Regimen Monograph

A - Regimen Name

IMAT Regimen

Imatinib

Disease Site	Sarcoma - Soft Tissue (Dermatofibrosarcoma protuberans - DFSP)
Intent	Palliative
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	In patients with unresectable, recurrent and/or metastatic DFSP

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B - Drug Regimen

iMAtinib	400* mg	PO	BID

(This drug is not currently publicly funded for this regimen and intent)

(Total daily dose = 800mg; Outpatient prescription in multiples of 100mg and 400mg tablets)
*The 800 mg daily dose should be given as 400 mg BID, to reduce iron exposure.

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C - Cycle Frequency

Continue treatment in the absence of unacceptable toxicity or disease progression.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Other Supportive Care:

- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.
- Patients should be tested for HBV infection prior to initiating treatment. Carriers of HBV must be monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

Also refer to CCO Antiemetic Recommendations.

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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 have been adapted from clinical trials or product monographs and could be considered.

Dose levels are 200mg, 300mg, 400mg, 600mg, and 800mg.

Indication	Daily Starting Dose	Escalate?	Hepatic Impairment		Renal Impairment (Clcr, ml/min)	
			Mild-Mod[4]	Severe[5]	20-59	<20
DFSP	800mg		1	2, 3	1	Discontinue

1. Start at 400 mg. For mild renal impairment only (Clcr = 40-59 mL/min), may consider escalation (if applicable in table) if inadequate efficacy providing lower dose well-tolerated.
2. Initially, start at 200 mg. If no toxicity may ↑ to 300mg.
3. While on treatment: Hold until bilirubin < 1.5 x ULN and AST/ALT < 2.5 x ULN and then restart by ↓ 1 dose level
4. bilirubin >1.5 - 3 x ULN or AST/ALT > ULN with bilirubin ≤ 1.5 x ULN
5. bilirubin > 3 x ULN or AST/ALT > 5 x ULN

Dosage with toxicity

Toxicity	Action
Fluid retention (grade 3,4)	Hold until ≤ grade 1; resume with 1 dose level ↓
Rash (grade 3, 4)	Hold until ≤ grade 1; resume with 1 dose level ↓ or discontinue
Hypotension / Hypersensitivity reaction	Hold, treat supportively, consider steroids
Bleeding	Hold; consider discontinuing if severe
Pneumonitis	Hold, investigate, consider discontinuing if confirmed
DRESS	Consider discontinuing

Dosage with myelosuppression:

	ANC (x 10^9/L)	Platelets (x 10^9/L)	Action
Starting dose 800mg	< 1	< 50	• Hold until ANC ≥ 1.5 x 10^9/L and platelets ≥ 75 x 10^9/L and then resume treatment with one dose level ↓ • If recurs, hold until recovery; resume by further ↓ one dose level

Hepatic Impairment

Imatinib is excreted via the liver and increased exposure is likely in the presence of hepatic impairment. See dosage table.

Renal Impairment

Imatinib is not excreted via the kidney to a significant extent; however, increased exposure and adverse effects are correlated with renal impairment. Exercise caution in patients with mild to moderate renal impairment. See dosage table.

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F - Adverse Effects

Refer to imatinib drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Fluid retention (may be severe) • Nausea, vomiting • Musculoskeletal pain • ↑ LFTs (May be severe) • Diarrhea • Rash (may be severe) • Fatigue	• Hypersensitivity reaction • Arrhythmia • Hemolysis • GI obstruction • GI perforation • Pancreatitis • Pneumonitis

• Headache • CNS (dizziness, insomnia, anxiety, depression) • Cough, dyspnea • Abnormal electrolytes • Myelosuppression ± infection, bleeding (may be severe, including CNS, GI hemorrhage)	• Renal failure • Rhabdomyolysis • Arterial thromboembolism • Venous thromboembolism • Pulmonary hypertension • Cardiotoxicity • Subdural hemorrhage • Tumour lysis syndrome • DRESS • Avascular necrosis • Hypothyroidism (not usually severe) • Atypical infections (including HBV reactivation)

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G - Interactions

Refer to imatinib drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to imatinib drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Brain imaging for patients suspected of having subdural hemorrhage; as clinically indicated
- CBC; weekly for first month, biweekly for second month, and as indicated thereafter (e.g. every 2 to 3 months)
- Electrolytes and serum creatinine; baseline and regular
- INR for patients taking warfarin, especially when starting treatment and with imatinib dose adjustments; baseline and regular

- Liver function tests; baseline and monthly or as clinically indicated
- LVEF, in patients with known underlying heart disease or in elderly patients; baseline and as clinically indicated
- Platelet counts and prothrombin time when imatinib is used concurrently with anticoagulants, prostacyclins, or other medications that increase bleeding risk; baseline and periodic
- TSH levels in patients with previous thyroidectomy or patients on replacement therapy; baseline and regular
- Serum or urine pregnancy test in women of childbearing potential; within one week before starting treatment
- HBV infection status: Prior to starting treatment; consult infectious disease if positive
- For carriers of HBV: signs and symptoms of active HBV infection; At each visit during treatment and for several months after treatment discontinues
- Clinical assessment of fluid retention, bleeding, infection, cardiac effects, thromboembolism, rhabdomyolysis, tumour lysis syndrome and gastrointestinal effects, pneumonitis, rash; regular

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

Suggested Clinical Monitoring

- EKG and troponin in patients with hypereosinophilia and cardiac involvement

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J - Administrative Information

Outpatient prescription for home administration

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K - References

BCR-ABL Tyrosine Kinase Inhibitors [GLEEVEC (imatinib mesylate), TASIGNA (nilotinib), BOSULIF (bosutinib), SPRYCEL (dasatinib), ICLUSIG (ponatinib hydrochloride)] - Risk of Hepatitis B Reactivation. Health Canada, May 4, 2016. [Accessed May 13, 2016]. Available from: http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/58222a-eng.php

Imatinib drug monograph, Cancer Care Ontario

Lebbé C, Kerob D, Porcher R, et al. Imatinib mesylate as a preoperative therapy in dermatofibrosarcoma: Results of a multicentric phase II study on 25 patients. Journal of Clinical Oncology 2007 (ASCO Annual Meeting Proceedings); 25(18S): 10032.

McArthur GA, Demetri GD, van Oosterom A, et al. Molecular and clinical analysis of locally advanced dermatofibrosarcoma protuberans treated with imatinib: imatinib target exploration consortium study B2225. JCO 2005; 23(4); 866-73.

June 2019 Updated emetic risk category

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M - Disclaimer

Regimen Abstracts

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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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