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| **Clinical Policy Title:** | alpelisib |
| **Policy Number:** | RxA.250 |
| **Drug(s) Applied:** | Piqray® |
| **Original Policy Date:** | 02/07/2020 |
| **Last Review Date:** | 06/10/2021 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Alpelisib (Piqray®) is a phosphoinositide 3-kinase (PI3K) inhibitor. It 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 a Food and Drug Administration approved test following progression on or after an endocrine-based regimen.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| alpelisib (Piqray®) | Breast cancer | In combination with fulvestrant: 300 mg orally once daily with food | 300 mg/day |

## Dosage Forms

- Tablets: 50 mg, 150 mg, 200 mg

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

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

1. Diagnosis of recurrent or stage IV HR-positive, HER2-negative, PIK3CA mutation positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years or older;
4. Disease has all of the following characteristics (a, b, c, and d):
   a. Hormone receptor-positive (i.e., estrogen or progesterone receptor [ER/PR]-positive);
   b. Human epidermal growth factor receptor 2-negative;
   c. Advanced (locally recurrent) or metastatic;
   d. Positive for PIK3CA mutation;
5. Prescribed in combination with fulvestrant;

6. Disease has progressed on or after endocrine therapy (*see Appendix B for examples*);
7. 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 Food and Drug Administration-approved or recommended by National Comprehensive Cancer Network.

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**II. Continued Therapy Approval**

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is currently receiving alpelisib for breast cancer and has received this medication for at least 30 days;
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 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 Food and Drug Administration-approved or recommended by National Comprehensive Cancer Network.*

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

**III. Appendices**

**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
SJS: Stevens-Johnson Syndrome
EM: erythema multiforme
TEN: toxic epidermal necrolysis
DRESS: drug reaction with eosinophilia and systemic symptoms

**APPENDIX B: Therapeutic Alternatives**

*Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.*

| Drug Name | Dosing Regimen | Dose Limit/Maximum Dose |
|---|---|---|
| **Endocrine Therapy** | | |

| Drug Name | Dosing Regimen | Dose Limit/Maximum Dose |
|---|---|---|
| anastrozole (Arimidex®) | 1 mg orally once daily | 1 mg/day |
| exemestane (Aromasin®) | 25 mg orally once daily | 25 mg/day |
| Fareston® (toremifene) | 60 mg orally once daily | 60 mg/day |
| Faslodex® (fulvestrant) | 500 mg intramuscularly 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 orally once daily | 2.5 mg/day |
| tamoxifen (Soltamox®) | 20 to 40 mg orally once daily | 40 mg/day |
| megestrol acetate | 40 mg orally 4 times a day | 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 to any of its components.

- Boxed Warning(s):
  - None reported.

**APPENDIX D: General Information**

- Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson Syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with Piqray®.
- In the SOLAR-1 study, SJS and EM were reported in 0.4% and 1.1% of the patients, respectively. Drug reaction with eosinophilia and systemic symptoms (DRESS) was reported in patients treated with Piqray® in the postmarketing setting. If signs or symptoms of SCARs occur, interrupt Piqray® until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, permanently discontinue Piqray®. Do not reintroduce Piqray®in patients who have experienced previous severe cutaneous adverse reactions during Piqray® treatment.
- If a SCAR is not confirmed, Piqray® may require dose modifications, topical corticosteroids, or oral antihistamine treatment. Advise patients of the signs and symptoms of SCARs (e.g., a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy).

**References**


1. Piqray® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2021. Available at: https://www.us.Piqray®.com/metastatic-breast-cancer/. Accessed March 08, 2021.
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4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed March 08, 2021.
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| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 01/2020 | 02/07/2020 |
| Policy reviewed.<br>1. Formatting updated.<br>2. Clinical criteria updated.<br>3. References updated.<br>4. Clinical policy title updated.<br>5. Drug(s) Applied updated.<br>6. Lines of Business updated.<br>7. Continued therapy criteria updated. | 06/29/2020 | 09/14/2020 |
| Policy was reviewed:<br>1. Appendix A: Abbreviation/ Acronym Key was updated.<br>2. Appendix B: Fixed header verbiage was updated as 'Below are suggested therapeutic alternatives.'<br>3. Appendix B: Discontinued brand Nolvadex® was removed.<br>4. Appendix D: General Information was added.<br>5. References were updated. | 03/10/2021 | 06/10/2021 |