Original Effective Date: 08/01/2022
Current Effective Date: 11/29/2023
Last P&T Approval/Version: 10/25/2023
Next Review Due By: 10/2024
Policy Number: C23736-A

Vijoice (alpelisib)

PRODUCTS AFFECTED

Vijoice (alpelisib)
*Piqray (alpelisib) – SEE STANDARD ONCOLOGY (C16154-A)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
PIK3CA Related Overgrowth Spectrum (PROS)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PIK3CA RELATED OVERGROWTH SPECTRUM (PROS):
   1. Documentation of a diagnosis of PIK3CA Related Overgrowth Spectrum (PROS)
      AND
   2. Documentation of a mutation in the PIK3CA gene [DOCUMENTATION REQUIRED]

AND

3. Prescriber attests that member has at least one target lesion identified on imaging.
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Vijoice (alpelisib) include: Severe hypersensitivity to Vijoice (alpelisib) or to any of its ingredients, pregnancy, lactation, and coadministration with strong CYP3A4 inducers]

CONTINUATION OF THERAPY:

A. PIK3CA RELATED OVERGROWTH SPECTRUM (PROS):
   1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   2. Documentation of positive response to therapy as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (i.e., documentation of a reduction in the target lesion volume and without new lesions or clinical improvement)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified specialist in genetic disorders or vascular disorders [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
2 years of age and older

QUANTITY:
Pediatric patients (2 years of age to less than 6 years of age): 50 mg taken orally once daily
Pediatric patients (6 years of age to less than 18 years of age): maximum 125 mg taken orally once daily
Adult patients (18 years of age and older): 250 mg taken orally once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
PIK3CA-Related Overgrowth Spectrum Agents - PI3K Inhibitor

FDA-APPROVED USES:
Indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy.

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).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
PIK3CA-related overgrowth spectrum (PROS) includes a group of genetic disorders that leads to overgrowth of various body parts due to changes (mutations) in the gene PIK3CA. This gene is involved in making a protein that helps regulate cell growth, division and survival. A broad array of disorders falls within this spectrum, with some overlap of symptoms between the different disorders. Syndromes within the spectrum may also overlap genetically, meaning they may share specific PIK3CA gene mutations in cells in the areas of the body that are affected. Since PIK3CA mutations in these disorders are not present in all cells, only certain areas of the body are overgrown, ranging from isolated digits to whole limbs, trunk, or brain. Different tissues may be involved individually or in combination such as fat, muscle, bone, nerve, brain and blood vessels. Genetic mutations that cause these disorders are not passed down from parent to child but instead result from changes to genes during development in the womb. Symptoms associated with these disorders can be present at birth (congenital) or appear later in early childhood. Overgrowth may stop in childhood or continue into adulthood.

Different subtypes within PROS include: CLAPO syndrome, CLOVES syndrome, DCMO, DMEG, FAH/FAO/HHML, FAVA, FIL, HMEG, Klippel-Trenaunay syndrome (KTS), LON, macrodactyly, MCAP and muscular hemihyperplasia (HH). Symptoms vary widely and depend on which part of the body overgrows, ranging from intellectual disability, seizures and autism when the brain is involved to blood clots when blood vessels are affected. Some PROS syndromes affect a wider range of body systems while others are more limited in which parts of the body overgrow.

Diagnosis of PROS is based on genetic testing for PIK3CA genetic variants. Testing for somatic conditions includes biopsy of tissue affected by overgrowth. Detection of a PIK3CA mutation in biopsied tissue may be difficult because these mutations are detected at widely varying levels in affected cells and tissues.

The Food and Drug Administration (FDA) granted accelerated approval to Vijoice® (alpelisib) for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-related overgrowth spectrum (PROS) who require systemic therapy. The approval was based on real-world evidence from a global, site-based, retrospective, non-interventional medical chart review of the EPIK-P1 trial (ClinicalTrials.gov Identifier: NCT04285723), which included 57 patients aged 2 years or older with PROS who were treated with Vijoice 50mg to 250mg orally once daily as part of an expanded access program for compassionate use. The primary endpoint was the proportion of patients with radiological response at week 24, defined as achieving at least a 20% reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions), confirmed by at least 1 subsequent imaging assessment, in the absence of a 20% or greater increase from baseline in any target lesion, progression of non-target lesions, or appearance of a new lesion.

Among 37 efficacy evaluable patients, results showed that 27% (n=10/37; 95% CI, 14-44) had a confirmed response at week 24. The median duration of response was not reached (95% CI, 0.9+, 42.9+ months), with 70% of patients having a response duration of at least 6 months and 60% having a response duration of at least 12 months. Moreover, 74% (n=23/31) of patients with imaging at baseline showed a mean reduction of 13.7% in target lesion volume. None of the patients experienced disease progression at the time of primary analysis.
At week 24, improvements in pain (90%; n=20/22), fatigue (76%; n=32/42), vascular malformation

(79%; n=30/38), limb asymmetry (69%; n=20/29), and disseminated intravascular coagulation (55%; n=16/29) were observed.
The most common adverse reactions reported were diarrhea (16%), stomatitis (16%), and hyperglycemia (12%). The most common grade 3/4 adverse event was cellulitis. Additionally, severe hypersensitivity, severe cutaneous adverse reactions, and pneumonitis have been reported with the use of alpelisib. Continued approval of Vijoice may be contingent upon verification and description of clinical benefit in a confirmatory trial. The accelerated approval was based on response rate and duration of response.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Vijoice (alpelisib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Vijoice (alpelisib) include: Severe hypersensitivity to Vijoice (alpelisib) or to any of its ingredients, pregnancy, lactation, and coadministration with strong CYP3A4 inducers.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Vijoice TBPK 50MG
Vijoice TBPK 125MG
Vijoice TBPK 200 & 50MG

REFERENCES

1. Vijoice (alpelisib) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; November 2022.
2. 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.
3. National Center for Advancing Translational Sciences. Genetic and Rare Diseases Information Center. PIK3CA-related overgrowth spectrum. Updated January 2022.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Prescriber Requirements	Q4 2023
REVISION- Notable revisions: Products Affected Continuation of Therapy Quantity Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q1 2023
NEW CRITERIA ESTABLISHED	Q3 2022