Clinical Policy: Alpelisib (Vijoice only)

Reference Number: PA.CP.PHAR.430
Effective Date: 08/2023
Last Review Date: 07/2025

Description
Alpelisib (Vijoice®) is a phosphoinositide 3-kinase (PI3K) inhibitor.

FDA Approved Indication(s)
Vijoice is indicated for the treatment of adult and pediatric patients 2 years of age or 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.*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Vijoice is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. PIK3CA Related Overgrowth Spectrum (must meet all)**:**

1. Request is for Vijoice;
2. Diagnosis of PROS;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Documented evidence for PIK3CA gene mutation;
   b. If unable to perform biopsy to confirm PIK3CA gene mutation, member meets all of the following (i, ii, and iii):
      i. Congenital or early childhood onset (birth to the age of eight);
      ii. Overgrowth that is sporadic and mosaic (other terms: patchy, irregular);
      iii. Either of any two clinical spectrum features from Category A or any one isolated feature from Category B (see Appendix E);
5. Member's condition is severe or life-threatening requiring systemic therapy as determined by treating physician;
6. For non-cutaneous lesions, member has at least one target lesion identified on imaging within the last 6 months;
7. Dose does not exceed any of the following (a, b, or c):
   a. Age 2-5 years: 50 mg (1 tablet or oral granules packet) per day;
   b. Age 6-17 years: 125 mg (1 tablet) per day;
   c. Age ≥ 18 years: 250 mg (two 125 mg tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. PIK3CA Related Overgrowth Spectrum (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Request is for Vijoice;
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following (a, b or c):
    a. Reduction in size, volume, and/or total number of measurable lesions from baseline via subsequent imaging scan;
    b. Improvement in at least one sign, symptom, or complication of PROS (e.g., pain, fatigue, vascular malformation, limb asymmetry, disseminated intravascular coagulation);
    c. Improvement in functional status (e.g., mobility, performance, work/school attendance);
4. If request is for a dose increase, new dose does not exceed any of the following (a, b, or c):
    a. Age 2-5 years: 50 mg (1 tablet or oral granules packet) per day;
    b. Age 6-17 years: 125 mg (1 tablet) per day;
    c. Age ≥ 18 years: 250 mg (two 125 mg tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
PROS: PIK3CA-related overgrowth spectrum

Appendix B: Therapeutic Alternatives
N/A

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): severe hypersensitivity to Piqray or Vijoice or to any of its components
- Boxed warning(s): none reported

Appendix D: General Information
Subdivisions of PROS
- CLAPO syndrome: capillary malformation of the lower lip, lymphatic malformation of the face and neck, asymmetry, and partial/generalized overgrowth
- CLOVES syndrome: congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal
- Diffuse capillary malformation with overgrowth
- Dysplastic megalencephaly
- Fibroadipose hyperplasia/fibroadipose overgrowth/hemihyperplasia-multiple lipomatosis syndrome
- Fibroadipose vascular anomaly
- Facial infiltrating lipomatosis
- Hemimegalencephaly
- Klippel-Trenaunay syndrome
- Lipomatosis of nerve
- Macodactyly
- Megalencephaly-capillary malformation syndrome
- Muscular hemihyperplasia

Appendix E: National Institutes of Health (NIH) Workshop Recommended Clinical Features of PROS

Category A (spectrum) - 2 or more features	**Category B (isolated features) – any 1 feature**
• Overgrowth: adipose, muscle, nerve, skeletal • Vascular malformations: capillary, venous, arteriovenous malformation, lymphatic • Epidermal nevus	• Large, isolated lymphatic malformation • Isolated macrodactyly or overgrown, splayed feed/hands, overgrown limbs • Truncal adipose overgrowth • Hemimegaloencephaly (bilateral), dysplastic megalencephaly, focal cortical dysplasia • Epidermal nevus • Seborrheic keratoses • Benign lichenoid keratoses

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Vijoice	PROS	Pediatric patients (2 to < 18 years of age): 50 mg PO daily with food. Consider a dose increase to 125 mg PO daily in pediatric patients ≥ 6 years old for response optimization after 24 weeks of treatment with Vijoice at 50 mg once daily Adult patients: 250 mg PO daily with food *Oral granules may be used to administer a 50 mg daily dose only. Do not use multiple 50 mg packets or a partial packet of oral granules for patients prescribed a 125 mg or a 250 mg dose. Do not combine oral granules and tablets to achieve the prescribed dose.	• Age 2 – 5: 50 mg/day • Age 6-17: 125 mg/day • Age ≥ 18: 250 mg/day

VI. Product Availability

Drug Name	Availability
Vijoice	Tablets: 50 mg, 125 mg, 200 mg Oral granules single-use packet: 50 mg

VII. References

1. Vijoice Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2024. Available at: https://www.novartis.us/sites/www.novartis.us/files/vijoice.pdf. Accessed May 19, 2025.
2. Micromedex® ® DRUGDEX® [Internet database]. Ann Arbor, Michigan: Merative™. Updated periodically. Accessed May 29, 2025.
3. Douzgou S, Rawson M, Faivre L, et al. A standard of care for individuals with PIK3CA-related disorders: an international expert consensus statement. Clinical Genetics. 2022; 101:32-47.
4. Canaud G, Lopez Gutierrez JC, Irvine A, et al. EPIK-P1: Retrospective chart review study of patients (pts) with PIK3CA-related overgrowth spectrum (PROS) who have received alpelisib (ALP) as part of a compassionate use programme. Annals of Oncology. 2021; 32(S5):S127.
5. Canuad G, Hammill AM, Adams D, Vikkula M, and Keppler-Noreuil KM. A review of mechanisms of disease across PIK3CA-related disorders with vascular manifestations. Orphanet J Rare Dis. 2021;16:306.
6. PIK3CA-related overgrowth spectrum. National Organization for Rare Disorders (NORD). 2025. Available at: https://rarediseases.org/rare-diseases/pik3ca-related-overgrowth-spectrum/. Accessed May 29, 2025.
7. Keppler-Noreuil KM, Rios JJ, Parker VE, et al. PIK3CA-related overgrowth spectrum (PROS): diagnostic and testing eligibility criteria, differential diagnosis, and evaluation. Am J Med Genet A. 2015;167A:287-95.

Reviews, Revisions, and Approvals	Date
Policy created	07/2023
3Q 2024 annual review: no significant changes; RT4: added oral granules dosage form per updated prescribing information; references reviewed and updated.	07/2024
3Q 2025 annual review: no significant changes; references reviewed and updated.	07/2025