

PHARMACY COVERAGE GUIDELINE

ZYDELIG® (idelalisib) oral tablet Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**

Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacypercet@azblue.com.

Medical Necessity Requirements for ZYDELIG (idelalisib)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication

- Relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, for individuals where rituximab alone is appropriate due to comorbidities
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

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Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- Negative pregnancy test for women of childbearing potential
- Serum liver tests: alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 1

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (If available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No FDA labeled contraindications such as anaphylaxis or history of toxic epidermal necrolysis
- No significant interacting drugs such as strong cytochrome P450 3A (CYP3A) inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin)
- Will not be used with another phosphatidylinositol 3 kinase (PI3K) inhibitor (e.g., Copiktra (duvelisib), Piqray (alpelisib), Itovebi (inavolisib), Aliqopa (copanlisib))
- Will not be used with drugs that cause liver toxicity
- Will not be used with drugs that cause diarrhea

Additional Requirements

- Will not be used as first line therapy for any diagnosis including CLL, small lymphocytic lymphoma (SLL), follicular lymphoma (FL), or other indolent non Hodgkin lymphomas
- Will not be used with bendamustine and rituximab, or in combination with rituximab for FL, SLL, or other indolent non Hodgkin lymphomas
- Individual is on prophylaxis for *Pneumocystis jiroveci* during treatment
- Will not be used with sensitive 3A4 substrates (e.g., alprazolam, atorvastatin, amlodipine, budesonide, buspirone, felodipine, lovastatin, midazolam, simvastatin, triazolam, others)

Documentation Requirements

- A completed request form must be submitted including:
 - Chart notes
 - Lab results (ALT, AST, bilirubin, pregnancy test, ECOG status)
 - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year
-

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification

- Continues to be seen by a physician specializing in or is in consultation with an Oncologist

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Clinical Response

- Documented evidence of efficacy, disease stability, and/or improvement
- No significant unacceptable adverse drug reactions that may exclude continued use

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Recurrent hepatotoxicity or aspartate transferase greater than 20 times upper limit of normal or bilirubin greater than 10 times upper limit of normal
- Life threatening diarrhea or colitis
- Symptomatic pneumonitis or organizing pneumonia
- *Pneumocystis jiroveci* pneumonia infection
- Intestinal perforation
- Stevens Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms
- Other severe or life threatening cutaneous reactions
- Serious hypersensitivity or anaphylaxis
- Other severe or life threatening cutaneous reactions
- Serious hypersensitivity or anaphylaxis
- Any recurrence of other severe or life threatening drug reaction

Additional Requirements

- No use with strong cytochrome P450 3A (CYP3A) inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin)
- No use with another phosphatidylinositol 3 kinase (PI3K) inhibitor (e.g., Copiktra (duvelisib), Piqray (alpelisib), Itovebi (inavolisib), Aliqopa (copanlisib))

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year
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Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

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1. Off-Label Use of Non-Cancer Medications
 2. Off-Label Use of Cancer Medications
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Description:

Zydelig (idelalisib) is indicated for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) used in combination with rituximab in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.

Limitations of Use:

- Zydelig is not indicated and is not recommended for first-line treatment of any patient, including patients with CLL, small cell lymphocytic lymphoma (SLL), follicular lymphoma (FL), and other indolent non-Hodgkin lymphomas.
- Zydelig is not indicated and is not recommended in combination with bendamustine and rituximab, or in combination with rituximab for the treatment of patients with FL, SLL, and other indolent non-Hodgkin's lymphomas

Zydelig (idelalisib) is a kinase inhibitor that targets malignant B cells. It is an inhibitor of phosphatidylinositol 3-kinase (PI3K δ), which is expressed in normal and malignant B-cells. Idelalisib induces apoptosis and inhibits proliferation in cell lines derived from malignant B-cells and in primary tumor cells. It 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. Treatment of lymphoma cells with idelalisib resulted in inhibition of chemotaxis and adhesion, and reduced cell viability.

CLL is characterized by progressive accumulation of small, mature lymphocytic leukemia cells in the peripheral blood, bone marrow, and lymphoid tissue. In CLL the abnormal lymphocytes are predominantly found in the blood.

Deletions in chromosomes 13q, 17p, and 11q; and trisomy 12 are recognized as negative prognostic factors of the disease affecting prognosis and drug resistance. The 17p deletion is associated with poor outcomes that include a short treatment-free interval, short survival, and poor response to chemotherapy. This deletion is more common in patients who have received prior therapy. Choice of therapy is made based on prognosis, age, comorbid conditions, and cytogenetic abnormalities.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

Resources:

Zydelig (idelalisib) tab product information, revised by Gilead Sciences, Inc. 02/2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 24, 2025.

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2026 – Updated October 10, 2025. Available at <https://www.nccn.org>. Accessed November 11, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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