RXADVANCE
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| **Clinical Policy Title:** | acalabrutinib |
| **Policy Number:** | RxA.54 |
| **Drug(s) Applied:** | Calquence® |
| **Original Policy Date:** | 03/06/2020 |
| **Last Review Date:** | 12/07/2020 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Acalabrutinib (Calquence®) is a Bruton tyrosine kinase (BTK) inhibitor. It is indicated for:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy.
  This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefits in confirmatory trials.
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| acalabrutinib (Calquence®) | Mantle cell lymphoma<br>Chronic lymphocytic leukemia<br>Small lymphocytic lymphoma | 100 mg by mouth approximately every 12 hours | 400 mg/day |

## Dosage Forms

- Capsule: 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. Mantle Cell Lymphoma** (must meet all)**:**

1. Diagnosis of MCL as a single-agent, second-line therapy;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Previously received at least one prior therapy (see Appendix B);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant

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off-label use (prescriber must submit supporting evidence);

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

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

1. Diagnosis of CLL or SLL as preferred therapy for relapsed or refractory disease as single agent therapy or in combination with Obinutuzumab.
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Previously received at least one prior therapy (see Appendix B);
5. If refractory to ibrutinib (Imbruvica®), member does not have BTK C481S mutations;
6. Request meets one of the following (a or b):
    a. Dose does not exceed 400 mg (4 capsules) 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

**C. Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma (off-label use)** (must meet all):

1. Diagnosis of Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma - Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed as a single agent therapy as alternative therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease;
5. Dose is within FDA-approved maximum limit for an FDA approved indication or 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

## II. Therapy Approval

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

1. Member is currently receiving the medication that has been authorized by RxAdvance , or documentation supports that member is currently receiving acalabrutinib (Calquence®) 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 400 mg (4 capsules) 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**
**Commercial:** 12 months
**Medicaid:** 12 months

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## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**

BTK: Bruton tyrosine kinase
CLL: Chronic lymphocytic leukemia
FDA: Food and Drug Administration
MCL: Mantle cell lymphoma
SLL: Small lymphocytic lymphoma
NCCN: National Comprehensive Cancer Network

**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 |
|---|---|---|
| CALGB (rituximab + methotrexate + cyclophosphophamide, doxorubicin, vincristine, prednisone; etoposide, cytarabine, rituximab; carmustine, etoposide, cyclophosphamide/autologous stem cell rescue; rituximab) | Varies | Varies |
| HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab | Varies | Varies |
| NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine) | Varies | Varies |
| RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine) | Varies | Varies |
| RDHAP (rituximab, dexamethasone, cisplatin, cytarabine) | Varies | Varies |
| RCHOP/RICE (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, ifosfamide, carboplatin, etoposide) | Varies | Varies |
| Bendeka® (bendamustine) + Rituxan® (rituximab) | Varies | Varies |
| VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone) | Varies | Varies |
| CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab) | Varies | Varies |
| Revlimid® (lenalidomide) + Rituxan® (rituximab) | Varies | Varies |
| **Without del(17p)/TP53 mutation** | | |
| Leukeran® (chlorambucil) + Gazyva® (obinutuzumab) | Varies | Varies |
| Imbruvica® (ibrutinib) | Varies | Varies |

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| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Leukeran® (chlorambucil) + Arzerra® (ofatumumab) | Varies | Varies |
| Leukeran® (chlorambucil) + Rituxan® (rituximab) | Varies | Varies |
| bendamustine (Bendeka®, Treanda®)+ CD20 monoclonal antibody (e.g., rituximab, ofatumumab, obinutuzumab) | Varies | Varies |
| FR/FCR (fludarabine, rituximab ± cyclophosphamide) | Varies | Varies |
| **With del(17p)/TP53 mutation** | | |
| Campath® (alemutuzumab) ± Rituxan® (rituximab) | Varies | Varies |
| High-dose methylprednisolone + Rituxan® (rituximab) | Varies | Varies |
| Gazyva® (obinutuzumab) | 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):
  - None
- Boxed Warning(s):
  - None

**APPENDIX D: General Information**

- Per NCCN: Due to lack of activity, Calquence® should not be used for ibrutinib-refractory CLL cells with BTK C481S mutations. Calquence® can however be used in cases of ibrutinib intolerance.

**References**

1. Calquence Prescribing Information. Wilmington, DE; AstraZeneca Pharmaceuticals LP: November 2019. Available at www.calquence.com. Accessed October 14, 2020.
2. National Comprehensive Cancer Network. B-cell Lymphomas Version 4.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf Accessed October 14, 2020.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. October 14, 2020.
4. National Comprehensive Cancer Network. Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma. Version 1.2021- September 1, 2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf . Accessed on October 26, 2020.

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 02/2020 | 03/06/2020 |

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| Policy was reviewed:<br>1. Clinical policy title Table updated.<br>2. Line of Business Policy Applies to was updated to “All lines of business”.<br>3. Dosing Regimen Abbreviated forms PO and BID replaced with by mouth and Twice a day.<br>4. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance”.<br>5. Appendix A Abbreviation/Acronym Key added.<br>6. Appendix B Therapeutic Alternatives language rephrased.<br>7. References were reviewed and updated.<br>8. Added initial approval criteria for Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma per NCCN 2A recommendation. | 10/26/2020 | 12/07/2020 |

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