Clinical Policy: Idelalisib (Zydelig)
Reference Number: CP.PHAR.133
Effective Date: 12.01.18
Last Review Date: 11.18
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Idelalisib (Zydelig®) is a kinase inhibitor.

FDA Approved Indication(s)
Zydelig is indicated for the treatment of:
- 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
- Relapsed follicular B-cell non-Hodgkin lymphoma (FL) in patients who have received at least two prior systemic therapies*
- Relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior systemic therapies*

*Accelerated approval was granted for FL and SLL based on overall response rate. Improvement in patient survival or disease related symptoms has not been established. Continued approval for these indications may be contingent upon verification of clinical benefit in confirmatory trials.

Limitation(s) of use:
- Zydelig is not indicated and is not recommended for first-line treatment of any patient.
- Zydelig is not indicated and is not recommended in combination with bendamustine and/or rituximab for the treatment of FL.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Zydelig is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Chronic Lymphocytic Leukemia (must meet all):
      1. Diagnosis of CLL;
      2. Prescribed by or in consultation with an oncologist or hematologist;
      3. Age ≥ 18 years;
      4. Disease is relapsed or refractory to first-line therapy (e.g., obinutuzumab, ibrutinib, ofatumumab, rituximab, fludarabine, alemtuzumab, alkylator therapy [e.g., bendamustine, chlorambucil, cyclophosphamide]);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg per day (2 tablets per day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

B. **Follicular B-Cell Non-Hodgkin Lymphoma** (must meet all):
   1. Diagnosis of FL;
   2. Prescribed by or in consultation with an oncologist or hematologist;
   3. Age ≥ 18 years;
   4. Member has received at least 2 prior systemic therapies (e.g., rituximab, obinutuzumab, doxorubicin, vincristine, alkylator therapy [e.g., bendamustine, chlorambucil, cyclophosphamide], lenalidomide);

5. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg per day (2 tablets per day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

C. **Small Lymphocytic Lymphoma** (must meet all):
   1. Diagnosis of SLL;
   2. Prescribed by or in consultation with an oncologist or hematologist;
   3. Age ≥ 18 years;
   4. Disease is relapsed or refractory to first-line therapy (e.g., obinutuzumab, ibrutinib, ofatumumab, rituximab, fludarabine, alemtuzumab, alkylator therapy [e.g., bendamustine, chlorambucil, cyclophosphamide]);

5. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg per day (2 tablets per day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

D. **Other Non-Hodgkin Lymphomas (off-label)** (must meet all):
   1. Diagnosis of one of the following non-Hodgkin lymphomas (a or b):
      a. Mucosa-associated lymphoid tissue (MALT) lymphoma (gastric or nongastric);
      b. Marginal zone lymphoma (nodal or splenic);
   2. Prescribed by or in consultation with an oncologist or hematologist;
   3. Age ≥ 18 years;
   4. Disease is refractory to both alkylator (e.g., bendamustine, chlorambucil, cyclophosphamide) and rituximab therapy;

5. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg per day (2 tablets per day);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**
E. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. All Indications in Section I (must meet all):
      1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Zydelig for a covered indication and has received this medication for at least 30 days;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, request meets one of the following (a or b):
         a. New dose does not exceed 300 mg per day (2 tablets per day);
         b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   
     Approval duration: 12 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

     Approval duration: Duration of request or 6 months (whichever is less); or

      2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   CLL: chronic lymphocytic leukemia       NCCN: National Comprehensive Cancer
   FDA: Food and Drug Administration       Network
   FL: follicular B-cell non-Hodgkin       SLL: small lymphocytic lymphoma
   lymphoma

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imbruvica® (ibrutinib)</strong></td>
<td><strong>CLL</strong>&lt;br&gt;Three 140 mg capsules (420 mg) PO QD</td>
<td>420 mg/day</td>
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<tr>
<td><strong>Leukeran® (chlorambucil)</strong></td>
<td><strong>CLL, SLL, FL</strong>&lt;br&gt;0.1 to 0.2 mg/kg PO QD (4 to 10 mg per day)</td>
<td>0.2 mg/kg daily</td>
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<tr>
<td><strong>Rituxan® (rituximab)</strong></td>
<td><strong>CLL</strong>&lt;br&gt;375 mg/m² IV infusion the day prior to the initiation of fludarabine/cyclophosphamide chemotherapy, then 500 mg/m² on Day 1 of cycles 2-6 (every 28 days)&lt;br&gt;&lt;br&gt;<strong>FL</strong>&lt;br&gt;375 mg/m² IV infusion once weekly for 4 doses (relapsed) or up to 8 doses (untreated)</td>
<td>500 mg/m²</td>
</tr>
<tr>
<td><strong>Gazyva™ (obinutuzumab) and Leukeran® (chlorambucil)</strong></td>
<td><strong>CLL, SLL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>Arzerra® (ofatumumab) and Leukeran® (chlorambucil)</strong></td>
<td><strong>CLL, SLL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>FCR</strong>&lt;br&gt;fludarabine (Fludara®), cyclophosphamide (Cytoxan®) and Rituxan® (rituximab)</td>
<td><strong>CLL, SLL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>FR</strong>&lt;br&gt;fludarabine (Fludara®) and Rituxan® (rituximab)</td>
<td><strong>CLL, SLL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>BR</strong>&lt;br&gt;Treanda® (bendamustine) and Rituxan® (rituximab)</td>
<td><strong>CLL, SLL, FL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td><strong>PCR</strong>&lt;br&gt;Nipent®(pentostatin), cyclophosphamide</td>
<td><strong>CLL, SLL</strong>&lt;br&gt;Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
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<tr>
<td>(Cytoxan) and Rituxan® (rituximab)</td>
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<tr>
<td>R-CHOP</td>
<td>FL</td>
<td>Varies</td>
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<tr>
<td>Rituxan® (rituximab), cyclophosphamide (Cytoxan®), doxorubicin , vincristine (Vincasar PFS®), and prednisone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>R-CVP</td>
<td>FL</td>
<td>Varies</td>
</tr>
<tr>
<td>Rituxan® (rituximab), cyclophosphamide (Cytoxan®), vincristine (Vincasar PFS®), and prednisone</td>
<td>Varies</td>
<td>Varies</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): history of serious allergic reactions including anaphylaxis and toxic epidermal necrolysis
- Boxed warning(s): fatal and serious toxicities-hepatic, severe diarrhea, colitis, pneumonitis, infections, and intestinal perforation

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLL, FL, SLL</td>
<td>150 mg PO BID</td>
<td>300 mg per day</td>
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<tr>
<td>If resuming Zydelig after interruption for other severe or life-threatening toxicities, reduce the dose to 100 mg BID.</td>
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</table>

VI. Product Availability
- Tablets: 150 mg, 100 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created: adapted from previously approved HIM.PA.SP49 and CP.CPA.278 Idelalisib (Zydelig) (both to be retired); new policy for Centene Medicaid; summarized NCCN and FDA-approved uses for improved clarity; added age requirement and specialist involvement in care; removed primary cutaneous B-cell lymphoma as a covered off-label indication (disease not listed in the NCCN compendium for Zydelig); updated continued therapy section to include language for continuity of care; references reviewed and updated.</td>
<td>07.11.18</td>
<td>11.18</td>
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</tbody>
</table>

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise
professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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