

Regimen Monograph

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A - Regimen Name

PAZO Regimen

Pazopanib

Disease Site

Sarcoma
Soft Tissue

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

Treatment of adult patients with selective subtypes* of advanced soft tissue sarcoma who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo)adjuvant therapy. Patients were required to have disease progression on or after, or be intolerant to, anthracycline-based regimen in the pivotal phase III study in STS.

*the pivotal trial excluded adipocytic sarcoma, GIST, rhabdomyosarcoma that was not alveolar or pleomorphic, chondrosarcoma, osteosarcoma, Ewing's sarcoma, primitive neuroectodermal tumours, DFSP, inflammatory myofibroblastic sarcoma, malignant mesothelioma and mixed mesodermal tumours of the uterus.

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B - Drug Regimen

[pazopanib](#)

800 mg

PO

Daily

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

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C - Cycle Frequency

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

- 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:

- Hypertension must be controlled before starting pazopanib.
- Electrolytes should be maintained within the normal range.
- Patients at risk of tumour lysis syndrome should have appropriate prophylaxis and be monitored closely.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

VEGF inhibitors may impair wound healing; pazopanib should be stopped at least 7 days prior to planned surgery.

Dosage with toxicity

Dose levels: 800mg, 600mg, 400mg, (200mg can be considered if benefit outweighs risk). Doses reduced for toxicity should not be re-escalated.

Toxicity / Event	Action
Mild myelosuppression	Hold until ANC $\geq 1.5 \times 10^9/L$ and Platelets $\geq 100 \times 10^9/L$
Persistent hypertension despite anti-hypertensive therapy	Reduce dose; see Management of Angiogenesis Inhibitor (AI)-Induced Hypertension
Urine protein ≥ 3 grams/24h	Hold until urine protein < 3 grams/24h; restart with $\downarrow 1$ dose level. Discontinue if recurs or develops severe nephrotic syndrome.
Hepatotoxicity	See table below
Serious infections	Consider hold or discontinuing pazopanib
Planned surgery	Hold for at least 7 days pre-surgery
Pneumonitis/ILD	Hold and investigate. If confirmed, discontinue
Retinal detachment	Hold and refer to ophthalmologist for treatment.* Once resolved, consider risk vs. benefit of restarting. Discontinue if recurs.
Wound dehiscence	Discontinue
Nephrotic syndrome, arterial thromboembolism, significant bleeding, grade 4 related organ toxicity, perforation, fistula, RPLS/PRES, thrombotic microangiopathy	
Uncontrollable hypertension or hypertensive crisis	

* Recommendation for ocular toxicity with VEGF inhibitors (Renouf 2012)

Hepatic Impairment During Treatment

Bilirubin during treatment		ALT / AST during treatment	Action
		3 – 8 x ULN (isolated ↑)	Continue treatment; LFTs weekly until ≤ grade 1 or baseline
		> 8 X ULN	Hold until ≤ grade 1. May restart if appropriate, ↓ to 400mg once daily; LFTs weekly x 8. Discontinue permanently if LFTs > 3 x ULN recurs.
>2 x ULN*	AND	> 3 x ULN	Discontinue permanently. Monitor liver function until recovery to grade 1 or baseline.
> ULN (isolated ↑) AND no signs and symptoms of liver injury	AND	< ULN	Caution; no dose adjustment needed. Investigate underlying cause.

* if mild and related to Gilbert's syndrome may treat as if isolated AST/ALT elevations.

Hepatic Impairment

Pazopanib should not be used in patients with baseline bilirubin > 1.5 x ULN and AST or ALT > 2 x ULN, or who have moderate-severe hepatic impairment. Avoid concomitant statins.

Clearance decreased by 50% in patients with moderate hepatic impairment and dose-limiting toxicity was observed at 400mg.

Use caution in patients with mild hepatic impairment as it has not been formally studied in these patients.

Renal Impairment

No dose adjustments are recommended for patients with mild or moderate renal impairment. Not recommended for use in patients with severe renal impairment (< 30 mL/min) as it has not been studied in this patient population.

Dosage in the Elderly

No dose adjustment required. Patients over age 60 may be at greater risk of elevated liver enzymes (ALT > 3 x ULN). Although no other differences in response were found between older and younger patients, older patients may be more sensitive to adverse effects.

Dosage Based on Ethnicity:

Myelosuppression and hand-foot syndrome were observed more frequently in East Asian patients.

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F - Adverse Effects

Refer to [pazopanib](#) 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
<ul style="list-style-type: none"> • Diarrhea 	<ul style="list-style-type: none"> • Hypertension (may be severe) • Hair or skin colour changes • Nausea, vomiting 	<ul style="list-style-type: none"> • Musculoskeletal pain • Anorexia • Cough/dyspnea • Fatigue • ↑ LFTs (may be severe) • Hemorrhage (may be severe) • Abdominal pain • Headache • Dizziness 	<ul style="list-style-type: none"> • Cardiotoxicity • Venous thromboembolism • Arterial thromboembolism • Artery aneurysm /dissection • ↑ QT interval, bradycardia • GI, GU fistula, perforation • RPLS/PRES • Pneumothorax • Pneumonitis • Proteinuria • Thrombotic microangiopathy • Retinal detachment • Pancreatitis • Hyper- / hypoglycemia • Hypothyroidism • Myelosuppression +/- infection • Tumour lysis syndrome

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G - Interactions

Refer to [pazopanib](#) drug monograph(s) for additional details

- Avoid co-administration with inhibitors that simultaneously target P-gp, BCRP and/or CYP3A4 (e.g. lapatinib) due to risk of increased pazopanib exposure.
- Avoid co-administration with strong CYP3A4 inducers or CYP3A4 substrates with narrow therapeutic ranges.
- Avoid co-administration with strong CYP3A4 inhibitors; if must co-administer, reduce pazopanib to 400mg daily (or lower if toxicity occurs).
- Avoid co-administration with CYP2C8 and CYP2D6 substrates with narrow therapeutic ranges.
- Avoid co-administration with inducers and strong inhibitors of P-gp and BCRP.
- Monitor patients for additive effects when co-administered with drugs that ↑ QT interval, ↑ risk of bleeding, ↑ risk of hepatotoxicity, and those that decrease heart rate.
- Avoid drugs that increase the gastric pH (i.e. PPIs, H2-antagonists) due to decreased pazopanib absorption and exposure; consider antacids and separate dosing by several hours.

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H - Drug Administration and Special Precautions

Refer to [pazopanib](#) drug monograph(s) for additional details.

Administration

- Swallow tablet(s) whole with a glass of water.
- Do not cut, crush or chew tablets, as this may increase drug exposure and side effects.
- Take each dose on an empty stomach, at least 1 hour before or 2 hours after a meal. Administration with meals doubles exposure.
- Avoid grapefruit, starfruit, Seville oranges, their juices or products during treatment.
- A missed dose may be taken if there are more than 12 hours until the next dose.
- Store between 15-30°C.

Contraindications:

- Patients who are hypersensitive to the drug or its components
- Patients less than 2 years of age

Other Warnings/Precautions:

- Pazopanib should not be used in patients who have had a thrombotic event within the past 6 months and is not recommended in patients with a history of hemoptysis, cerebral or significant GI bleeding in the past 6 months.
- Use with caution in patients:
 - with risk factors for Torsades de Pointes (history of QT prolongation, antiarrhythmics, medications that prolong the QT interval, cardiac disease, electrolyte disturbances, diabetes or autonomic neuropathy);
 - with bradycardia at baseline, a history of syncope or arrhythmia, ischemic heart disease or congestive heart failure;
 - with an increased risk of or a history of thrombotic events;
 - with a significant risk of hemorrhage;
 - at risk of GI perforation or fistula;
 - with hypothyroidism;
 - on medications that can lead to bradycardia or which are hepatotoxic.
- Pazopanib is not indicated for use in combination with other anticancer agents; increased toxicity and/or mortality has been observed in combination with pemetrexed, lapatinib, or pembrolizumab.

Pregnancy and Lactation

- This regimen is not recommended or 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

- Blood pressure; Baseline (2 readings separated by 24 hours for patients on anti-hypertensives at baseline), then within one week after starting pazopanib, and at each visit
- Liver function tests; Baseline, at weeks 2, 4, 6, 8, at months 3 and 4, then as clinically indicated; monitor more frequently in patients with known HLA-B*57-01 allele
- CBC; Baseline and at each visit
- Renal function tests; Baseline and at each visit
- Urinalysis; Baseline and at each visit
- ECG; Baseline and as clinically indicated
- Electrolytes, including magnesium, calcium, phosphate; Baseline and as clinically indicated
- Blood glucose, lipase and amylase; Baseline and as clinically indicated
- Thyroid function tests; Baseline and as clinically indicated
- LVEF in patients at risk (including those who have received prior anthracyclines); Baseline and as clinically indicated
- Signs and symptoms of tumour lysis syndrome in patients at risk; Baseline and as clinically indicated
- 24 hour urine protein in patients with worsening proteinuria; As clinically indicated
- Clinical toxicity assessment of hypertension, pneumonitis, thromboembolism, diarrhea, bleeding, infection, wound healing, fatigue, GI fistula/perforation, lung, neurologic or ocular effects; 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

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

Renouf DJ, Velazquez-Martin JP, Simpson R, Siu LL, Bedard PL. Ocular toxicity of targeted therapies. J Clin Oncol. 2012 Sep 10;30(26):3277-86.

Van der Graaf WTA, Blay JY, Chawla SP, et al. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2012; 379(9829):1879-86.

December 2024 Updated Premedication and Supportive Measures, Dose Modifications, Adverse Effects, Interactions, Drug Administration and Special Precautions, and Monitoring sections

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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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