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Itovebi

Description

Itovebi (inavolisib)

Background
Itovebi (inavolisib) is an inhibitor of phosphatidylinositol-3-kinase (PI3K) with inhibitory activity predominantly against PI3Kα. In vitro, Itovebi induced the degradation of mutated PI3K catalytic alpha subunit P110α (encoded by the PIK3CA gene), inhibited phosphorylation of downstream target AKT, reduced cellular proliferation, and induced apoptosis in PIK3CA-mutated breast cancer cell lines. In vivo, Itovebi reduced tumor growth in PIK3CA-mutated, estrogen receptor-positive, breast cancer xenograft models. The combination of Itovebi with palbociclib and fulvestrant increased tumor growth inhibition compared to each treatment alone or the doublet combinations (1).

Regulatory Status
FDA-approved indication: Itovebi is a kinase inhibitor indicated in combination with palbociclib and fulvestrant for the treatment of adults with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy (1).

Itovebi carries warnings regarding hyperglycemia, stomatitis, and diarrhea. Anti-hyperglycemics, corticosteroid-containing mouthwash, and antidiarrheal medications should be considered as clinically indicated. Interrupt, dose reduce, or discontinue Itovebi based on severity of symptoms (1).

Itovebi can cause fetal harm when administered in pregnant women. Females of reproductive potential should be advised to use effective non-hormonal contraception during treatment with Itovebi and for 1 week after the last dose. Male patients with female partners of reproductive potential should use effective contraception during treatment with Itovebi and for 1 week after the last dose (1).

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

Related policies
Piqray

Policy

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

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Locally 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 palbociclib (Ibrance) and fulvestrant (Faslodex)
5. Following recurrence on or after completing adjuvant endocrine therapy

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

Locally advanced or metastatic breast cancer

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Used in combination with palbociclib (Ibrance) and fulvestrant (Faslodex)
3. Female patients of reproductive potential **only**: patient will be advised to use effective non-hormonal contraception during treatment with Itovebi and for 1 week after the last dose
4. Male patients with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Itovebi and for 1 week after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 9 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Itovebi is a kinase inhibitor indicated in combination with palbociclib and fulvestrant for the treatment of adults with PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer. Itovebi may cause hyperglycemia, stomatitis, diarrhea, and embryo-fetal toxicity. The safety and effectiveness of Itovebi 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 Itovebi while maintaining optimal therapeutic outcomes.

References

1. Itovebi [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2024.
2. NCCN Drugs & Biologics Compendium® Inavolisib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.

Policy History

Date	Action
November 2024	Addition to PA
December 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.