Regimen Monograph

A - Regimen Name

PNAT Regimen

Ponatinib

Disease Site

Hematologic
Leukemia - Acute Lymphoblastic (ALL)

Intent

Curative
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 Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in patients who are T315I mutation positive, or where there is prior TKI resistance or intolerance to imatinib and dasatinib

(Refer to EAP criteria)

Supplementary Public Funding

ponatinib
Exceptional Access Program (ponatinib - For the treatment of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), according to specific clinical criteria) (EAP Website)

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B - Drug Regimen

ponatinib	45 mg	PO	Daily

See drug monograph; may consider lower starting dose in selected patients with hepatic impairment or those taking concomitant strong CYP3A4 inhibitors.

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C - Cycle Frequency

Consider discontinuation if a hematologic response has not been achieved by 3 months.

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Febrile Neutropenia Risk: Low

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:

- Ensure adequate hydration and correct hyperuricemia before starting ponatinib.
- 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.

Patients' cardiovascular status should be assessed and risk factors managed prior to starting treatment and monitored during treatment.

Dosage with toxicity

Dose levels: 45 mg, 30 mg, 15 mg (if further dose reduction indicated, discontinue)

Doses reduced for toxicity may be re-escalated after toxicity has resolved, if clinically appropriate.

Toxicity	Severity	Action/ponatinib dose
Myelosuppression	ANC < 1 x 10^9/L or platelets < 50 x 10^9/L (unrelated to disease)	1st occurrence: Hold* until recovery, restart at the same dose. 2nd occurrence: Hold* until recovery, restart at ↓ 1 dose level from previous dose. 3rd occurrence: Hold* until recovery, restart at ↓ 1 dose level from previous dose.
Hemorrhage	Grade 3 or 4	Hold and investigate. Consider the risk vs. benefit of restarting.
LFTs	AST/ALT > 3 x ULN	Hold until recovery to ≤ grade 1, restart at ↓ 1 dose level from previous dose.
	AST/ALT ≥ 3 x ULN AND total bilirubin > 2 x ULN AND ALP < 2 x ULN	Discontinue
Suspected Pancreatitis	Asymptomatic Amylase/lipase > 2 x ULN	Hold until recovery to ≤ grade 1 then restart at ↓1 dose level from previous dose.
	Amylase/Lipase elevations and symptomatic	Hold and investigate for pancreatitis.
	Grade 3 pancreatitis	Hold until recovery to < grade 2 then restart at ↓ 1 dose level from previous dose.
	Grade 4 pancreatitis	Discontinue
Hypertriglyceridemia	Grade 3 or 4	Manage patient appropriately to reduce pancreatitis risk.

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Cardiac/ATE/VTE	Arterial or venous thromboembolic event	Discontinue unless benefit outweighs risk
	Blurred or decreased vision	Hold and refer for ophthalmic examination for suspected vascular occlusion. Consider the risk vs. benefit of restarting.
	LVEF < 50% and > 10% below baseline and asymptomatic	Hold until recovery. Discontinue if does not resolve within 4 weeks or is ≥ grade 3.
	Symptomatic CHF	Discontinue
	Arrhythmias	Hold and investigate.
	Hypertension	Treat to normalize blood pressure. Hold if not medically controlled and evaluate for renal artery stenosis.
Fluid retention		Hold, reduce or discontinue ponatinib as clinically indicated.
RPLS / PRES	Any	Hold if suspected Discontinue if confirmed or Restart if resolved and only if benefits outweigh risks
Other non-hematologic toxicity	Grade 3 or 4	Hold until recovery. Restart at ↓ 1 dose level from previous dose. If grade 4, consider discontinuation.
Major surgical procedures		Consider hold prior to surgery. Restart based on clinical judgement of adequate wound healing.
*Restart once ANC ≥ 1.5 x 10^9/L and platelets ≥ 75 x 10^9/L		

Hepatic Impairment

The recommended starting dose is 30 mg once daily in patients with hepatic impairment (Child-Pugh A, B or C). There was an increase in adverse effects in patients with severe hepatic impairment.

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Renal Impairment

Renal excretion is not a major route of elimination. Dosage adjustment is not recommended, but ponatinib has not been studied in patients with CrCl < 50 ml/min or end-stage renal disease.

Dosage in the Elderly

Patients aged 65 and older were more likely to experience reduced efficacy and adverse effects compared to younger patients. The dose should be selected with caution given the greater frequency of decreased hepatic, renal and cardiac function, other diseases and drug therapies in older patients.

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F - Adverse Effects

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

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Increased amylase/lipase • Rash (may be severe) • Myelosuppression +/- infection, bleeding (may be severe) • Abdominal pain • Fluid retention (may be severe, including effusions)	• Headache • Constipation • Arterial thromboembolism (may be severe) • Fatigue • Increased LFTs (may be severe) • Musculoskeletal pain • Hypertension (may be severe) • Nausea, vomiting • Eye disorders (may be severe including retinal vascular disorders) • Peripheral neuropathy	• Cardiotoxicity • Arrhythmia (atrial fibrillation) • Venous thromboembolism • Artery aneurysm / dissection • Tumour lysis syndrome • GI perforation • Atypical infections (including HBV reactivation) • Hypothyroidism • Hyperglycemia • Pulmonary hypertension • Pancreatitis • RPLS / PRES

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G - Interactions

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

- Ponatinib is metabolized by CYP3A4 and is susceptible to drug interactions with inhibitors and inducers of this isoenzyme.
- Consider reducing the ponatinib starting dose to 30 mg when given with strong CYP3A4 inhibitors.
- Avoid strong CYP3A4 inducers, if possible. Caution and monitor for reduced efficacy if used together.
- There is no need to adjust the dose or separate administration with drugs that raise gastric pH.
- Caution and monitor with P-gp or BCRP substrates.

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H - Drug Administration and Special Precautions

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

Administration:

- Ponatinib should be swallowed whole with or without food.
- Tablets should not be crushed, chewed or dissolved.
- If a dose is missed, an additional dose should not be taken. Patients should take the next dose at the usual time.
- Store at room temperature (15^{o}C to 30^{o}C) in the original package.

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components
- Patients who have uncontrolled hypertension or other unmanaged cardiac risk factors
- Patients with a history of myocardial infarction, prior revascularization or stroke unless the potential benefit outweighs the risk
- Patients with dehydration or untreated hyperuricemia

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Warnings/Precautions:

- Patients aged 65 and older experienced reduced efficacy and increased adverse effects.
- Use with caution in patients .with a prior history of ischemia, hypertension, congestive heart failure or conditions that may impair left ventricular function, diabetes or hyperlipidemia.
- Use with caution in patients with hepatic impairment.
- Use with caution in patients at risk of bleeding, those receiving antiplatelets and/or anticoagulants.
- Use with caution in patients with a history of pancreatitis or alcohol abuse.
- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation:

- Ponatinib is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose. It is unknown whether ponatinib affects the effectiveness of oral contraceptives. An alternative method of contraception should be used.
- Breastfeeding is not recommended.
- Fertility effects: Likely

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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

- Blood pressure; Baseline and as clinically indicated; ensure hypertension is controlled to minimize risk of arterial thromboembolism
- Calcium, phosphate; Baseline and as clinically indicated
- CBC; Baseline, every 2 weeks for the first 3 months, and then monthly and as clinically indicated
- Eye exam and fundoscopy; Baseline, with blurred vision and as clinically indicated
- Lipase, amylase; Baseline, every 2 weeks for the first 2 months, and then periodically or as clinically indicated

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- Liver function tests; Baseline, at least monthly and as clinically indicated
- LVEF; Baseline, 3 months after treatment initiation, and as clinically indicated
- Clinical toxicity assessment for bleeding, infection, thromboembolism, fluid retention (including regular weight monitoring), hypertension, cardiac and GI effects, tumour lysis syndrome, ocular and neurologic effects; Baseline and at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Cortes JE, Kim DW, Pinilla-Ibarz J, et al; PACE Investigators. A phase 2 trial of ponatinib in Philadelphia chromosome-positive leukemias. N Engl J Med. 2013 Nov 7;369(19):1783-96.

Couban S, Savoie L, Mourad YA, et al. Evidence-based guidelines for the use of tyrosine kinase inhibitors in adults with Philadelphia chromosome-positive or BCR-ABL-positive acute lymphoblastic leukemia: a Canadian consensus. Curr Oncol. 2014 Apr;21(2):e265-309.

Ponatinib drug monograph, Cancer Care Ontario.

December 2025 removed information on controlled distribution program

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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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