Clinical Policy: Idelalisib (Zydelig)

Reference Number: CP.PHAR.133
Effective Date: 12.01.18
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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.

Limitation(s) of use:

- Zydelig is not indicated and is not recommended for first-line treatment of any patient, including patients with CLL, small 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 lymphomas.

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 idelalisib and Zydelig are **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 as evidenced by prior therapy with both of the following (a and b; *see Appendix B for examples*);*
   a. BTK inihibitor (e.g., Calquence®, Brukinsa®, Imbruvica®, Jayprica®);
   b. Venclexta®;
   **Prior authorization may be required.*
5. Prescribed as a single agent (*off-label*) or in combination with rituximab;
6. For Zydelig requests, member must use idelalisib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*

a. Dose does not exceed (i and ii):
   i. 300 mg per day;
   ii. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Small Lymphocytic Leukemia (off-label) (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 as evidenced by prior therapy with both of the following (a and b; *see Appendix B for examples*);*
   a. BTK inihibitor (e.g., Calquence, Brukinsa, Imbruvica, Jaypirca);
   b. Venclexta;

   **Prior authorization may be required.*
5. Prescribed as a single agent or in combination with rituximab;
6. For Zydelig requests, member must use idelalisib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed (i and ii):
      i. 300 mg per day;
      ii. 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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. For Zydelig requests, member must use idelalisib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed (i and ii):
      i. 300 mg per day;
      ii. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
FL: follicular B-cell non-Hodgkin lymphoma
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic 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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
CLL/SLL *Examples of first-line, second-line and subsequent therapies:* • Gazyva® (obinutuzumab) ± Calquence (acalabrutinib) ± Venclexta (venetoclax) • Imbruvica (ibrutinib) ± Gazyva (obinutuzumab) or Venclexta (venetoclax) or rituximab (Rituxan, Truxima, Riabni) • Brukinsa (zanubritinib) • Jaypirca (pirtobrutinib) • Venclexta (venetoclax) ± Gazyva (obinutuzumab) or rituximab (Rituxan®, Truxima®, Riabni™)	Varies	Varies

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

Indication	Dosing Regimen	Maximum Dose
CLL	150 mg PO BID	300 mg per day

VI. Product Availability

Tablets: 100 mg, 150 mg

VII. References

1. Zydelig Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; February 2022. Available at http://www.zydelig.com. Accessed July 24, 2026.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 24, 2026.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 24, 2026.
4. Gilead. Gilead statement on Zydelig U.S. indication for follicular lymphoma and small lymphocytic leukemia. Company statements. Published January 14, 2022. Available at: https://www.gilead.com/company/company-statements/2022/gilead-statement-on-zydelig-us-indication-for-follicular-lymphoma-and-small-lymphocytic-leukemia. Accessed July 24, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; added redirection to generic if available; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.29.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	08.07.23	11.23
4Q 2024 annual review: for CLL/SLL, revised prior therapy requirement from at least one prior therapy to prior therapy with BTK inhibitor and Venclxta-based regimens per NCCN; updated Appendix B per NCCN; references reviewed and updated.	08.06.24	11.24
4Q 2025 annual review: for CLL, added step therapy bypass for IL HIM per IL HB 5395; for all indications, extended initial approval duration for Medicaid and HIM from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	07.15.25	11.25
4Q 2026 annual review: added ICHRA line of business; references reviewed and updated.	07.24.26	11.26

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.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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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