PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 04/13/2022

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]

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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Vijoice is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **PIK3CA-Related Overgrowth Spectrum (PROS).** Approve for the duration noted if the patient meets ONE of the following criteria (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 the following criteria (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 that 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 the following criteria (i, ii and ii):
     - **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 RECOMMENDED FOR APPROVAL

Coverage of Vijoice is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Vijoice® tablets [prescribing information]. East Hanover, NJ: Novartis; April 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 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.
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 11, 2022.
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 July 8. [Epub ahead of print].