RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	idelalisib
Policy Number:	RxA.581
Drug(s) Applied:	Zydelig®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Idelalisib (Zydelig®) is a kinase inhibitor. It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
idelalisib (Zydelig®)	CLL, FL, SLL	150 mg PO BID	300 mg per day

Dosage Forms

- Tablets: 150 mg, 100 mg

Clinical Policy

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

i. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):

1. Diagnosis of CLL or SLL;
2. Prescribed by or in consultation with an oncologist or hematologist;

3. Age 18 years of age or older;
4. Relapsed/refractory disease after ≥ one prior therapy (see Appendix B for examples);
   *Prior authorization may be required.
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
Commercial: 6 months
Medicaid: 6 months

B. Follicular and Marginal Zone Lymphomas (must meet all)**:**

1. One of the following diagnoses (a or b):
   a. FL;
   b. Marginal zone lymphoma (off-label) (i, ii, or iii)
      i. Splenic marginal zone lymphoma;
      ii. Nodal marginal zone lymphoma;
      iii. Extranodal marginal zone lymphoma (a or b):
         a) Gastric MALT lymphoma;
         b) Nongastric MALT lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age 18 years of age or older;
4. Relapsed/refractory disease after ≥ 2 prior therapies (see Appendix B for examples);*
   *Prior authorization may be required.
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
Commercial: 6 months
Medicaid: 6 months

ii. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication that has been authorised by RxAdvance or member has met initial approval criteria for the 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).

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

Approval Duration
Commercial: 12 months
Medicaid: 12 months

iii. Appendices

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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
CLL/SLL Examples of first-line, second-line and subsequent therapies: • FCR (fludarabine, cyclophosphamide, rituximab) • HDMP (high dose methylprednisolone) + rituximab • Single-agent examples: Imbruvica® (ibrutinib); Venclexta® (venetoclax) ± Gazyva® (obinutuzumab) or rituximab; Campath® (alemtuzumab) ± rituximab; Gazyva®; Copiktra® (duvelisib); Calquence® (acalabrutinib); Revlimid® (lenalidomide) ± rituximab; Arzerra® (ofatumumab) ± FC (fludarabine, cyclophosphamide); Leukeran® (chlorambucil) + rituximab	Varies	Varies
Follicular Lymphoma Examples of first-line, second-line and subsequent therapies: • bendamustine + Gazyva® or rituximab	Varies	Varies
• CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva® or rituximab • CVP (cyclophosphamide, vincristine, prednisone) + Gazyva® or rituximab • Single-agent examples: rituximab; Revlimid ± rituximab		
Marginal Zone Lymphomas Examples of first-line, second-line and subsequent therapies: • bendamustine + rituximab • RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • Single-agent examples: rituximab; Leukeran® ± rituximab; cyclophosphamide ± rituximab; Imbruvica®; Revlimid ± rituximab; Copiktra®; Aliqopa® (copanlisib)	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. Brand name might be non-preferred when generic is preferred.

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.

APPENDIX D: General Information

- Zydelig® is used when follicular lymphoma returns after treatment with at least 2 prior medicines. Zydelig® should not be used as the first medicine to treat people who have been diagnosed with follicular lymphoma, and should not be used in combination with bendamustine and/or Rituxan® (rituximab) to treat people with follicular lymphoma.
- Zydelig® works differently from chemotherapy because it blocks a specific protein in B cells called PI3K delta. PI3K delta sends signals to cancerous B cells, telling them to multiply and helping them survive. Zydelig® blocks these signals, helping to slow the growth of lymphoma cells.

References

1. Zydelig Prescribing Information. Foster City, CA: Gilead Sciences, Inc.; October 2018. Available at http://www.zydelig.com. Accessed October 09, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 09, 2020.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed October 09, 2020.
4. National Comprehensive Cancer Network. B-cell lymphomas Version 4.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed October 09, 2020.
5. NCI Dictionary of Cancer Terms. National Cancer Institute website. https://www.cancer.gov/publications/dictionaries/cancer-terms. Accessed October 09, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated as “idelalisib”. 2. Lines of business policy applies to all lines of business. 3. HIM removed and approval duration updated. 4. Continued therapy criteria II.A.1. was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 5. Appendix D updated. 6. References were reviewed and updated.	10/09/2020	12/07/2020