Vijoice (alpelisib) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
06-01-2024	12-01-2022

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Vijoice® (alpelisib) Tablets	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		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

PIK3CA-Related Overgrowth Spectrum (PROS)	PIK3CA-related overgrowth spectrum (PROS) is a group of genetic disorders that result in overgrowth of various body parts due to mutations in the PIK3CA gene. A broad number of disorders fall into the spectrum, with some genetic and symptom overlap between the different disorders. The PIK3CA gene is involved in making a protein that helps regulate cell growth, division, and survival. Mutations to the PIK3CA gene happen spontaneously during development in the womb. There are a number of subtypes of PROS and include:(2) • CLAPO (capillary malformation of the lower lip, lymphatic malformation of the face and neck, asymmetry of face and limbs, and partial or generalized overgrowth involving one or more body segments) syndrome • Congenital lipomatous (fatty) overgrowth, vascular malformations, epidermal nevi, and scoliosis/skeletal/spinal anomalies (CLOVES) syndrome • Diffuse capillary malformation with overgrowth (DCMO) • Dysplastic megalencephaly (DMEG) • Fibroadipose hyperplasia (FAH)/fibroadipose overgrowth (FAO) • Hemihyperplasia multiple lipomatosis (HHML) syndrome • Fibro-adipose vascular anomaly (FAVA) • Facial infiltrating lipomatosis (FIL) • Hemimegalencephaly (HME) • Klippel-Trenaunay syndrome (KTS) • Lipomatosis of nerve (LON) • Macrodactyly • Megalencephaly-capillary malformation (MCAP) syndrome • Muscular hemihyperplasia (HH) PROS is caused by somatic mutations in the PIK3CA gene. There are a variety of activating mutations of the PIK3CA gene associated with each syndrome with some genetic overlap between the different syndromes. These somatic mutations occur during prenatal development and are said to be somatic mosaic mutations, where the mutations are present in only certain cells of the body affecting only certain areas of the body, leading to overgrowth in only certain body regions or asymmetrically.(2)

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	The PIK3CA gene leads to the creation of the protein known as p110a, and mutations in this gene result in an abnormally active PI3K enzyme. With increased activity, affected cells grow and divide more rapidly, leading to abnormal bone, soft tissue and blood vessel growth. PIK3CA mutations may also cause overgrowth by influencing the effects of growth factors and hormones on nearby and distant cells. Mutations in the PIK3CA gene have been found in certain cancers of the lower GI tract, the ovaries, breasts, brain and liver. Currently, most patients with PROS do not appear to be at a significantly higher risk for cancer. The only cancer reported in PROS to date has been Wilms tumor, the most common pediatric kidney cancer in very young children.(2)
	
	Due to the phenotypic overlap and variability, the diagnosis of PROS can be complicated. Referral to a physician with expertise in the diagnosis and treatment of PROS is recommended. Biopsy of the overgrown tissue and genetic testing for PIK3CA variants are required to confirm the diagnosis of PROS.(2,3,4) The National Institute of Health (NIH) Clinical Diagnostic Criteria for PROS include the following:(3)
	
	• Required:
	  ○ Presence of somatic PIK3CA mutation*
	  ○ Congenital or early childhood onset
	  ○ Overgrowth sporadic and mosaic
	  ○ Features described in either A or B
	• A: Spectrum (two or more features)**
	  ○ Overgrowth
	  ○ Vascular malformations
	  ○ Epidermal nevus
	• B: Isolated features
	  ○ Large isolated lymphatic malformations
	  ○ Isolated macrodactyly OR overgrown splayed feet/hands, overgrown limbs
	  ○ Truncal adipose overgrowth
	  ○ Hemimegalencephaly (bilateral)/dysplastic megalencephaly/focal cortical dysplasia
	  ○ Epidermal nevus
	  ○ Seborrheic keratoses
	  ○ Benign lichenoid keratoses
	
	*- If no mutation identified, consider as presumptive PROS
	**- Typically progressive
	
	Treatment is dependent on the syndrome and symptoms present. Treatment options can include the following:(2)
	
	• Laser ablation may be used for vascular anomalies.
	• Surgical removal of vascular malformations may be helpful. Sclerotherapy or embolization may be performed alone or in conjunction with surgery.
	• Surgical removal or debulking may be an option for tissue overgrowth of limbs, digits, or soft tissue, but abnormal tissue may regrow, requiring repeated surgical interventions.
	• Orthopedic options may include surgical closure of growth plates in joints or shoe lifts.
	• Physical, occupational, and speech therapy along with special education may be warranted depending on motor and intellectual disabilities present.
	• Megalencephaly requires referral to a neurosurgeon for potential surgical treatments for Chiari malformations or hydrocephalus, or medications for seizures.

Efficacy	The efficacy of Vijoice was assessed in EPIK-P1 (NCT04285723), a single-arm clinical study in patients who were treated as part of an expanded access program for compassionate use. Eligible patients 2 years of age and older with PIK3CA-related overgrowth spectrum (PROS) who received Vijoice had clinical manifestations of PROS that were assessed by the treating physician as severe or life-threatening and

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	necessitating systemic treatment and had documented evidence of mutation in the PIK3CA gene.(1) The efficacy of Vijoice was evaluated in a total of 37 patients with at least one target lesion identified on imaging performed within 24 weeks prior to receipt of the first dose of Vijoice. Ninety-two percent of patients had congenital overgrowth and 8% had early childhood-onset. The major efficacy outcome measure for the study was the proportion of patients with radiological response at week 24 as determined by blinded independent central review (BICR), defined as a greater than or equal to 20% reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions) confirmed by at least one subsequent imaging assessment, in the absence of a greater than or equal to 20% increase from baseline in any target lesion, progression of non-target lesions, or appearance of a new lesion. An additional efficacy outcome measure was duration of response, defined as the time from the first documented response to the date of the first documented disease progression or death due to any cause. Of the patients treated with Vijoice 10 were considered responders, and of those patients 7 sustained response for greater than or equal to 6 months and 6 sustained response for greater than or equal to 12 months.(1)
Safety	Vijoice is contraindicated in patients with severe hypersensitivity to alpelisib or any of its ingredients.(1)

REFERENCES

Number	Reference
1	Vijoice prescribing information. Novartis Pharmaceuticals Corp. November 2022.
2	National Organization for Rare Disorders (NORD) Rare Disease Database. PIK3CA-Related Overgrowth Spectrum (PROS). Accessed at: https://rarediseases.org/rare-diseases/pik3ca-related-overgrowth-spectrum/
3	Keppler-Noreuil KM, Rios JJ, Parker VER, et al. PIK3CA-Related Overgrowth Spectrum (PROS): Diagnostic and Testing Eligibility Criteria, Differential Diagnosis, and Evaluation. Am J Med Genet A. 2015 Feb;0(2):287–295.
4	Kuentz P, St-Onge J, Duffourd Y, et al. Molecular Diagnosis of PIK3CA-Related Overgrowth Spectrum (PROS) in 162 Patients and Recommendations for Genetic Testing. Genet Med. 2017 Sep;19(9):989-997.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Vijoice	alpelisib (pros) pak ; alpelisib (pros) tab therapy pack	125 MG ; 200 & 50 MG ; 50 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Vijoice	Alpelisib (PROS) Pak	200 & 50 MG	56	Tablets	28	DAYS			

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Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Vijoice	Alpelisib (PROS) Tab Therapy Pack	50 MG	28	Tablets	28	DAYS			
Vijoice	Alpelisib (PROS) Tab Therapy Pack	125 MG	28	Tablets	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vijoice	alpelisib (pros) pak ; alpelisib (pros) tab therapy pack	125 MG ; 200 & 50 MG ; 50 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Vijoice	Alpelisib (PROS) Pak	200 & 50 MG	Medicaid
Vijoice	Alpelisib (PROS) Tab Therapy Pack	50 MG	Medicaid
Vijoice	Alpelisib (PROS) Tab Therapy Pack	125 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Vijoice

      1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**
   B. ALL of the following:
      1. The patient has a diagnosis of PIK3CA-Related Overgrowth Spectrum (PROS) confirmed by ALL of the following:
         A. Presence of somatic PIK3CA mutation **AND**
         B. Congenital or early childhood onset **AND**
         C. Overgrowth sporadic and mosaic **AND**
         D. ONE of the following:
            1. The patient has at least TWO of the following features:
               A. Overgrowth
               B. Vascular malformations
               C. Epidermal nevus **OR**
            2. The patient has at least ONE of the following features:
               A. Large isolated lymphatic malformations

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Module	Clinical Criteria for Approval
	B. Isolated macrodactyly OR overgrown splayed feet/hands, overgrown limbs C. Truncal adipose overgrowth D. Hemimegalencephaly (bilateral)/dysplastic megalencephaly/focal cortical dysplasia E. Epidermal nevus F. Seborrheic keratoses G. Benign lichenoid keratoses **AND** 2. The patient has severe manifestations of PROS that requires systemic therapy **AND** 3. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., experienced in PROS) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient has NOT had disease progression (e.g., increase in lesion number, increase in lesion volume) with the requested agent (medical records required) **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., experienced in PROS) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval**: up to 6 months for initial; up to 12 months for renewal

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