Iclusig® (ponatinib) – Expanded indication

- On December 18, 2020, Takeda announced the FDA approval of Icusig (ponatinib), 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.
    - Iclusig was previously approved in patients with CP CML for whom no other tyrosine kinase inhibitor therapy are indicated.
- Iclusig is also approved for the treatment of adult patients with:
    - Accelerated phase or blast phase CML or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other kinase inhibitors are indicated.
    - T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL.
- The updated drug label includes an optimized, response-based Iclusig dosing regimen in CP CML with a daily starting dose of 45 mg and, upon achieving ≤ 1% BCR-ABL1^{IS}, dose reduction to 15 mg.
    - BCR-ABL1 is an abnormal tyrosine kinase that is expressed in CML and Ph+ ALL.
- The approval of Iclusig for the expanded indication was based on data from the OPTIC trial, as well as five-year data from the PACE trial. OPTIC was a dose-optimization study in patients with CP CML whose disease was considered to be resistant or resistant/intolerant to at least 2 prior kinase inhibitors or who had the T315I mutation. The major efficacy outcome measure was ≤ 1% BCR-ABL1^{IS} at 12 months.
    - At 12 months and in the 93 patients initiating therapy with Iclusig 45 mg daily, 42% (95% CI: 32, 53) achieved ≤ 1% BCR-ABL1^{IS}.
- PACE was a single-arm, multi-cohort, open-label study in patients with CML and Ph+ ALL whose disease was considered to be resistant or intolerant to a prior kinase inhibitor. A total of 267 patients with CP CML were eligible for the efficacy analysis. The major efficacy outcome measure for patients with CP-CML was major cytogenetic response (MCyR).
    - By 12 months, 55% (95% CI 49, 62) achieved MCyR with Iclusig.
- Iclusig carries a boxed warning for arterial occlusive events, venous thromboembolic events, heart failure, and hepatotoxicity.
- The recommended starting dosage of Iclusig for CP CML is 45 mg orally once daily with a reduction to 15 mg orally once daily upon achievement of ≤ 1% BCR-ABL1^{IS}. 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.
    - Iclusig should be continued until loss of response at the re-escalated dose or unacceptable toxicity.
    - Iclusig discontinuation should be considered if hematologic response has not occurred by 3 months.

Continued . . .

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

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