PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral – Bruton's Tyrosine Kinase Inhibitor) – Calquence Prior Authorization Policy
- Calquence® (acalabrutinib tablets – AstraZeneca)

REVIEW DATE: 06/11/2025; selected revision 06/18/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Calquence, a Bruton’s tyrosine kinase (BTK) inhibitor, is indicated in adults for the following uses:[1]

- **Chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL)**.
- **Mantle cell lymphoma**, previously untreated, in combination with bendamustine and rituximab in patients who are ineligible for autologous hematopoietic stem cell transplantation (HSCT).
- **Mantle cell lymphoma**, in patients who have received at least one prior therapy.

Guidelines

Calquence is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **B-Cell Lymphomas**: NCCN guidelines (version 2.2025 – February 10, 2025) address mantle cell lymphoma and marginal zone lymphoma.[2,5] Calquence is recommended as one of several "preferred" agents as second-line and subsequent therapy for mantle cell lymphoma (category 2A); there is a footnote that states that Calquence has not been shown to be effective for Imbruvica® (ibrutinib tablets, capsules, or oral solution)-refractory mantle cell lymphoma with *BTK* C481S mutations. . Calquence can also be used in combination with rituximab as pre-treatment in order to limit the number of cycles of aggressive induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen (category 2A). Calquence is also recommended as "preferred" aggressive induction therapy (category 2B), "preferred" less aggressive induction therapy in combination with rituximab (category 2A), and maintenance therapy with chemotherapy (category 2B). For marginal zone lymphoma, NCCN guidelines recommend Calquence as a "preferred" regimen for second-line and subsequent therapy including patients who are older or infirm (category 2A).
- **CLL/SLL**: NCCN guidelines (version 3.2025 – April 2, 2025) list Calquence ± Gazyva® (obinutuzumab intravenous infusion) as a "preferred" first-line therapy option for patients with deletion(17p)/TP53 mutation (category 2A) or without deletion(17p)/TP53 mutation (category 1); Venclexta + Calquence ± Gazyva® (obinutuzumab intravenous infusion) is also listed as a "preferred" first-line option for patients with deletion(17p)/TP53 mutation (category 2A) .[3,5] The guidelines also list single-agent Calquence as a "preferred" second-line or third-line therapy for patients with or without deletion(17p)/TP53 mutation (category 1); there is a footnote that states that Calquence has not been shown to be effective for Imbruvica-refractory CLL with *BTK* C481S mutations. Patients with Imbruvica intolerance have been successfully treated with Calquence or Brukinsa without recurrence of symptoms.
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 3.2025 – February 6, 2025) recommend single-agent Calquence as "other recommended regimen" for previously treated disease (category 2A).[4,5]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Calquence. All approvals are provided for the duration noted below.

- **Calquence® (acalabrutinib tablets - AstraZeneca)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia.** Approve for 1 year if the patient is ≥ 18 years of age.

2. **Mantle Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient meets ONE of the following (a or b):
         a) Patient has tried at least one systemic regimen; OR
         Note: Examples of a systemic regimen contain one or more of the following products: rituximab, dexamethasone, cytarabine, carboplatin, cisplatin, oxaliplatin, cyclophosphamide, doxorubicin, vincristine, prednisone, methotrexate, bendamustine, bortezomib, or lenalidomide.
         b) According to the prescriber, patient is not a candidate for a chemotherapy regimen; OR
      ii. Calquence is used in combination with rituximab.

3. **Small Lymphocytic Lymphoma.** Approve for 1 year if the patient is ≥ 18 years of age.

Other Uses with Supportive Evidence

4. **Marginal Zone Lymphoma**. Approve for 1 year if the patient meets BOTH of the following (A and B):
   Note: Marginal zone lymphoma includes gastric mucosa-associated lymphoid tissue (MALT) lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma.
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one systemic regimen.
   Note: Examples of a systemic regimen contain one or more of the following products: bendamustine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, lenalidomide, or chlorambucil.

5. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one systemic regimen.
   Note: Examples of a systemic regimen contain one or more of the following products: Brukinsa (zanubrutinib capsules), Imbruvica (ibrutinib tablets, capsules, and oral solution), rituximab, bendamustine, cyclophosphamide, dexamethasone, bortezomib, Kyprolis (carfilzomib intravenous infusion), or Ninlaro (ixazomib capsule).

CONDITIONS NOT COVERED

- **Calquence® (acalabrutinib tablets - AstraZeneca)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Calquence ® tablets [prescribing information]. Wilmington, DE: AstraZeneca; January 2025.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 6, 2025.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2025 – April 2, 2025). © 2025 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 6, 2025.
4. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2025 – February 6, 2025). © 2025 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 6, 2025.
5. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 6, 2025. Search term: acalabrutinib.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/12/2023
Annual Revision	**Mantle Cell Lymphoma**: Criterion which states "Calquence is used in combination with rituximab" was added as an option for approval.	06/12/2024
Update	**01/17/2025**: The overview section was updated to include new FDA approved indication of Previously untreated mantle cell lymphoma, in combination with bendamustine and rituximab in patients who are ineligible for autologous hematopoietic stem cell transplantation (HSCT).	--
Update	**04/08/2025**: The policy name was changed from "Oncology – Calquence PA Policy" to "Oncology (Oral - Bruton's Tyrosine Kinase Inhibitor) – Calquence PA Policy".	--
Annual Revision	**Mantle Cell Lymphoma:** The wording of "systemic regimen" was reworded to "chemotherapy regimen" for the option of approval which previously stated "according to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail)." **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Kyprolis (carfilzomib intravenous infusion), or Ninlaro (ixazomib capsule) were added to the note and fludarabine or cladribine were removed from the note.	06/11/2025
Selected Revision	**Mantle Cell Lymphoma:** The wording "i.e., an elderly patient who is frail" was removed from the requirement which previously stated, "according to the prescriber, patient is not a candidate for a chemotherapy regimen (i.e., an elderly patient who is frail)."	06/18/2025