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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 21, 2019
Subject:	Piqray	**Page:**	1 of 5

Last Review Date: March 7, 2025

Piqray

Description

Piqray (alpelisib)

Background
Piqray (alpelisib) is an inhibitor of phosphatidylinositol-3-kinase (PI3K) with inhibitory activity predominantly against PI3Kα. In breast cancer cell lines, alpelisib inhibited the phosphorylation of PI3K downstream targets, including Akt and showed activity in cell lines harboring a PIK3CA mutation. PI3K inhibition by alpelisib treatment has been shown to induce an increase in estrogen receptor (ER) transcription in breast cancer cells. The combination of alpelisib and fulvestrant demonstrated increased anti-tumor activity compared to either treatment alone (1).

Regulatory Status
FDA-approved indication: Piqray is indicated in combination with fulvestrant for the treatment of adults 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 (1).

Piqray has warnings regarding severe hypersensitivity, hyperglycemia, pneumonitis, diarrhea, and severe cutaneous reactions. Severe cutaneous reactions, including Stevens-Johnson syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) were reported in patients treated with Piqray (1).

Piqray may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception during treatment with Piqray and for 1

week after the last dose. Male patients with female partners of reproductive potential should be advised to use condoms and effective contraception during treatment with Piqray and for 1 week after the last dose (1).

The safety and effectiveness of Piqray in pediatric patients less than 18 years of age have not been established (1).

Related policies
Itovebvi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Piqray may be considered **medically necessary** if the conditions indicated below are met.

Piqray may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Advanced or metastatic breast cancer

AND ALL of the following:

1. Hormone receptor (HR)-positive
2. Human epidermal growth factor receptor 2 (HER2)-negative
3. PIK3CA-mutated as detected by an FDA-approved test
4. Used in combination with fulvestrant (Faslodex)
5. Patient has had disease progression on or after an endocrine-based regimen
6. Prescriber agrees to monitor for **ALL** of the following:

   a. Severe cutaneous reactions, such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS)
   b. Pneumonitis
7. Prescriber agrees to monitor for elevated glucose and decrease the dose or discontinue therapy as required
8. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Piqray and for 1 week after the last dose
9. Male patients with female partners of reproductive potential **only**: patient will be advised to use condoms and effective contraception during treatment and for 1 week after the last dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Advanced or metastatic breast cancer

AND ALL of the following:

1. Used in combination with fulvestrant (Faslodex)
2. **NO** disease progression or unacceptable toxicity
3. Prescriber agrees to monitor for **ALL** of the following:
   a. Severe cutaneous reactions, such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS)
   b. Pneumonitis
4. Prescriber agrees to monitor for elevated glucose and decrease the dose or discontinue therapy as required
5. Female patients of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Piqray and for 1 week after the last dose

6. Male patients with female partners of reproductive potential **only**: patient will be advised to use condoms and effective contraception during treatment and for 1 week after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Strength	Quantity Limit
300 mg daily dose (2 x 150 mg)	168 tablets per 84 days **OR**
250 mg daily dose (1 x 200 mg + 1 x 50 mg)	168 tablets per 84 days **OR**
200 mg daily dose (1 x 200 mg)	84 tablets per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Piqray (alpelisib) is an inhibitor of phosphatidylinositol-3-kinase (PI3K) indicated in combination with fulvestrant for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer. Piqray has warnings regarding severe hypersensitivity, hyperglycemia, pneumonitis, diarrhea, fetal harm and severe cutaneous reactions. The safety and effectiveness of Piqray in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Piqray while maintaining optimal therapeutic outcomes.

References

1. Piqray [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2024.
2. NCCN Drugs & Biologics Compendium® Alpelisib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
June 2019	Addition to PA
September 2019	Annual review. Revised hyperglycemia monitoring requirement to prescriber agrees to monitor for elevated glucose and decrease dose or discontinue therapy as required per SME
June 2020	Annual review
September 2021	Annual editorial review and reference update. Revised monitoring requirement to monitoring for “Severe cutaneous reactions, such as Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS)”
April 2022	Adjusted contraception requirement to align with indication, only male patients with female partners of reproductive potential are to be advised to use condoms and effective contraception. Added clarification under renewal indicating female patients must be postmenopausal per PI
June 2022	Annual review and reference update
September 2022	Annual review and reference update
June 2023	Annual review and reference update
February 2024	Per PI update, removed requirement for female patients to be postmenopausal and added contraception requirement for female patients
March 2024	Annual review and reference update
June 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.