Regimen Monograph

A - Regimen Name

IFNA(IND-MNT(SC)) Regimen

Interferon alfa-2b (IV Induction followed by SC maintenance)

Disease Site	Melanoma
Intent	Adjuvant 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	For treatment of adult patients with high-risk malignant melanoma who are rendered disease-free following resection
Supplementary Public Funding	**interferon alfa-2b** New Drug Funding Program (Interferon - Melanoma)

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B - Drug Regimen

Induction IV:

interferon alfa-2b	20 million units /m²	IV (in hospital or cancer clinic)	Days 1 to 5 each week for 4 weeks

then

(Continued on next page)

Maintenance SC:

interferon alfa-2b	10 million units /m²	SC	3 times weekly on alternate days, for 48 weeks (Self-administered)

(Outpatient prescription in 18 MU, 30 MU and 60 MU pens, also available in vials of 10 MU/mL)

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C - Cycle Frequency

Induction IV CYCLE of 28 DAYS
Given in hospital or cancer centre (for initial cycle)

SUBSEQUENT MAINTENANCE CYCLES OF 28 DAYS
For a usual total of 48 weeks

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:
Routine prophylaxis of flu-like symptoms with acetaminophen 500-1000 mg before each dose (especially if this adverse effect occurs with early doses).

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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

Doses should be held or reduced (50%) for severe toxicity. Consider permanent discontinuation if recurs.

Toxicity	Action	Dose (% of previous dose)
Colitis, pancreatitis Pulmonary infiltrates/ Pulmonary function impairment Ischemic disorders Autoimmune disorders New or worsening ophthalmological disorders Severe depression, suicidal behaviour, psychosis, hallucinations, aggressive behaviour Severe hypersensitivity reaction Severe exacerbation of pre-existing neuropsychiatric, autoimmune, ischemic or infective conditions.	Discontinue	Not applicable
Transient rashes	May continue treatment; treat symptomatically	No change
Thyroid dysfunction	Continue if TSH normalized after medication	No change

Dosage with myelosuppression:

- Reduce dose or hold dose for significant myelosuppression.

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Hepatic Impairment

Do not use in patients with autoimmune hepatitis.

LFTs (AST and/or ALT)	Action	Dose (% of previous dose)
5 – 10 x ULN	Hold until recovery	50%
> 10 x ULN	Discontinue	Not applicable

Renal Impairment

Caution if CrCl < 50 mL/min. Contraindicated in combination therapy with ribavirin in patients with CrCl < 50 ml/min.

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F - Adverse Effects

Refer to interferon alfa-2b drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Flu-like symptoms (ie. fever, fatigue, headache, myalgia, rigors/chills) • Injection site reactions • Anorexia, nausea, diarrhea, vomiting • Increases in hepatic function tests (may be severe) • Rash (may be severe) • Alopecia • CNS effects (may be severe)	• Pneumonitis, Pancreatitis • Autoimmune disorders • Retinopathy, retinal vein/artery occlusion, detachment • Arterial and venous embolism • Arrhythmia, cardiac failure • Renal failure, rhabdomyolysis • Anemia (may be aplastic or hemolytic) • Photosensitivity • Anaphylaxis

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G - Interactions

Refer to interferon alfa-2b drug monograph(s) for additional details

May potentiate effects of radiation therapy

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H - Drug Administration and Special Precautions

Refer to interferon alfa-2b drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- **INDUCTION IV**

- Clinical toxicity assessment of flu-like symptoms, neurotoxicity, psychiatric, ophthalmic, endocrine, cardiovascular, pulmonary, autoimmune, GI adverse effects; regular
- Baseline ophthalmologic evaluation
- Baseline and regular CBC
- Baseline and routine liver and renal function tests and electrolytes
- Baseline and regular thyroid function tests

MAINTENANCE SC

- Clinical toxicity assessment of flu-like symptoms, neurotoxicity, psychiatric, ophthalmic, endocrine, cardiovascular, pulmonary, autoimmune, GI adverse effects; regular
- CBC at baseline and intermittently as required.
- Baseline and intermittent liver & renal function tests.
- Regular thyroid function tests
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- ECG in patients with pre-existing cardiovascular disease or advanced cancer; baseline and regular
- Blood glucose tests in diabetic patients; baseline and regular
- Triglyceride levels; baseline and regular
- Opthalmoscopy; regular

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J - Administrative Information

Maintenance phase: Outpatient prescription for home administration

Approximate Patient Visit	IV induction: 1 to 1.5 hours
Pharmacy Workload (average time per visit)	(IV) 8.432 minutes
Nursing Workload (average time per visit)	(IV) 49.167 minutes

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K - References

Interferon alfa-2b drug monograph, Cancer Care Ontario Drug Formulary 2014.

Kirkwood JM, Ibrahim IG, Sosmas JA, et al. High-Dose interferon Alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLHIQS-21 vaccine in patients with resected stage 11B-III melanoma: result of intergroup trial E 1694/59512/C509801. J Clin Oncol May 1 ,2001; 19(9): 2370-2380.

Kirkwood JM, Strawderman MH, Ernstoff MS, et al. Interferon alfa-2b adjuvant therapy of high-risk resected cutaneous melanoma: the Eastern Cooperative Oncology Group trial EST 1684. J Clin Oncol, 1996; 14: 7-17.

PEBC Advice Documents or Guidelines

- Systemic Adjuvant Therapy for Patients at High Risk for Recurrent Melanoma

April 2016 Replaced regimen category with evidence-informed

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L - Other Notes

Interferon Alfa is not listed in the Ontario Drug Benefit Formulary for malignant melanoma. Confirm coverage with other third party prescription plans.

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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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