

CP-CML

DOSING GUIDE

Utilize an optimized dosing strategy for adults with CP-CML[1]

INDICATIONS AND USAGE

ICLUSIG is a indicated for the treatment of adult patients with:

- Chronic phase (CP) Chronic Myeloid Leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors.
- Accelerated phase (AP) or blast phase (BP) CML for whom no other kinase inhibitors are indicated.
- T315I-positive CML (chronic phase, accelerated phase, or blast phase).

Limitations of Use: ICLUSIG is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

IMPORTANT SAFETY INFORMATION

WARNING: ARTERIAL OCCLUSIVE EVENTS, VENOUS THROMBOEMBOLIC EVENTS, HEART FAILURE, and HEPATOTOXICITY

See full prescribing information for complete boxed warning.

- Arterial occlusive events (AOEs), including fatalities, have occurred in ICLUSIG-treated patients. AOEs included fatal myocardial infarction, stroke, stenosis of large arterial vessels of the brain, severe peripheral vascular disease, and the need for urgent revascularization procedures. Patients with and without cardiovascular risk factors, including patients age 50 years or younger, experienced these events. Monitor for evidence of AOEs. Interrupt or discontinue ICLUSIG based on severity. Consider benefit-risk to guide a decision to restart ICLUSIG.
- Venous thromboembolic events (VTEs) have occurred in ICLUSIG-treated patients. Monitor for evidence of VTEs. Interrupt or discontinue ICLUSIG based on severity.
- Heart failure, including fatalities, occurred in ICLUSIG-treated patients. Monitor for heart failure and manage patients as clinically indicated. Interrupt or discontinue ICLUSIG for new or worsening heart failure.
- Hepatotoxicity, liver failure and death have occurred in ICLUSIG-treated patients. Monitor liver function tests. Interrupt or discontinue ICLUSIG based on severity.

ICLUSIG optimized dosing[1]

45 mg→15 mg for patients who achieve ≤1% BCR::ABL1[IS]

The OPTIC trial established an optimized dosing strategy in CP-CML.

Follow the 3 Rs:

Respond with 45 mg

Start at 45 mg

- Start at 30 mg orally once daily in patients taking strong CYP3A inhibitors and in patients with pre-existing hepatic impairment (Child-Pugh A, B, or C)

Reduce to 15 mg

Reduce the dose to 15 mg orally once daily after ≤1% BCR::ABL1[IS] is achieved

- Consider discontinuing ICLUSIG if hematologic response has not occurred by 3 months

Remain on 15 mg for as long as response is maintained

Patients can continue with the 15-mg, once-daily dose of ICLUSIG for as long as they maintain response

- Patients who lose response can have their dose re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily
- Patients taking 15 mg orally once daily who experience an adverse reaction can have their dose reduced to 10 mg orally once daily once the adverse reaction resolves

ICLUSIG | **One pill** | **Once a day** | **With or without food**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

Important dosing considerations[1]

- ICLUSIG is an oral, once-daily TKI
  - Tablets should be swallowed whole. Do not crush, break, cut, or chew tablets
  - ICLUSIG can be taken with or without food
  - If a dose is missed, take the next dose at the regularly scheduled time the next day
- ICLUSIG is available in 45-, 30-, 15-, and 10-mg tablet strengths
- There are recommended dosage modifications for ARs including: AOEs, VTEs, heart failure, hepatotoxicity, pancreatitis and elevated lipase, myelosuppression, and non-hematologic adverse reactions (hypertension, neuropathy, hemorrhage, fluid retention, and cardiac arrhythmias)
  - Table 1 of the full Prescribing Information contains the complete ICLUSIG dosage modifications for ARs depending on severity
  - These dosage modifications can be found within this guide, starting on page 4
- Consider the efficacy and safety of ICLUSIG in relation to the dose for your patients:
  - In PACE, the dose intensity-safety relationship indicated that there are significant increases in Grade ≥3 adverse reactions (hypertension, thrombocytopenia, pancreatitis, neutropenia, rash, ALT increase, AST increase, lipase increase, myelosuppression) over the dose range of 15 mg to 45 mg. In addition to dose, increased age and history of ischemia, hypertension, diabetes, or hypercholesterolemia were also contributory factors to a higher incidence of AOEs
  - In OPTIC, an exposure-response relationship between ponatinib exposure and molecular response rate at 12 months was observed. A relationship between higher ponatinib exposures and higher incidence of adverse reactions, including thrombocytopenia (Grade ≥3) and AOEs, was observed

ALT=alanine aminotransferase; AOE=arterial occlusive event; AP-CML=accelerated phase chronic myeloid leukemia; AR=adverse reaction; AST=aspartate aminotransferase; BCR-ABL1[IS]=BCR-ABL1 International Scale; BP-CML=blast phase chronic myeloid leukemia; CP-CML=chronic phase chronic myeloid leukemia; TKI=tyrosine kinase inhibitor.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Arterial Occlusive Events (AOEs): AOEs, including fatalities, have occurred in patients who received ICLUSIG. These included cardiovascular, cerebrovascular, and peripheral vascular events, and occurred in patients with and without cardiovascular risk factors. Monitor for evidence of AOEs. Interrupt, then resume at the same or decreased dose, or discontinue ICLUSIG based on recurrence/severity. Consider benefit-risk before restarting ICLUSIG.

Venous Thromboembolic Events (VTEs): Serious or severe VTEs have occurred in patients who received ICLUSIG, including events such as deep vein thrombosis, embolism, pulmonary embolism, superficial vein thrombosis, thrombosis, jugular vein thrombosis, superficial thrombophlebitis, retinal vein occlusion, and retinal vein thrombosis with vision loss. Monitor for evidence of VTEs. Interrupt, then resume at the same or decreased dose, or discontinue ICLUSIG based on recurrence/severity.

ICLUSIG® (ponatinib) tablets 45mg / 30mg / 15mg / 10mg

Dosage modifications for adverse reactions[1]

Recommended dosage modifications of ICLUSIG for adverse reactions are provided in Table 1 of the Prescribing Information and recommended dose reductions of ICLUSIG for adverse reactions are presented in Table 2.

Recommended dosage modifications for AOEs and VTEs[1]

Adverse Reaction	Severity	ICLUSIG Dosage Modifications
AOE: cardiovascular or cerebrovascular	Grade 1	Interrupt ICLUSIG until resolved, then resume at same dose.
	Grade 2	Interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
	Grade 3 or 4	Discontinue ICLUSIG.
AOE: peripheral vascular and other or **VTE**	Grade 1	Interrupt ICLUSIG until resolved, then resume at same dose.
	Grade 2	Interrupt ICLUSIG until Grade 0 or 1, then resume at same dose. If recurrence, interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose.
	Grade 3	Interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
	Grade 4	Discontinue ICLUSIG.

Monitor for evidence of AOEs or VTEs. Interrupt, then resume at the same or decreased dose or discontinue ICLUSIG based on recurrence/severity. For AOEs, consider benefit-risk to guide a decision to restart ICLUSIG

AOE=arterial occlusive event; VTE=venous thromboembolic event.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Heart Failure: Fatal, serious, or severe heart failure events have occurred, including increased brain natriuretic peptide (BNP), left ventricular hypertrophy, left ventricular dysfunction, congestive cardiac failure, cardiac failure, left atrial dilatation, and decreased ejection fraction. Monitor for signs or symptoms of heart failure and manage as clinically indicated. Interrupt, then resume at reduced dose, or discontinue ICLUSIG for new or worsening heart failure.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

Additional dosage modifications

Recommended dosage modifications for heart failure[1]

Severity	ICLUSIG Dosage Modifications
Grade 2 or 3	Interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.
Grade 4	Discontinue ICLUSIG.

Monitor patients for signs or symptoms consistent with heart failure and manage heart failure as clinically indicated. Interrupt, then resume at reduced dose or discontinue ICLUSIG for new or worsening heart failure

Recommended dosage modifications for hepatotoxicity[1]

Severity	ICLUSIG Dosage Modifications
AST or ALT greater than 3 times ULN	Interrupt ICLUSIG until Grade 0 or 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.

Liver function tests: Recommended to monitor at baseline, then at least monthly or as clinically indicated[1]

Recommended dosage modifications for myelosuppression[1]

Severity	ICLUSIG Dosage Modifications
ANC less than 1 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 platelet at least 75 x 10^9/L, then resume at same dose. If recurrence, interrupt ICLUSIG until resolution, then resume at next lower dose.

Complete blood count monitoring: Recommended every 2 weeks for the first 3 months and then monthly or as clinically indicated[1]

ALT=alanine aminotransferase; ANC=absolute neutrophil count; AST=aspartate aminotransferase; ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatotoxicity: ICLUSIG can cause hepatotoxicity, including liver failure and death. Fulminant hepatic failure leading to death has occurred. The most frequent hepatotoxic events were elevations of ALT, AST, GGT, bilirubin, and alkaline phosphatase, and decreased albumin and blood fibrinogen. Monitor liver function tests at baseline, then at least monthly or as clinically indicated. Interrupt, then resume at a reduced dose, or discontinue ICLUSIG based on recurrence/severity.

ICLUSIG® (ponatinib) tablets 45mg / 30mg / 15mg / 10mg

Additional dosage modifications[1]

Recommended dosage modifications for pancreatitis and elevated lipase

Severity	ICLUSIG Dosage Modifications
Serum lipase greater than 1 to 1.5 times ULN	Consider interrupting ICLUSIG until resolution, then resume at same dose.
Serum lipase greater than 1.5 to 2 times ULN, 2 to 5 times ULN and asymptomatic, or asymptomatic radiologic pancreatitis	Interrupt ICLUSIG until Grade 0 or 1 (<1.5 times ULN), then resume at next lower dose.
Serum lipase greater than 2 to 5 times ULN and symptomatic, symptomatic Grade 3 pancreatitis, or serum lipase greater than 5 times ULN and asymptomatic	Interrupt ICLUSIG until complete resolution of symptoms and after recovery of lipase elevation Grade 0 or 1, then resume at next lower dose.
Symptomatic pancreatitis and serum lipase greater than 5 times ULN	Discontinue ICLUSIG.

Monitor serum lipase: Recommended every 2 weeks for the first 2 months and then monthly or as clinically indicated. Consider additional serum lipase monitoring in patients with a history of pancreatitis or alcohol abuse.[1] Interrupt, then resume at the same or reduced dose or discontinue ICLUSIG based on severity. Evaluate for pancreatitis when lipase elevation is accompanied by abdominal symptoms

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypertension: Serious or severe hypertension, including hypertensive crisis, has occurred. Patients may require urgent intervention for hypertension with confusion, headache, chest pain, or shortness of breath. Monitor blood pressure at baseline and as clinically indicated and manage as clinically indicated. Interrupt, dose reduce, or discontinue ICLUSIG if hypertension is not medically controlled. For significant worsening, labile or treatment-resistant hypertension, interrupt ICLUSIG and consider evaluating for renal artery stenosis.

Pancreatitis: Serious or severe pancreatitis has occurred. Elevations of lipase and amylase also occurred. In the majority of cases that led to dose modification or treatment discontinuation, pancreatitis resolved within 2-3 weeks. Monitor serum lipase every 2 weeks for the first 2 months and then monthly or as clinically indicated. Consider additional serum lipase monitoring in patients with a history of pancreatitis or alcohol abuse. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on severity. Evaluate for pancreatitis when lipase elevation is accompanied by abdominal symptoms.

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Additional dosage modifications[1]

Recommended dosage modifications for other non-hematologic adverse reactions (hypertension, neuropathy, hemorrhage, fluid retention, and cardiac arrhythmias)

Severity	ICLUSIG Dosage Modifications
Grade 1	Interrupt ICLUSIG until resolved, then resume at same dose.
Grade 2	Interrupt ICLUSIG until Grade 0 or 1, then resume at same dose. If recurrence, interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose.
Grade 3 or 4	Interrupt ICLUSIG until Grade 0 or 1, then resume at next lower dose. Discontinue ICLUSIG if recurrence.

Monitor patients for evidence or symptoms of hypertension, neuropathy, hemorrhage, fluid retention, and cardiac arrhythmias while on ICLUSIG. Manage patients as clinically indicated. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on recurrence/severity. Refer to Section 5 (5.5, 5.8, 5.10, 5.11, 5.12) of the full Prescribing Information for the monitoring recommendations for these specific warnings

Dose reductions

Recommended dose reductions for adverse reactions

Dose Reduction	Dosage for Patients with CP-CML	Dosage for Patients with AP-CML, BP-CML, and Ph+ ALL Monotherapy
First	30 mg orally once daily	30 mg orally once daily.
Second	15 mg orally once daily	15 mg orally once daily.
Third	10 mg orally once daily	Permanently discontinue ICLUSIG in patients unable to tolerate 15 mg orally once daily.
Subsequent Reduction	Permanently discontinue ICLUSIG in patients unable to tolerate 10 mg orally once daily.	

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Increased Toxicity in Newly Diagnosed Chronic Phase CML: In a prospective randomized clinical trial in the first-line treatment of newly diagnosed patients with CP-CML, single agent ICLUSIG increased the risk of serious adverse reactions. The trial was halted for safety. ICLUSIG is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML.

Neuropathy: Peripheral and cranial neuropathy occurred in ICLUSIG-treated patients, including Grade 3 or 4 events. Monitor for symptoms such as hypoesthesia, hyperesthesia, paresthesia, discomfort, a burning sensation, neuropathic pain, or weakness. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on recurrence/severity.

ICLUSIG® (ponatinib) tablets 45mg / 30mg / 15mg / 10mg

Considerations for strong CYP3A inhibitors and inducers[1]

Strong CYP3A inhibitors



Avoid coadministration of strong CYP3A inhibitors during treatment with ICLUSIG

Coadministration increases ponatinib plasma concentrations, which may increase the risk of ICLUSIG adverse reactions



If coadministration of a strong CYP3A inhibitor cannot be avoided, reduce the ICLUSIG once-daily dose from:

- **45 mg→30 mg**
- **30 mg→15 mg**
- **15 mg→10 mg**

If the patient's dose has already been reduced to 10 mg orally, once daily, avoid coadministration of ICLUSIG with a strong CYP3A inhibitor



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 CYPA3 inducers

Avoid coadministration with a strong CYP3A inducer unless benefit outweighs the risk of decreased ponatinib exposure. Monitor patients for reduced efficacy. Selecting concomitant medication with no or minimal CYP3A induction potential is recommended.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Ocular Toxicity: Serious or severe ocular toxicities leading to blindness and blurred vision have occurred. The most frequent ocular toxicities were dry eye, blurred vision, and eye pain. Retinal toxicities included retinal vein occlusion, retinal hemorrhage, age-related macular degeneration, arteriosclerotic retinopathy, retinal vascular disorder, macular edema, and vitreous floaters. Conduct comprehensive eye exams at baseline and periodically during treatment.

Hemorrhage: Fatal and serious hemorrhages have occurred. Intracranial hemorrhage, gastrointestinal hemorrhage, and subdural hematoma were the most frequently reported serious hemorrhages. Most hemorrhages occurred in patients with Grade 4 thrombocytopenia. Monitor for hemorrhage and manage as clinically indicated. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on recurrence/severity.

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Recommendations for specific populations[1]

Pregnancy

Based on findings in animals and its mechanism of action, ICLUSIG can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus.

Lactation

Because of the potential for serious adverse reactions in the breastfed child from ICLUSIG, advise women not to breastfeed during treatment with ICLUSIG and for 1 week following the last dose.

Females and males of reproductive potential

ICLUSIG can cause fetal harm when administered to pregnant women. Verify the pregnancy status of females of reproductive potential prior to initiating ICLUSIG. Advise females of reproductive potential to use effective contraception during treatment with ICLUSIG and for 3 weeks after the last dose. Advise females of reproductive potential of the potential for reduced fertility from ICLUSIG.

Pediatric use

Safety and effectiveness of ICLUSIG have not been established in pediatric patients.

Geriatric use

Patients aged 65 years or older are more likely to experience adverse reactions including vascular occlusion, decreased platelet count, peripheral edema, increased lipase, dyspnea, asthenia, muscle spasms, and decreased appetite. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Hepatic impairment

Patients with hepatic impairment are more likely to experience adverse reactions compared to patients with normal hepatic function. Reduce the starting dose of ICLUSIG for patients with pre-existing hepatic impairment (Child-Pugh A, B, or C). The safety of multiple doses, or doses higher than 30 mg, has not been studied in patients with hepatic impairment.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Fluid Retention: Fatal and serious events, including one instance of fatal brain edema and serious events of pleural effusion, pericardial effusion, and angioedema have occurred. The most frequent occurrences of fluid retention in patients who received ICLUSIG were peripheral edema, pleural effusion, hydrothorax, pericardial effusion, and peripheral swelling. Monitor for fluid retention and manage as clinically indicated. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on recurrence/severity.

Cardiac Arrhythmias: Cardiac arrhythmias, including ventricular and atrial arrhythmias, tachycardia, bradycardia, cardio-respiratory arrest, syncope, atrial fibrillation, and supraventricular tachycardia, have occurred, including some patients with serious or severe (Grade 3 or 4) events leading to hospitalization. Monitor for signs and symptoms suggestive of slow heart rate (fainting, dizziness) or rapid heart rate (chest pain, palpitations, or dizziness) and manage patients as clinically indicated. Interrupt, then resume at the same or reduced dose, or discontinue ICLUSIG based on recurrence/severity.

ICLUSIG®
(ponatinib) tablets
45mg / 30mg / 15mg / 10mg

Available doses of ICLUSIG[1]

Strength	NDC number	Description	Presentation
10 mg	63020-536-30	Oval, white to off-white, biconvex film-coated tablets with debossed "NZ" on one side and plain on the other side	30 tablets in a wide-mouth white high density polyethylene (HDPE) bottle with a desiccant canister and induction-sealed, child-resistant closure.
15 mg	63020-535-30	Round, white, biconvex film-coated tablets with debossed "A5" on one side and plain on the other side	30 tablets in a wide-mouth white HDPE bottle with a desiccant canister and induction-sealed, child-resistant closure.
	63020-535-60		60 tablets in a wide-mouth white HDPE bottle with a desiccant canister and induction-sealed, child-resistant closure.
30 mg	63020-533-30	Round, white, biconvex film-coated tablets with debossed "C7" on one side and plain on the other side	30 tablets in a wide-mouth white HDPE bottle with a desiccant canister and induction-sealed, child-resistant closure.
45 mg	63020-534-30	Round, white, biconvex film-coated tablets with debossed "AP4" on one side and plain on the other side	30 tablets in a wide-mouth white HDPE bottle with a desiccant canister and induction-sealed, child-resistant closure.

All tablet strengths of ICLUSIG are taken orally, once daily, with or without food[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Myelosuppression: Grade 3 or 4 neutropenia, thrombocytopenia, and anemia have occurred. Obtain complete blood counts every 2 weeks for the first 3 months and then monthly or as clinically indicated. Interrupt ICLUSIG if ANC <1 × 10^9/L or platelets <50 × 10^9/L, and resume when ANC ≥1.5 × 10^9/L and platelets ≥75 × 10^9/L, at same or reduced dose.

Tumor Lysis Syndrome (TLS): Serious TLS has occurred. Ensure adequate hydration and treat elevated uric acid prior to initiating ICLUSIG.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS has been reported. Patients can present with hypertension, seizure, headache, decreased alertness, altered mental functioning, vision loss, and other visual and neurological disturbances. MRI is necessary to confirm diagnosis. Interrupt ICLUSIG until resolution. The safety of resumption of ICLUSIG upon resolution of RPLS is unknown.

Impaired Wound Healing and Gastrointestinal Perforation: Impaired wound healing occurred in patients receiving ICLUSIG. Withhold ICLUSIG for at least 1 week before elective surgery and for at least 2 weeks after major surgery until adequate wound healing. Gastrointestinal perforation or fistula have occurred. Permanently discontinue ICLUSIG in patients with gastrointestinal perforation.

Embryo-Fetal Toxicity: ICLUSIG can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to the fetus. Females of reproductive potential should use effective contraception during treatment with ICLUSIG and for 3 weeks after the last dose.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

The most common adverse reactions (occurring in >20% of patients) are:

- ICLUSIG as a single agent: rash and related conditions, arthralgia, abdominal pain, fatigue, headache, constipation, hypertension, dry skin, hepatotoxicity, fluid retention and edema, pyrexia, pancreatitis/lipase elevation, nausea, hemorrhage, anemia, AOEs, and cardiac arrythmias. The most common Grade 3 or 4 laboratory abnormalities (>20%) are platelet count decreased, neutrophil cell count decreased, and white blood cell decreased.
- ICLUSIG in combination with chemotherapy: hepatotoxicity, arthralgia, rash and related conditions, headache, pyrexia, abdominal pain, constipation, fatigue, nausea, oral mucositis, hypertension, pancreatitis/lipase elevation, neuropathy peripheral, hemorrhage, febrile neutropenia, fluid retention and edema, vomiting, paresthesia, and cardiac arrhythmias. The most common Grade 3 or 4 laboratory abnormalities (>20%) are decreased white blood cell count, decreased neutrophil cell count, decreased platelet count, decreased lymphocyte cell count, decreased hemoglobin, increased lipase and increased alanine aminotransferase.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals at 1-844-817-6468 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Avoid coadministration or reduce ICLUSIG dose if coadministration cannot be avoided.

Strong CYP3A Inducers: Avoid coadministration.

Reference:

1. ICLUSIG (ponatinib) [prescribing information]. Cambridge, MA: Takeda Pharmaceuticals U.S.A., Inc. 10/2025.

ICLUSIG®
(ponatinib) tablets
45mg / 30mg / 15mg / 10mg



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45mg / 30mg / 15mg / 10mg

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed during treatment with ICLUSIG and for 1 week following last dose.

Females and Males of Reproductive Potential: Verify pregnancy status of females of reproductive potential prior to initiating ICLUSIG. Ponatinib may impair fertility in females, and it is not known if these effects are reversible.

Pre-existing Hepatic Impairment: For patients with CP-CML, AP-CML, BP-CML, and Ph+ ALL receiving monotherapy, reduce the starting dose of ICLUSIG to 30 mg orally once daily for patients with pre-existing hepatic impairment. For patients with newly diagnosed Ph+ ALL, no dosage adjustment is recommended when administering ICLUSIG to patients with mild hepatic impairment.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning.

Visit ICLUSIG.com/hcp for more information on ICLUSIG.



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