DRUG NAME: VINDESINE

SYNONYM(S): Desacetylvinblastine amide, DAVA, DVA, VDS

COMMON TRADE NAME(S): ELDISINE®

CLASSIFICATION: Mitotic Inhibitor

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

MECHANISM OF ACTION: [1]

Vindesine is a vinca alkaloid which is a synthetic derivative of vinblastine. Vindesine binds to the microtubular proteins of the mitotic spindle, leading to crystallization of the microtubule and mitotic arrest or cell death. The vinca alkaloids are considered to be cell cycle phase-specific.

PHARMACOKINETICS: [1,2,3,4,5,6,7,8,9,10]

Oral Absorption	not absorbed orally	
Distribution	rapid distribution to superficial and deep tissue compartments	
	cross blood brain barrier?	no
	Vd	8.11 L/kg, 58-600 L
	PPB	no information found
Metabolism	metabolized in liver	
	active metabolite(s)	no information found
	inactive metabolite(s)	no information found
Excretion	major route of excretion is biliary system	
	urine	19% within 84 hours
	t½ α	3 minutes
	t½ β	0.8-1.7 hours
	t½ γ	20-24 hours
	Cl	no information found

USES: [3,10,11]

* Acute lymphocytic leukemia

Less frequent uses include:
- Breast cancer
- Chronic myelogenous leukemia
- Colorectal cancer
- * Lung cancer, non-small cell
- Renal cell cancer

* Health Protection Branch approved indication.

SPECIAL PRECAUTIONS: [3]

Vindesine may be lethal if injected intrathecally. The Compendium of Pharmaceuticals and Specialties (CPS) and the United States Pharmacopeia (USP) require that vindesine be dispensed in an overwrap bearing the statements "Do not remove covering until moment of injection. Fatal if given intrathecally. For intravenous use only."

Vindesine is potentially ***mutagenic and carcinogenic***. Its safe use in ***pregnancy*** and its effects on ***fertility*** have not been established. ***Breast feeding*** is not recommended due to potential secretion into breast milk.

SIDE EFFECTS: [3,10,11]

ORGAN SITE	SIDE EFFECT	ONSET			
dermatologic	alopecia (common)		E		
	rash (rare)		E		
extravasation hazard (refer to Appendix 2)	**VESICANT**	I			
gastrointestinal	mild nausea and vomiting	I			
	mild stomatitis (rare)		E		
	abdominal cramping (autonomic neuropathy)		E		
	constipation (rare, autonomic neuropathy)		E		
	paralytic ileus (rare, autonomic neuropathy)		E		
hypersensitivity	Type I (anaphylactoid, rare)	I			
hematologic	myelosuppression nadir 3-6 days, recovery 7-10 days		E		
	thrombocytopenia or thrombocytosis (rare)		E		
injection site	chemical phlebitis	I			
neurologic	peripheral neuropathy		E		
	jaw pain (may be severe, cranial nerve neuropathy)	I			

Dose-limiting side effects are underlined.
I = immediate (onset in hours to days); E = early (days to weeks);

D = delayed (weeks to months); L = late (months to years)

The ***tissue necrosis*** that happens with ***extravasation*** may happen days to weeks after the treatment. Patients must be observed for delayed reactions and prior injection sites carefully inspected.

Neurotoxicity with the vinca alkaloids is qualitatively similar but quantitatively different (vincristine> vindesine>vinblastine). The peripheral paresthesia is similar to vincristine neurotoxicity with symptoms appearing after 3-4 courses. Hepatic dysfunction increases vindesine's neurotoxic potential. ***Peripheral neuropathy*** manifests initially as distal paresthesias, proximal muscle weakness and loss of deep tendon reflexes. ***Autonomic neuropathy:*** Abdominal cramping is common with infrequent constipation. Paralytic ileus is rarely dose limiting. Urinary retention and postural hypotension have been noted rarely. ***Cranial nerve neuropathy:*** Hoarseness and sometimes severe transient jaw pain are infrequent. Cortical blindness has been described.

INTERACTIONS: [3,12]

AGENT	EFFECT	MECHANISM	MANAGEMENT
mitomycin	acute bronchospasm has occurred minutes to hours after administration of vindesine in some patients previously or simultaneously treated with mitomycin	unknown	caution
phenytoin	decreased phenytoin serum levels	possibly decreased absorption or increased metabolism of phenytoin	monitor phenytoin serum level; adjust phenytoin dose prn

SOLUTION PREPARATION AND COMPATIBILITY: [3,14,15]

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Injection: 5 mg vial; also contains mannitol. May also contain sodium hydroxide and/or sulfuric acid. Store in refrigerator.

Reconstitute powder with 5 mL bacteriostatic NS to a final concentration of 1 mg/mL.

Reconstituted solution for injection: Stable for 24 hours at room temperature and 14 days when refrigerated. Trissel states stability of 30 days under refrigeration.

Diluted solution for infusion: Dilutions in D5W or NS are stable at least 24 hours at room temperature protected from light. Electrolyte-containing solutions, such as lactated Ringer's, are not recommended since precipitation may occur.

It is recommended that vindesine ***not be mixed with other drugs.***

PARENTERAL ADMINISTRATION: [13,15]

Subcutaneous	not used due to corrosive nature
Intramuscular	not used due to corrosive nature
Direct intravenous	Preferred method due to need for frequent monitoring for signs of extravasation. Via small (21 or 23) gauge needle into tubing of running IV. Push slowly, over 1-3 minutes, so that drip of IV solution does not stop or reverse. Check for blood return before administration and after every 2-3 mL of drug. If no blood return, stop the injection and assess the IV site. Flush with 20 mL NS or D5W after administration to clear any remaining drug from tubing.
Intermittent infusion	slow IV push preferred
Continuous infusion	in appropriate volume over 5-7 days, secure venous access required
Intraperitoneal	no information available on this route
Intrapleural	no information available on this route
Intrathecal	not used due to corrosive nature
Intra-arterial	no information available on this route
Intravesical	no information available on this route

DOSAGE GUIDELINES: [3,16,17]

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 white blood cell count. Dosage may be reduced and/or delayed in patients with bone marrow depression due to cytotoxic/radiation therapy.

***Adults*:**

Intravenous: q1-2w: 2-4 mg/m^2
q3-4w: 1.5 mg/m^2/day x 5-7 days as a continuous infusion

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

Dosage in hepatic failure:

Bilirubin (µmol/L)	% usual dose
25-50	50%
>50	omit

***Children*:**

Intravenous: q1w: 4 mg/m^2
biw (twice weekly): 2 mg/m^2

VINDESINE FACT SHEET
FOR THE HEALTH CARE PROFESSIONAL

OTHER NAMES	vindesine sulfate, desacetylvinblastine amide, DAVA, DVA, VDS, ELDESINE®
USES	many (refer to monograph)
DOSAGE FORMS	injection: 5 mg vial for reconstitution (refrigerate)

USUAL DOSE RANGE	Adults: 2-4 mg/m^2 q1-2w 1.5 mg/m^2/day x 5-7 days q3-4w Children: 4 mg/m^2 IV q1w 2 mg/m^2 IV twice weekly
DOSE REDUCTIONS	low WBC, RBC, platelets (myelosuppression) liver (hepatic) failure nerve problems (neurotoxicity)

IV COMPATIBILITY	normal saline, dextrose 5%
ROUTES	direct IV (preferred) intermittent IV (VAD preferred) continuous IV (via VAD)
EXTRAVASATION HAZARD Management	**VESICANT** (tissue damage on extravasation) stop IV, aspirate, elevate limb, warm intermittent compresses

ONSET	**SIDE EFFECT** * may be life-threatening side effects in ***bold, italic*** type are common
IMMEDIATE (hours to days)	* anaphylaxis (rare) nausea and vomiting (uncommon, usually mild) jaw pain (may be severe, rare; cranial nerve neuropathy)
EARLY (days to weeks)	* ***low WBC, RBC, platelets*** (***myelosuppression***, nadir 3-6 days, recovery 7-10 days) increased platelet count (thrombocytosis, rare) ***hair loss*** (***alopecia***, common, usually mild) ***nerve problems*** (peripheral, cranial nerve and autonomic neuropathy) gastrointestinal problems (***abdominal cramping***, constipation - rare, paralytic ileus - rare; autonomic neuropathy) vein irritation at injection site (phlebitis) mouth sores (rare, stomatitis) rash (rare)

CONTRAINDICATIONS	known hypersensitivity to vindesine

	pregnancy and breast feeding
SIGNIFICANT INTERACTIONS *increases toxicity	phenytoin (DILANTIN®), *mitomycin (MUTAMYCIN®)
LABORATORY MONITORING	each treatment: CBC, electrolytes, liver function

TEACHING AIDS	· *For the Patient: Vindesine* · *Chemotherapy and You: a Guide to Self-help During Treatment*

NOTES:
- **Intrathecal administration of vindesine is absolutely contraindicated.** Care must be taken to avoid accidental intrathecal administration which could be fatal.
- Peripheral neuropathy includes the loss of deep tendon reflex at the ankle, numbness, parethesia and motor weakness.
- Cranial nerve neuropathy includes jaw pain and hoarseness. Jaw pain may require analgesics and does not usually require a dose modification.
- Autonomic neuropathy includes constipation, abdominal pain, paralytic ileus and urinary retention. High enemas or stimulant laxatives may be required.
- May cause severe irritation, and rarely corneal ulceration, if accidental contamination of the eye occurs. Wash the eye with water immediately and thoroughly.

FOR THE PATIENT: Vindesine

Other names: ELDESINE®

- **Vindesine** (vin-DESS-een) is a drug that is used to treat some kinds of cancer. It is a clear liquid that is injected into a vein.
- A **blood sample** will be taken before each treatment. The dose and timing of your chemotherapy may be changed based on your blood counts and/or other side effects.
- Other drugs such as phenytoin (DILANTIN®) may **interact** with vindesine. Tell your doctor if you are taking this or any other drugs as your dose may need to be changed. Check with your doctor or pharmacist before you start taking any new drugs.
- The **drinking of alcohol** (in small amounts) will not affect the safety or usefulness of vindesine.
- Vindesine may damage sperm and may harm the baby if used during pregnancy. It is best to **use birth control** while being treated with vindesine. Tell your doctor right away if you or your partner becomes pregnant. **Do not breast feed** during treatment.
- **Tell** doctors or dentists that you are being treated with vindesine before you receive any treatment from them.

SIDE EFFECTS	MANAGEMENT
Vindesine **burns** if it leaks under the skin.	Tell your nurse or doctor ***immediately*** if you feel burning, stinging or any other change while the drug is being given.
Pain or tenderness may occur where the needle was placed.	·Apply warm compresses or soak in warm water for 15-20 minutes several times a day.
Nausea rarely occurs with vindesine. Most people have little or no nausea.	·Drink plenty of liquids. ·Eat often in small amounts.
Constipation may occur.	·Exercise if you can. ·Drink plenty of fluids. ·Add prunes or prune juice. ·Eat foods high in fibre such as bran, whole grain breads and cereals, nuts, raw fruits and raw vegetables.
Your **white blood cells** will decrease 3-6 days after your treatment. They will return to normal 7-10 days after your last treatment. White blood cells protect your body by fighting bacteria (germs) that cause infection.	To help prevent infection: ·Wash your hands often and always after using the bathroom. ·Take care of your skin and mouth. ·Avoid crowds and people who are sick.

SIDE EFFECTS	MANAGEMENT
When they are low, **you are at greater risk of having an infection**.	·Call your doctor ***immediately*** at the first sign of an infection such as fever (over 100°F or 38°C), chills, cough, sore throat or burning when you pass urine.
Your **platelets** may decrease 3-6 days after your treatment. They will return to normal 7-10 days after your last treatment. Platelets help to make your blood clot when you hurt yourself. **You may bruise or bleed more easily than usual**.	To help prevent bleeding problems: ·Try not to bruise, cut or burn yourself. ·Clean your nose by blowing gently, do not pick your nose. ·Avoid constipation. ·For minor pain, take acetaminophen (eg, TYLENOL®). Do not take ASA (eg, ASPIRIN®) or ibuprofen (eg, ADVIL®).
Hair loss is common and may begin within a few days or weeks of treatment. Your hair may thin or you may become totally bald. Your scalp may feel tender. You may also lose hair on your face and body. Your hair will grow back once your treatments are over an sometimes between treatments. Colour and texture may change.	·Use a gentle baby shampoo and soft brush. ·Avoid hair spray, bleaches, dyes and perms. ·Protect your scalp with a hat, scarf or wig in cold weather. Some extended health plans will pay part of the cost of a wig. ·Cover your head or apply sunblock on sunny days. ·Apply mineral oil to your scalp to reduce itching. ·If you lose your eyelashes and eyebrows, protect your eyes from dust and grit with a broad-rimmed hat and glasses.
Numbness of the fingers or toes may occur. This will slowly return to normal once your treatments are over. This may take several months.	·Be careful when handling items that are sharp, hot or cold. ·Tell your doctor at your next visit especially if you have trouble with buttons, writing or picking up small objects.

SEE YOUR DOCTOR OR GET EMERGENCY HELP *IMMEDIATELY* IF YOU HAVE:

- Signs of an **infection** such as fever (over 100°F or 38°C); chills; cough; sore throat; pain or burning when you pass urine; redness, pain or swelling of any area of your body; sores forming anywhere on your body.
- Signs of **bleeding problems** such as black, tarry stools; blood in urine; pinpoint red spots on skin.

SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:

- Trouble in walking or climbing stairs.
- Severe constipation or stomach cramps.
- Trouble passing urine, frequent need to pass urine or bed-wetting.

CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:

- Uncontrolled nausea, vomiting or constipation.
- Easy bruising or bleeding.
- Severe jaw pain or headache.
- Redness, swelling, pain or sores where the needle was placed.
- Redness, swelling, pain or sores on your lips, tongue, mouth or throat.

REPORT ADDITIONAL PROBLEMS TO YOUR DOCTOR.

See ***Chemotherapy and You: a Guide to Self-help During Treatment*** available free from the Canadian Cancer Society for more information on managing side effects.

Notes:

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