PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/21/2016**
LAST REVIEW DATE:	**2/17/2022**
LAST CRITERIA REVISION DATE:	**2/17/2022**
ARCHIVE DATE:	

ZYDELIG® (idelalisib) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Zydelig (idelalisib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Combination therapy with rituximab, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL), in combination with rituximab, for whom rituximab alone would be considered appropriate therapy due to other co-morbidities

     b. Relapsed follicular B-cell non-Hodgkin lymphoma (FL) who have received at least two prior systemic therapies and **will not be used** in combination with bendamustine and/or rituximab

     c. Relapsed small lymphocytic lymphoma (SLL) who have received at least two prior systemic therapies

     d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. **Will not be used** as first-line therapy for any of the above diagnoses described in criteria #3

  5. Individual is on prophylaxis for *Pneumocystis jiroveci* during treatment

  6. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Negative pregnancy test in a woman of childbearing potential
     b. Serum liver tests (ALT, AST, and bilirubin)
     c. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-1

  7. There are **NO** FDA-label contraindications, such as
     a. Toxic epidermal necrolysis with any drug

  8. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Zydelig (idelalisib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

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2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. Documented evidence of efficacy, disease stability and/or improvement
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Recurrent hepatotoxicity or AST > 20 times upper limit of normal (ULN) or bilirubin > 10 ULN
        ii. Life-threatening diarrhea
        iii. Symptomatic pneumonitis
        iv. *Pneumocystis jiroveci* pneumonia infection
        v. Intestinal perforation
        vi. Stevens-Johnson syndrome, toxic epidermal necrolysis, or drug rash with eosinophilia and systemic symptoms (DRESS)
        vii. Other severe or life-threatening cutaneous reactions
        viii. Serious hypersensitivity or anaphylaxis
        ix. Any recurrence of other severe or life-threatening drug reaction

5. There are no significant interacting drugs

Renewal duration: 12 months

- 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:

    1. **Off-Label Use of Non-cancer Medications**

    2. **Off-Label Use of Cancer Medications**

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; it is also indicated for relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies; and it is indicated for relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies. It is not indicated and is not recommended for first line therapy for any patient.

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Zydelig (idelalisib) is a kinase inhibitor that targets malignant B cells. It is an inhibitor of phosphatidylinositol 3-kinase (PI3Kδ), 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/SLL are different expressions of the same disease and are managed in the same way. CLL and SLL are 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, while in SLL the bulk is found in the lymph nodes, bone marrow, and other lymphoid tissues.

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.

Non-Hodgkin lymphoma (NHL) consists of a diverse group of malignant neoplasms variously derived from B-cell progenitors, T-cell progenitors, mature B-cells, mature T-cells, or (rarely) natural killer (NK) cells. Follicular lymphoma (FL) is the most common slow growing (indolent) form of NHL. Common symptoms of FL include enlargement of the lymph nodes in the neck, underarms, abdomen, or groin, as well as fatigue, shortness of breath, night sweats, and weight loss. Some patients with FL develop a transformed lymphoma, which is often more aggressive and usually requires more intensive treatments. FL is characterized by multiple relapses after treatment, although many can go into a remission.

Resources:

Zydelig (idelalisib) product information, revised by Gilead Sciences, Inc. 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 06, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 5.2021 – Updated September 22,2021. Available at https://www.nccn.org. Accessed December 02, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2022 – Updated September 08, 2021. Available at https://www.nccn.org. Accessed December 02, 2021.

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.