673 respectively, although other regimens tend now to be preferred. The vinca alkaloids are also active in gestational trophoblastic tumours (p.650), and vinblastine is also used in the therapy of invasive bladder cancer (p.659); it may be used in the adjuvant or palliative treatment of non-small-cell lung cancer (p.668) and in the palliative care of advanced breast cancer (p.661) and mycosis fungoides (p.657). It has been used in malignancies of the kidney (p.667). Vinca alkaloids are also used to treat Kaposi's sarcoma (p.675).

Preparations

BP 2008: Vinblastine Injection;
USP 31: Vinblastine Sulfate for Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Blastovin; Velbe†; Xintoprost†; ***Austral.:*** Velbe; ***Austria:*** Velbe; ***Belg.:*** Velbe; Vinblasin; ***Braz.:*** Rabinefil†; Velban†; ***Chile:*** Lemblastine; Velbe†; ***Denm.:*** Velbe; ***Fin.:*** Velbe†; ***Fr.:*** Velbe; ***Ger.:*** Cellblastin†; Velbe†; ***Gr.:*** Velbe; ***Hong Kong:*** Velbe†; ***India:*** Cytoblastin; ***Israel:*** Blastovin; ***Ital.:*** Velbe; ***Mex.:*** Ifabla†; Lemblastine; Velbe†; ***Neth.:*** Blastivin; Velbe; ***Norw.:*** Velbe; ***Philipp.:*** Velbastine; ***Port.:*** Solblastin; Velbe†; ***Swed.:*** Velbe; ***Switz.:*** Velbe; ***UK:*** Velbe; ***USA:*** Velban; ***Venez.:*** Velbe†.

Vincristine Sulfate *(USAN, rINNM)*

Compound 37231; Leurocristine Sulphate; NSC-67574; 22-Oxovincaleukoblastine Sulphate; Sulfato de vincristina; Vincristine, sulfate de; Vincristine Sulphate *(BANM)*; Vincristini sulfas; Vinkristiinisulfaatti; Vinkristin Sülfat; Vinkristino sulfatas; Vinkristinsulfat; Vinkristin-sulfát; Vinkrisztin-szulfát; Winkrystyny siarczan.

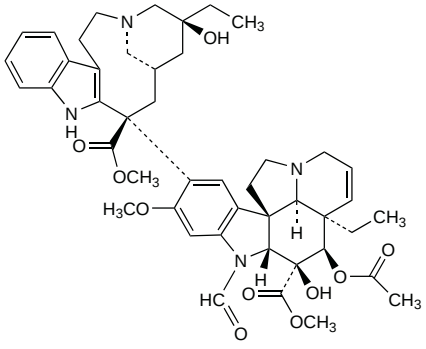
Винкристина Сульфат

$C_{46}H_{56}N_4O_{10},H_2SO_4$ = 923.0.

CAS — 57-22-7 (vincristine); 2068-78-2 (vincristine sulfate).

ATC — L01CA02.

ATC Vet — QL01CA02.



(vincristine)

Description. Vincristine sulfate is the sulfate of an alkaloid, 22-oxovincaleukoblastine, obtained from *Catharanthus roseus* (*Vinca rosea*) (Apocynaceae).

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Vincristine Sulphate). A white or slightly yellowish, very hygroscopic, crystalline powder. It loses not more than 12% of its weight on drying. Freely soluble in water; slightly soluble in alcohol. A 0.1% solution in water has a pH of 3.5 to 4.5. Store at a temperature not exceeding –20° in airtight glass containers. Protect from light.

USP 31 (Vincristine Sulfate). A white to slightly yellow, odourless, hygroscopic, amorphous or crystalline powder. It loses not more than 12% of its weight on drying. Freely soluble in water; slightly soluble in alcohol; soluble in methyl alcohol. A 0.1% solution in water has a pH of 3.5 to 4.5. Store at a temperature between –25° and –20° in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Vinblastine Sulfate, p.786.

Bone-marrow depression occurs less commonly than with vinblastine but neurological and neuromuscular effects are more severe with vincristine and are dose-limiting. Walking may be impaired and the neurological effects may not be reversed for several months after the drug is stopped. Convulsions, often with hypertension, have occurred. Constipation is common and there may be abdominal pain. Urinary disturbances have occurred and alopecia is frequent.

Folinic acid has been given for the treatment of overdosage: suggested doses are as much as 100 mg of folinic acid intravenously every 3 hours for 24 hours, then every 6 hours for at least 48 hours. However, this is unlikely to be of benefit in reversing neuromuscular toxicity. For mention of the use of glutamic acid in managing the usually fatal consequences of inadvertent intrathecal dosage, see below.

Because severe constipation and impaction of faeces often occur with vincristine, laxatives or enemas may be necessary to ensure regular bowel function. Vincristine should be given with caution to patients with pre-existing neuromuscular disease and is contra-indicated in patients with the demyelinating form of Charcot-Marie-Tooth syndrome (see under Effects on the Nervous System, below). Doses may need to be adjusted in patients with hepatic impairment. Care should also be taken in elderly patients, who may be more susceptible to neurotoxicity.

Administration error. *Inadvertent intrathecal doses of vincristine result in ascending paralysis and death.*[1,2] However, in one case[1] treatment immediately after the error, and consisting of removal of contaminated spinal fluid and flushing with lactated Ringer's solution and fresh frozen plasma diluted in lactated Ringer's solution, plus intravenous and oral glutamic acid, was reported successful in stabilising neurological dysfunction and preventing death. A similar case of successful treatment has subsequently been reported,[3] in which immediate CSF aspiration and irrigation (with lactated Ringer's solution containing fresh frozen plasma to bind vincristine) for 6 days was combined with intravenous folate, glutamic acid, and pyridoxine. The role of neuroprotectant drugs in these cases is uncertain, although a study involving 84 patients found that glutamic acid 1.5 g daily given orally in divided doses during a 6-week induction chemotherapy course decreased vincristine-induced neurotoxicity.[4] One manufacturer (*Lilly*) has stated that the roles of glutamic acid, folinic acid, and pyridoxine remain unclear.

While early recognition and immediate treatment with cerebrospinal fluid drainage and exchange may improve survival,[5] fatalities still occur despite these measures.[5,6] Recommendations[2,6] have been made in order to prevent further errors occurring, including restrictions on the prescription, administration, and storage of intrathecal drugs. In the UK, recommendations state that vinca alkaloids for intravenous use in adults or children over 10 years should be diluted to a maximum concentration of 100 micrograms/mL (vincristine) or a volume of at least 20 mL (vinblastine, vindesine, or vinorelbine) and labelled with a clear warning of the consequences of use by other routes. Higher concentrations may be used in children under 10 years, and in certain specialised centres.[2]

1. Dyke RW. Treatment of inadvertent intrathecal injection of vincristine. *N Engl J Med* 1989; **321:** 1270–1.
2. Department of Health. Updated national guidance on the safe administration of intrathecal chemotherapy (HSC 2003/010, 2 October 2003). Available at: http://www.dh.gov.uk/assetRoot/04/06/43/17/04064317.pdf (accessed 01/07/04)
3. Qweider M, *et al.* Inadvertent intrathecal vincristine administration: a neurosurgical emergency. Case report. *J Neurosurg Spine* 2007; **6:** 280–3.
4. Jackson DV, *et al.* Amelioration of vincristine neurotoxicity by glutamic acid. *Am J Med* 1988; **84:** 1016–22.
5. Alcaraz A, *et al.* Intrathecal vincristine: fatal myeloencephalopathy despite cerebrospinal fluid perfusion. *J Toxicol Clin Toxicol* 2002; **40:** 557–61.
6. Fernandez CV, *et al.* Intrathecal vincristine: an analysis of reasons for recurrent fatal chemotherapeutic error with recommendations for prevention. *J Pediatr Hematol Oncol* 1998; **20:** 587–90.

Effects on the nervous system. In its most typical form, vincristine neurotoxicity[1] manifests as a mixed sensorimotor neuropathy of the distal type. The earliest symptoms are sensory changes in the form of paraesthesias, accompanied by impairment and ultimately loss of deep tendon reflexes. In more severe forms, impairment of motor function occurs with wrist drop and foot drop, ataxia and gait abnormalities, and occasionally progressive quadriparesis.

In contrast to these peripheral neuropathies, which are usually associated with long-term usage, there may be short-term autonomic neuropathy resulting in constipation and occasionally ileus, abdominal pain, atony of the urinary bladder (which may lead to urinary retention), orthostatic hypotension, and rarely, impotence. Effects on the cranial nerves may result in ptosis, hoarseness (due to laryngeal nerve paralysis), or optic neuropathies. Effects on the CNS are rare, probably in part because of poor penetration into CSF, but include excessive release of antidiuretic hormone and consequent hyponatraemia.

Hallucinations have occurred[2] and effects on the special senses have been reported: both bilateral optic atrophy and blindness,[3] and profound neurological deafness (which was largely reversible on drug withdrawal)[4] have occurred. Convulsions associated with hypertension are another feature of vincristine toxicity.[5]

Toxicity is related to both the cumulative and the individual dose.[1] It usually begins in adults after receiving a total of 5 to 6 mg, and is significant by the time a cumulative dose of 15 to 20 mg is reached. If individual doses are low (less than 2 mg) or intervals between doses are longer than the usual week, patients can tolerate higher cumulative doses. Children tolerate vincristine better than adults, but the elderly are particularly prone to neurotoxicity. Patients with existing neurological disorders such as poliomyelitis or the Charcot-Marie-Tooth syndrome may be at increased risk of neurotoxicity.[6-9] It has been suggested that increased neurotoxicity may be associated with the use of ready-to-use solutions rather than reconstituted lyophilised preparations but this has not been proved.[10-14]

There is no good treatment for the effects of vincristine on the nervous system: symptoms are largely reversible once dosage is interrupted, and should be managed with appropriate symptomatic care.[1] However, there is some suggestion that glutamic acid may be of benefit in treating neurotoxicity—see Administration Error, above. For the use of dinoprost to alleviate ileus induced by vinca alkaloids, see p.2007.

1. Legha SS. Vincristine neurotoxicity: pathophysiology and management. *Med Toxicol* 1986; **1:** 421–7.
2. Holland JF, *et al.* Vincristine treatment of advanced cancer: a cooperative study of 392 cases. *Cancer Res* 1973; **33:** 1258–64.
3. Awidi AS. Blindness and vincristine. *Ann Intern Med* 1980; **93:** 781.
4. Yousif H, *et al.* Partially reversible nerve deafness due to vincristine. *Postgrad Med J* 1990; **66:** 688–9.
5. Ito S, *et al.* Seizures and hypertension complicating vincristine therapy in children. *Clin Pharmacol Ther* 1995; **57:** 208.
6. Hogan-Dann CM, *et al.* Polyneuropathy following vincristine therapy in two patients with Charcot-Marie-Tooth syndrome. *JAMA* 1984; **252:** 2862–3.
7. Miller BR. Neurotoxicity and vincristine. *JAMA* 1985; **253:** 2045.
8. Chauncey TR, *et al.* Vincristine neurotoxicity. *JAMA* 1985; **254:** 507.
9. Griffiths JD, *et al.* Vincristine neurotoxicity in Charcot-Marie-Tooth syndrome. *Med J Aust* 1985; **143:** 305–6.
10. Arnold AM, *et al.* Acute vincristine neurotoxicity. *Lancet* 1985; **i:** 346.
11. Jalihal S, Roebuck N. Acute vincristine neurotoxicity. *Lancet* 1985; **i:** 637.
12. Davies CE, *et al.* Acute vincristine neurotoxicity. *Lancet* 1985; **i:** 637–8.
13. Warrier RP, Ducos R. Acute vincristine neurotoxicity. *Lancet* 1985; **i:** 980.
14. Gennery BA. Vincristine neurotoxicity. *Lancet* 1985; **ii:** 385.

Handling and disposal. For a method for the destruction of vincristine *wastes*, see under Vinblastine Sulfate, p.786.

Urine and faeces produced for up to 4 and 7 days respectively after a dose of vincristine 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.

Porphyria. Vincristine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems, although there is conflicting evidence of porphyrinogenicity.

Interactions

For a general outline of antineoplastic drug interactions, see p.642. Use of vincristine with drugs that inhibit cytochromes of the CYP3A subfamily may result in decreased metabolism of vincristine and increased toxicity. If vincristine is used with asparaginase it should be given 12 to 24 hours before the enzyme: giving asparaginase with or before vincristine may reduce vincristine clearance and increase toxicity. For reports of vascular toxicity and Raynaud's syndrome associated with the use of vinca alkaloids with bleomycin and other drugs see Effects on the Cardiovascular System, p.636.

Antibacterials. Severe neurotoxicity has occurred when *isoniazid* was added to the regimen of a patient receiving vincristine.[1]

1. Carrión C, *et al.* Possible vincristine-isoniazid interaction. *Ann Pharmacother* 1995; **29:** 201.

Antiepileptics. A pharmacokinetic study showed that systemic clearance of vincristine was 63% higher when it was given with *phenytoin* or *carbamazepine*, two inducers of the cytochrome P450 isoenzyme CYP3A4. The clinical significance of this finding is unknown.[1]

1. Villikka K, *et al.* Cytochrome P450-inducing antiepileptics increase the clearance of vincristine in patients with brain tumours. *Clin Pharmacol Ther* 1999; **66:** 589–93.

Antifungals. Toxicity has been reported to be increased in children who received *itraconazole* with or without nifedipine dur-

ing treatment involving vincristine.[1-4] Itraconazole is presumed to potentiate the toxicity of vincristine either by inhibition of cytochrome P450 isoenzymes, thus reducing the clearance of vincristine,[1-4] or by inhibiting the P-glycoprotein efflux pump,[2,3] and increasing intracellular concentrations of vincristine. Nifedipine also decreases the clearance of vincristine, by similar mechanisms,[1,3,4] and can theoretically further potentiate toxicity.

1. Murphy JA, *et al.* Vincristine toxicity in five children with acute lymphoblastic leukaemia. *Lancet* 1995; **346:** 443.
2. Jeng MR, Feusner J. Itraconazole-enhanced vincristine neurotoxicity in a child with acute lymphoblastic leukemia. *Pediatr Hematol Oncol* 2001; **18:** 137–42.
3. Sathiapalan RK, El-Solh H. Enhanced vincristine neurotoxicity from drug interactions: case report and review of literature. *Pediatr Hematol Oncol* 2001; **18:** 543–6.
4. Kamaluddin M, *et al.* Potentiation of vincristine toxicity by itraconazole in children with lymphoid malignancies. *Acta Paediatr* 2001; **90:** 1204–7.

Nifedipine. Vincristine toxicity may be potentiated by nifedipine, see Antifungals, above.

Pharmacokinetics

Vincristine is not reliably absorbed from the gastrointestinal tract. After intravenous injection it disappears rapidly from the blood. It is extensively protein bound and is reported to be concentrated in blood platelets. It is metabolised in the liver and excreted primarily in the bile; about 70 to 80% of a dose is found in faeces, as unchanged drug and metabolites, while 10 to 20% appears in the urine. The terminal half-life is reported to be about 85 hours but may range from about 19 to 155 hours. Vincristine does not appear to cross the blood-brain barrier in significant amounts.

Uses and Administration

Vincristine is an antineoplastic agent that may act similarly to vinblastine (p.786) by arresting mitosis at the metaphase. Significant cross-resistance with vinblastine has not been reported although pleiotropic resistance may occur.

Vincristine sulfate is used mainly in combination chemotherapy regimens for acute and chronic leukaemias, lymphomas, including Hodgkin's disease and non-Hodgkin's lymphomas, and multiple myeloma. It is also used for tumours of the breast, lung, head and neck, and soft-tissue sarcomas, as well as for paediatric solid tumours including Ewing's sarcoma, rhabdomyosarcoma, neuroblastoma, Wilms' tumour, retinoblastoma, and medulloblastoma. Vincristine has also been used in idiopathic thrombocytopenic purpura refractory to other agents. See also the cross-references given below.

Vincristine sulfate is given by intravenous injection. It has been given as a solution containing 1 mg/mL. However, UK guidelines recommend that for patients over the age of 10 years, solutions of vincristine should generally be diluted to a maximum concentration of 100 micrograms/mL and to a volume of at least 10 mL, to avoid inadvertent intrathecal use; higher concentrations can be used for children under 10 years of age. Care should be taken to avoid extravasation and the injection may be given over 1 minute into a freely-running intravenous infusion (usually sodium chloride 0.9%) if preferred.

The usual adult intravenous dose of vincristine sulfate is 1.4 to 1.5 mg/m^2 once weekly, up to a maximum weekly dose of 2 mg (see also Administration, below). For children weighing over 10 kg, the suggested dose is 1.4 to 2 mg/m^2 once weekly, up to a maximum weekly dose of 2 mg. For those weighing less than 10 kg, the suggested initial dose is 50 micrograms/kg, once weekly.

Blood counts should be carried out before giving each dose. Dosage reduction is recommended in patients with hepatic impairment (see below).

A liposomal formulation of vincristine is under investigation for the treatment of acute lymphoblastic leukaemia.

Action. Results *in vitro* suggested[1] a selective action of vincristine against lymphocytes of patients with chronic lymphocytic leukaemia; lymphocytes of healthy subjects were not so affected. A further study[2] confirmed these findings, and also found marked variation in vincristine susceptibility among individual chronic lymphocytic leukaemic cells. This suggests that vincristine may have effects other than arrest of mitosis.

1. Vilpo J, Vilpo L. Selective toxicity of vincristine against chronic lymphocytic leukaemia in vitro. *Lancet* 1996; **347:** 1491–2.
2. Vilpo JA, *et al.* Selective toxicity of vincristine against chronic lymphocytic leukemia cells in vitro. *Eur J Haematol* 2000; **65:** 370–8.

Administration. Although a maximum single dose of 2 mg is recommended for vincristine sulfate to reduce neurotoxicity, a review[1] has suggested that this guideline is overly rigid, since it does not take into account interindividual variations in pharmacokinetics and susceptibility to toxicity, which may be considerable. Furthermore the authors considered the evidence for effectiveness of this dosage limitation to be equivocal. They suggested beginning therapy at 1.4 mg/m^2 and adjusting subsequent doses according to toxicity.

For UK recommendations on dilution of intravenous vinca alkaloids see Administration Error, under Adverse Effects, above.

1. McCune JS, Lindley C. Appropriateness of maximum-dose guidelines for vincristine. *Am J Health-Syst Pharm* 1997; **54:** 1755–8.

Administration in hepatic impairment. Licensed product information states that the dose of vincristine should be reduced by 50% in patients having a serum bilirubin value above 3 mg per 100 mL (51 micromoles/litre).

Amyloidosis. For mention of regimens including vincristine used in the management of amyloidosis, see p.743.

Blood disorders, non-malignant. Vincristine may be employed in the treatment of various auto-immune blood disorders, see under Vinblastine, p.786.

Malignant neoplasms. Vincristine is widely used in the treatment of malignant neoplasms. It is a fundamental part of potentially curative regimens for acute lymphoblastic leukaemia, Hodgkin's disease and aggressive non-Hodgkins lymphomas (see p.651, p.655 and p.656). It has also been used in chronic lymphocytic leukaemia (p.653) and in other non-Hodgkin's lymphomas including AIDS-related lymphoma (p.657), Burkitt's lymphoma (p.657) and mycosis fungoides (p.657). Other haematological malignancies in which it may be tried include multiple myeloma (p.658). Among the solid neoplasms, vincristine is used in regimens to treat gestational trophoblastic tumours (p.650), tumours of the brain (p.660), head and neck (p.666), Wilms' tumour (p.667), small-cell lung cancer (p.668), and thymoma (p.674). It is also employed in regimens for neuroblastoma (p.674), retinoblastoma (p.675), and some sarcomas including sarcomas of bone, Kaposi's sarcoma, and rhabdomyosarcoma (see p.675, p.675, and p.676).

Preparations

BP 2008: Vincristine Injection;
USP 31: Vincristine Sulfate for Injection; Vincristine Sulfate Injection.

Proprietary Preparations (details are given in Part 3)
Arg.: Vinces; ***Austral.:*** Oncovin; ***Austria:*** Oncovin; ***Belg.:*** Oncovin; Vincrisin; ***Braz.:*** Biocrist†; Oncovin†; Tecnocris; Vincizina; Vincrifil†; Vincristex†; Vinracine†; ***Chile:*** Citomid; Oncovin†; ***Cz.:*** Citomid†; ***Denm.:*** Oncovin; ***Fin.:*** Oncovin†; ***Fr.:*** Oncovin; ***Ger.:*** Cellcristin; Farmistin†; Onkocristin; ***Gr.:*** Oncovin; ***India:*** Biocristine; Cytocristin; Neocristin; ***Malaysia:*** Vinracine; ***Mex.:*** Citomid; Ifavin†; Oncovin; Vinblax†; Vincasar†; Vintec; ***Norw.:*** Oncovin†; ***Philipp.:*** Alcavixin; Nevexitin; ***Port.:*** Faulcris†; Oncovin†; ***Rus.:*** Citomid (Цитомид)†; ***S.Afr.:*** Oncovin†; ***Spain:*** Vincrisul; ***Swed.:*** Oncovin; ***Switz.:*** Oncovin; ***Thai.:*** Citomid; ***UK:*** Oncovin; ***USA:*** Oncovin; Vincasar PFS; ***Venez.:*** Oncovin†.

Vindesine Sulfate *(USAN, rINNM)*

Compound 112531 (vindesine); Desacetyl Vinblastine Amide Sulfate; LY-099094; NSC-245467 (vindesine or vindesine sulfate); Sulfato de vindesina; Vindesiinisulfaatti; Vindésine, sulfate de; Vindesine Sulphate *(BANM)*; Vindesini sulfas; Vindesinsulfat; Vindesin-sulfát; Vindezino sulfatas; Vindezin-szulfát. 3-Carbamoyl-4-*O*-deacetyl-3-de(methoxycarbonyl)vincaleukoblastine sulfate.

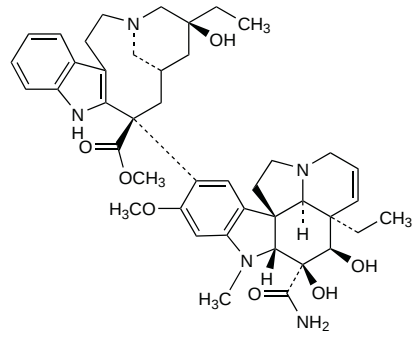
Виндезина Сульфат

$C_{43}H_{55}N_5O_7,H_2SO_4$ = 852.0.

CAS — 53643-48-4 (vindesine); 59917-39-4 (vindesine sulfate).

ATC — L01CA03.

ATC Vet — QL01CA03.



(vindesine)

Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).
Ph. Eur. 6.2 (Vindesine Sulphate). A white or almost white, hygroscopic, amorphous substance. Freely soluble in water and in methyl alcohol; practically insoluble in cyclohexane. The pH of a 0.5% solution in water is 3.5 to 5.5. Store in airtight polypropylene containers with a polypropylene cap, at a temperature not exceeding –50°.

Adverse Effects, Treatment, and Precautions

As for Vinblastine Sulfate, p.786.

The main dose-limiting effect of vindesine is granulocytopenia, with the nadir of the white cell count usually occurring 3 to 5 days after a dose and recovery after a further 4 to 5 days. Although neurotoxicity occurs it may be less severe than that seen with vincristine (see p.787). Alopecia is the most common adverse effect.

Folinic acid has been suggested for the treatment of overdosage by analogy with vincristine.

Vindesine should not be given by the intrathecal route, as this may produce fatal toxicity. Care should be taken if acute abdominal pain occurs: further doses may result in paralytic ileus.

Administration error. *Inadvertent intrathecal doses of vinca alkaloids result in ascending paralysis and death.* In a 10-year-old child accidentally given an intrathecal injection of vindesine, treatment with folinic acid and dexamethasone produced transient recovery but symptoms subsequently recurred and the patient died of progressive ascending paralysis.[1] The CNS showed changes at necropsy similar to those seen after intrathecal vincristine. Other fatal cases[2] have subsequently been reported. For reference to the successful treatment of inadvertent intrathecal dosage of vincristine, and UK recommendations on dilution of vinca alkaloids to avoid intrathecal use, see p.787.

1. Robbins G. Accidental intrathecal injection of vindesine. *BMJ* 1985; **291:** 1094.
2. Nisse P, *et al.* Administration accidentelle intrathécale de vindésine: à propos de 2 cas mortels. *Therapie* 2007; **62:** 360–1.

Interactions

As for Vinblastine Sulfate, p.786.

Pharmacokinetics

The pharmacokinetics of vindesine are similar to those of the other vinca alkaloids. After intravenous doses elimination from the blood is triphasic; the drug is rapidly distributed to body tissues. The terminal half-life is reported to be about 20 hours. It is metabolised primarily in the liver and excreted in bile and urine.

Uses and Administration

Vindesine sulfate is an antineoplastic agent derived from vinblastine (see p.785); like the other vinca alkaloids it causes mitotic arrest in metaphase by binding to microtubular protein. It is used in the treatment of refractory acute lymphoblastic or chronic myeloid leukaemias, and malignant melanoma. It has also been tried in malignant neoplasms of the breast, and lung. See also the cross references given below.

Vindesine sulfate is given weekly by intravenous injection. It may be given as a solution containing 1 mg/mL in sodium chloride injection 0.9%. However, UK guidelines recommend that for patients over the age of 10 years, solutions of vindesine should generally be di-