



TYKERB (lapatinib)

Preferred product: generic lapatinib

RATIONALE FOR INCLUSION IN PA PROGRAM

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



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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).

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.



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4. NCCN Drugs & Biologics Compendium® Lapatinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.