Acatinib

Acalabrutinib INN

Composition
Acatinib 100 Capsule: Each capsule contains Acalabrutinib INN 100 mg.

Pharmacology
Acalabrutinib is a small-molecule inhibitor of Bruton tyrosine kinase (BTK). Acalabrutinib and its active metabolite, ACP-5862, form a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B cell antigen receptor (BCR) and cytokine receptor pathways. In B cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. In nonclinical studies, acalabrutinib inhibited BTK-mediated activation of downstream signaling proteins CD86 and CD69 and inhibited malignant B-cell proliferation and tumor growth in mouse xenograft models.

Indications
Acalabrutinib is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy and for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Dosage and Administration
For patients with MCL, CLL, or SLL, the recommended dosage of Acalabrutinib is 100 mg taken orally approximately every 12 hours until disease progression or unacceptable toxicity.Start Acalabrutinib at Cycle 1 (each cycle is 28 days). Start obinutuzumab at Cycle 2 for a total of 6 cycles and refer to the obinutuzumab prescribing information for recommended dosing. Administer Acalabrutinib prior to obinutuzumab when given on the same day.

Adverse Reactions
- Serious and Opportunistic Infections
- Hemorrhage
- Cytopenias
- Second Primary Malignancies
- Atrial Fibrillation and Flutter

Warnings and Precautions
Serious and Opportunistic Infections
Fatal and serious infections, including opportunistic infections, have occurred in patients with hematologic malignancies treated with Acalabrutinib.
Hemorrhage
Fatal and serious hemorrhagic events have occurred in patients with hematologic malignancies treated with Acalabrutinib.
Cytopenias
Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with Acalabrutinib. Grade 4 neutropenia developed in 12% of patients. Monitor complete blood counts regularly during treatment. Interrupt treatment, reduce the dose, or discontinue treatment as warranted.
Second Primary Malignancies
Second primary malignancies, including skin cancers and other solid tumors, occurred in 12% of 1029 patients exposed to Acalabrutinib in clinical trials. The most frequent second primary malignancy was skin cancer, reported in 6% of patients. Monitor patients for skin cancers and advise protection from sun exposure.

Contraindications
None.

Use in Specific Populations
Use in Pregnancy
Acalabrutinib may cause fetal harm and dystocia when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk.
Lactation
No data are available regarding the presence of Acalabrutinib or its active metabolite in human milk, its effects on the breastfed child, or on milk production. Acalabrutinib and its active metabolite were present in the milk of lactating rats. Due to the potential for adverse reactions in a breastfed child from Acalabrutinib, advise lactating women not to breastfeed while taking Acalabrutinib and for 2 weeks after the last dose.
Pediatric Use
The safety and efficacy of Acalabrutinib in pediatric patients have not been established.
Geriatric Use
Patients with CLL or MCL in clinical trials of Acalabrutinib, 68% were 65 years of age or older, and 24% were 75 years of age or older. Among patients 65 years of age or older, 59% had Grade 3 or higher adverse reactions and 39% had serious adverse reactions. Among patients younger than age 65, 45% had Grade 3 or higher adverse reactions and 25% had serious adverse reactions. No clinically relevant differences in efficacy were observed between patients ≥ 65 years and younger.

Storage
Do not store above 25ºC. Protect from light. Keep out of reach of children.

Packaging
Acatinib 100 Capsule: Each HDPE container of Acatinib 100 contains 60's capsule, a silica gel desiccant and polyester coil with a child resistant closure.

Manufactured by
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh

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