Regimen Monograph

A - Regimen Name

IDEL Regimen

Idelalisib

Disease Site	Hematologic - Lymphoma - Non-Hodgkin's Low Grade
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	Monotherapy for the treatment of patients with follicular lymphoma who have received at least two prior systemic therapies and are refractory to both rituximab and an alkylating agent.

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B - Drug Regimen

idelalisib	150 mg	PO	BID

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

(available as 150 mg and 100 mg tablets)

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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

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

A supply of loperamide should be provided for diarrhea.

Advise patients to avoid sun exposure or use sufficient sun protection.

Antibiotic prophylaxis for PCP/PJP is required during treatment and for 2 to 6 months after discontinuation of treatment.

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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

Dose levels: 150 mg bid, 100 mg bid, discontinue if further dose modification required.

Toxicity	Grade	Action/idelalisib dose
Diarrhea/colitis	1	Provide supportive care (e.g. loperamide) and continue at the same dose.
	2	Provide supportive care, hold and monitor until resolved to ≤ grade 1.

		Restart at the same dose.
	3 or 4	Provide supportive care, hold. Consider addition of anti-inflammatory agent (e.g. sulfasalazine, budesonide). Monitor until resolved to ≤ grade 1. Restart at ↓ 1 dose level
Toxicity	**Grade**	**Action/idelalisib dose**
Neutropenia Or Thrombocytopenia	3	Continue at the same dose and monitor CBC.
	4	Hold until ANC ≥ 0.5 x 10^9/L and ≥ platelets 25 x 10^9/L. Restart at ↓ 1 dose level
ALT/AST elevation	1 or 2	Continue at the same dose and monitor LFTs.
	3 or 4	Hold until ALT/AST ≤ 1 x ULN. Restart at ↓ 1 dose level Discontinue for recurrent hepatotoxicity.
Pneumonitis / organizing pneumnonia	Any grade	Hold and evaluate for respiratory symptoms. • If no infectious origin found and pneumonitis is likely drug-related, discontinue idelalisib. Consider steroids especially if severe • If infectious origin found, monitor/treat until resolved. Restart at ↓ 1 dose level.
CMV infection/viremia		Discontinuation if evidence of CMV infection or viremia (positive PCR or antigen test)
Signs and symptoms of PML	Any	Hold and investigate; refer to neurologist. Discontinue if confirmed.
Signs and symptoms of PCP/PJP		Discontinue
Rash	2	Hold until ≤ grade 1. Restart at the same dose.
	3 or 4	Hold until ≤ grade 1. Restart at ↓ 1 dose level. Discontinue if severe cutaneous reactions (e.g. TEN)
Hypersensitivity	3 or 4	Discontinue, treat appropriately.

Hepatic Impairment

AUC is increased with hepatic impairment, but no dosage adjustment is required in mild to moderate hepatic impairment (monitor closely). Insufficient data for patients with severe hepatic impairment. Patients with baseline ALT/AST > 2.5 x ULN or bilirubin > 1.5 x ULN were excluded from clinical trials.

Renal Impairment

No dosage adjustment is required for mild, moderate or severe renal impairment.

Dosage in the Elderly

No dosage adjustment is required for elderly patients. The incidence of severe adverse events was higher among patients aged 65 and older compared to younger patients, but age had no clinically relevant effect on drug exposure.

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F - Adverse Effects

Refer to idelalisib 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
• Increased triglycerides • Increased	• Diarrhea (may be severe) • Fatigue • Cough, dyspnea	• Rash (may be severe)	• Hypersensitivity • Pneumonitis (including

LFTs (may be severe)	• Nausea, vomiting • Fever • Abdominal pain • Myelosuppression +/- infection (including atypical), bleeding (may be severe)	• Anorexia • Insomnia • Headache • Edema	organizing pneumonia) • PML

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G - Interactions

Refer to idelalisib drug monograph(s) for additional details

- Idelalisib is a substrate for CYP3A4 and is susceptible to drugs interactions with inducers and inhibitors of this isoenzyme. Avoid strong CYP3A4 inducers and inhibitors where possible.
- Idelalisib is also a CYP3A4 inhibitor. Caution and monitor with substrates that have a narrow therapeutic index.
- Idelalisib may reduce the effectiveness of oral contraceptives. Caution and consider an alternative method of contraception.

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H - Drug Administration and Special Precautions

Refer to idelalisib drug monograph(s) for additional details

Administration

- May be administered with or without food
- If a dose is missed, it may be taken within 6 hours of the missed dose. If a dose is missed by more than 6 hours, it should not be taken; the next dose should be taken as scheduled.
- Dispense only in original container with intact seal
- Store below $30^{o}C$

Contraindications

- in first line CLL and early line indolent NHL outside of a clinical trial
- patients who have a hypersensitivity to this drug or any of its components

Warnings/precautions

- Idelalisib should not be started in patients with any evidence of ongoing systemic bacterial, fungal or viral infections.
- not recommended in patients with ongoing inflammatory bowel disease given the risk of severe diarrhea
- not recommended in patients with active hepatitis or liver disease

Pregnancy & lactation

- Idelalisib is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 1 month after the last dose. Idelalisib may reduce the effectiveness of hormonal contraceptives (refer to drug interactions). Consider additional alternative methods of contraception.
- Breastfeeding is not recommended.

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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.

Recommended Clinical Monitoring

- CBC; Baseline, every 2 weeks for the first 6 months, and at least weekly with grade 3 or 4 myelosuppression.
- CMV PCR/Antigen; baseline and regular
- Liver function tests; Baseline, every 2 weeks for the first 3 months, thereafter every 1 to 3 months, and as clinically indicated. Weekly with hepatotoxicity until within ULN.
- Clinical toxicity assessment for GI, skin, respiratory toxicity, hypersensitivity, bleeding and infection (including opportunistic, CMV); 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

Gopal AK, Kahl BS, de Vos S, et al. PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma. N Engl J Med. 2014 Mar 13;370(11):1008-18.

Idelalisib drug monograph, Cancer Care Ontario.

June 2019 Updated emetic risk category

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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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