Regimen Monograph

A - Regimen Name

EPIRIFOS Regimen

EPIrubicin-Ifosfamide

Disease Site	Sarcoma - Soft Tissue
Intent	Adjuvant
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	Intensified adjuvant chemotherapy treatment for Soft Tissue Sarcoma.

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B - Drug Regimen

ifosfamide	1800 mg /m²	IV	Day 1 to 5
mesna	360 mg /m²	IV immediately before ifosfamide, then 4 and 8 hours post-ifosfamide	Days 1 to 5
EPIrubicin	60 mg /m²	IV	Days 1 and 2
filgrastim	300 mcg	Subcut per day	Daily on days 8 to 15

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 5 cycles, or until evidence of disease progression or limited by drug toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: High

Other Supportive Care:

- Ifosfamide:
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration.
- Inadequate total hydration may result in dose-related hemorrhagic cystitis

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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.

Dosage with toxicity

Hematologic Toxicities: See Appendix 6 for general recommendations.

Hepatic Impairment

Bilirubin		AST / ALT	Actions
1 - 2 x ULN	and/or	2 - 4 x ULN	REDUCE Epirubicin to 50% dose
2 – 4 x ULN	and/or	> 4 x ULN	REDUCE Epirubicin to 25%-50% dose
> 4 x ULN	and/or	OMIT	Omit dose

The dose of ifosfamide should be adjusted in the presence of hepatic impairment.

Renal Impairment

Clearance or Creatinine Levels	Actions
If CrCl <0.5mL/sec or Serum Creatinine > 185µmol/L	REDUCE Ifosfamide to 75 % dose
If CrCl <0.2mL/sec or Serum Creatinine >300µmol/L	REDUCE Ifosfamide to 67 % dose

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F - Adverse Effects

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

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Alopecia • Dysgeusia • Mucositis • Nausea, vomiting • Fatigue • Diarrhea • Abdominal pain • Hemorrhagic cystitis	• Hypersensitivity • Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • Pneumonitis • Pancreatitis • Rhabdomyolysis

• Neurotoxicity (may be severe) • Flu-like symptoms • Myelosuppression +/- infection, bleeding (may be severe) • Bone pain	• Vision changes • SIADH

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G - Interactions

Refer to ifosfamide, mesna, EPIrubicin, filgrastim drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to ifosfamide, mesna, EPIrubicin, filgrastim drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and before each cycle.
- Baseline and regular liver function tests.
- Baseline and regular renal function tests (including electrolytes and magnesium) and urinalysis.
- Cardiac examination especially with risk factors (including prior therapy with doxorubicin, mitoxantrone, or other cardiotoxic drug), or a cumulative epirubicin dose of > 900 mg/m^2.
- Clinical toxicity (including stomatitis, neurotoxicity, cystitis, local toxicity, cardiotoxicity) assessment; 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	4.5 hours
Pharmacy Workload (average time per visit)	31.2 minutes
Nursing Workload (average time per visit)	54.667 minutes

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K - References

Epirubicin, ifosfamide, mesna drug monographs, Cancer Care Ontario.

Frustaci S, Gherlinzoni F, De Paoli A, et al. Adjuvant chemotherapy for adult soft tissue sarcomas of the extremities and girdles: results of the Italian ramomized cooperative trial.
J of Clin Oncol 2001;19(5): 1238-47.

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L - Other Notes

Sarcomas are rare tumours and as such benefit from referral to specialized centres where there will be access to multidisciplinary expertise including good radiology, orthopedic and thoracic surgery, medical oncology, radiation oncology, pathology, and other supportive care disciplines.

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the

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Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

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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