Clinical Policy: Alpelisib (Piqray, Vijoice)

Reference Number: ERX.SPA.341
Effective Date: 09.01.19
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Piqray is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Piqray and Vijoice are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Request is for Piqray;
2. Diagnosis of breast cancer;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Disease has all of the following characteristics (a, b, c, and d):
   a. HR-positive (i.e., estrogen or progesterone receptor [ER/PR]-positive);
   b. HER2-negative;
   c. Advanced (locally recurrent) or metastatic;
   d. Positive for PIK3CA mutation;
6. Piqray is prescribed in combination with fulvestrant;
7. Disease has progressed on or after an endocrine therapy (*see Appendix B*);
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 300 mg (two tablets) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

B. PIK3CA-Related Overgrowth Spectrum (must meet all)**:**
1. Request is for Vijoice;
2. Diagnosis of PROS;
3. Age ≥ 2 years;
4. Documented evidence for PIK3CA gene mutation;
5. Member's condition is severe or life-threatening requiring systemic therapy as deemed by treating physician;
6. Member has at least one target lesion identified on imaging;
7. Dose does not exceed any of the following (a, b, or c):
   a. Age 2-5 years: 50 mg (1 tablet) per day;
   b. Age 6-17 years: 125 mg (1 tablet) per day;
   c. Age ≥ 18 years: 250 mg (2 tablets) per day.

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Piqray for breast cancer and has received this medication for at least 30 days;
2. Request is for Piqray;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 300 mg (two 150 mg tablets) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

B. PIK3CA-Related Overgrowth Spectrum (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Vijoice;
3. Member is responding positively to therapy as evidenced by subsequent imaging scan with a reduction in sum of measurable lesion volume assessed across 1 to 3 target lesions;
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) per day;
   b. Age 6-17 years: 125 mg (1 tablet) per day;
   c. Age ≥ 18 years: 250 mg (2 tablets) per day.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ER: estrogen receptor
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
NCCN: National Comprehensive Cancer Network
PR: progesterone receptor
PROS: PIK3CA-related overgrowth spectrum

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Endocrine Therapy		
anastrozole (Arimidex®)	1 mg PO QD	1 mg/day
exemestane (Aromasin®)	25 mg PO QD	25 mg/day
Fareston® (toremifene)	60 mg PO QD	60 mg/day
fulvestrant (Faslodex®)	500 mg IM into the buttocks slowly (1 - 2 minutes per injection) as two 5 mL injections, one in each buttock, on days 1, 15, 29 and once monthly thereafter	500 mg/day
letrozole (Femara®)	2.5 mg PO QD	2.5 mg/day
tamoxifen (Nolvadex®, Soltamox®)	20 to 40 mg PO QD	40 mg/day
megestrol acetate	40 mg PO QID	160 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Piqray	Breast cancer	In combination with fulvestrant: 300 mg PO QD with food	300 mg/day
Vijoice	PROS	Pediatric patients (2 to less than 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	• Age 2 – 5: 50 mg/day • Age 6-17: 125 mg/day • Age >18: 250 mg/day

VI. Product Availability

Drug Name	Availability
Piqray	Tablets: 50 mg, 150 mg, 200 mg
Vijoice	Tablets: 50 mg, 125 mg, 200 mg

VII. References

1. Piqray Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021. Available at: https://www.novartis.us/sites/www.novartis.us/files/piqray.pdf. Accessed April 8, 2022.
2. Vijoice Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2022. Available at: https://www.novartis.us/sites/www.novartis.us/files/vijoice.pdf. Accessed April 22, 2022.
3. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed April 8, 2022.
4. National Comprehensive Cancer Network. Breast Cancer Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed April 8, 2022.
5. Douzou S, Rawson M, Baselga E, Danielpour 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.
6. 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.
7. 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.
8. PIK3CA-related overgrowth spectrum. National Organization for Rare Disorders (NORD). 2022. Available at: https://rarediseases.org/rare-diseases/pik3ca-related-overgrowth-spectrum/. Accessed April 22, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.09.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	04.30.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated,	05.05.21	08.21
3Q 2022 annual review: RT4: newly approved agent Vijoice for PROS added to policy; references reviewed and updated.	05.17.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of

medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.