Regimen Monograph

A - Regimen Name

VIP Regimen

Etoposide (VP-16)-Ifosfamide-PLATINOL® (CISplatin)

Disease Site	Genitourinary - Testis
Intent	Curative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	First or second line treatment of testicular cancer with curative intent.

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B - Drug Regimen

CISplatin (Round to nearest 1mg)	20 mg /m²	IV	Days 1 to 5
ifosfamide (Round to nearest 25mg; maximum dose = 1.75 g)	1200 mg /m²	IV	Days 1 to 5

etoposide (Round to nearest 10mg)	75 mg /m²	IV	Days 1 to 5

(continued on next page)

mesna (Round to nearest 10 mg) **AND**	240 mg /m²	IV	Days 1 to 5, immediately before ifosfamide
mesna (Round to nearest 10 mg)	240 mg /m²	IV	Days 1 to 5, at 4 and 8 hours after ifosfamide
May substitute doses at 4 and 8 hours post-ifosfamide with:			
mesna (Round to nearest 10 mg)	480 mg /m²	PO	Days 1 to 5, at 4 and 8 hours after ifosfamide

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 3 or 4 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: High

Febrile Neutropenia Risk: High

Other Supportive Care:

Fertility counselling and sperm bank should be routinely offered.

Also refer to CCO Antiemetic Summary

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations are in use at some centres.

As dose modification may compromise treatment efficacy, it is recommended that modification of this regimen be done only after discussion with a medical oncologist experienced in the treatment of testicular cancer.

Dosage with toxicity

Hematologic Toxicities: Primary prophylaxis with G-CSF at dose 5–10mcg/kg SC x 10 days, starting on Day 6 is recommended, because of the extreme myelosuppressive effect of the regimen, especially when given as second line.

Hepatic Impairment

Dosage modification should be individualized.

Renal Impairment

Dosage modification should be individualized.

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F - Adverse Effects

Refer to CISplatin, ifosfamide, etoposide, mesna drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life Threatening
• Nausea and vomiting • Nephrotoxicity (may be severe) • Electrolyte abnormalities • Neurotoxicity and ototoxicity	• Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism

(may be severe) • Myelosuppression ± infection / bleeding (may be severe) • Hyperuricemia • Alopecia • Mucositis, diarrhea • Encephalopathy, neuropathy (may be severe) • Hemorrhagic cystitis (may be severe)	• Hypersensitivity • ↑ LFTs • Pancreatitis • Pneumonitis • SIADH • Rhabdomyolysis • Secondary malignancy • Hemolysis / hemolytic uremic syndrome / disseminated intravascular coagulation • Vasculitis • Seizures • Raynaud's • Rash

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G - Interactions

Refer to CISplatin, ifosfamide, etoposide, mesna drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to CISplatin, ifosfamide, etoposide, mesna drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Baseline and regular liver and renal function tests (including electrolytes and magnesium), and urinalysis.
- Clinical toxicity assessment (including GI toxicity, neurotoxicity, ototoxicity, infection, bleeding); at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	7 hours
Pharmacy Workload (average time per visit)	41.24 minutes
Nursing Workload (average time per visit)	59.167 minutes

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K - References

Cisplatin, etoposide, ifosfamide and mesna drug monographs, Cancer Care Ontario.

Loehrer PJ, Einhorn LH, Williams SD, VP-16 plus ifosfamide plus cisplatin as salvage therapy in refractory germ cell cancer. J Clin Oncol, 1986; 4:1528-1536.

Loehrer PJ Sr, Lauer R, Roth BJ, et al. Salvage therapy in recurrent germ cell cancer: ifosfamide and cisplatin plus either vinblastine or etoposide. Ann Intern Med, 1988; 109: 540-546.

Nichols CR, Catalano PJ, Crawford ED, et. al. Randomized comparison of cisplatin and etoposide and either belomycin or ifosfamide in treatment of advanced disseminated germ cell tumours: an Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B Study. J Clin Oncol 1998 Apr; 16(4): 1287-93.

April 2016 Replaced regimen category with evidence-informed

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M - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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The format and content of the drug monographs, regimen monographs, appendices and symptom management

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