



Drug Coverage Policy

Effective Date.....9/1/2024
Coverage Policy Number IP0481
Policy Title.....Vijoice

Vijoice

- Vijoice® (alpelisib tablets - Novartis)

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 Healthcare Coverage Policy

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 Vioice 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 Vioice 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 $\geq 20\%$ reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions), in the absence of a $\geq 20\%$ 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 Vioice 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

Medical Necessity Criteria

Vioice is considered medically necessary when the following criteria are met:

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 Vioice.** Approve for 1 year if the patient meets ALL of the following (i, ii and iii):
- i.** Patient has been established on Vioice for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Vioice is reviewed under criterion A (Initial Therapy).
 - ii.** Patient has experienced a reduction in volume from baseline (prior to initiating Vioice) 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 Vioice).

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

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

References

1. Vioice® tablets [prescribing information]. East Hanover, NJ: Novartis; November 2022.
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. Canaud 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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Updated coverage policy title from <i>Alpelsib</i> to <i>Vijoice</i> .	9/1/2024

The policy effective date is in force until updated or retired.

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