BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/21/16**
SECTION: DRUGS	**LAST REVIEW DATE: 1/18/18**
	LAST CRITERIA REVISION DATE: 1/18/18
	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.**

ZYDELIG® (idelalisib) oral tablet (cont.)

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.

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.

Zydelig (idelalisib)

Medication class:
Antineoplastic Agent, Phosphatidylinositol 3-kinase Inhibitor

FDA-approved indication(s):
- Relapsed chronic lymphocytic leukemia (CLL) (in combination with rituximab) when rituximab alone is appropriate therapy due to other comorbidities
- Relapsed follicular B-cell non-Hodgkin lymphoma after at least 2 prior systemic therapies
- Relapsed small lymphocytic lymphoma (SLL) after at least 2 prior systemic therapies

ZYDELIG® (idelalisib) oral tablet (cont.)

Limitations of use:
- Idelalisib is not indicated or recommended for first-line treatment of CLL, follicular B-cell non-Hodgkin lymphoma, or SLL

Recommended Dose:
- 150 mg twice daily

Maximum dosage
- Not stated

Available Dosage Forms:
- 100 mg and 150 mg tablets

Warnings, Precautions, and other Clinical Information:
- Recurrence of severe or life-threatening toxicity on a re-challenge should result in permanent discontinuation of Zydelig
- Serious hepatotoxicity has been reported, interrupt, reduce dose, or discontinue Zydelig if it occurs
- Avoid use with other drugs that cause liver toxicity
- Safety and efficacy data are not available in patients with baseline ALT or AST > 2.5 x ULN or bilirubin > 1.5 x ULN, as these patients were excluded from studies
- Serious and severe diarrhea or colitis has been reported, interrupt, reduce dose, or discontinue Zydelig if it occurs, diarrhea due to Zydelig responds poorly to anti-motility agents
- Avoid use with other drugs that cause diarrhea
- Permanently discontinue for any of the following: AST/ALT > 20x ULN, bilirubin > 10x ULN, or life-threatening diarrhea
- Serious pneumonitis has been reported, interrupt or discontinue Zydelig if it occurs
- Serious intestinal perforations has been reported, discontinue Zydelig if it occurs
- Consider prophylaxis for *Pneumocystis jirovecii* pneumonia while on Zydelig
- Interrupt Zydelig if suspect *Pneumocystis jirovecii* infection, permanently discontinue if infection is confirmed
- Severe cutaneous reaction (Stevens-Johnson syndrome or toxic epidermal necrolysis) have been reported, interrupt Zydelig if suspected, if confirmed permanently discontinue
- Permanently discontinue if serious allergic reaction occurs
- Avoid use of strong CYP3A4 inducers such as carbamazepine, phenytoin, rifampin, or St. John's wort
- Zydelig is a strong CYP3A4 inhibitor, avoid use with CYP3A4 substrates
- Woman of child bearing potential should be warned against becoming pregnant
- Woman who is breast feeding an infant or child should stop breast feeding
- There is no information on use in patients with creatinine clearance < 15 mL/min

ZYDELIG® (idelalisib) oral tablet (cont.)

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 an Oncologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:
   - Relapsed chronic lymphocytic leukemia (CLL)
     - Has relapsed after at least **one** prior therapy for CLL
       - Some examples of NCCN category 1 CLL therapy include (listed alphabetically):
         - Fludarabine + cyclophosphamide + rituximab
         - Ibrutinib
         - Obinutuzumab + chlorambucil
         - NCCN category 2A regimens (listed alphabetically):
           - Bendamustine + rituximab (or obinutuzumab or ofatumumab)
           - Fludarabine + rituximab
           - Ofatumumab + chlorambucil
           - Rituximab + chlorambucil
     - Zydelig will be used in combination with rituximab

   - Relapsed small lymphocytic lymphoma (SLL)
     - Has failed at least **two** prior systemic therapies
       - Some examples of NCCN category 1 CLL therapy include (listed alphabetically):
         - Fludarabine + cyclophosphamide + rituximab
         - Ibrutinib
         - Obinutuzumab + chlorambucil
         - NCCN category 2A regimens (listed alphabetically):
           - Bendamustine + rituximab (or obinutuzumab or ofatumumab)
           - Ofatumumab + chlorambucil
           - Rituximab + chlorambucil

   - Relapsed follicular B-cell non-Hodgkin lymphoma (FL)
     - Has failed at least **two** prior systemic therapies (an alkylating agent and rituximab)

4. **ALL** of the following baseline tests have been completed before initiation of treatment:
   - Serum liver tests (ALT, AST, and bilirubin)
   - Complete blood count

5. There are **NO** contraindications:
   - Contraindications include:
     - History of serious allergic reactions including anaphylaxis and toxic epidermal necrolysis

Initial approval duration: 6 months

ZYDELIG® (idelalisib) oral tablet (cont.)

- **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 an Oncologist

2. Individual's condition does not show evidence of progressive disease while on therapy
   - Worsening is defined as:
     - Disease has progressed

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Hepatotoxicity
       - Signs and symptoms may include: right sided abdominal pain, bruising, yellow skin or eyes, dark brown urine, severe nausea or vomiting, fatigue, light colored pale stools, itching, confusion
     - Severe and persistent GI events – perforation
       - Signs and symptoms may include: nausea, diarrhea (# BMs $\geq$ 6/d) , dyspepsia, vomiting, abdominal pain, dehydration
     - Pneumonitis
       - Signs and symptoms may include: fever, shortness of breath, cough, chest tightness or pain, headache, weight loss, fatigue
     - Infections
       - Signs and symptoms may include: fever, cough, chills, weakness, shortness of breath, chest pain
     - Stevens-Johnson syndrome and toxic epidermal necrolysis
       - Signs and symptoms may include: progressive skin rash, hives, blistering, oral ulcers
     - Anaphylaxis
       - Signs and symptoms may include: hives over neck and face, itching, nasal congestion, difficulty breathing, swelling of lips, mouth, tongue or throat

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

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.

ZYDELIG® (idelalisib) oral tablet (cont.)

Zydelig. Package Insert. Reference ID 205858-GS-000-PI. Revised by manufacturer 7/2014. Accessed 11-18-2015.

Zydelig. Package Insert. Revised by manufacturer 09/2016. Accessed 12-04-2016

Zydelig. Package Insert. Revised by manufacturer 11/2017. Accessed 12-22-2017

NCCN Clinical Practice Guidelines in Oncology: Chronic lymphocytic leukemia/Small lymphocytic lymphoma. Version 2.2018, Oct 23, 2017. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

NCCN Clinical Practice Guidelines in Oncology: B-cell Lymphomas. Version 7.2017, Dec 5, 2017. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

UpToDate: Overview of the treatment of chronic lymphocytic leukemia. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/overview-of-the-treatment-of-chronic-lymphocytic-leukemia?search=chronic%20lymphocytic%20leukemia&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2

UpToDate: Treatment of relapsed or refractory chronic lymphocytic leukemia. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-chronic-lymphocytic-leukemia?search=chronic%20lymphocytic%20leukemia&source=search_result&selectedTitle=7~150&usage_type=default&display_rank=8

UpToDate: Pathobiology of follicular lymphoma. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/pathobiology-of-follicular-lymphoma?search=follicular%20B-cell%20non-Hodgkin%20lymphoma&source=search_result&selectedTitle=13~150&usage_type=default&display_rank=13#H26244291

UpToDate: Treatment of relapsed or refractory follicular lymphoma. Current through Nov 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-follicular-lymphoma?source=related_link#H22

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.