ICLUSIG®
(ponatinib) tablets

ICLUSIG Dosing Guide

Learn about response-based, once-daily oral dosing with ICLUSIG

ICLUSIG (ponatinib tablets) is indicated for:

- the treatment of adult patients with chronic phase (CP), accelerated phase (AP), or blast phase (BP) chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom other tyrosine kinase inhibitor (TKI) therapy is not appropriate, including CML or Ph+ ALL that is T315I mutation positive or where there is prior TKI resistance or intolerance.

Response-based, once-daily oral dosing with ICLUSIG

Before starting treatment with ICLUSIG, the cardiovascular status of the patient should be assessed and cardiovascular risk factors should be actively managed. Cardiovascular status should continue to be monitored and therapy optimized during treatment with ICLUSIG.

CP-CML

1 Start at 45 mg

The recommended starting dosage of ICLUSIG is 45 mg orally once daily.

2 Reduce to 15 mg

Dosage can be reduced to 15 mg orally once daily upon achievement of molecular response (≤1% BCR-ABL1[IS]).

3 Dose based on response

Patients with loss of response can re-escalate the dose of ICLUSIG to a previously tolerated dosage of 30 mg or 45 mg orally once daily. Continue ICLUSIG until loss of response at the re-escalated dose or unacceptable toxicity. Consider discontinuing ICLUSIG if hematologic response has not occurred by 3 months.

AP-CML, BP-CML, and Ph+ ALL

1 Start at 45 mg

The recommended starting dosage of ICLUSIG is 45 mg orally once daily.

2 Maintain at 45 mg

Continue ICLUSIG until loss of response or unacceptable toxicity.

3 Dose based on response

Consider reducing the dose of ICLUSIG for patients with accelerated phase (AP) CML who have achieved a major cytogenetic response. Consider discontinuing ICLUSIG if response has not occurred by 3 months.

AP-CML=accelerated phase chronic myeloid leukemia; BCR-ABL1[IS]= BCR-ABL1 International Scale; BP-CML=blast phase chronic myeloid leukemia; CP-CML=chronic phase chronic myeloid leukemia; Ph+ ALL=Philadelphia chromosome positive acute lymphoblastic leukemia.

Available strengths



ICLUSIG 15 mg

Tablet shown at actual size

Recommended dose reductions for ICLUSIG for adverse reactions

Dose reduction	Dosage for patients with CP-CML	Dosage for patients with AP-CML, BP-CML, and Ph+ ALL
First	30 mg orally once daily	30 mg orally once daily
Second	Reduce to 15 mg orally once daily	Reduce to 15 mg orally once daily
Subsequent reduction	Permanently discontinue ICLUSIG in patients unable to tolerate 15 mg orally once daily	Permanently discontinue ICLUSIG in patients unable to tolerate 15 mg orally once daily

AP-CML=accelerated phase chronic myeloid leukemia; BP-CML=blast phase chronic myeloid leukemia; CP-CML=chronic phase chronic myeloid leukemia; Ph+ ALL=Philadelphia chromosome positive acute lymphoblastic leukemia.

ICLUSIG® (ponatinib) tablets

Dose modifications to help manage adverse reactions

Adverse reaction	Severity	ICLUSIG dose modification
Arterial occlusive event (AOE): cardiovascular or cerebrovascular	Grade 1	Interrupt ICLUSIG until resolved, then resume at same dose.
	Grade 2	Interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
	Grade 3 or 4	Discontinue ICLUSIG.
AOE: peripheral vascular and other **or Venous thromboembolic event (VTE)**	Grade 1	Interrupt ICLUSIG until resolved, then resume at same dose.
	Grade 2	Interrupt ICLUSIG until ≤ Grade 1, then resume at same dose. If recurrence, interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose.
	Grade 3	Interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
	Grade 4	Discontinue ICLUSIG.
Heart failure	Grade 2 or 3	Interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
	Grade 4	Discontinue ICLUSIG.
Hepatic toxicity	AST or ALT greater than 3 times ULN	Interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose.
	AST or ALT at least 3 times ULN concurrent with bilirubin greater than 2 times ULN and alkaline phosphatase less than 2 times ULN	Discontinue ICLUSIG.
Pancreatitis and elevation of lipase/amylase	Asymptomatic Grade 2 pancreatitis and/or elevation of lipase/amylase greater than 1.5 – 2.0 times ULN or greater than 2.0 – 5.0 times ULN and asymptomatic	Consider interrupting ICLUSIG until resolution then resume at same dose.
	Elevation of lipase/amylase greater than 5.0 times ULN and asymptomatic	Interrupt ICLUSIG until ≤ Grade 1 (less than 1.5 times ULN) then resume at next lower dose.
	Grade 3 pancreatitis or elevation of lipase/amylase greater than 2.0 – 5.0 times ULN and symptomatic	Interrupt ICLUSIG until complete resolution of symptoms and after recovery of lipase elevation ≤ Grade 1, then resume at next lower dose.
	Grade 4 pancreatitis or elevation of lipase/amylase greater than 5.0 times ULN and symptomatic	Discontinue ICLUSIG.
Myelosuppression	ANC less than 1.0 x 10^9/L or platelets less than 50 x 10^9/L	Interrupt ICLUSIG until ANC at least 1.5 x 10^9/L and platelets at least 75 x 10^9/L, then resume at same dose. If recurrence, interrupt ICLUSIG until resolution, then resume at next lower dose.
Other non-hematologic adverse reactions	Grade 2	Interrupt ICLUSIG until ≤ Grade 1, then resume at same dose. If recurrence, interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose.
	Grade 3 or 4	Interrupt ICLUSIG until ≤ Grade 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.

Grading based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0.
ANC=absolute neutrophil count; ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

Consult the product monograph at https://takeda.info/en-ca-iclusigpm for complete dosing recommendations. The product monograph is also available by calling 1-800-268-2772.

ICLUSIG® (ponatinib) tablets

Considerations for strong CYP3A inhibitors and inducers

Strong CYP3A inhibitors

Ponatinib is primarily metabolized by CYP3A4. Therefore, concomitant use of substances which inhibit CYP3A may increase ponatinib plasma concentrations.

Avoid co-administration of ICLUSIG with strong CYP3A inhibitors such as clarithromycin, itraconazole, ketoconazole, nelfinavir, ritonavir, voriconazole, posaconazole, and grapefruit juice.

If co-administration of a strong CYP3A inhibitor cannot be avoided, reduce the ICLUSIG dosage

Current ICLUSIG dosage	Recommended ICLUSIG dosage with a strong CYP3A inhibitor
45 mg orally once daily	30 mg orally once daily
30 mg orally once daily	15 mg orally once daily
15 mg orally once daily	Discontinue ICLUSIG

After the strong CYP3A inhibitor has been discontinued for 3 to 5 elimination half-lives, resume the ICLUSIG dosage that was tolerated prior to initiating the strong CYP3A inhibitor.

Strong CYP3A inducers

Ponatinib is primarily metabolized by CYP3A4. Therefore, concomitant use of CYP3A inducers may decrease ponatinib plasma concentrations. Co-administration of ICLUSIG with strong CYP3A inducers (such as carbamazepine, phenobarbital, phenytoin, rifabutin, rifampicin, and St. John's Wort) should be avoided unless the benefit outweighs the possible risk of decreased ponatinib exposure.

Monitor patients for signs of reduced efficacy. Selection of concomitant medications with no or minimal CYP3A induction potential is recommended.

Important safety information

Consult the product monograph at https://takeda.info/en-ca-iclusigpm for important information about:

- Contraindications in patients with unmanaged cardiovascular risk factors, including uncontrolled hypertension; and patients who are not adequately hydrated and with uncorrected high uric acid levels.
- The most serious warnings and precautions regarding arterial occlusive events (AOEs), venous thromboembolic events (VTEs), heart failure, hemorrhage events, hepatotoxicity, myelosuppression, pancreatitis, and elevations in serum lipase or amylase.
- Other relevant warnings and precautions regarding hepatic impairment, renal impairment, co-administration with strong CYP3A inhibitors, hypertension (including hypertensive crisis), cardiac arrythmias, fluid retention, gastrointestinal perforation and impaired wound healing, myelosuppression, hepatotoxicity, pancreatitis and serum lipase, hepatitis B virus reactivation, tumour lysis syndrome, monitoring and laboratory tests, including cardiovascular status, blood pressure, complete blood count, liver function tests, serum amylase/lipase, left ventricular ejection fraction (LVEF), evidence of VTEs, comprehensive eye exams, hydration and uric acid levels, weight, phosphate, neurologic adverse events, ophthalmologic adverse events, posterior reversible encephalopathy syndrome (PRES), caution in patients driving and operating machinery, fertility, and pregnant and nursing women. Contains lactose.
- Conditions of clinical use, adverse reactions, drug interactions and dosing instructions.

The product monograph is also available by calling 1-800-268-2772.

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Reference: Takeda Canada Inc. ICLUSIG (ponatinib tablets) Product Monograph. February 24, 2025.

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Date of preparation: January 2026
PRMCDA/CA/ICL/0007E

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REVIEWED BY PAAB