Regimen Monograph

A - Regimen Name

NILO Regimen

Nilotinib

Disease Site

Hematologic
Leukemia - Chronic Myeloid (CML)

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

- For the treatment of patients with chronic phase Philadelphia chromosome positive chronic myeloid leukemia (Ph+CML)
- For the treatment of accelerated phase Ph+ CML in patients with resistance to or intolerance to imatinib

Supplementary Public Funding	**niLOtinib** Exceptional Access Program (niLOtinib - Chronic phase Ph+ CML, with specific criteria) (EAP Website)
	niLOtinib Exceptional Access Program (niLOtinib - Accelerated phase Ph+ CML with documented resistance or intolerance to imatinib therapy, with specific criteria) (EAP Website)

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B - Drug Regimen

Newly diagnosed Ph+ CML (chronic phase):

niLOtinib	300 mg	PO	BID (every 12 hours)

Resistant or Intolerant Ph+ CML (chronic phase) or CML (accelerated phase):

niLOtinib	400 mg	PO	BID (every 12 hours)

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C - Cycle Frequency

CONTINUOUS TREATMENT

To response; discontinue with disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Other Supportive Care:

- Use of allopurinol and hydration to reduce the risk of tumour lysis syndrome are recommended, especially in patients with high tumour load or renal impairment.
- See Nilotinib monograph for possible drug interactions with antiemetics or other supportive medications.

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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.

Dosage with toxicity

Dosage with hematologic toxicities: Exclude underlying disease causality.

Dose	**Counts (X 10^9/L)**	**Action**		**Time required for recovery (Platelets > 50 X 10^9/L and/or ANC > 1 X 10^9/L)**	**Subsequent Dose**
Newly diagnosed at 300 mg BID OR Resistant or intolerant at 400 mg BID	ANC < 1 and/or Platelet counts <50	Hold and monitor counts	AND	≤ 2 weeks	Resume at prior dose
				> 2 weeks	Restart at 400 mg once daily

Dosage with QT prolongation:

QTc	Action		QTc monitoring	Subsequent Dose
QTc > 480 msec	Hold; correct hypokalemia and hypomagnesemia. Review concomitant medications.	AND	QTcF < 450 msec or within 20 msec of baseline within 2 weeks	Resume at prior dose
			QTcF = 450 – 480 msec after 2 weeks	Restart at 400 mg once daily*
			No recovery	Discontinue
QTc > 480 msec at 400 mg daily	Discontinue	-	-	-

*repeat ECG 7 days after any dosage adjustment

Dosage with non-hematologic toxicities:

Toxicity	Action
≥ Grade 3 LFTs or ↑ lipase / amylase	Hold; resume at 400 mg once daily when ≤ Grade 1
Symptomatic lipase or amylase ↑	Hold, investigate. May resume at 400 mg once daily if ≤ grade 1
Other clinically significant moderate, or severe (≥ Grade 3, including fluid retention)	Hold; resume at 400 mg once daily when resolved. Consider re-escalation to starting dose if clinically appropriate.

Hepatic Impairment

Increased nilotinib exposure was observed in patients with hepatic impairment. Clinical studies excluded patients with ALT/AST > 2.5 x ULN and total bilirubin > 1.5 x ULN. Dose adjustment is not required for mild to moderate hepatic impairment at baseline. Use with caution; monitor LFTs and QTc interval regularly. Consider dose reduction in patients with severe impairment and use with extreme caution. Use the table above for hepatic toxicity.

Renal Impairment

Nilotinib and its metabolites are minimally excreted by the kidney. Although dose adjustments are not anticipated, patients with creatinine > 1.5 x ULN were excluded from clinical trials. Patients with renal impairment may be at increased risk of TLS.

Dosage in the Elderly

No differences in safety and efficacy were observed in patients ≥ 65 years of age.

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F - Adverse Effects

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

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
	• Rash (may be severe)	• Headache • Nausea, vomiting • QT interval prolonged • Fatigue • Myelosuppression ± infection, bleeding (may be severe) • Musculoskeletal pain • Constipation • Abdominal pain • Alopecia	• ↑ Lipase, amylase • Cardiotoxicity, arrhythmia • Hypersensitivity • Pneumonitis; Interstitial lung disease • Rhabdomyolysis • Sudden death • Arterial thromboembolism Venous thromboembolism • Hepatic failure • Renal failure • GI perforation • TLS • Vasculitis • Optic neuritis • Fluid retention • Pulmonary hypertension

			• Pancreatitis • Secondary malignancies • Atypical infections (including HBV reactivation)

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G - Interactions

Refer to nilotinib drug monograph(s) for additional details.

- Nilotinib is an inhibitor of CYP3A4, CYP2C8, CYP2C9, CYP2D6, UGT1A1 and inducer of CYP2B6, CYP2C8, and CYP2C9. This may result in interactions with substrates of these enzymes (i.e. increased exposure to HMG CoA reductase inhibitors, or statins).
- Avoid concomitant use with CYP3A4 inhibitors and inducers; consider dose adjustment for substrates with narrow therapeutic index.
- Caution with p-glycoprotein substrates and inhibitors, acid reducing agents, alcohol, CYP2D6 substrates, CYP 2B6 substrates, UGT1A1 substrates, CYP 2C9 substrates, CYP 2C8 substrates, and drugs that can affect electrolyte levels.
- Nilotinib absorption is increased when taken with food, which can result in higher serum concentrations and toxicity
- Yogurt has been shown to result in significant increases in nilotinib bioavailability. Do not use yogurt to disperse the capsule contents.
- Concomitant use of antiemetics, including metoclopramide, prochlorperazine, ondansetron, dolasetron and others may have additive effects on QT interval prolongation.

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H - Drug Administration and Special Precautions

Refer to nilotinib drug monograph(s) for additional details.

Administration:

- Nilotinib should be swallowed whole with a glass of water on an empty stomach, at least 1 hour before and 2 hours after food.
- If patient has trouble swallowing the capsules, may open the capsule and mix the content of each capsule in 1 teaspoon of applesauce and swallow immediately. Do not mix with other foods or liquids or use more applesauce than described above.
- Avoid grapefruit, starfruit, Seville oranges, their juices or products during treatment.
- If a dose is missed, take the next dose as scheduled. Do not replace missed doses.
- Store at room temperature (15-30°C) in the original package.

Contraindications:

- Patients who have a hypersensitivity to nilotinib or to any of its excipients
- Long QT syndrome, persistent QTc > 480 msec
- Uncorrectable hypokalemia or hypomagnesemia

Warnings/Precautions:

- Consultation with a liver disease expert is recommended prior to starting nilotinib in chronic HBV carriers (including those with active disease), and for patients who test positive for HBV infection while on treatment
- The risk of QT prolongation is increased when nilotinib is taken with food, in patients who have had high-dose anthracyclines, patients with uncontrolled or significant cardiac disease (i.e. MI, CHF, unstable angina, etc) or with hypokalemia or hypomagnesemia.
- Avoid drugs that can prolong QT including antiemetics, antiarrhythmics and strong CYP3A4 inhibitors (Refer to Interactions section).
- Exercise caution in patients with risk factors for atherosclerosis.
- Use with caution in patients with risk of tumour lysis (high tumour burden or decreased renal function).
- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- Patients with Gilbert's Syndrome may experience an ↑ in indirect bilirubin levels.
- Caution is recommended in patients with hepatic impairment or a previous history of pancreatitis.

Pregnancy/Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available)
- Fertility effects: Probable

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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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; baseline and regular; every 2 weeks for the first 2 months and then monthly, or as clinically indicated thereafter
- ECG; baseline, seven days after initiation and following dose adjustments, then periodically thereafter
- Electrolytes, including phosphorus, potassium, calcium and magnesium; baseline and regular
- Fasting blood glucose and creatine kinase (CK); baseline and regular
- Lipase, amylase; baseline and regular; also monitor following dose adjustments or as clinically indicated
- Liver function tests; baseline and regular, also monitor following dose adjustments or as clinically indicated
- Monitoring for tumor lysis syndrome (including phosphate, uric acid, LDH); baseline and initial treatment period until tumour burden significantly reduced
- Renal function tests; baseline and regular
- Weight and other signs and symptoms of fluid retention; baseline and regular

- Clinical assessment of toxicity (e.g. GI effects, fluid retention, rash, hemorrhage, cardiovascular effects, infections, hyperglycemia, pneumonitis, etc.); regular
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Close INR monitoring for patients on warfarin; baseline and as clinically indicated

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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

Giles FJ, le Coutre PD, Pinilla-Ibarz J, et al. Nilotinib in imatinib-resistant or imatinib-intolerant patients with chronic myeloid leukemia in chronic phase: 48-month follow-up results of a phase II study. Leukemia. 2013;27(1):107-12.

Kantarjian HM, Hochhaus A, Saglio G, et al. Nilotinib versus imatinib for the treatment of patients with newly diagnosed chronic phase, Philadelphia chromosome-positive, chronic myeloid leukaemia: 24-month minimum follow-up of the phase 3 randomised ENESTnd trial. Lancet Oncol. 2011 Sep;12(9):841-51.

Larson RA, Hochhaus A, Hughes TP, et al. Nilotinib vs imatinib in patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase: ENESTnd 3-year follow-up. Leukemia. 2012 Oct;26(10):2197-203.

Le Coutre P, Ottmann OG, Giles F, et al. Nilotinib (formerly AMN107), a highly selective BCR-ABL tyrosine kinase inhibitor, is active in patients with imatinib-resistant or -intolerant accelerated phase chronic myelogenous leukemia. Blood 2008; 111 (4): 1834-9.

Le Coutre PD, Giles FJ, Hochhaus A, et al. Nilotinib in patients with Ph+ chronic myeloid leukemia in accelerated phase following imatinib resistance or intolerance: 24-month follow-up results. Leukemia. 2012 Jun;26(6):1189-94.

Nilotinib drug monograph, Ontario Health (Cancer Care Ontario).

Saglio G, Kim DW, Issaragrisil S, et al. Nilotinib versus imatinib for newly diagnosed chronic myeloid myeloma. N Engl J Med 2010; 362: 2251-9.

July 2025 Updated Pregnancy/Lactation section

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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 information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

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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