BlueCross BlueShield Federal Employee Program

ZYDELIG (idelalisib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Zydelig (idelalisib) is an inhibitor of phosphatidylinositol 3-kinase (PI3Kδ), which is expressed in normal and malignant B-cells. Zydelig induces apoptosis and inhibits proliferation of cell lines derived from malignant B-cells and in primary tumor cells. Zydelig inhibits several cell signaling pathways, including B-cell receptor (BCR) signaling and the CXCR4 and CXCR5 signaling, which are involved in trafficking and homing of B-cells to the lymph nodes and bone marrow (1).

Regulatory Status

FDA-approved indication: Zydelig is a kinase inhibitor indicated for the treatment of patients with (1):

1. Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.

Off-Label Uses: (2-3)

1. Relapsed or refractory CLL as a single agent
2. Relapsed or refractory SLL as a single agent

Limitations of Use: (1)

Zydelig is not indicated and is not recommended for first-line treatment of any patient.

Zydelig carries a boxed warning alerting patients and health care professionals of fatal and serious toxicities including liver toxicity, diarrhea, and colon inflammation (colitis); lung inflammation (pneumonitis); and intestinal perforation. Physicians should monitor for development of these conditions and interrupt and then reduce or discontinue Zydelig as clinically appropriate (1).

Physicians should monitor hepatic function prior to and during treatment, as clinically indicated, in all patients every 2 weeks for the first 3 months of treatment, every 4 weeks for the next 3 months, then every 1 to 3 months thereafter. If the ALT or AST rises above 3 times the upper limit of normal, the hepatic function should be monitored weekly until resolved. Withhold Zydelig if the ALT or AST is greater than 5 times the upper limit of normal, and continue to monitor AST, ALT and total bilirubin weekly until the abnormality is resolved. Concurrent use of Zydelig with other drugs that may cause liver toxicity should be avoided. Zydelig should be discontinued with recurrent hepatotoxicity (1).

Treatment-emergent Grade 3 or 4 neutropenia may occur in patients treated with Zydelig. Blood counts should be monitored at least every two weeks for the first 6 months of therapy, and at least weekly in patients while neutrophil counts are less than 1.0 Gi/L (1).

Zydelig may cause fetal harm when administered to a pregnant woman. If Zydelig is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus (1).

Treatment should be continued until disease progression or unacceptable toxicity. The optimal and safe dosing regimen for patients who receive treatment longer than several months is unknown (1).

Safety and effectiveness of Zydelig in children less than 18 years of age have not been established (1).

Summary

Zydelig is indicated, in combination with rituximab, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) for whom rituximab alone would be considered appropriate therapy due to other co-morbidities. Zydelig is also used off-label for the treatment of patients with refractory CLL and for relapsed or refractory small lymphocytic lymphoma (SLL). Zydelig carries a boxed warning alerting patients and health care professionals of fatal and serious toxicities including liver toxicity, diarrhea, and colon inflammation (colitis); lung inflammation (pneumonitis); and intestinal perforation. Physicians should monitor for development of these conditions and interrupt and then reduce or discontinue Zydelig as clinically appropriate. Safety and effectiveness of Zydelig in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Zydelig while maintaining optimal therapeutic outcomes.

References

1. Zydelig [package insert]. Foster City, CA: Gilead Sciences, Inc.; February 2024.
2. NCCN Drugs & Biologics Compendium®. Idelalisib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 14, 2025.