BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.21.049

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	August 22, 2014
Subject:	Zydelig	**Page:**	1 of 6

Last Review Date: March 8, 2024

Zydelig

Description

Zydelig (idelalisib)

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).

Related policies
Copiktra

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zydelig may be considered **medically necessary** if the conditions indicated below are met.

Zydelig may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsed or refractory chronic lymphocytic leukemia (CLL)
2. Relapsed or refractory small lymphocytic lymphoma (SLL)

AND ALL of the following:

a. Prior therapy with an alkylator and rituximab therapy
b. Prescriber agrees to monitor hepatic function prior to and during treatment and to interrupt, reduce, or discontinue Zydelig as clinically appropriate
c. Prescriber agrees to monitor for the development of severe diarrhea, colitis, pneumonitis, and intestinal perforation and to interrupt, reduce, or discontinue Zydelig as clinically appropriate

Prior – Approval *Renewal* Requirements

Age 18 years of age and older

Diagnoses

Patient must have **ONE** of the following:

1. Relapsed or refractory chronic lymphocytic leukemia (CLL)
2. Relapsed or refractory small lymphocytic lymphoma (SLL)

AND ALL of the following:

a. Prescriber agrees to monitor hepatic function prior to and during treatment and to interrupt, reduce, or discontinue Zydelig as clinically appropriate
b. Prescriber agrees to monitor for the development of severe diarrhea, colitis, pneumonitis, and intestinal perforation and to interrupt, reduce, or discontinue Zydelig as clinically appropriate

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

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 2022.
2. NCCN Drugs & Biologics Compendium®. Idelalisib 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

Policy History

Date	Action
August 2014	Addition to PA
September 2014	Annual review and update
December 2014	Annual editorial review and reference update
December 2015	Annual review
June 2016	Annual editorial review and reference update Removal of patient must have a current prior authorization for Rituxan (rituximab) and must be used in combination with Rituxan (rituximab) from CLL. Removal of patient has received two prior systemic therapies from SLL. Removal of no disease progression or unacceptable toxicity from renewal. Addition of indications: primary cutaneous B-cell lymphoma with **ONE** of the following subtypes: primary cutaneous marginal zone lymphoma, or follicle center lymphoma; recurrent or progressive gastric mucosa associated lymphoid tissue (MALT) lymphoma; refractory or progressive non-gastric MALT lymphoma; refractory or progressive splenic marginal zone lymphoma Policy change from 5.04.49 to 5.21.49
September 2016	Annual review
June 2017	Annual editorial review and reference update
March 2018	Annual editorial review and reference update Addition of the requirement of “prior therapy with an alkylator and rituximab therapy” per SME Reworded the Primary cutaneous B-cell lymphoma indication
June 2018	Annual editorial review
March 2019	Annual review and reference update
June 2020	Annual review and reference update
June 2021	Annual review and reference update
June 2022	Per PI update removal of indication: relapsed follicular B-cell non-Hodgkin lymphoma, Per NCCN removal of indications: primary cutaneous marginal zone lymphoma, or follicle center lymphoma; recurrent or progressive gastric mucosa associated lymphoid tissue (MALT) lymphoma; refractory or progressive non-gastric MALT lymphoma; refractory or progressive splenic marginal zone lymphoma
September 2022	Annual review and reference update
December 2022	Annual review and reference update
March 2023	Annual review and reference update

March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.