Iclusig® (ponatinib) – Expanded indication

- On March 19, 2024, Takeda announced the FDA approval of Iclusig (ponatinib), in combination with chemotherapy, for treatment of adult patients with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).
    - This indication is approved under accelerated approval based on minimal residual disease (MRD)-negative complete remission (CR) at the end of induction. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s).
- Iclusig is also approved as monotherapy in Ph+ ALL for whom no other kinase inhibitors are indicated or T315I-positive Ph+ ALL.
- In addition to Ph+ ALL, Iclusig is approved for different uses for chronic myeloid leukemia (CML). This includes:
    - Chronic phase CML with resistance or intolerance to at least two prior kinase inhibitors
    - Accelerated phase or blast phase CML for whom no other kinase inhibitors are indicated
    - T315I-positive CML (chronic phase, accelerated phase, or blast phase).
- The approval of Iclusig for the expanded indication was based on PhALLCON, a randomized, active-controlled, open-label study in 245 patients with newly diagnosed Ph+ ALL. Patients were randomized to receive either Iclusig or imatinib in combination with chemotherapy (imatinib in combination with chemotherapy is an unapproved regimen in adult patients). Efficacy was based on the MRD-negative CR rate at the end of induction.
    - MRD-negative CR at the end of induction was achieved in 30% of patients in the Iclusig arm vs. 12% of patients in the imatinib arm (risk difference 0.18, 95% CI: 0.08, 0.28; p = 0.0004).
- Iclusig carries a boxed warning for arterial occlusive events, venous thromboembolic events, heart failure, and hepatotoxicity.
- The most common adverse reactions (> 20%) with Iclusig, in combination with chemotherapy, were hepatic dysfunction, 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%) with Iclusig, in combination with chemotherapy, were decreased white blood cell count, decreased neutrophil cell count, decreased platelet count, decreased lymphocyte cell count, decreased hemoglobin, increased lipase, and increased alanine aminotransferase.
- The recommended starting dose of Iclusig (in combination with chemotherapy) for the treatment of newly diagnosed Ph+ ALL is 30 mg orally once daily with a reduction to 15 mg orally once daily upon achievement of MRD-negative CR at the end of induction. Iclusig should be continued in combination with chemotherapy for up to 20 cycles until loss of response or unacceptable toxicity.

Continued . . .

— Refer to the Iclusig drug label for dosing for all its other uses and indications.

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