DRUG NAME: Vinblastine

SYNONYM(S): VBL,[1] Vincaleukoblastine Sulfate,[2] VLB[2]

COMMON TRADE NAME(S): vinblastine sulfate injection

CLASSIFICATION: mitotic inhibitor[1]

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Vinblastine is the salt of a naturally-occurring vinca alkaloid obtained from the flowering herb periwinkle[1,2] Vinca alkaloids act by preventing the polymerization of tubulin to form microtubules, as well as inducing depolymerization of formed tubules.[1] Vinblastine may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization.[1-3] Vinca alkaloids are cell cycle phase-specific for M phase and S phase.[3,4] Vinblastine exerts some immunosuppressive activity.[1,2,4] Cross-resistance with vincristine has been reported.[1]

PHARMACOKINETICS:

Oral Absorption	not given orally due to incomplete and variable absorption	
Distribution	extensive binding to tissue and formed peripheral blood elements[5]	
	cross blood brain barrier?	poorly; not in therapeutic concentrations
	volume of distribution[3]	27.3 L/kg
	plasma protein binding[3]	99%
Metabolism	primarily hepatic, involves the CYP3A hepatic enzyme system[2]	
	active metabolite	desacetylvinblastine
	inactive metabolite(s)[4]	yes
Excretion	primarily bilary/fecal, some renal excretion[6]	
	urine[3]	yes, <1% as unchanged drug
	feces[3]	95%, via bile[2]
	terminal half life[6]	25 h
	clearance[5]	0.74 L/hr/kg

Adapted from standard reference[1] unless specified otherwise.

USES:

Primary uses:
Fibromatosis
Germ cell tumour[2,8]
*Kaposi's sarcoma
Lung cancer, non-small cell[2,9]
*Lymphoma, Hodgkin's
*Lymphoma, non-Hodgkin's
*Mycosis fungoides
*Testicular cancer
Ureter, transitional cell cancer[10,11]

Other uses:
Bladder cancer[2]
*Breast cancer
*Choriocarcinoma
*Histiocytosis X
Melanoma[2]

*Health Canada approved indication

SPECIAL PRECAUTIONS:

Inadvertent administration of vinblastine by the intrathecal (IT) route is nearly always **fatal** and is a medical emergency.[2] **All** vinblastine doses dispensed should be labelled with an auxiliary label and a medication label, both stating **"WARNING: FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES"**.[12]

Use with caution in patients with preexisting pulmonary dysfunction, ischemic cardiovascular disease, and in patients receiving other potentially ototoxic medications such as platinum-containing antineoplastics.[2,4]

Elderly patients with cachexia or skin ulcers may develop a more profound leukopenia; avoid vinblastine use.[1]

Carcinogenicity: Vinblastine is potentially carcinogenic.[4,5]

Mutagenicity: Vinblastine is potentially mutagenic[4]; vinblastine is not mutagenic in Ames test.[5] No information found regarding clastogenicity in mammalian *in vitro* and *in vivo* chromosome tests.

Fertility: Aspermia has been reported.[1] Animal studies have demonstrated degenerative changes in germ cells.[1] In humans, vinblastine-related oligospermia is typically temporary (6-24 months); recovery of normal spermatogenesis can be expected.[13]

Pregnancy: FDA Pregnancy Category D.[3] There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective). Use of vinblastine for selected patients with coincident Hodgkin's lymphoma and pregnancy has been reported without evidence of fetal toxicity.[13]

Breastfeeding is not recommended due to the potential secretion into breast milk.[2,3]

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.[13,14] When placebo-controlled trials are available, adverse events are included if the incidence is ≥5% higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
auditory/hearing	hearing impairment; related to eighth cranial nerve damage, may be partial or total, temporary or permanent[2]; see paragraph following the **Side Effects** table
blood/bone marrow/ febrile neutropenia	myelosuppression (>10%)[4]
	anemia[2]; typically not significant
	leukopenia; dose-related, nadir days 4-10 with recovery within another 7-14 days, with high-dose therapy recovery may take ≥21 days[2]
	thrombocytopenia (1-5%)[6]; typically mild and transient, but significant platelet count depression may occur in patients who have bone marrow infiltrated with disease or who have received prior radiation therapy or chemotherapy
cardiovascular (general)	angina pectoris,[2] myocardial infarction,[2] coronary ischemia[2]
	hypertension (1-10%)[3,4]
constitutional symptoms	fatigue (1-10%)[4]
	fever[2]

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in ***bold, italics***	
dermatology/skin	*extravasation hazard: vesicant*[15]
	alopecia[2] (>10%)[3,4]; including loss of body hair; typically incomplete, re-growth may occur during treatment
	photosensitivity[2] (1-10%)[3,4]
	rash/dermatitis (1-10%)[3,4]
endocrine	SIADH[3] (<1%)[4]; typically with high-dose[16,17]
gastrointestinal	*emetogenic potential: rare*[18]
	anorexia
	constipation (1-10%)[3]; related to autonomic neuropathy,[4,19] see paragraph following the **Side Effects** table
	diarrhea (1-10%)[4]
	ileus (1-10%)[3,4]; related to autonomic neuropathy,[19] see paragraph following the **Side Effects** table
	mucositis (1-10%)[3]
	nausea and vomiting (1-10%)[3]; typically mild,[3] usually lasts[2] < 24 h
hemorrhage	bleeding from old rectal ulcers[2]
	hemorrhagic enterocolitis (<1%)[3,4]
	rectal bleeding (<1%)[4,6]
metabolic/laboratory	hyperuricemia[2] (1-10%)[3,4]
musculoskeletal	cramps[13]
	weakness
neurology	depression (1-10%)[3,4]
	paresthesias (20%),[20] neurotoxicity (<1%);[3] see paragraph following the **Side Effects** table
pain	abdominal pain (1-10%)[3]; related to autonomic neuropathy[19]
	face, jaw and/or parotid gland pain; see paragraph following the **Side Effects** table
	headache (1-10%)[3,4]
	muscle pain
	pain at the tumour site (1-5%)[6]; immediate or delayed, may be severe
pulmonary	acute shortness of breath and bronchospasm (1-10%)[4]; see paragraph following the **Side Effects** table
renal/genitourinary	urinary retention[3] (1-10%)[3,4]; related to autonomic neuropathy,[4] see paragraph following the **Side Effects** table
sexual/reproductive function	aspermia, oligospermia[13]; reversible, typical duration 6-24 months[13]
syndromes	tumour lysis syndrome[2]
vascular	Raynaud's phenomenon (1-10%)[3,4]; reported in patients receiving vinblastine and bleomycin +/- cisplatin[2]

Adapted from standard reference[1] unless specified otherwise.

Neurotoxicity (<1%)[3] The vinca alkaloids can cause central and peripheral, including autonomic, neurotoxicity. Risk of neurotoxicity may be increased with high-dose or prolonged therapy.[2,4,20] Neurotoxicity may occur days to weeks after starting treatment,[4] with recovery typically occurring weeks to months after stopping therapy.[21] Neurologic effects are typically much less common and severe than with vincristine.[2,4,5,20] Mild paresthesia (20%)[20] is the most frequently reported neurologic toxicity and is usually reversible on discontinuation of vinblastine. Other neurologic toxicities may include numbness, neuritis, muscle cramps,[13] loss of deep tendon reflexes, headache, malaise, weakness, dizziness, seizures, depression, psychoses, severe face and jaw pain, severe immediate or delayed pain at the tumour site, bone pain, vocal cord paralysis, ocular toxicities including ptosis, and dysfunction of the autonomic system.[1,2,21] High doses (>20 mg) can cause autonomic neuropathy including urinary retention, orthostatic hypotension, and constipation.[4] Patients receiving vinblastine should receive opioid analgesics with caution due to the risk of additive autonomic neuropathy which may result in severe constipation.[13] An appropriate bowel routine to prevent or treat constipation should be initiated prior to starting vinblastine treatment.[14]

Severe jaw or parotid gland pain can occur within a few hours of the first dose of vinblastine. This is not an indication to stop treatment or modify the dose; treat with analgesics.[4]

Ototoxicity due to eighth cranial nerve damage manifests as dizziness, nystagmus, vertigo, and hearing impairment. Hearing impairment may be partial or total, temporary or permanent.[2] Use vinblastine with caution in patients receiving other potentially ototoxic medications such as platinum-containing antineoplastics.[2,4]

Acute shortness of breath and bronchospasm (1-10%)[4] has occurred with vinca alkaloids and is more frequent with concomitant mitomycin.[2,4] Symptoms may occur minutes to hours after vinblastine injection[2,4] or up to 2 weeks after a mitomycin dose.[2] Symptoms may be characterized by cough, dyspnea, hypoxemia, and interstitial infiltration.[16] Aggressive treatment may be required.[2,4] Progressive dyspnea has occurred; do not readminister vinblastine.[2,4] Patients with preexisting pulmonary dysfunction may have increased risk of respiratory toxicity with vinblastine.[4]

Tumour lysis syndrome may result from cell lysis by cytotoxic chemotherapy and may lead to electrolyte disturbances or acute renal failure.[22] It is most likely with highly proliferative tumours of massive burden, such as leukemias, high-grade lymphomas, and myeloproliferative diseases. The risk may be increased in patients with preexisting renal dysfunction, especially ureteral obstruction. Suggested prophylactic measures for high-risk patients[23]:

- aggressive hydration
- allopurinol
- if possible, discontinuation of drugs that cause hyperuricemia (e.g., thiazide diuretics) or acidic urine (e.g., salicylates)
- monitoring of electrolytes, calcium, phosphate, renal function, LDH, and uric acid
- electrolyte replacement as required
- alkalinization of urine, if the uric acid level is elevated, use sodium bicarbonate IV or PO titrated to maintain urine pH > 7

INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
azole antifungal agents [2,24] (e.g., itraconozole, ketoconazole, voriconazole)	increased toxic effect of vinblastine	possible inhibition of vinblastine metabolism (CYP 3A4)	avoid combination; if used concomitantly, decrease dose of vinblastine and monitor for toxicity
carbamazepine[24]	decreased therapeutic effect of vinblastine	possible increase in vinblastine metabolism (CYP 3A4)	avoid combination if possible

AGENT	EFFECT	MECHANISM	MANAGEMENT
erythromycin[2,24]	increased toxic effect of vinblastine	possible inhibition of vinblastine metabolism (CYP 3A4)	avoid combination; if used concomitantly decrease dose of vinblastine and monitor for toxicity
mitomycin[2,4]	acute shortness of breath and severe bronchospasm have occurred following use of vinblastine in patients who had received mitomycin simultaneously or within 2 weeks	unknown	avoid combination if possible; use with caution
phenytoin[24]	decreased therapeutic effect of phenytoin	decreased absorption and/or increased metabolism of phenytoin	monitor phenytoin serum levels

Vinblastine is a potent CYP 3A4 inhibitor; therefore, vinblastine may increase the levels/effects of drugs or herbs that are CYP3A4 substrates.[2]

Vinblastine is a major CYP3A4 substrate; therefore, drugs or herbs that are CYP3A4 inducers may decrease the levels/effects of vinblastine. Likewise, drugs or herbs that are CYP3A4 inhibitors may increase the levels/effects of vinblastine.[2]

SUPPLY AND STORAGE:

Injection: Hospira Healthcare Corporation supplies vinblastine as single use 10 mg/10 mL vials. Store in the refrigerator and protect from light.[1]

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

SOLUTION PREPARATION AND COMPATIBILITY:

For basic information on the current brand used at the BC Cancer Agency, see Chemotherapy Preparation and Stability Chart in Appendix.

Compatibility: consult detailed reference

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold***, ***italics***

Subcutaneous	not used due to corrosive nature[2,4]
Intramuscular	not used due to corrosive nature[4]
Direct intravenous	**NOT USED DUE TO THE RISK OF INADVERTENT INTRATHECAL ADMINISTRATION[25-27]**
Intermittent infusion	**over** 5-**15 minutes**[19]; • dilution in large volumes of diluent (≥100 mL) and/or administration over prolonged periods (≥30 minutes) is not recommended due to increased vein irritation and risk of extravasation[28,29]; infusions of 3-8 h have sometimes been used for specific clinical indications[30,31] • see ***Prevention and Management of Extravasation of Chemotherapy***

BCCA administration guideline noted in ***bold***, ***italics***

Continuous infusion	not recommended due to increased vein irritation and risk of extravasation following administration of large volumes (≥100 mL) of diluted vinblastine and/or administration over prolonged periods (≥30 minutes)[28,29]; has sometimes been used for specific clinical indications[5,19]
Intraperitoneal	not used due to corrosive nature[32]
Intrapleural	not used due to corrosive nature[32]
Intrathecal	**ABSOLUTELY CONTRAINDICATED; INTRATHECAL INJECTION CAN BE FATAL**[1]
Intra-arterial	investigational, has been used[33]
Intravesical	no information found
Intralesional	investigational, has been used[16,34]

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

***Adults*:**

BCCA usual dose noted in ***bold, italics***

	Cycle Length:	
**Intravenous:*	***1-4 weeks[1,7,35]:***	***6 mg/m^2 (range 3.7-18.5 mg/m^2) IV for one dose on day 1 (total dose per cycle 6 mg/m^2 [range 3.7-18.5 mg/m^2])***
	2 weeks[36]:	***6-10 mg IV for one dose on day 1 (total dose per cycle 6-10 mg)***
	3 weeks[8]:	***0.11 mg/kg IV once daily for 2 consecutive days starting on day 1 (total dose per cycle 0.22 mg/kg)***
	4 weeks[37]:	***6 mg/m^2 IV for one dose on days 1 and 15 (total dose per cycle 12 mg/m^2)***
	4 weeks[10]:	***4 mg/m^2 IV for one dose on days 1 and 8 (total dose per cycle 8 mg/m^2)***
	4 weeks[11]:	***3 mg/m^2 IV for one dose on days 2, 15, and 22 (total dose per cycle 9 mg/m^2)***
	n/a[9]:	***5 mg/m^2 IV for one dose on days 1, 8, 15, 22, and 29 (total dose 25 mg/m^2)***

*maximum weekly dose[2]: 18.5 mg/m^2

Concurrent radiation: investigational, has been used[38]

Dosage in myelosuppression: modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"

Dosage in renal failure: no adjustment required[16,39]

Dosage in hepatic failure[4]: adjustment required; suggested dose adjustment:

Serum bilirubin (micromol/L)	Dose
25-50	50%
>50	25%

Dosage in dialysis: not removed by hemodialysis[3]

Children:

†*Intravenous:*

Cycle Length:

1-2 weeks[1,40,41]: 2.5-6 mg/m^2 (range 2.5-12.5 mg/m^2) IV for one dose on day 1
(total dose per cycle 2.5-6 mg/m^2 [range 2.5-12.5 mg/m^2])

7-10 days[40]: 0.4 mg/kg IV for one dose on day 1
(total dose per cycle 0.4 mg/kg)

3 weeks[40]: 0.2 mg/kg IV once daily for 2 consecutive days starting on day 1
(total dose per cycle 0.2 mg/kg)

†maximum weekly dose[40]: 12.5 mg/m^2

REFERENCES:

1. Mayne Pharma (Canada) Inc. Vinblastine sulfate injection® product monograph. Montreal, Quebec; 10 August 2003.
2. McEvoy GK, editor. AHFS 2007 Drug Information. Bethesda, Maryland: American Society of Health-System Pharmacists, Inc. p. 1225-1228.
3. Rose BD editor. Vinblastine. UpToDate 15.1 ed. Waltham, Massachusetts: UpToDate®; 2007.
4. Repchinsky C editor. Vinblastine, CPhA monograph, Compendium of Pharmaceuticals and Specialties. Ottawa, Ontario: Canadian Pharmacists Association; 2006.
5. Chabner BA, Longo DL. Cancer Chemotherapy and Biotherapy. 4th ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2006. p. 240-253.
6. USPDI® Drug Information for the Health Care Professional (database on the Internet). Vinblastine (Systemic). Thompson MICROMEDEX®, 2007. Available at: www.micromedex.com. Accessed 18 May 2007.
7. BC Cancer Agency Sarcoma Tumour Group. (SAMV) BCCA Protocol Summary for Palliative Therapy for Aggressive Fibromatosis Using Weekly or Alternate Week Methotrexate and Vinblastine Intravenously. Vancouver, British Columbia: BC Cancer Agency; 1 April 2007.
8. BC Cancer Agency Genitourinary Tumour Group. (GUVEIP) BCCA Protocol Summary for Consolidation/Salvage Treatment for Germ Cell Cancer Using Vinblastine, Cisplatin, Ifosfamide and Mesna. Vancouver, British Columbia: BC Cancer Agency; 1 February 2007.
9. BC Cancer Agency Lung Tumour Group. (LUCMT-1) BCCA Protocol Summary for Combined Chemotherapy and Radiation Treatment for Stage 3 Non-Small Cell Lung Cancer. Vancouver, British Columbia: BC Cancer Agency; 1 January 2005.
10. BC Cancer Agency Genitourinary Tumour Group. (GUBCV) BCCA Protocol Summary for Therapy for Transitional Cell Cancers Using Carboplatin-Vinblastine. Vancouver, British Columbia: BC Cancer Agency; 16 January 2007.
11. BC Cancer Agency Genitourinary Tumour Group. (GUMVAC) BCCA Protocol Summary for Therapy for Transitional Cell Cancer of the Urothelium using Methotrexate, Vinblastine, Doxorubicin, and Cisplatin. Vancouver, British Columbia: BC Cancer Agency; 1 February 2007.
12. BC Cancer Agency Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy V-40: Labeling of Vinca Alkaloid Preparations. Vancouver, British Columbia: BC Cancer Agency; 1 February 2008.
13. Joseph Connors MD. BC Cancer Agency Lymphoma Tumour Group. Personal communication. 28 June 2007; .
14. Nevin Murray MD. BC Cancer Agency Genitourinary Tumour Group. Personal communication. 20 July 2007; .
15. BC Cancer Agency Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer Agency; 1 September 2006.
16. DRUGDEX® Evaluations (database on the Internet). Vinblastine. Thomson MICROMEDEX®, 2007. Available at: www.micromedex.com. Accessed 18 May 2007.
17. MARTINDALE - The Complete Drug Reference (database on the Internet). Vinblastine sulfate. Thomson MICROMEDEX®, 2007. Available at: http://www.micromedex.com/. Accessed 18 May 2007.
18. BC Cancer Agency. (SCNAUSEA) Guidelines for Prevention and Treatment of Chemotherapy-induced Nausea and Vomiting in Adults. Vancouver, British Columbia: BC Cancer Agency; 1 November 2005.
19. Solimando Jr DA. Cancer chemotherapy update: Updates of vinblastine and vincristine. Hosp Pharm 1997;32(4):475-482.

20. Wen PW, Plotkin SR. Neurologic complications of cancer chemotherapy. UpToDate 15.1, 8 December 2006. Available at: www.uptodate.com. Accessed 18 May 2007.
21. Parentin F, Liberali T, Perissutti P, et al. Unilateral palpebral ptosis associated with vinblastine therapy. Neuro-ophthalmol 2005;29(3):133-135.
22. DeVita VT, Hellman S, Rosenberg SA. Cancer Principles & Practice of Oncology. 6th ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2001. p. 2640.
23. Leukemia/Bone Marrow Transplant Program of British Columbia. Leukemia/BMT Manual. 4th ed. Vancouver, British Columbia: Vancouver Hospital and Health Sciences Centre / BC Cancer Agency; 2003. p. 27.
24. Drug Interaction Facts (database on the Internet). Vinblastine. Facts and Comparisons 4.0, 2007. Available at: http://online.factsandcomparisons.com;. Accessed 18 May 2007.
25. Institute for Safe Medication Practices Canada. 2014-15 Targeted Medication Safety Best Practices for Hospitals - Best Practice #1: Dispense vinCRIStine (and other vinca alkaloids) in a minibag of a compatible solution and not in a syringe. Canada: Institute for Safe Medication Practices Canada; 2014.
26. World Health Organization. Information Exchange System - Vincristine (and other vinca alkaloids) should only be given intravenously via a minibag. Alert No. 115 ed. Geneva, Switzerland: World Health Organization; 18 July 2007.
27. Institute for Safe Medication Practices Canada. ISMP Safety Bulletin - Published data supports dispensing vincristine in minibags as a system safeguard. Canada: Institute for Safe Medication Practices Canada; 03 October 2001.
28. Hospira Healthcare Corporation. Vinblastine Sulfate injection® product monograph. Saint-Laurent, Quebec; 18 June 2007.
29. Lexi-Drugs® (database on the Internet). VinBLAStine. Lexi-Comp Inc., 3 November 2014. Available at: http://online.lexi.com. Accessed 20 November 2014.
30. Repchinsky C, editor. Vinblastine CPhA monograph, Compendium of Pharmaceuticals and Specialties (eCPS). Canadian Pharmacists Association, Last revised: Mar 2009. Available at: https://www.e-therapeutics.ca/. Accessed 20 November 2014.
31. AHFS Drug Information® (database on the Internet). Vinblastine sulfate. Lexi-Comp Inc., 1 January 2009. Available at: http://online.lexi.com. Accessed 18 November 2014.
32. Trissel L. Handbook on injectable drugs. 13th ed. Bethesda, Maryland: American Society of Health-System Pharmacists; 2005. p. 1469-1474.
33. Melichar B, Dvorak J, Jandik P, et al. Intraarterial chemotherapy of malignant melanoma metastatic to the liver. Hepatogastroenterology 2001;48(42):1711-5.
34. Dezube BJ, Groopman JE. AIDS-related Kaposi's sarcoma: Clinical features and treatment. UpToDate 15.1, 8 January 2007. Available at: www.uptodate.com. Accessed 18 May 2007.
35. BC Cancer Agency Lymphoma Tumour Group. (LYPALL) BCCA Protocol Summary for Lymphoma Palliative Chemotherapy. Vancouver, British Columbia: BC Cancer Agency; 1 Feb 2007.
36. BC Cancer Agency Kaposi's Sarcoma Tumour Group. (KSVB) BCCA Protocol Summary for Palliative Treatment for Kaposi's Sarcoma using Vinblastine Alternating with Vincristine. Vancouver, British Columbia: BC Cancer Agency; 1 September 2002.
37. BC Cancer Agency Lymphoma Tumour Group. (LYABVD) BCCA Protocol Summary for Treatment of Hodgkin's Disaese with Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine. Vancouver, British Columbia: BC Cancer Agency; 1 February 2007.
38. Kragelj B, Jereb B, Kragelj L, et al. Concurrent vinblastine and radiation therapy in bladder cancer. Cancer 1992;70(12):2885-2890.
39. Aronoff GR, Berns JS, Brier ME, Golper TA, et al. Drug Prescribing in Renal Failure: Dosing guidelines for adults. 4th ed. Philadelphia, Pennsylvania: American College of Physicians; 1999. p. 74.
40. Rose BD editor. Vinblastine: pediatric drug information. www.uptodate.com ed. Waltham, Massachusetts: UpToDate 15.1; 2007.
41. Pizzo P, Poplack D. Principles and Practice of Pediatric Oncology. 5th ed. Philadelphia, Pennsylvania: Lippincott Williams & Wilkins; 2006. p. 302.