

Regimen Monograph

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A - Regimen Name

SORA Regimen

SORAfenib

Disease Site Gastrointestinal
 Hepatobiliary / Liver / Bile Duct

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 advanced hepatocellular carcinoma (HCC) in patients who have Child-Pugh Class A disease, ECOG status 0-2, and either had disease progression while being treated with transarterial chemoembolization (TACE) or are not suitable for TACE.

Supplementary Public Funding [SORAfenib](#)
Exceptional Access Program (SORAfenib - Advanced hepatocellular carcinoma, with specific criteria)

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B - Drug Regimen[SORAfenib](#)

400 mg

PO

BID

[back to top](#)**C - Cycle Frequency****CONTINUOUS TREATMENT**

Until disease progression or unacceptable toxicity.

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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.

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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. See appendix 6 for general recommendations. Hypokalemia, hypomagnesemia and hypocalcemia should be corrected before sorafenib treatment.

Dosage with toxicity**Dose levels:**

Dose level	Sorafenib dose
0	800mg daily dose (400mg bid)
-1	600mg daily dose (400mg and 200mg, 12 hours apart)
-2	400mg daily dose (200mg bid)
-3	200mg daily dose (200mg od)

Toxicity grade	Occurrence	Dose modification
Grade 1 skin	Any	Continue treatment with sorafenib and consider topical/supportive therapy for symptomatic relief.
Grade 2 skin	1 st	Continue treatment, supportive care. Consider ↓ 2 dose levels for 28 days; if does not improve hold for at least 7 days until ≤ grade 1 and restart at 400mg daily. If ≤ grade 1 x 28 days, consider re-escalating to full dose.
	2 nd or 3 rd	As for 1 st occurrence, but do not re-escalate if hold required.
	4 th	Consider discontinuing sorafenib.
Grade 3 skin	1 st	Supportive care and hold at least 7 days until ≤ grade 1, restart by ↓ 2 dose levels; if ≤ grade 1 x 28 days, consider re-escalating to full dose.
	2 nd	As for 1 st occurrence, but do not re-escalate.
	3 rd	Consider discontinuing sorafenib.
Grade 3 non-hematological/related organ	1 st	Hold until recovery to ≤ grade 2; ↓ 2 dose levels
	2 nd	Discontinue
Cardiac ischemia and/or infarction	Any	Hold; consider discontinuing
↑LFTs	Any	Hold if severe and rule out other causes. Discontinue if drug-induced hepatitis.
GI perforation, severe hypertension despite treatment, cardiac failure, ≥ grade 3 bleeding, pneumonitis, SJS or TEN, Grade 4 non-hematological/related organ	Any	Discontinue

Hepatic Impairment

Patients with hepatocellular carcinoma (HCC) and Child-Pugh B hepatic impairment have greater systemic exposure than Child-Pugh A patients, although this difference is not seen in non-HCC patients. Exercise caution and monitor closely when treating Child-Pugh B patients with sorafenib, due to the heterogenous nature of this population. Sorafenib has not been studied in patients with Child-Pugh C hepatic impairment.

Miller 2009 suggested the following dose modifications in patients with HCC:

Child-Pugh		Bilirubin	Albumin	Dose
A	AND	$\leq 1.5 \times \text{ULN}$		400mg bid
B	AND/OR	$> 1.5 - 3 \times \text{ULN}$		200mg bid
C	AND/OR	$> 3 \times \text{ULN}$		Do not treat – severe toxicity likely
			≤ 25	200mg daily

Renal Impairment

Although the product monograph suggests that no dose adjustments are required in patients with mild, moderate, or severe renal impairment not requiring dialysis, a pharmacokinetic study (Miller 2009) suggested the following:

Creatinine clearance	Dose
$> 40 \text{ mL/min}$	400mg BID
$20-40 \text{ mL/min}$	200mg BID
$< 20 \text{ mL/min}$	No information; avoid or use with extreme caution

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F - Adverse Effects

Refer to [SORAfenib](#) 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
<ul style="list-style-type: none"> • Abnormal electrolytes • Myelosuppression +/- infection, bleeding (may be severe) • Diarrhea • Increased amylase/lipase (may be severe) • Rash (may be severe) • Fatigue • Increased LFTs (may be severe) • Hand-foot syndrome • Alopecia 	<ul style="list-style-type: none"> • Nausea, vomiting • Hypertension • Anorexia, weight loss • Hemorrhage (may be severe) • Cough, dyspnea (may be severe) • Neuropathy • Abdominal pain • Mucositis • Musculoskeletal pain • Headache 	<ul style="list-style-type: none"> • Cholecystitis • Hypo/hyperthyroidism • Arterial thromboembolism • Venous thromboembolism • Artery aneurysm / dissection • Cardiotoxicity • Hypersensitivity • Pancreatitis • PRES • GI perforation • Osteonecrosis of the jaw • Renal failure • Rhabdomyolysis • Vasculitis • Secondary malignancy

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

Administration

- Oral self-administration; drug available by outpatient prescription.
- Prescribed dose should be administered orally on an empty stomach, or with a low-fat or moderate-fat meal with a large glass of water.
- Store at room temperature (15-30°C).

Contraindications

- Patients who have a hypersensitivity to this drug or any of its components

Warnings/Precautions

- Concomitant warfarin or antiplatelet agents should be used cautiously.
- Temporary hold is recommended for patients undergoing major surgery.
- Hypokalemia, hypomagnesemia and hypocalcemia should be corrected before treatment.
- Due to the potential risk of bleeding, tracheal, bronchial, and esophageal infiltration should be treated with localized therapy before starting sorafenib in DTC patients.
- Sorafenib may impair exogenous thyroid suppression in DTC patients.
- Sorafenib should be administered with caution in patients who have bradycardia or with increased risk of developing prolongation of the QT interval/Torsades de pointes (i.e. hypokalemia or hypomagnesemia, congenital long QT syndrome, history of cardiac disease or arrhythmias, concomitant anti-arrhythmic or other medications that may prolong QT interval). Patients with unstable coronary artery disease or recent MI (within 6 months) were excluded from clinical trials.

Pregnancy/Lactation

- Sorafenib is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **2 weeks** after the last dose.
 - Breastfeeding is not recommended.
 - Sorafenib impairs male and female fertility.
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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; weekly for first 6 weeks of treatment, then periodically thereafter
- CBC; baseline and regular
- Thyroid function tests; baseline and regular
- ECG during therapy; baseline and periodic
- Electrolytes, including phosphate and calcium; baseline and regular
- INR, for patients on warfarin; regular, especially at initiation, or discontinuation or change of dose.
- Liver function tests, amylase and lipase; baseline and regular
- Clinical toxicity ratings (bleeding, hypertension, skin changes, diarrhea, pancreatitis, congestive heart failure, hepatitis, secondary malignancies); regular
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

Suggested Clinical Monitoring

- LVEF, especially in patients with cardiac risk factors; baseline and periodic
- Dental evaluation before starting treatment with preventative dentistry as needed

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Cheng AL, Kang YK, Chen ZD, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. *Lancet Oncology* 2009; 10: 25-34.

Hollebecque A, Cattani S, Romano O, et al. Safety and efficacy of sorafenib in hepatocellular carcinoma: the impact of the Child-Pugh score. *Aliment Pharmacol Ther* 2011;34(10):1193-201.

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Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. *NEJM* 2008;359:378-90.

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Pinter M, Sieghart W, Graziadel I, et al. Sorafenib in Unresectable Hepatocellular Carcinoma from Mild to Advanced Stage Liver Cirrhosis. *Oncologist* 2009;14(1):70-6.

Pressiani T, Boni C, Rimassa L, et al. Sorafenib in patients with Child-Pugh class A and B advanced hepatocellular carcinoma: a prospective feasibility analysis. *Ann Oncol* 2013;24(2):406-11.

Sorafenib drug monograph, Cancer Care Ontario.

Wörns MA, Weinmann A, Pfingst K, et al. Safety and efficacy of sorafenib in patients with advanced hepatocellular carcinoma in consideration of concomitant stage of liver cirrhosis. *J Clin Gastroenterol* 2009;43(5):489-95.

Zhu AX, Clark JW. Commentary: Sorafenib Use in Patients with Advanced Hepatocellular Carcinoma and Underlying Child-Pugh B Cirrhosis—Evidence and Controversy. *The Oncologist* 2009; 14: accepted Jan 5, 2009. (e-pub ahead of print)

PEBC Advice Documents or Guidelines

- [Non-Surgical Management of Advanced Hepatocellular Carcinoma](#)

March 2023 Updated Rationale/uses 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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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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