zanubrutinib (Brukinsa™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO172

Description

Zanubrutinib (Brukinsa) is an orally administered Bruton's Tyrosine Kinase (BTK) inhibitor.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
zanubrutinib (Brukinsa)	80 mg tablets	Treatment of adult patients with mantle cell lymphoma who have received at least one prior therapy	120 tablets/30 days

Initial Evaluation

I. Zanubrutinib (Brukinsa) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   C. A diagnosis of **Mantle Cell Lymphoma (MCL)** when the following are met:
      1. Member has received one prior therapy [e.g. chemotherapy, rituximab (Rituxan), or lenalidomide (Revlimid)]; **AND**
      2. Member has not previously progressed on a BTK inhibitor [e.g. ibrutinib (Imbruvica), acalabrutinib (Calquence)]

II. Zanubrutinib (Brukinsa) is considered investigational when used for all other conditions, including but not limited to:
   A. Chronic Lymphocytic Leukemia (CLL)
   B. Diffuse Large B-cell Lymphoma (DLBCL)
   C. Follicular Lymphoma (FL)
   D. Hairy Cell Leukemia (HCL)
   E. Graft-versus Host Disease (GvHD)
   F. Marginal Zone Lymphoma (MZL)
   G. Indolent Non-Hodgkin Lymphoma (iNHL)
   H. Small Lymphocytic Lymphoma (SLL)

I. Waldenstrom Macgroglobulinemia (WM)
J. MCL first-line therapy
K. MCL combination therapy

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. The member has exhibited improvement or stability of disease symptoms (e.g. no signs of disease progression)

Supporting Evidence

I. Zanubrutinib (Brukinsa) was studied in one open-label, single-arm, Phase 2 trial, and one Phase 1/2 safety and pharmacokinetic trial in 118 patients with MCL who had progressed on prior systemic therapy. The primary efficacy outcome was the overall response rate (ORR) which was 84% in both trials. Secondary efficacy outcomes were complete response (CR), partial response (PR), and duration of response (DoR). The percentage of patients with a CR was 59% and 22% for the Phase 2 trial and Phase 1/2 trial, respectively. The percentage of patients with a PR was 24% and 62% for the Phase 2 trial and Phase 1/2 trial, respectively. Median DoR in months was 19.5 and 18.5 for the Phase 2 trial and Phase 1/2 trial, respectively. Progression-free survival was evaluated in the Phase 2 trial, and found 74.6% of patients at 12 months were progression-free.
II. Zanubrutinib (Brukinsa) was FDA-approved under the accelerated approval pathway based on ORR. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Finalized data has not been published on these trials at this time.
III. The safety profile of zanubrutinib (Brukinsa) is similar to that of other BTK inhibitors [e.g. ibrutinib (Imbruvica), acalabrutinib (Calquence)]. The most common side effects are: upper respiratory tract infection, diarrhea, rash, pneumonia, and musculoskeletal pain. There are no specific contraindications to using zanubrutinib (Brukinsa); however, warnings and precautions include: serious cytopenias (e.g. neutropenia, thrombocytopenia, anemia), infections, cardiac arrhythmias, second primary malignancies (most commonly skin cancer), hemorrhage, and embryo-fetal toxicity. Zanubrutinib (Brukinsa) showed a 23% dose interruption rate, a 1% dose reduction rate, and a 7% discontinuation rate due to intolerable adverse events in clinical trials.

IV. Zanubrutinib (Brukinsa) was studied in a head-to-head trial against ibrutinib (Imbruvica) in patients with Waldenstrom's Macroglobulinemia. Zanubrutinib (Brukinsa) had lower rates of atrial fibrillation (2% vs 15%), minor bleeding (48.5% vs 59.2%), major hemorrhage (5.9% vs 9.2%), and diarrhea (20.8% vs 31.6%) compared to ibrutinib (Imbruvica), respectively. The rate of neutropenia was 29.7% and 13.3% for zanubrutinib (Brukinsa) and ibrutinib (Imbruvica), respectively.

V. For the treatment of MCL the National Comprehensive Cancer Network guidelines recommend initial induction therapy with chemotherapy. Those that respond well to initial treatment are candidates for an autologous stem cell transplant followed by rituximab for three years. Recommended second-line therapies are BTK inhibitors [e.g. acalabrutinib (Calquence), ibrutinib (Imbruvica), zanubrutinib (Brukinsa)], lenalidomide (Revlimid), and venetoclax (Venclaxta).

Investigational or Not Medically Necessary Uses

I. The following indications do not have sufficient evidence to support the use of zanubrutinib (Brukinsa) at this time:
   A. Chronic Lymphocytic Leukemia (CLL)
   B. Diffuse Large B-cell Lymphoma (DLBCL)
   C. Follicular Lymphoma (FL)
   D. Hairy Cell Leukemia (HCL)
   E. Graft-versus Host Disease (GvHD)
   F. Marginal Zone Lymphoma (MZL)
   G. Indolent Non-Hodgkin Lymphoma (iNHL)
   H. Small Lymphocytic Lymphoma (SLL)
   I. Waldenstrom Macgroglobulinemia (WM)
   J. MCL first-line therapy
   K. MCL combination therapy

References

I. Brukinsa [Prescribing Information]. Beigene USA, Inc.: San Mateo, CA. November 2019.
II. Brukinsa [Manufacturer e-dossier]. Beigene USA, Inc.: San Mateo, CA. November 2019.
III. Nasdaq Investors. BeiGene Announces Results of Phase 3 ASPEN Trial of Zanubrutinib Compared to Ibrutinib for the Treatment of Patients with Waldenstrom's Macroglobulinemia. http://ir.beigene.com/news-releases/news-release-details/beigene-announces-results-phase-3-aspen-trial-zanubrutinib?loc=US. Written December 16, 2019. Accessed December 19, 2019.
IV. National Comprehensive Cancer Network. NCCN Clinical Practice Guideline in Oncology. B-cell lymphomas. Version 6.2019. November 26, 2019.

Policy Implementation/Update:

Last Reviewed: 02/2020	
Action and Summary of Changes	**Date**
Policy created	02/2020