09-J4000-28

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Reviewed: 04/09/25

Revised: 05/15/25

Subject: Alpelisib (Vijoice)

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DESCRIPTION:

On April 5, 2022, the FDA granted accelerated approval to Vijoice (alpelisib) for adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-related overgrowth spectrum (PROS) who require systemic therapy. Vijoice is a kinase inhibitor that works by inhibiting the PI3K pathway and is the first FDA-approved treatment for PROS. PROS is a group of rare conditions characterized by focal or segmental overgrowth of parts of the body due to mutations in the PIK3CA gene. Prior to the approval of Vijoice, the only treatment options for PROS were surgery or interventional radiology.

The safety and efficacy of alpelisib were evaluated in EPIK-P1 (n=57), a single-arm retrospective chart review of patients with PROS who have received alpelisib as part of a compassionate use program. Patients (median age, 14 years; 44% were 2 to 11 years) had at least one target lesion identified on imaging, with most having congenital overgrowth (92%) and early childhood-onset (8%). Various manifestations of PROS were included; congenital lipomatous overgrowth, vascular malformations, epidermal nevi, and skeletal/spinal/scoliosis abnormalities (CLOVES, 81%); megalencephaly-capillary malformation polymicrogyria; Klippel-Trenaunay syndrome; and facial infiltrating lipomatosis).

The primary outcome measure for the study was the proportion of patients with response at 24 weeks (+/- 4 weeks), defined by achieving at least 20% reduction from the index date in the sum of measurable target lesion volume (one to three lesions, via central review of imaging scans), provided that none of the individual target lesions have ≥20% increase from index date and in absence of progression of non-target lesions and without new lesions. An additional secondary outcome measure was duration of response, defined as the time from first documented response to the date of the first documented disease progression or death due to any cause.

While 57 patients were enrolled in the study, 20 patients did not have sufficient data to evaluate efficacy. Of the 37 patients included in the efficacy population, 27% had a radiological response at Week 24, and 60% had a response lasting 12 months or longer. The most common adverse events (AEs) of any grade were diarrhea (16%), stomatitis (16%), and hyperglycemia (12%).

Additional clinical trials evaluating long-term efficacy and safety of alpelisib in PROS are being conducted.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of alpelisib (Vijoice) **meets the definition of medical necessity** for **ALL** of the following criteria are met:

1. Member is diagnosed with PIK3CA-Related Overgrowth Spectrum (PROS)

   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.

2. Member has a mutation in the PIK3CA gene – laboratory documentation must be provided
3. Member has at least one severe manifestation of PROS – documentation from the medical record must be provide
4. Member has at least one PROS-related measurable lesion defined as a lesion with longest diameter of at least 2 cm – documentation from the medical record must be submitted
5. Alpelisib is prescribed by or in consultation with a physician specializing in genetic disorders
6. Member is at least 2 years of age
7. Dose does not exceed 250 mg daily

Approval duration: 6 months

Continuation of alpelisib (Vijoice) **meets the definition of medical necessity** for **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida in the past two years for PROS or other FDA-approved diagnosis, OR the member has previously met all indication-specific initiation criteria
2. Member has a mutation in the PIK3CA gene – laboratory documentation must be provided
3. Member demonstrates a reduction in PROS-related lesion volume from baseline (prior to initiation of alpelisib) – documentation from the medical record must be provided
4. Alpelisib is prescribed by or in consultation with a physician specializing in genetic disorders
5. Member is at least 2 years of age
6. Dose does not exceed 250 mg daily

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Pediatric patients (2 to less than 18 years of age): 50 mg taken orally once daily with food. Consider a dose increase to 125 mg once daily in pediatric patients ≥ 6 years old for response optimization (clinical/radiological) after 24 weeks of treatment at 50 mg once daily. When a pediatric patient turns 18 years old, consider a gradual dose increase up to 250 mg.
- Adult patients: 250 mg taken orally once daily with food

Dose Adjustments

- See FDA approved labeling for dose adjustments due to adverse reactions

Drug Availability

- Tablets: 50 mg, 125 mg, and 200 mg
- Oral Granules: 50 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Severe hypersensitivity to alpelisib or any of its ingredients

Precautions/Warnings

- Severe Hypersensitivity: Permanently discontinue

- Severe Cutaneous Adverse Reactions (SCARs)
- Hyperglycemia
- Pneumonitis
- Diarrhea
- Embryo-Fetal Toxicity

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

Q04.3	Other reduction deformities of brain
Q04.5	Megalencephaly
Q04.8	Other specified congenital malformation of brain
Q27.8	Other specified congenital malformations of peripheral vascular system
Q27.9	Congenital malformations of peripheral vascular system, unspecified
Q74.0	Other congenital malformations of lower limb(s), including shoulder girdle
Q74.2	Other congenital malformations of lower limb(s), including pelvic girdle
Q87.2	Congenital malformation syndromes predominantly involving limbs.
Q87.3	Congenital malformation syndromes involving early overgrowth
Q87.8	Other specified congenital malformation syndromes, not elsewhere classified
Q89.9	89.9 Congenital malformation, unspecified.

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Canaud G, 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. Presented at the 2021 ESMO Virtual Congress; September 17–21, 2021. https://www.esmo.org/newsroom/press-office/early-signs-ofefficacy-of-new-targeted-agents-and-immunotherapies-reported-for-multiple-cancers-at-esmo-congress-2021
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 4/1/25]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 4/1/25]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 4/1/25].
5. Novartis. Vijoice (alpelisib) tablet. 2024 [cited 8/6/24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=638069a4-aee0-46c9-9e21-54ad449c163c.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 4/1/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 04/09/25.

GUIDELINE UPDATE INFORMATION:

07/01/22	New Medical Coverage Guideline.
08/15/24	Review and revision to guidline; consisting of updating position statement and references.
10/15/24	Revision to guideline; consisting of updating dosage/administration.
05/15/25	Review and revision to guidline; consisting of updating references.