# sonrotoclax (Beqalzi™)

EOCCO POLICY

## Policy Type: PA/SP  Pharmacy Coverage Policy: EOCCO350

### Description

Sonrotoclax (Beqalzi) is an orally administered B-cell lymphoma 2 (BCL-2) inhibitor.

### Length of Authorization

- Initial: 12 months
- Renewal: 12 months

### Quantity Limits

| Product Name | Indication | Dosage Form | Quantity Limit |
|---|---|---|---|
| sonrotoclax (Beqalzi) | Mantle cell lymphoma | Starter pack | 44 tablets/ 30 days |
| | | 80 mg tablet | 120 tablets/ 30 days |
| | | 20 mg tablet | 28 tablets/ 28 days |
| | | **Restart packs** | |
| | | 1 mg wallet | 11 tablets/ 28 days |
| | | 5 mg wallet | 11 tablets/ 28 days |
| | | 20 mg wallet | 11 tablets/ 28 days |
| | | 80 mg wallet | 11 tablets/ 28 days |

### Initial Evaluation

I. **Sonrotoclax (Beqalzi)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   B. Medication will not be used in combination with any other oncology therapy; **AND**
   C. A diagnosis of **relapsed or refractory mantle cell lymphoma (MCL)** when the following are met:
      1. Member has progressed on, or was intolerant to one systemic therapy from each of the following modalities:
         i. Covalent Bruton Tyrosine Kinase inhibitor (BTKi) [e.g., ibrutinib (Imbruvica), acalabrutinib (Calquence), zanubrutinib (Brukinsa)]; **AND**
         ii. Additional systemic therapy (e.g., lenalidomide, rituximab, stem cell transplant, etc.); **AND**
      2. Member has progressed on, is refractory to, or is not a candidate for allogenic stem cell transplant; **AND**
      3. Provider attestation that all standard therapies have been exhausted or are inappropriate; **AND**
      4. Provider attestation that member is not a candidate for clinical trial participation

II. Sonrotoclax (Beqalzi) is considered investigational when used for all other conditions, including but not limited to:

A. Newly diagnosed mantle cell lymphoma (MCL)
B. Sonrotoclax (Beqalzi) used in combination with other oncology therapy
C. Chronic lymphocytic leukemia (CLL) and/or small lymphocytic lymphoma (SLL)
D. Waldenström Macroglobulinemia
E. Follicular lymphoma
F. Amyloid light-chain (AL) amyloidosis

## Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication will not be used in combination with any other oncology therapy; **AND**
IV. Disease response to treatment defined by stabilization of disease or decrease in tumor size or tumor spread, or no signs of disease progression

## Supporting Evidence

I. Mantle cell lymphoma (MCL) is an aggressive form of non-Hodgkin lymphoma (NHL) resulting from a malignant transformation of B-cells in the outer edge of a lymph node follicle (the mantle zone). Mantle cell lymphoma compromises of about 3-10% of NHL cases and predominantly affects older men between 60-70 years of age. Most patients have advanced stage disease at the time of diagnosis with approximately 75% presenting with lymphadenopathy and the remaining 25% presenting with extranodal disease. Given the complexity of management of MCL, treatment must be initiated by, in or consultation with, an oncologist.
II. Sonrotoclax (Beqalzi) has been studied in clinical trials as monotherapy only. There is insufficient evidence to support the efficacy and safety of sonrotoclax (Beqalzi) in combination with other oncology therapies.
III. For the treatment of relapsed/refractory (r/r) MCL, the National Comprehensive Cancer Network (NCCN) guidelines prefer treatment with a covalent BTK inhibitor [i.e., acalabrutinib (Calquence), ibrutinib (Imbruvica), zanubrutinib (Brukinsa)] as standard of care (SOC) if the patient has not progressed on one already, and an alternate rituximab-based regimen if they have (Category 2A). Second-line rituximab-based regimens include rituximab with chemoimmunotherapy, rituximab with ibrutinib (Imbruvica), and rituximab with venetoclax (Venclexta). Other second-line regimens include ibrutinib (Imbruvica) with venetoclax (Venclexta). If there is progression on covalent BTKi's, NCCN recommends subsequent treatment with a non-covalent BTK inhibitor—pirtobrutinib (Jaypirca), and T-cell mediated therapies (i.e., CAR-T cell therapy, bispecific antibodies) (Category 2A).
    - Preferred therapy in r/r MCL: Covalent BTKi (continuous)—acalabrutinib (Calquence), zanubrutinib (Brukinsa), or lenalidomide (continuous) with rituximab

i. Other recommended therapy: covalent BTKi (continuous)—ibrutinib (Imbruvica)± Rituximab

- Useful in certain circumstances: Bendamustine + rituximab, bortezomib ± rituximab, dexamethasone/cytarabine (DHA) + platinum (carboplatin, cisplatin, or oxaliplatin) + rituximab, gemcitabine/oxaliplatin (GEMOX) + rituximab, ibrutinib (continuous)/venetoclax (Venclexta), RBAC500, venetoclax (Venclexta) ± rituximab
- Progressive disease after prior covalent BTKi: non-covalent BTki—pirtobrutinib (Jaypirca), T-cell mediated therapy: lisocabtagene maraleucel (Breyanzi), brexucabtagene autoleucel (Tecartus), glofitamab-gxbm (Columvi), monsunetzumab-axgb (Lunsumio), polatzumab (Vedotin)

IV. Sonrotoclax (Beqalzi) was studied in a single-arm, open-label, multicenter Phase 1/2 (BGB-11417-201) study. In the pivotal Phase 2 portion, 103 participants were given a ramp up phase and continued 320 mg daily until disease progression or unacceptable toxicity. The primary efficacy outcome was overall response rate (ORR). Key secondary endpoints were complete response (CR), progression-free survival (PFS), median duration of response (DOR), time to response (TTR), and overall survival (OS). The median age of participants was 68 years, 75.7% of patients (n=87) were male, and 87.8% of patients (n=101) had stage III or IV MCL. Most participants at baseline had at least three prior lines of therapy (59.1%), including treatment with at least two prior BTK inhibitors (15.7%) including pirtobrutinib (Jaypirca) (12.2%), CAR-T cell therapy (2.6%), and autologous stem-cell transplant (14.8%). The single arm, open-label BGB-11417-201 study is of low quality. The study had a small sample size, lacked a comparator, and it was not adequately randomized. There is low confidence that the sonrotoclax (Beqalzi) provides a clinically objective and/or meaningful benefit for R/R MCL because overall response rate (ORR), DOR, PFS, and CR are surrogate markers that do not directly correlate with clinically significant outcomes, such as effects on morbidity or mortality. Therefore, major uncertainty lies in the validity of the results and applicability to patients. Confirmation of benefit is required from a Phase 3, randomized controlled trial. The majority of participants received at least three lines of prior therapy, therefore, benefit of sonrotoclax (Beqalzi) for patients without prior use of standard of care is unknown. National Comprehensive Cancer Network guidelines have been updated to include sonrotoclax (Beqalzi) in a new third-line and subsequent therapy treatment category for MCL (category 2A). Trial of a BTKi and an additional systemic therapy (e.g., lenalidomide, rituximab, stem cell transplant, etc.) is clinically appropriate, cost-effective, and aligns with the labeled indication and how sonrotocalx (Beqalzi) was studied in clinical trials.

V. Allogenic stem cell transplant (ASCT) is historically the standard of care in r/r MCL prior to the modern establishment of BTKi's in this disease space. Patients in the BGB-11417-201 study included 14.8% with prior ASCT. Consideration for or attestation that member is not a candidate of ASCT is warranted prior to use of sonrototoclax (Beqalzi).

VI. National Comprehensive Cancer Network guidelines have been updated to include sonrotoclax (Beqalzi) in a new third-line and subsequent therapy treatment category for MCL (category 2A). However, guidelines do not specify a limit to the number of chemotherapy regimens that can be attempted prior to use of the third-line treatment recommendation. Confirmatory trials for sonrotoclax (Beqalzi) included patients with progression on multiple lines of therapy, ranging

from one to eight prior lines of therapy. There are no head-head trials comparing the safety and efficacy of sonrotoclax (Beqalzi) to BTK inhibitors and other SOC treatment options for R/R MCL. The study design, endpoints, and efficacy results of sonrotoclax (Beqalzi), when indirectly compared, are similar to that of other secondary/subsequent-line treatments that are FDA-approved for R/R MCL. Ensuring all standard of care therapies have been exhausted prior to use of sonrotoclax (Beqalzi) is both clinically appropriate and cost effective.

VII. Guidelines recommend clinical trials as an option in the consolidation/additional therapy space after at least two lines of therapy in r/r MCL. Provider attestation that member is not a candidate for clinical trial participation is required. Clinical trials may represent the most suitable approach to treatment of rare cancers such as MCL at this time. As of July 2026, there are numerous recruiting clinical trials across the United States (e.g., NCT07719556, NCT07199296, NCT06496308, NCT07453095, etc.).

**Investigational or Not Medically Necessary Uses**

I. Sonrotoclax (Beqalzi) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Newly diagnosed MCL
      i. Sonrotoclax (Beqalzi) has only been FDA-approved in the setting of r/r MCL. There is insufficient evidence to support the safety and efficacy of sonrotoclax (Beqalzi) in treatment naïve patients without prior progression on a BTK inhibitor and anti-CD-20 chemoimmunotherapy regimens.
   B. Sonrotoclax (Beqalzi) used in combination with other oncology therapy
      i. There is currently a confirmatory, active comparator, Phase 3 (CELESTIAL-RRMCL) study underway that will evaluate the safety and efficacy of sonrotoclax (Beqalzi) plus zanubrutinib (Brukinsa) vs placebo in r/r MCL. The study is currently recruiting and is expected to be completed in 2032. There is also currently a Phase 2, randomized (BRAZAN) study to evaluate bendamustine, rituximab, cytarabine (AraC), and zanubrutinib, followed by maintenance therapy with zanubrutinib and rituximab with or without sonrotoclax (Beqalzi) for the treatment of newly diagnosed MCL. The study is active and expected to be completed in 2039. There is insufficient evidence for the use of sonrotoclax (Beqalzi) in combination with other oncology therapy for the treatment of MCL.
   C. Chronic lymphocytic leukemia (CLL) and/or small lymphocytic lymphoma (SLL)
      i. There are currently multiple Phase 2 studies underway to evaluate sonrotoclax (Beqalzi) alone and in combination with Zanubrutinib (Brukinsa) in the setting of treatment-naïve chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). These studies are in progress. Sonrotoclax (Beqalzi) is not FDA-approved in the setting of CLL/SLL and use of sonrotoclax (Beqalzi) in these disease settings is insufficiently supported.
   D. Waldenström Macroglobulinemia

i. Sonrotoclax (Beqalzi) has not been FDA-approved for use in the setting of Waldenström Macroglubulinemia. There is currently a phase II, multicenter, OLE study of sonrotoclax (Beqalzi), zanubrutinib (Brukinsa) and rituximab in with r/r Waldenström's Macroglobulinemia. The study is active and is expected to be completed by august 2028. There is insufficient efficacy and safety evidence for the use of sonrotoclax (Beqalzi) in Waldenström's Macroglobulinemia.

E. Follicular lymphoma
   i. Sonrotoclax (Beqalzi) has not been FDA-approved for use in the setting of follicular lymphoma. There is currently a Phase II, multicenter, single-arm study of sonrotoclax (Beqalzi), zanubrutinib (Brukinsa) and rituximab in previously untreated patients with follicular lymphoma (FLOURISH). The study is not yet recruiting and is expected to be completed by september 2029. There is insufficient efficacy and safety evidence for the use of sonrotoclax (Beqalzi) in follicular lymphoma.

F. Amyloid light-chain (AL) amyloidosis
   i. Sonrotoclax (Beqalzi) has not been FDA-approved for use in the setting of AL amyloidosis. There is currently a Phase II, interventional study of sonrotoclax (Beqalzi) used in combination with and without daratumumab in newly diagnosed patients with AL amyloidosis. The study is not yet recruiting and is expected to be completed by 2029. There is insufficient efficacy and safety evidence for the use of sonrotoclax (Beqalzi) in AL amyloidosis.

## Appendix

I. Table 1: Ramp-up dosing schedule

| Week Number | Days | Daily Dose | Number of Tablets per Dose |
|---|---|---|---|
| **Week 1** | Days 1 to 3 | 1 mg | One 1 mg tablet |
| | Days 4 to 7 | 2 mg | Two 1 mg tablets |
| **Week 2** | Days 1 to 3 | 5 mg | One 5 mg tablet |
| | Days 4 to 7 | 10 mg | Two 5 mg tablets |
| **Week 3** | Days 1 to 3 | 20 mg | One 20 mg tablet |
| | Days 4 to 7 | 40 mg | Two 20 mg tablets |
| **Week 4** | Days 1 to 3 | 80 mg | One 80 mg tablet |
| | Days 4 to 7 | 160 mg | Two 80 mg tablets |

**The Starter Pack provides the first 4 weeks of BEQALZI*

## References

1. Beqalzi. Package Insert. BeOne Medicines, Inc; 2026.
2. National Comprehensive Cancer Network. B-Cell lymphomas. May 20, 2026. Accessed July 29, 2026. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

3. Hematology Advisor. FDA Grants Accelerated Approval to Beqalzi for R/R Mantle Cell Lymphoma. Updated May 14, 2026. Accessed July 29, 2026. FDA Grants Accelerated Approval to Beqalzi for R/R Mantle Cell Lymphoma - Hematology Advisor
4. Eyre TA, Song Y, Hermine O, et al. Phase I/II Study of Sonrotoclax (BGB-11417) Monotherapy in Patients With Mantle Cell Lymphoma Previously Treated With Anti-CD20 Therapy and a Bruton Tyrosine Kinase Inhibitor. *J Clin Oncol*. Published online July 1, 2026. doi:10.1200/JCO-26-00550
5. Sonrotoclax. Drug Facts and Comparisons. Facts & Comparisons eAnswers. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed July 29, 2026. http://online.factsandcomparisons.com

### Related Policies

*Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.*

| Policy Name | Disease state |
|---|---|
| zanubrutinib (Brukinsa™) policy | Relapsed or refractory mantle cell lymphoma (R/R MCL) |
| | Relapsed or refractory follicular lymphoma (FL) |
| | Waldenström's macroglobulinemia i |
| | Chronic lymphocytic leukemia (CLL), Small lymphocytic lymphoma (SLL) |
| | Relapsed or refractory marginal zone lymphoma |
| venetoclax (Venclexta®) policy | Chronic lymphocytic leukemia (CLL), Small lymphocytic lymphoma (SLL) |
| | Acute myeloid leukemia |
| | Relapsed or refractory mantle cell lymphoma (R/R MCL) |
| pirtobrutinib (Jaypirca™) policy | Relapsed or refractory mantle cell lymphoma (R/R MCL) |
| | Chronic lymphocytic leukemia (CLL), Small lymphocytic lymphoma (SLL) |
| acalabrutinib (Calquence®) policy | Relapsed or refractory mantle cell lymphoma (R/R MCL) |
| | Chronic lymphocytic leukemia (CLL), Small lymphocytic lymphoma (SLL) |

### Policy Implementation/Update:

| Action and Summary of Changes | Date |
|---|---|
| Policy created | 11/2026 |