Effective Date **10/1/2023**
Next Review Date… **10/1/2024**
Coverage Policy Number **IP0481**

Alpelisib

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Related Coverage Resources

Quantity Limitations - (1201)

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. 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.

Overview

This policy supports medical necessity review for alpelisib tablets **(Vijoice®)**.

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

Medical Necessity Criteria

Alpelisib (Vijoice) is considered medically necessary when the following are met:

1. **PIK3CA-Related Overgrowth Spectrum (PROS).** Individual meets **ALL** of the following criteria (A, B, C, and D):
   A. Individual is 2 years of age or older
   B. According to the prescriber the individual has at least one severe clinical manifestation of PROS (for example, excessive tissue growth, blood vessel malformations, scoliosis, vascular tumors, cardiac or renal manifestations, and those that require systemic treatment)
   C. Individual has a *PIK3CA* pathogenic or likely pathogenic variant as confirmed by genetic testing

D. The medication is prescribed by, or in consultation with, a physician that specializes in treatment of genetic disorders

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.

Reauthorization Criteria

Alpelisib (Vijoice) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response, including the following:

1. Individual has experienced a reduction in at least one lesion volume as confirmed by radiographic imaging from baseline
2. Individual has experienced an improvement at least one sign or symptom of PROS from baseline (for example, pain, fatigue, vascular malformation, limb asymmetry, or disseminated intravascular coagulation)

Authorization Duration

Initial approval duration: up to 6 months.
Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Vijoice, a kinase inhibitor, is indicated for the treatment of adults and pediatric patients ≥ 2 years of age with severe manifestations of phosphatidylinositol- 4,5-bisphosphate 3-kinase catalytic subunit alpha **(PIK3CA)-Related Overgrowth Spectrum** (PROS) 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]

References

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3. Canaud G, Lopez Gutierrez JC, Irvine A, et al. EPIK-P1: retrospective chart review study of patients with PIK3CA-related overgrowth spectrum who have received alpelisib as part of a compassionate use programme [abstract]. Presented at : The 2021 European Society for Medical Oncology (ESMO) Congress; virtual; September 16-21, 2021.
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.
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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.