Vinorelbine: Drug information

(For additional information see "Vinorelbine: Patient drug information" and see "Vinorelbine: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Experienced physician:

Vinorelbine tartrate injection should be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents.

Not for intrathecal use:

This product is for intravenous (IV) use only. Intrathecal administration of other vinca alkaloids has resulted in death. Syringes containing this product should be labeled “Warning — for IV use only. Fatal if given intrathecally.”

Bone marrow suppression:

Severe granulocytopenia resulting in increased susceptibility to infection may occur. Granulocyte counts should be greater than or equal to 1000 cells/mm^3 prior to the administration of vinorelbine tartrate. The dosage should be adjusted according to complete blood counts with differentials obtained on the day of treatment.

Extravasation:

It is extremely important that the IV's needle or catheter be properly positioned before vinorelbine tartrate is injected. Administration of vinorelbine tartrate may result in extravasation causing local tissue necrosis or thrombophlebitis.

Brand Names: US

Navelbine

Brand Names: Canada

Navelbine; Vinorelbine Injection, USP; Vinorelbine Tartrate for Injection

Pharmacologic Category

Antineoplastic Agent, Antimicrotubular; Antineoplastic Agent, Vinca Alkaloid

Dosing: Adult

Non-small cell lung cancer (NSCLC): IV:

Single-agent therapy: 30 mg/m^2 every 7 days until disease progression or unacceptable toxicity

Combination therapy: 25-30 mg/m^2 every 7 days (in combination with cisplatin)

Off-label dosing: 25 mg/m^2 days 1 and 8 every 21 days (in combination with cisplatin and cetuximab) for up to 6 cycles (Pirker, 2009) **or** 25-30 mg/m^2 days 1, 8, and 15 every 28 days (in combination with gemcitabine) for 6 cycles **or** until disease progression or unacceptable toxicity (Herbst, 2002; Greco, 2007)

Breast cancer, metastatic (off-label use): IV: 25 mg/m^2 every 7 days (as a single agent) until disease progression or unacceptable toxicity (Zelek, 2001) **or** 30 mg/m^2 every 7 days (as a single agent); after 13 weeks, may administer every 14 days for patient convenience, continue until disease progression or unacceptable toxicity (Vogel, 1999) **or** 25 mg/m^2 every 7 days (in combination with trastuzumab) until disease progression or unacceptable toxicity (Burstein, 2001; Burstein 2007) **or** 30 or 35 mg/m^2 days 1 and 8 every 21 days (in combination with trastuzumab) until disease progression or unacceptable toxicity (Andersson, 2011)

Cervical cancer (off-label use): IV: 30 mg/m^2 days 1 and 8 of a of a 21-day treatment cycle (Muggia, 2004; Muggia, 2005)

Hodgkin lymphoma, relapsed or refractory (off-label use): IV:

GVD regimen: 15 mg/m^2 (post-transplant patients) or 20 mg/m^2 (transplant-naïve patients) on days 1 and 8 of a 21-day cycle (in combination with gemcitabine and doxorubicin liposomal) for 2 to 6 cycles (Bartlett, 2007)

IGEV regimen: 20 mg/m^2 on day 1 of a 21-day cycle (in combination with ifosfamide, mesna, gemcitabine, and prednisolone) for 4 cycles (Santoro, 2007)

Malignant pleural mesothelioma (off-label use): IV: 30 mg/m^2 (maximum dose: 60 mg) every 7 days per 6-week treatment cycle, continue until disease progression (Stebbing, 2009) **or** 30 mg/m^2 (maximum dose: 60 mg) every 7 days for 6 weeks, off 2 weeks, then repeat cycle (Muers, 2008)

Ovarian cancer, relapsed (off-label use): IV: 25 mg/m^2 every 7 days (Bajetta, 1996) **or** 30 mg/m^2 days 1 and 8 of a 21-day treatment cycle (Rothenberg, 2004) until disease progression or unacceptable toxicity

Salivary gland cancer, recurrent (off-label use): IV: 25 mg/m^2 on days 1 and 8 of a 21-day cycle (in combination with cisplatin) for a minimum of 3 cycles and for up to 6 cycles (Airoldi, 2001) **or** 30 mg/m^2 every 7 days (monotherapy) for a minimum of 9 weeks and for up to 6 cycles (Airoldi, 2001)

Small cell lung cancer, refractory (off-label use): IV: 25 or 30 mg/m^2 every 7 days until disease progression or unacceptable toxicity (Furuse, 1996; Jessem, 1993)

Soft tissue sarcoma, advanced (off-label use): IV: 25 mg/m^2 days 1 and 8 of a 21-day treatment cycle (in combination with gemcitabine) until disease progression or unacceptable toxicity (Dileo, 2007)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

Renal insufficiency: No dosage adjustment necessary.

Hemodialysis: Initial: IV: Reduce dose to 20 mg/m^2/week; administer either after dialysis (on dialysis

days) or on nondialysis days (Janus, 2010)

Dosing: Hepatic Impairment

Note: In patients with concurrent hematologic toxicity and hepatic impairment, administer the lower of the doses determined from the adjustment recommendations.

Administer with caution in patients with hepatic insufficiency. In patients who develop hyperbilirubinemia during treatment with vinorelbine, the dose should be adjusted for total bilirubin as follows:

Serum bilirubin ≤2 mg/dL: Administer 100% of dose

Serum bilirubin 2.1-3 mg/dL: Administer 50% of dose (Ecklund, 2005; Floyd, 2006; Superfin, 2006)

Serum bilirubin >3 mg/dL: Administer 25% of dose (Ecklund, 2005; Floyd, 2006; Superfin, 2006)

Patients (breast cancer) with extensive liver metastases (>75% of liver volume): Administer 50% of dose (Ecklund, 2005; Superfin, 2006)

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012).

Dosing: Adjustment for Toxicity

Note: In patients with concurrent hematologic toxicity and hepatic impairment, administer the lower of the doses determined from the adjustment recommendations.

Dosage adjustment in hematological toxicity (based on granulocyte counts):

Granulocytes ≥1500 cells/mm^3 on day of treatment: Administer 100% of starting dose.

Granulocytes 1000-1499 cells/mm^3 on day of treatment: Administer 50% of starting dose.

Granulocytes <1000 cells/mm^3 on day of treatment: Do not administer. Repeat granulocyte count in 1 week. If 3 consecutive doses are held because granulocyte count is <1000 cells/mm^3, discontinue vinorelbine.

Adjustment: For patients who, during treatment, have experienced fever or sepsis while granulocytopenic or had 2 consecutive weekly doses held due to granulocytopenia, subsequent doses of vinorelbine should be:

75% of starting dose for granulocytes ≥1500 cells/mm^3

37.5% of starting dose for granulocytes 1000-1499 cells/mm^3

Dosage adjustment for neurotoxicity: Neurotoxicity ≥grade 2: Discontinue treatment

Dosage adjustment for other adverse events: Severe adverse events: Reduce dose or discontinue treatment

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Intravenous:

Navelbine: 10 mg/mL (1 mL); 50 mg/5 mL (5 mL)

Generic: 10 mg/mL (1 mL); 50 mg/5 mL (5 mL)

Solution, Intravenous [preservative free]:

Generic: 10 mg/mL (1 mL); 50 mg/5 mL (5 mL)

Generic Equivalent Available (US) Yes

Administration **For IV use only; FATAL IF GIVEN INTRATHECALLY.** Administer as a direct intravenous push or rapid bolus, over 6-10 minutes (up to 30 minutes). Longer infusions may increase the risk of pain and phlebitis. Intravenous doses should be followed by at least 75-125 mL of saline or D_5W to reduce the incidence of phlebitis and inflammation.

Vesicant; ensure proper needle or catheter position prior to administration. Avoid extravasation.

Extravasation management: If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do **NOT** flush the line); initiate hyaluronidase antidote; remove needle/cannula; apply dry warm compresses for 20 minutes 4 times a day for 1-2 days; elevate extremity (Perez Fidalgo, 2012). Remaining portion of the vinorelbine dose should be infused through a separate vein.

Hyaluronidase: If needle/cannula still in place, administer 1-6 mL hyaluronidase (150 units/mL) into the existing IV line; the usual dose is 1 mL hyaluronidase for each 1 mL of extravasated drug (Perez Fidalgo, 2012; Schulmeister, 2011). If needle/cannula was removed, inject 1-6 mL (150 units/mL) subcutaneously in a clockwise manner using 1mL for each 1 mL of drug extravasated (Schulmeister, 2011) **or** administer 1 mL (150 units/mL) as 5 separate 0.2 mL injections (using a 25-gauge needle) subcutaneously into the extravasation site (Polovich, 2009).

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use Treatment of non-small cell lung cancer (NSCLC)

Use: Off-Label

Breast cancer, metastatic; Cervical cancer, persistent or recurrent; Hodgkin lymphoma, relapsed or refractory (GVD regimen); Hodgkin lymphoma, relapsed or refractory (IGEV regimen); Malignant pleural mesothelioma; Ovarian cancer, relapsed; Salivary gland cancer, recurrent; Small cell lung cancer, refractory; Soft tissue sarcoma, advanced

Medication Safety Issues

Sound-alike/look-alike issues:

Vinorelbine may be confused with vinBLAStine, vinCRIStine

Vinorelbine (50 mg/5 mL; Hospira manufacturer) may be confused with conventional cytarabine (100 mg/5 mL; Hospira manufacturer) due to similar packaging; potential for inadvertent intrathecal administration of vinorelbine may occur (ISMP, [Smetzer 2015]).

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Administration issues:

Vinorelbine is intended **for IV use only**: Inadvertent intrathecal administration of other vinca alkaloids has resulted in death. Syringes containing vinorelbine should be labeled **"For IV use only. Fatal if given intrathecally."** Vinorelbine should **NOT** be prepared during the preparation of any intrathecal medications. After preparation, keep vinorelbine in a location **away** from the separate storage location recommended for intrathecal medications.

Adverse Reactions Reported with single-agent therapy.

>10%:

Central nervous system: Fatigue (27%), peripheral neuropathy (25%; grade 3: 1%; grade 4: <1%)

Dermatologic: Alopecia (12% to 30%)

Gastrointestinal: Nausea (31% to 44%; grade 3: 1% to 2%), constipation (35%; grade 3: 3%), vomiting (20% to 31%; grade 3: 1% to 2%), diarrhea (12% to 17%)

Hematologic & oncologic: Leukopenia (83% to 92%; grade 4: 6% to 15%), granulocytopenia (90%; grade 4: 36%; nadir: 7 to 10 days; recovery 14 to 21 days), neutropenia (85%; grade 4: 28%), anemia (83%; grades 3/4: 9%)

Hepatic: Increased serum AST (67%; grade 3: 5%; grade 4: 1%), increased serum bilirubin (total bilirubin: 5% to 13%; grade 3: 4%; grade 4: 3%)

Local: Injection site reaction (22% to 28%; includes erythema at injection site, vein discoloration), pain at injection site (16%)

Neuromuscular & skeletal: Weakness (36%)

Renal: Increased serum creatinine (13%)

1% to 10%:

Cardiovascular: Localized phlebitis (7% to 10%), chest pain (5%)

Central nervous system: Decreased deep tendon reflex (<5%)

Dermatologic: Skin rash (<5%)

Gastrointestinal: Paralytic ileus (1%)

Hematologic & oncologic: Febrile neutropenia (≤8%; grade 4: ≤4%), thrombocytopenia (3% to 5%; grades 3/4: 1%)

Infection: Sepsis (≤8%; grade 4: ≤4%)

Neuromuscular & skeletal: Arthralgia (<5%), myalgia (<5%), jaw pain (<5%)

Otic: Ototoxicity (≤1%)

Respiratory: Dyspnea (7%)

<1%, postmarketing, and/or case reports: Abdominal pain, anaphylaxis, angioedema, back pain, deep vein thrombosis, dysphagia, esophagitis, flushing, headache, hemolytic-uremic syndrome, hemorrhagic cystitis, hypersensitivity reaction, hypertension, hyponatremia, hypotension, intestinal necrosis, intestinal obstruction, intestinal perforation, interstitial pulmonary disease, ischemic heart disease, localized rash, mucositis, myasthenia, myocardial infarction (rare), pancreatitis, pneumonia, pruritus, pulmonary edema, pulmonary embolism, radiation recall phenomenon (dermatitis, esophagitis), skin blister, SIADH (syndrome of inappropriate antidiuretic hormone secretion), tachycardia, thromboembolism, thrombotic thrombocytopenic purpura, tumor pain, unsteady gait, urticaria, urticaria at injection site, vasodilatation

Contraindications

Pretreatment granulocyte counts <1000/mm^3

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: **[U.S. Boxed Warning]: Severe granulocytopenia may occur with treatment (may lead to infection); granulocyte counts should be ≥1000 cells/mm^3 prior to treatment initiation; dosage adjustment may be required based on blood counts (monitor blood counts prior to each dose).** Granulocytopenia is a dose-limiting toxicity; nadir is generally 7-10 days after administration and recovery occurs within the following 7-14 days. Monitor closely for infections and/or fever in patients with severe granulocytopenia. Use with extreme caution in patients with compromised marrow reserve due to prior chemotherapy or radiation therapy.

• Extravasation: **[U.S. Boxed Warning]: Vesicant; ensure proper catheter or needle position prior to (and during) infusion. Avoid extravasation. Extravasation may cause local tissue necrosis and/or thrombophlebitis.**

• Gastrointestinal toxicity: May cause severe constipation (grade 3-4), paralytic ileus, intestinal obstruction, necrosis, and/or perforation; some events were fatal. Oral vinorelbine (not available in the U.S.) is associated with a moderate antiemetic potential; antiemetics are recommended to prevent nausea/vomiting (Dupuis, 2011; Roila, 2010); IV vinorelbine has a minimal emetic potential (Dupuis, 2011; Roila, 2010).

• Neuropathy: May cause new-onset or worsening of pre-existing neuropathy; use with caution in patients with neuropathy. Monitor for new or worsening sign/symptoms of neuropathy. Dosage adjustment required.

• Pulmonary toxicity: Fatal cases of interstitial pulmonary changes and ARDS have been reported with single-agent therapy (mean onset of symptoms: 1 week). Promptly evaluate changes in baseline pulmonary symptoms or any new-onset pulmonary symptoms (eg, dyspnea, cough, hypoxia). Acute shortness of breath and severe bronchospasm have been reported with vinca alkaloids, usually when used in combination with mitomycin.

Disease-related concerns:

• Hepatic impairment: Vinorelbine elimination is predominantly hepatic. While there is no evidence that toxicity is enhanced in patients with elevated transaminases, use with caution in patients with severe hepatic injury or impairment; dosage modification required for elevated total bilirubin.

• Radiation therapy: May have radiosensitizing effects with prior or concurrent radiation therapy; radiation recall reactions may occur in patients who have received prior radiation therapy.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special handling:

• Hazardous agent: Avoid eye contamination (exposure may cause severe irritation).

Other warnings/precautions:

• Experienced physician: **[U.S. Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician.**

• NOT for intrathecal use: **[U.S. Boxed Warning]: For IV use only; intrathecal administration of other vinca alkaloids has resulted in death. If dispensed in a syringe, should be labeled "for intravenous use only - fatal if given intrathecally".** Vinorelbine should **NOT** be prepared during the preparation of any intrathecal medications. After preparation, keep vinorelbine in a location **away** from the separate storage location recommended for intrathecal medications.

Metabolism/Transport Effects

Substrate of CYP2D6 (minor), CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Ceritinib: May increase the serum concentration of CYP3A4 Substrates. Management: Use of ceritinib with a narrow therapeutic index CYP3A substrate (e.g., alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, tacrolimus) should be avoided when possible. *Risk C: Monitor therapy*

CISplatin: May enhance the adverse/toxic effect of Vinorelbine. Specifically, the combination may be associated with a higher risk of granulocytopenia. *Risk C: Monitor therapy*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Vinorelbine. *Risk C: Monitor therapy*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Gefitinib: May enhance the neutropenic effect of Vinorelbine. *Risk C: Monitor therapy*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Macrolide Antibiotics: May increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). Macrolides may also increase the distribution of Vinca Alkaloids into certain cells and/or tissues. Management: Consider an alternative to using a macrolide antibiotic when possible in order to avoid the potential for increased vinca alkaloid toxicity. **Exceptions:** Azithromycin (Systemic); Fidaxomicin; Roxithromycin; Spiramycin. *Risk D: Consider therapy modification*

MiFEPRIStone: May increase the serum concentration of CYP3A4 Substrates. Management: Minimize doses of CYP3A4 substrates, and monitor for increased concentrations/toxicity, during and 2 weeks following treatment with mifepristone. Avoid cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. *Risk D: Consider therapy modification*

MitoMYcin (Systemic): Antineoplastic Agents (Vinca Alkaloids) may enhance the adverse/toxic effect of MitoMYcin (Systemic). Specifically, the risk of pulmonary toxicity may be increased. *Risk C: Monitor therapy*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

PACLitaxel (Conventional): May enhance the neurotoxic effect of Vinorelbine. *Risk C: Monitor therapy*

PACLitaxel (Protein Bound): May enhance the neurotoxic effect of Vinorelbine. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Posaconazole: May enhance the adverse/toxic effect of Antineoplastic Agents (Vinca Alkaloids). Posaconazole may increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). Management: Avoid the concomitant use of posaconazole and vinca alkaloids when possible. If combined, monitor for increased vinca alkaloid toxicities (eg, neurotoxicity, gastrointestinal toxicity). *Risk D: Consider therapy modification*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tertomotide: Immunosuppressants may diminish the therapeutic effect of Tertomotide. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Voriconazole: May enhance the adverse/toxic effect of Antineoplastic Agents (Vinca Alkaloids). Voriconazole may increase the serum concentration of Antineoplastic Agents (Vinca Alkaloids). *Risk D: Consider therapy modification*

Pregnancy Risk Factor

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Pregnancy Implications

Animal reproduction studies have demonstrated embryotoxicity, fetotoxicity, decreased fetal weight, and delayed ossification. May cause fetal harm if administered during pregnancy. Women of childbearing potential should avoid becoming pregnant during vinorelbine treatment.

Breast-Feeding Considerations

It is not known if vinorelbine is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, breast-feeding should be discontinued during

treatment.

Monitoring Parameters CBC with differential and platelet count (prior to each dose, and after treatment), hepatic function tests; monitor for new-onset pulmonary symptoms (or worsening from baseline); monitor for neuropathy (new or worsening symptoms; monitor infusion site; monitor for signs symptoms of constipation/ileus

Mechanism of Action Semisynthetic vinca alkaloid which binds to tubulin and inhibits microtubule formation, therefore, arresting the cell at metaphase by disrupting the formation of the mitotic spindle; it is specific for the M and S phases. Vinorelbine may also interfere with nucleic acid and protein synthesis by blocking glutamic acid utilization.

Pharmacodynamics/Kinetics

Distribution: V_d: binds extensively to human platelets and lymphocytes (80% to 91%)

Children and Adolescents 2 to 17 years: 21.1 ± 12.2 L/kg (Johansen 2006)

Adults: 25 to 40 L/kg

Protein binding: 80% to 91%

Metabolism: Extensively hepatic, via CYP3A4, to two metabolites, deacetylvinorelbine (active) and vinorelbine N-oxide

Half-life elimination: Triphasic:

Children and Adolescents 2 to 17 years: Terminal: 16.5 ± 9.7 hours (Johansen 2006)

Adults: Terminal: 28 to 44 hours

Excretion: Feces (46%); urine (18%, 10% to 12% as unchanged drug)

Pricing: US

Solution (Navelbine Intravenous)

10 mg/mL (1 mL): $42.00

50 mg/5 mL (5 mL): $210.00

Solution (Vinorelbine Tartrate Intravenous)

10 mg/mL (1 mL): $24.00

50 mg/5 mL (5 mL): $108.00

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names Filcrin (UY); Navelbin (HN); Navelbine (AE, AR, AT, AU, BB, BG, BH, BM, BR, BS, BZ, CH, CL, CN, CY, CZ, DE, DK, EE, EG, ES, FI, FR, GB, GR, GY, ID, IE, IL, IQ, IR, IS, IT, JM,

JO, KR, KW, LB, LT, LU, LY, MT, MX, MY, NL, NO, NZ, OM, PH, PK, PL, QA, RO, RU, SA, SE, SI, SK, SR, SY, TH, TR, TT, TW, VN, YE); Navildez (CR, DO, GT, HN, NI, PA, SV); Navirel (UA); Neoben (UA); Viessia (CR, DO, GT, HN, NI, PA, SV); Vilne (EC); Vinbine (IN); Vinelbine (LK, ZW); Vinorel (BD); Vinorelsin (ID); Vinorgen (LK, PE, PY); Vinotec (LK); Vinotel (PH); Zinavin (CO)

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