PRIOR AUTHORIZATION POLICY

POLICY: Vijoice Prior Authorization Policy
- Vijoice® (alpelisib tablets and oral granules – Novartis)

REVIEW DATE: 05/15/2024; selected revision 06/19/2024

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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

Vijoice, a kinase inhibitor, is indicated for the treatment severe manifestations of phosphatidylinositol- 4,5-bisphosphate 3-kinase catalytic subunit alpha **(PIK3CA)-Related Overgrowth Spectrum** (PROS) in adults and pediatric patients ≥ 2 years of age who require systemic therapy.[1]

This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Disease Overview

PROS is a heterogeneous group of diseases caused by mutations in *PI3KCA* and characterized by a range of clinical features.[2] Examples of PROS include patients with congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal (CLOVES) syndrome; megalencephaly-capillary malformation (MCAP) syndrome; Klippel-Trenaunay syndrome (KTS); facial infiltrating lipomatosis (FIL); dysplastic megalencephaly (DMEG); hemimegalencephaly (HMEG); focal cortical dysplasia (FCD); or capillary vascular malformation of the lower lip, lymphatic malformations of the head and neck, asymmetry and partial or generalized overgrowth (CLAPO) syndrome.[2,3] The core

features are congenital or early-childhood onset of segmental/focal overgrowth, predominantly affecting the brain, limbs (including fingers and toes), trunk (including abdomen and chest), and face, all usually in an asymmetric distribution. PROS-related complications can include hemorrhages; embolisms; vascular or lymphatic anomalies; congenital neurological complications; developmental delays; functional impairments; organ abnormalities, including cardiac and renal; superficial infections; chronic pain; skeletal anomalies; and psychological impact.[3] The diagnosis of PROS is often suspected by clinical features of the syndrome and can be confirmed with genetic testing of the *PI3KCA* gene.[2] Review articles state that management of PROS includes treatment of the manifestations, such as surgery, laser therapy, sclerotherapy, or oral medications such as sirolimus.[2,3,6]

Clinical Efficacy

The efficacy of Vijoice was evaluated in one single-arm pivotal study in patients who were treated as part of an expanded access program for compassionate use.[1,3] Eligible patients with PROS were ≥ 2 years of age, had severe or life-threatening clinical manifestations of PROS necessitating systemic treatment, and had documented evidence of mutation in the *PIK3CA* gene as determined by a local laboratory. The efficacy of Vijoice was evaluated in a total of 37 patients with at least one target lesion identified on imaging. The major efficacy outcome measure for the study was the proportion of patients with radiological response at Week 24, defined as a ≥ 20% reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions), in the absence of a ≥ 20% increase from baseline in any target lesion, progression of non-target lesions, or appearance of a new lesion. This trial demonstrated that the response rate of Vijoice was 27% (10 out of 37 patients) and the proportion of patients with duration of response ≥ 6 months was 70% (60% of patients had duration of response ≥ 12 months)[1,3] Clinically meaningful improvement in PROS-related signs and symptoms (e.g., pain, fatigue, vascular malformation, limb asymmetry, or disseminated intravascular coagulation) were observed.[3]

POLICY STATEMENT

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

- **Vijoice® (alpelisib tablets and oral granules (Novartis)**

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 Indication

1. **PIK3CA-Related Overgrowth Spectrum (PROS).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   Note: Examples of PROS include congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal (CLOVES) syndrome; megalencephaly-capillary malformation (MCAP) syndrome; Klippel-Trenaunay

syndrome (KTS); facial infiltrating lipomatosis (FIL), dysplastic megalencephaly (DMEG); hemimegalencephaly (HMEG); focal cortical dysplasia (FCD); or capillary vascular malformation of the lower lip, lymphatic malformations of the head and neck, asymmetry and partial or generalized overgrowth (CLAPO) syndrome.

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 2 years of age; AND
- **ii.** Patient has at least one severe clinical manifestation of PROS, as determined by the prescriber; AND
  Note: Examples of severe clinical manifestations include excessive tissue growth, blood vessel malformations, scoliosis, vascular tumors, cardiac or renal manifestations, and those who require systemic treatment.
- **iii.** Patient has a *PIK3CA* mutation as confirmed by genetic testing; AND
- **iv.** The medication is being prescribed by or in consultation with a physician that specializes in treatment of genetic disorders.

B) Patient is Currently Receiving Vijoice. Approve for 1 year if the patient meets ALL of the following (i, ii and iii):
- **i.** Patient has been established on Vijoice for at least 6 months; AND
  Note: A patient who has received < 6 months of therapy or who is restarting therapy with Vijoice is reviewed under criterion A (Initial Therapy).
- **ii.** Patient has experienced a reduction in volume from baseline (prior to initiating Vijoice) in at least one lesion, as confirmed by measurement; AND
- **iii.** Patient has experienced an improvement in at least one sign or symptom of PROS from baseline (prior to initiating Vijoice).
  Note: Examples of signs or symptoms of PROS include pain, fatigue, vascular malformation, limb asymmetry, or disseminated intravascular coagulation.

CONDITIONS NOT COVERED

- **Vijoice® (alpelisib tablets and oral granules (Novartis)**

is(are) considered experimental, investigational or unproven for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Vijoice® tablets and oral granules [prescribing information]. East Hanover, NJ: Novartis; April 2024.
2. Mirzaa G, Graham JM Jr, Keppler-Noreuil K. PIK3CA-related overgrowth spectrum. 2013 Aug 15 [Updated 2021 Dec 23]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. Gene Reviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022.
3. Canaud G, Lopez Gutierrez JC, Irvine AD, et al. Alpelisib for treatment of patients with PIK3CA-related overgrowth spectrum (PROS). *Genet Med*. 2023; 25(12):100969.
4. Keppler-Noreuil K, Rios JJ, Parker V, et al. PIK3CA-related overgrowth spectrum (PROS): diagnostic and testing eligibility criteria, differential diagnosis, and evaluation. *Am J Med Genet A*. 2015;0(2):287-295.
5. National Center of Advancing Translational Sciences. Genetic and Rare Disease Information Center. PIK3CA-related overgrowth spectrum. Available at:

https://rarediseases.info.nih.gov/diseases/12182/pik3ca-related-overgrowth-spectrum. Created January 29, 2018. Accessed on April 24, 2024.
6. Canuad G, Hammil AM, Adams D. A review of mechanisms of disease across PIK3CA-related disorders with vascular manifestations. *Orphanet J Rare Dis*. 2021;16(1):306.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/10/2023
Annual Revision	No criteria changes.	05/15/2024
Selected Revision	Vijoice oral granules were added to the policy; same criteria for tablets applies to oral granules formulation.	06/19/2024