Regimen Monograph

A - Regimen Name

IVOS Regimen

Ivosidenib

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

Treatment of locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation in patients who were previously treated by at least one prior line of systemic therapy.

IDH1 R132 mutation should be confirmed using an appropriate diagnostic test prior to starting ivosidenib.

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B - Drug Regimen

ivosidenib	500 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: Low – 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:

- QTc should be < 450 ms prior to starting ivosidenib. In the presence of QTc 480-500 ms, treatment should only be initiated in exceptional cases if the benefits outweigh the risks.

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E - Dose Modifications

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

Dosage with toxicity

Dose Level	Ivosidenib Dose (mg daily)
0	500
-1	250
-2	Discontinue

Toxicity	Grade/Severity	Action
QTc Interval Prolongation	QTc > 480 to 500 ms	Hold until QTc ≤ 480 ms.* Resume** at same dose.
	QTc > 500 ms	Hold.* Monitor ECG† every 24 hours until QTc ≤ 480ms or within 30 ms of baseline. Resume** at 1 dose level ↓. May increase dose to 500 mg daily if alternative etiology for QTc prolongation is identified.
	QT prolongation with signs/symptoms of life-threatening ventricular arrhythmia	Discontinue.
Other Adverse Reactions	Grade 3	Hold until improvement to ≤ Grade 1 or baseline. Resume at same dose.
		First recurrence: Hold until improvement to ≤ Grade 1 or baseline. Resume at 1 dose level ↓, then return to original dose once toxicity resolves.
		Second recurrence: Discontinue.
	Grade 4	Hold until improvement to ≤ Grade 1 or baseline. Resume at 1 dose level ↓.
		Recurrence: Discontinue

* Monitor electrolyte levels and supplement as clinically indicated. Review and adjust concomitant medications known to prolong QTc intervals.

** Monitor ECGs at least weekly for 2 weeks and as clinically indicated.

† If QTc > 550 ms, consider continuous ECG monitoring until < 500 ms.

Hepatic Impairment

Hepatic Impairment	Ivosidenib Dose
Mild (Child-Pugh Class A)	No dose adjustment required.
Moderate (Child-Pugh Class B)	No data available. Use with caution and monitor closely.
Severe (Child-Pugh Class C)	

Renal Impairment

Creatinine Clearance*	Ivosidenib Dose
≥ 30	No dose adjustment required.
< 30	No data available. Use with caution and monitor closely.

*Reported as eGFR (mL/min/1.73 m^2)

Dosage in the Elderly

No dose adjustment is required. No overall differences in effectiveness or safety were observed between patients aged ≥ 65 years compared to younger patients. No data is available for patients ≥ 85 years old.

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F - Adverse Effects

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

Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Diarrhea • Nausea, vomiting • Fatigue • Abdominal pain	• QT interval prolonged • Peripheral neuropathy • ↑ bilirubin, LFTs • Cholestatic jaundice • Ascites • Myelosuppression ± bleeding

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G - Interactions

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

- Concomitant use with strong CYP3A4 inducers is **contraindicated** due to risk of lower ivosidenib exposure.
- Concomitant use with dabigatran is **contraindicated** due to risk of altered exposure of P-gp substrates.
- Avoid concomitant use with strong and moderate CYP3A4 inhibitors due to increased risk of ivosidenib toxicity. If they are administered concomitantly, ↓ ivosidenib dose to 250 mg once daily and closely monitor for QTc prolongation. Resume ivosidenib dose at 500 mg once daily after inhibitor has been discontinued for at least 5 half-lives.
- Avoid concomitant use with medications known to prolong QTc interval due to increased risk of QTc interval prolongation.
- Avoid concomitant use with OAT3, sensitive* OATP1B1 and OATP1B3 substrates due to increased risk of toxicity from these substrates.
- Avoid concomitant use with anti-fungals that are CYP3A4 substrates due to expected loss of anti-fungal efficacy.
- Avoid concomitant use with sensitive* substrates of CYP3A4, CYP2B6, CYP2C8, CYP2C9, and CYP2C19 due to risk of decreased substrate efficacy.

- Avoid concomitant use with UGT substrates due to risk of decreased substrate efficacy.
- Since the efficacy of hormonal contraceptives may be reduced, concomitant use of a non-hormonal (e.g. barrier) method of contraception is recommended during treatment and for at least 1 month after the last ivosidenib dose.
- Use with caution when concomitantly administering medications that affect electrolytes or reduce heart rate due to increased risk of QTc interval prolongation. Monitor and maintain electrolyte levels and heart rate within the normal range.

***Sensitive substrates** are those where minimal concentration changes from enzyme or transporter inhibition (or induction) may lead to serious adverse effects (or therapeutic failure).

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H - Drug Administration and Special Precautions

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

Administration

- Administer each dose on an empty stomach, at least 1 hour before or 2 hours after a meal.
- Tablets should be swallowed whole with water. Do not split, crush, or chew the tablets.
- Grapefruit, starfruit, Seville oranges, their juices or products should be avoided during treatment, due to risk of increased toxicity.
- If a dose is missed, administer the dose as soon as possible within 12 hours of missed dose. If the dose is missed by more than 12 hours, skip the dose and administer the next dose at the next planned time. Do not give extra tablets to make up for the missed dose.
- If patient vomits after taking a dose, do not administer a replacement dose. The next regular daily dose should be given on the next day.
- Store at 15°C - 30°C. Keep the bottle tightly closed in order to protect tablets from moisture.

Contraindications

- Patients who have a hypersensitivity to this drug or any of its components
- Patients taking strong CYP3A4 inducers or dabigatran
- Patients with congenital long QT syndrome

- Patients with a family history of sudden death or polymorphic ventricular arrythmia
- Patients with a QT/QTc interval > 500 ms, regardless of the correction method used

Other Warnings/ Precautions

- Ivosidenib contains lactose and should not be used in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption
- QTc interval prolongation has been reported following treatment with ivosidenib, and can increase the risk of ventricular arrhythmias including torsades de pointes. Clinical trials excluded patients with baseline QTc ≥ 450 ms or other factors that increased the risk of QT prolongation (e.g. history or family history of long QT syndrome, uncontrolled or significant cardiovascular disease, heart failure, hypokalemia). Closely monitor patients who have congestive heart failure or electrolyte abnormalities. Use with caution in patients who have low albumin levels or are underweight.
- Caution with driving or using machinery as dizziness may occur with treatment.

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: Unknown

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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, at each visit, and as clinically indicated
- Liver function tests; Baseline, at each visit, and as clinically indicated
- Renal function tests; Baseline, at each visit, and as clinically indicated
- ECG; Baseline and at least weekly during the first 3 weeks of treatment and then at least monthly for the duration of treatment. (More frequent monitoring may be necessary in patients with/at risk of QT prolongation.)
- Electrolytes, including sodium, potassium, calcium or magnesium; Baseline, at each visit, and as clinically indicated
- Clinical toxicity assessment for fatigue and GI 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

Abou-Alfa GK, Macarulla T, Javle MM, et al. Ivosidenib in IDH1-mutant, chemotherapy-refractory cholangiocarcinoma (ClarIDHy): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol. 2020 Jun;21(6):796-807. doi: 10.1016/S1470-2045(20)30157-1.

Ivosidenib drug monograph. Ontario Health (Cancer Care Ontario).

January 2026 New regimen monograph

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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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