The Ray of Hope for
All Known Single Point Mutations

ICLUSIG®
(ponatinib) tablets
45 mg, 15 mg

Iclusig® is indicated in adult patients with[1]:

- CP-, AP- or BP-CML resistant to dasatinib or nilotinib
- CP-, AP- or BP-CML intolerant to dasatinib or nilotinib and subsequent treatment with imatinib is not clinically appropriate
- Ph+ ALL resistant to dasatinib
- Ph+ ALL intolerant to dasatinib and subsequent treatment with imatinib is not clinically appropriate
- T315I+ CML or Ph+ ALL

Iclusig® is Recommended by Multiple International Guidelines

	CML	Ph+ ALL
NCCN Guidelines[2,3] (National Comprehensive Cancer Network®)	Ponatinib is a treatment option for patients with a T315I mutation and/or CP-CML with resistance or intolerance to at least 2 prior TKIs or for patients with AP-CML or BP-CML for whom no other TKI is indicated.	Ponatinib has activity against T315I mutations and is effective in treating patients with resistant or progressive disease on multiple TKIs
ESMO Guidelines[4,5] (ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE)	Ponatinib should be considered the agent of choice in patients with CML and T315I mutation, and in instances where other TKIs are not indicated. No other commercially available TKIs have activity against this mutated BCR-ABL.	In Ph+ ALL, the third-generation TKI ponatinib is currently the only option in patients progressing with the T315I mutation.

Iclusig® is Recommended for BCR-ABL1 Resistance Mutations

ELN European LeukemiaNet

ELN 2020 Recommendations for Treating CML[6]

Resistance Mutations	Recommended TKI(s)
T315I	**Ponatinib**
F317L/V/I/C, T315A	Nilotinib, Bosutinib, or **Ponatinib**
V299L	Nilotinib or **Ponatinib**
Y253H, E255V/K, F359V/I/C	Dasatinib, Bosutinib, or **Ponatinib**

AP-CML: accelerated phase chronic myeloid leukemia; BP-CML: blast phase chronic myeloid leukemia; CML: chronic myeloid leukemia; CP-CML: chronic phase chronic myeloid leukemia; ELN: European LeukemiaNet; ESMO: European Society for Medical Oncology; NCCN: National Comprehensive Cancer Network; Ph+ ALL: Philadelphia chromosome positive acute lymphoblastic leukemia; TKI: tyrosine kinase inhibitor.

References: 1. Iclusig® (Ponatinib) Hong Kong Prescribing Information revised Jan 2019. 2. NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia. National Comprehensive Cancer Network. Available at http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Version 3.2021 — January 13, 2021; Accessed: July 8, 2021. 3. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. National Comprehensive Cancer Network. Available at http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Version 1.2021 — April 6, 2021; Accessed: July 8, 2021. 4. Hochhaus A, et al. Chronic myeloid leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017 Jul 1;28(suppl_4):iv41-iv51. 5. Hoelzer D, et al. Acute lymphoblastic leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2016 Sep;27(suppl 5):v69-v82. 6. Hochhaus A, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. Leukemia. 2020 Apr;34(4):966-984.

Abbreviated Prescribing Information.
ICLUSIG® (ponatinib) 15 mg/45 mg tablets. **Indication:** in adult patients with (1) chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation; and (2) Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation. **Dosage:** Recommended starting dose: 45 mg once daily. Assess the patient's cardiovascular status before treatment initiation. Refer to the package insert for dose modification for management of toxicities. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Warnings and precautions:** Risk of myelosuppression; a complete blood count should be performed every 2 weeks for the first 3 months and then monthly or as clinically indicated. Monitoring for evidence of arterial occlusion and thromboembolism; interrupt treatment in such events. If decreased vision or blurred vision occurs, perform an ophthalmic examination (including fundoscopy). Reports of treatment-emergent hypertension; urgent clinical intervention required for hypertension associated with confusion, headache, chest pain, or shortness of breath. Discontinue treatment in patients developing serious heart failure. Caution recommended in patients with a history of pancreatitis or alcohol abuse. Patients with severe hypertriglyceridemia should be appropriately managed to avoid pancreatitis. Liver function tests should be performed prior to treatment initiation and monitored periodically, as clinically indicated. Interrupt treatment and evaluate patients for serious or severe haemorrhage. Monitor for active HBV infection in HBV carriers throughout therapy and for several months after treatment. Interrupt treatment in the event of posterior reversible encephalopathy syndrome. Caution recommended in patients with hepatic/renal impairment. Not advised in pregnancy; only used when clearly necessary. Stop breastfeeding during treatment & use effective contraception during treatment. **Drug interactions:** Caution in concomitant use with CYP3A inhibitors/inducers, transporter substrates (e.g. P-gp and BCRP) & anti-clotting agents in patients who may be at risk of bleeding events. **Adverse reactions:** pneumonia, pancreatitis, abdominal pain, atrial fibrillation, pyrexia, myocardial infarction, peripheral arterial occlusive disease, anaemia, angina pectoris, platelet count decreased, febrile neutropenia, hypertension, coronary artery disease cardiac failure congestive, cerebrovascular accident, sepsis, cellulitis, acute kidney injury, UTI and lipase increased. **Please see full Prescribing information for details.** (HKOP_ICLUSIG API_HK Revised May 2020)

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