Zydelig

Description

Zydelig (idelalisib)

Background
Zydelig, in combination with Rituxan (rituximab), treats patients whose chronic lymphocytic leukemia (CLL) has returned (relapsed), in patients for whom Rituxan would be considered appropriate therapy due to other existing medical conditions (co-morbidities). Zydelig, used alone, is used to treat patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) and small lymphocytic lymphoma (SLL), another type of non-Hodgkin lymphoma. Zydelig is intended to be used in patients who have received at least two prior systemic therapies. Zydelig targets a protein found in the cells of several types of blood cancer that helps cancer cells develop, grow, and spread (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.
2. Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies.
3. Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies.

Off-Label Uses: (2-3)

1. Relapsed or refractory CLL as a single agent
2. Relapsed or refractory SLL as a single agent
3. Refractory or progressive follicular lymphoma
4. Primary cutaneous B-cell lymphoma
   a. Primary cutaneous marginal zone lymphoma
   b. Follicle center lymphoma
5. Recurrent or progressive gastric mucosa associated lymphoid tissue (MALT) lymphoma
6. Refractory or progressive non-gastric MALT lymphoma
7. Refractory or progressive splenic marginal zone lymphoma

Limitation of use:
Zydelig is not indicated and is not recommended for first-line treatment of any patient (1).

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 that can occur in Zydelig-treated patients. 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 occurred in 31% of Zydelig-treated patients across clinical trials. Blood counts should be monitored at least every two weeks for the first 3 months of therapy, and at least weekly in patients while neutrophil counts are less than 1.0 G/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**
Aliqopa, Arzerra, Bendeka, Copiktra, Gazyva, Imbruvica, Revlimid, Rituxan, Treanda, Venclexta

**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** in patients 18 years of age or older with one of the following diagnosis: relapsed or refractory chronic lymphocytic leukemia (CLL), relapsed, refractory or progressive follicular B-cell non-Hodgkin lymphoma (FL), relapsed or refractory small lymphocytic lymphoma (SLL), B-cell nodal marginal zone 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; and if the conditions indicated below are met.

Zydelig may be considered **investigational** in patients less than 18 years of age and 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, refractory or progressive follicular B-cell non-Hodgkin lymphoma (FL)
3. Relapsed or refractory small lymphocytic lymphoma (SLL)
4. Relapsed or refractory B-cell nodal marginal zone lymphoma
5. Recurrent or progressive gastric mucosa associated lymphoid tissue (MALT) lymphoma

6. Refractory or progressive non-gastric MALT lymphoma

7. Refractory or progressive splenic marginal zone lymphoma

AND ALL of the following:
   a. Prior therapy with an alkylator and rituximab therapy
   b. Agreement to monitor hepatic function prior to and during treatment and to interrupt and then reduce, or discontinue Zydelig as clinically appropriate
   c. Agreement to monitor the development of severe diarrhea, colitis, pneumonitis, and intestinal perforation and to interrupt and then 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, refractory or progressive follicular B-cell non-Hodgkin lymphoma (FL)
3. Relapsed or refractory small lymphocytic lymphoma (SLL)
4. Relapsed or refractory B-cell lymphoma nodal marginal zone lymphoma
5. Recurrent or progressive gastric mucosa associated lymphoid tissue (MALT) lymphoma
6. Refractory or progressive non-gastric MALT lymphoma
7. Refractory or progressive splenic marginal zone lymphoma

AND ALL of the following:
   a. Agreement to monitor hepatic function prior to and during treatment and to interrupt and then reduce, or discontinue Zydelig as clinically appropriate
   b. Agreement to monitor the development of severe diarrhea, colitis, pneumonitis, and intestinal perforation and to interrupt and then reduce, or discontinue Zydelig as clinically appropriate
Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 12 months

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 indicated for the treatment of patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL). Zydelig is indicated for the treatment of patients with relapsed 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 that can occur in Zydelig-treated patients. 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 children 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
Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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</thead>
<tbody>
<tr>
<td>August 2014</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual review and update</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>December 2015</td>
<td>Annual review</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
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<td></td>
<td>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.</td>
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<td>Addition of indications: primary cutaneous B-cell lymphoma with <strong>ONE</strong> 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</td>
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<tr>
<td>September 2016</td>
<td>Policy change from 5.04.49 to 5.21.49</td>
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<tr>
<td>June 2017</td>
<td>Annual review</td>
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<tr>
<td>March 2018</td>
<td>Annual editorial review and reference update</td>
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<td>Addition of the requirement of “prior therapy with an alkylator and rituximab therapy” per SME</td>
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<tr>
<td>June 2018</td>
<td>Annual editorial review</td>
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<tr>
<td>March 2019</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.