Clinical Policy: Lapatinib (Tykerb)

Reference Number: ERX.SPA.81
Effective Date: 03.01.14
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Lapatinib (Tykerb®) is a kinase inhibitor.

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
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Age ≥ 18 years;
4. Disease is recurrent or metastatic (stage IV), and HER2-positive;
5. Tykerb is prescribed in combination with one of the following (a, b, or c):*
   a. Capecitabine, and one of the following (i or ii):
      i. Member has received prior therapy;
      ii. Member has extensive brain metastases;
   b. Trastuzumab, and member has received at least 2 prior therapies;
   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);

   **Prior authorization may be required.*
6. If member is a premenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);

7. For brand Tykerb requests, member must use generic lapatinib, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed 1,500 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Bone Cancer (off-label) (must meet all)**:**
1. Diagnosis of recurrent chordoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is EGFR-positive;
5. Prescribed as a single agent;
6. For brand Tykerb requests, member must use generic lapatinib, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

C. Colorectal Cancer (off-label) (must meet all)**:**
1. Diagnosis of unresectable, advanced, or metastatic colorectal cancer and both of the following (a and b):
   a. Disease is HER2 positive;
   b. Disease is RAS (i.e., both KRAS and NRAS) and BRAF wild-type;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyla®, Tykerb, Perjeta®);
5. Prescribed in combination with trastuzumab;*

**Prior authorization may be required.*

6. For brand Tykerb requests, member must use generic lapatinib, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Tykerb for a covered indication and has received this medication for at least 30 days;

2. Member is responding positively to therapy;
3. For brand Tykerb requests, member must use generic lapatinib, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 1,500 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EGFR: epidermal growth factor receptor
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

- NCCN recommendations in breast cancer:
  - 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	Advanced or metastatic: 1,250 mg PO QD on Days 1-21 continuously in combination with capecitabine 2,000 mg/m^2/day (administered PO in 2 doses approximately 12 hours apart) on Days 1-14 in a repeating 21-day cycle HER2-positive: 1,500 mg PO QD continuously in combination with letrozole 2.5 mg PO QD	1,500 mg/day 5,500 mg/day if taking a strong CYP3A4 inducer 500 mg/day if taking a strong CYP3A4 inhibitor

VI. Product Availability

Tablet: 250 mg

VII. References

1. Tykerb Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2022. Available at: https://www.tykerb.com. Accessed July 29, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 29, 2022.
3. National Comprehensive Cancer Network. Breast Cancer Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 29, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; references reviewed and updated.	07.02.18	11.18
4Q 2019 annual review: added bone cancer off-label use criteria per NCCN 2A recommendation; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.13.19	11.19
Added NCCN compendium-supported use of colorectal cancer in combination with trastuzumab; references reviewed and updated.	02.20.20	05.20
4Q 2020 annual review: updated the following off-label criteria per NCCN category 2A recommendations: chordoma- added that Tykerb must be prescribed as a single agent; colorectal cancer- added that disease must also be BRAF wild type; references reviewed and updated.	07.15.20	11.20
4Q 2021 annual review: added redirection to generic formulation; added criterion for ovarian ablation or suppression for premenopausal women being treated with Tykerb for breast cancer per NCCN Compendium; references reviewed and updated.	08.13.21	11.21
4Q 2022 annual review: per NCCN, for breast cancer, added requirement for prior therapy if prescribed in combination with capecitabine or trastuzumab (with bypass for brain metastases for capecitabine) and for colorectal cancer, added additional disease qualifier of unresectable; references reviewed and updated.	07.29.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional

medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.