Clinical Policy: Lapatinib (Tykerb)

Reference Number: PA.CP.PHAR.79
Effective Date: 01/18
Last Review Date: 10/18 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for lapatinib (Tykerb®) tablets for oral use.

FDA Approved Indication(s)
Tykerb is indicated in combination with:

- 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
- Letrozole for the treatment of postmenopausal women with hormone receptor (HR)-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated

Limitation(s) of use:

- Patients should have disease progression on trastuzumab prior to initiation of treatment with Tykerb in combination with capecitabine.
- Tykerb in combination with an aromatase inhibitor has not been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Tykerb is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Disease is recurrent or metastatic (stage IV), and HER2-positive;
4. Tykerb is prescribed in combination with one of the following (a, b, or c):
   a. Capecitabine;
   b. Trastuzumab;
   c. If HR-positive, an aromatase inhibitor (e.g., anastrozole, letrozole, exemestane), and:
      i. If male, an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1500 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, meets one of the following (a or b):
    a. New dose does not exceed 1500 mg 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).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Lapatinib is an inhibitor of the intracellular tyrosine kinase domains of both EGFR (ErbB1) and HER (ErbB2). Lapatinib inhibits ErbB-driven tumor cell growth in vitro and in various animal models.

- An *in vitro* additive effect was demonstrated when lapatinib and 5-FU (the active metabolite of capecitabine) were used in combination.
- Lapatinib also retained significant *in vitro* growth inhibitory activity against breast cancer cell lines selected for long-term growth in trastuzumab-containing medium.

Hormone receptor-positive (estrogen receptor-positive or progesterone receptor-positive) that coexpress HER2 tend to be resistant to established endocrine therapies. Similarly, hormone receptor-positive breast cancer cells that initially lack EGFR or HER2 upregulate these receptor proteins as the tumor becomes resistant to endocrine therapy.

Formulations:

Tykerb is available in 250 mg tablets for oral administration.

FDA Approved Indications:

Tykerb is a kinase inhibitor/oral tablet formulation indicated in combination with:

- Capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab.
    - Limitation of use: Patients should have disease progression on trastuzumab prior to initiation of treatment with Tykerb in combination with capecitabine.

- Letrozole for the treatment of postmenopausal women with hormone receptor-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated.

Appendices

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known severe hypersensitivity (e.g., anaphylaxis) to this product or any of its components
- Boxed warning(s): hepatotoxicity

Appendix D: General Information

- The NCCN recommends that men with HR-positive breast cancer be treated similarly to postmenopausal women, except that the use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.
- The NCCN supports use of Tykerb in premenopausal women with HR-positive breast cancer when used concomitantly with an aromatase inhibitor. Along with this combination therapy, patients should also be treated with ovarian ablation/suppression. Ovarian ablation can be achieved with surgical oophorectomy or ovarian irradiation. Ovarian suppression can be achieved with luteinizing hormone-releasing hormone agonists (e.g., goserelin, leuprolide).
- The NCCN also recommends use of Tykerb in combination with capecitabine for the treatment of recurrent brain metastases in patients with breast cancer that is responsive to Tykerb.
- HR-positive can be either estrogen receptor (ER)- or progesterone receptor (PR)-positive.

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; added COC; references reviewed and updated.	07/18	

References

1. Tykerb Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2017. Available at https://www.tykerb.com. Accessed July 5, 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 5, 2018.
3. National Comprehensive Cancer Network. Breast Cancer Version 1.2018. Available at www.NCCN.org. Accessed July 5, 2018.