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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	October 4, 2012
Subject:	Tykerb	**Page:**	1 of 5

Last Review Date: March 8, 2024

Tykerb

Description

Tykerb (**lapatinib**)

Preferred product: generic lapatinib

Background
Tykerb (lapatinib) is a kinase inhibitor of the intracellular kinase domains of both Epidermal Growth Factor Receptor (EGFR [ErbB1]) and of Human Epidermal Receptor Type 2 (HER 2 [ErbB2]) receptors. Tykerb inhibits ErbB-driven tumor cell growth in vitro and in various animal models (1).

Regulatory Status
FDA-approved indications: Tykerb (lapatinib) is a kinase inhibitor indicated in combination with: (1)

1. Capecitabine, for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
2. Letrozole (Femara) for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor and for whom hormonal therapy is indicated.

Limitation of Use:
Patients should have disease progression on trastuzumab prior to initiation of treatment with Tykerb in combination with capecitabine.

Off-Label Use:

Tykerb has also been shown to be effective for HER2+ gastric cancer when in combination with trastuzumab. The combination of Tykerb and trastuzumab has been shown to be superior to Tykerb alone in the second-line treatment of HER2+ breast cancer. The use of Tykerb in combination with trastuzumab has been shown to be safe and effective in metastatic HER2+ breast cancer. The treatment is recommended in the NCCN guidelines and is an accepted standard of care (2-4).

Tykerb carries a boxed warning for hepatotoxicity in clinical trials and post-marketing experience. The hepatotoxicity may be severe, and deaths have been reported. Patients should be monitored and Tykerb discontinued if patients experience severe changes in liver function tests (1).

Tykerb has warnings regarding decrease in left ventricular ejection fraction (LVEF), diarrhea, interstitial lung disease and pneumonitis, QT interval prolongation, severe cutaneous reactions and fetal harm. Tykerb should be discontinued if patients experience severe pulmonary symptoms. Female patients of reproductive potential must have pregnancy status verified prior to starting treatment with Tykerb. Female patients of reproductive potential and male patients with female partners of reproductive potential must be advised to use effective contraception during treatment with Tykerb and for 1 week after the last dose (1).

The safety and effectiveness of Tykerb have not been established in pediatric patients (1).

Related policies

Afinitor, Enhertu, Halaven, Herceptin Hylecta, Ibrance, Kadcyla, Margenza, Nerlynx, Perjeta, Phesgo, Trastuzumab, Tukysa

Policy

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

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

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

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. HER2+ advanced or metastatic breast cancer with **ONE** of the following:
    a. History of prior therapy with an anthracycline, a taxane, and trastuzumab
        i. Used in combination with capecitabine or trastuzumab
    b. Postmenopausal women for whom hormonal therapy is indicated
        i. Used in combination with letrozole or trastuzumab

2. HER2+ gastric cancer
    a. Used in conjunction with or after the use of trastuzumab

AND the following for **Brand Tykerb ONLY**:

1. Patient **MUST** have tried the preferred product (generic Tykerb: lapatinib) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Tykerb (lapatinib) is a kinase inhibitor of the intracellular kinase domains of both Epidermal Growth Factor Receptor (EGFR [ErbB1]) and of Human Epidermal Receptor Type 2 (HER 2

[ErbB2]) receptors. Tykerb inhibits ErbB-driven tumor cell growth in vitro and in various animal models. Tykerb is indicated to be used in combination with capecitabine in patients who have received prior therapy with an anthracycline, a taxane and trastuzumab. Tykerb is approved in combination with letrozole for the treatment of HER-2 overexpressing (positive) cancers in postmenopausal women for whom hormonal therapy is indicated. The use of Tykerb in combination with trastuzumab has been shown to be safe and effective in metastatic HER2+ breast cancer. Tykerb may also be used in HER2+ gastric cancer when used in conjunction with or after trastuzumab therapy. The safety and effectiveness of Tykerb have not been established in pediatric patients (1-4).

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

References

1. Tykerb [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2022.
2. Tanizaki J, Okamoto I, Takezawa K, et al. Synergistic antitumor effect of S-1 and HER2-targeting agents in gastric cancer with HER2 amplification. *Mol Cancer Ther.* 2010 May; 9 (5):1198-207.
3. Wainberg Z, Angehel A, Desai A, et al. Lapatinib, a dual EGFR and HER2 kinase inhibitor, selectively inhibits HER2-amplified human gastric cancer cells and is synergistic with trastuzumab in vitro and in vivo. *Clin Cancer Res.*2010 Mar 1; 16(5):1509-19.
4. NCCN Drugs & Biologics Compendium® Lapatinib 2024. National Comprehensive Cancer Network, Inc. Accessed on January 11, 2024.

Policy History

Date	Action
October 2012	New Addition
December 2012	Annual editorial review and update
January 2013	Addition of the indication of HER2+ gastric cancer when used in conjunction with or after trastuzumab (Herceptin) therapy.
March 2013	Annual editorial review and update
April 2013	Removal of the concurrent therapy with Xeloda and Femara requirement in breast cancer (7,8,9,10)
June 2013	Label Update
December 2013	Annual editorial review by the PMPC and update Combination therapy updated to reflect current requirements for postmenopausal women with HER2+ metastatic breast cancer
December 2014	Annual editorial review and reference update

February 2015	Addition of advanced breast cancer
June 2015	Annual editorial review
June 2016	Annual editorial review and reference update Policy number change from 5.04.23 to 5.21.23
June 2017	Annual editorial review and reference update
December 2017	Annual review
March 2018	Annual review
June 2019	Annual review and reference update
December 2019	Annual review
March 2020	Annual review and reference update
June 2020	Annual review
September 2020	Annual review
December 2020	Annual review
June 2021	Annual review and reference update
December 2021	Annual review and reference update. Added requirement that brand Tykerb has to t/f the preferred product lapatinib
September 2022	Annual review and reference update
June 2023	Annual review and reference update
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.