

Clinical Policy Title:	obinutuzumab
Policy Number:	RxA.385
Drug(s) Applied:	Gazyva®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Obinutuzumab is a CD20-directed cytolytic antibody. Obinutuzumab is indicated:

- In combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)
- In combination with bendamustine followed by obinutuzumab monotherapy, for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab- containing regimen
- In combination with chemotherapy followed by obinutuzumab monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
obinutuzumab (Gazyva®)	CLL/SLL	100 mg IV on day 1, 900 mg IV on day 2 of cycle 1, then 1000 mg IV on days 8 and 15 of cycle 1; begin the next cycle of therapy on day 29. For cycles 2 to 6, give obinutuzumab 1000 mg IV on day 1 repeated every 28 days. Administer obinutuzumab in combination with chlorambucil (0.5 mg/kg orally on day 1 and 15) in cycles 1 to 6.	See regimen
	FL	1000 mg IV on day 1, 8 and 15 of cycle 1, 1000 mg on day 1 of cycles 2-6 or cycles 2-8, and then 1000 mg every 2 months for up to 2 years. For patients with relapsed or refractory FL, administer in combination with bendamustine in six 28-day cycles. Patients who achieve stable disease,	See regimen

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Dosing Information			
Drug Name	Indication	Dosing Regimen	Maximum Dose
		<p>complete response or partial response to the initial 6 cycles should continue on 1000 mg as monotherapy for up to two years.</p> <p>For patients with previously untreated FL, administer obinutuzumab with one of the following chemotherapy regimens:</p> <ul style="list-style-type: none"> • Six 28-day cycles in combination with bendamustine • Six 21-day cycles in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), followed by 2 additional 21-day cycles of obinutuzumab alone • Eight 21-day cycles in combination with CVP (cyclophosphamide, vincristine, prednisone) <p>Patients with previously untreated FL who achieve a complete or partial response to the initial 6 or 8 cycles should continue on obinutuzumab 1000 mg as monotherapy for up to 2 years.</p>	

Dosage Forms

- Single-dose vial: 1,000 mg/40 mL (25 mg/mL)

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;
4. Request meets one of the following (a or b):*
 - a. After initial loading doses, dose does not exceed 1,000 mg per 28-day cycle;
 - 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

Commercial: 6 months

Medicaid: 6 months

HIM: 6 months

B. Follicular and other B-Cell Lymphomas (must meet all):

1. Diagnosis of one of the following B-cell lymphoma subtypes (a or b):
 - a. Follicular lymphoma (grade 1-2);
 - b. Other B-cell lymphomas (off-label):
 - i. Marginal zone lymphoma (a, b, or c):
 - a) Splenic marginal zone lymphoma;
 - b) Nodal marginal zone lymphoma;
 - c) Extranodal marginal zone lymphoma (1 or 2):
 - 1) Gastric mucosa-associated lymphoid tissue lymphoma;
 - 2) Non-gastric mucosa-associated lymphoid tissue lymphoma;
 - ii. Histologic transformation of nodal marginal zone lymphoma to diffuse large B-cell lymphoma;
 - iii. Diffuse large B-cell lymphoma;
 - iv. High-grade B-cell lymphoma;
 - v. Mantle cell lymphoma;
 - vi. Castleman's disease;
 - vii. Post-transplant lymphoproliferative disorders;
 - viii. AIDS-related B-cell lymphoma;
 - ix. Burkitt lymphoma;
2. If not FL, one of the following uses (a or b):
 - a. Used as a substitute* for rituximab in patients experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens- Johnson syndrome, lichenoid dermatitis, vesicobullous dermatitis, and toxic epidermal necrolysis;
*Re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.
 - b. If marginal zone lymphoma (i or ii):
 - i. Maintenance therapy if disease is rituximab-refractory, recurrent and has been treated with obinutuzumab and bendamustine;
 - ii. Second-line or subsequent therapy in combination with bendamustine (see Appendix B for examples of prior therapy);
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥18 years;
5. Request meets one of the following (a or b):**
 - a. After initial loading doses, dose does not exceed 1,000 mg per 28-day cycle;
 - 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

Commercial: 6 months

Medicaid: 6 months

HIM: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy.
2. Member is currently receiving obinutuzumab for a covered indication and has received this medication for at least 30 days;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):*
 - a. After initial loading doses, new dose does not exceed 1,000 mg per 28-day cycle;
 - 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

HIM: 12 Months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

- CLL: Chronic Lymphocytic Leukemia
- FDA: Food and Drug Administration
- FL: Follicular Lymphoma
- MALT: Mucosa-Associated Lymphoid Tissue
- NCCN: National Comprehensive Cancer Network
- NHL: Non-Hodgkin Lymphoma
- 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 <u>Examples of first-line, second-line and subsequent therapies:</u> <ul style="list-style-type: none"> • ibrutinib • acalabrutinib ± obinutuzumab • venetoclax + obinutuzumab • chlorambucil + obinutuzumab • high-dose methylprednisolone + rituximab • ibrutinib + obinutuzumab • chlorambucil • rituximab 	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<p>Marginal Zone Lymphomas</p> <p><u>Examples of first-line, second-line and subsequent therapies:</u></p> <ul style="list-style-type: none"> • bendamustine + rituximab • RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • <u>Single-agent examples:</u> rituximab; Leukeran® (chlorambucil) ± rituximab; cyclophosphamide ± rituximab; Imbruvica® (ibrutinib); Revlimid® (lenalidomide) ± rituximab; Copiktra® (duvelisib); 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.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Patients with known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or any of the excipients, including serum sickness with prior obinutuzumab use.
- Boxed warning(s):
 - Hepatitis B virus reactivation and progressive multifocal leukoencephalopathy

APPENDIX D: General Information

Not applicable

References

1. Gazyva Prescribing Information. South San Francisco, CA: Genentech, Inc.; March 2020. Available at: <https://www.gazyva.com/>. Accessed July 23, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 23, 2020.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cli.pdf. Accessed July 23, 2020.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 23, 2020.
5. Gazyva. In: Lexicomp Online Drug Database [database on the Internet]. Hudson, Ohio: Lexicomp, Inc.; 2020 [updated June 18, 20]. Available at: <http://online.lexi.com>. Subscription required to view. Accessed July 23, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy updated. <ol style="list-style-type: none"> 1. Formatting updated. 2. Policy updated. 3. Continued criteria for approval updated. 4. Approval duration updated. 5. Reference updated. 	07/23/2020	09/14/2020