Clinical Policy: Lapatinib (Tykerb)

Reference Number: CP.PHAR.79
Effective Date: 10.01.11
Last Review Date: 11.24
Line of Business: Commercial, HIM, 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.

It is the policy of health plans affiliated with Centene Corporation® 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. Member meets both of the following (a and b):
   a. Disease is recurrent, advanced, or metastatic (stage IV);
   b. 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 3 prior therapies;
c. Both of the following (i and ii):
   i. If HR-positive, an aromatase inhibitor (e.g., anastrozole, letrozole, exemestane);
   ii. 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Bone Cancer (off-label) (must meet all)**:**

1. Diagnosis of recurrent conventional or chondroid 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit 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, 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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.novartis.com/us-en/sites/novartis_us/files/tykerb.pdf. Accessed July 12, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 8, 2024.
3. National Comprehensive Cancer Network. Breast Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed August 8, 2024.
4. National Comprehensive Cancer Network. Colon Cancer Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed August 8, 2024.
5. National Comprehensive Cancer Network. Bone Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed August 12, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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	08.13.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
premenopausal women being treated with Tykerb for breast cancer per NCCN Compendium; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; added legacy Wellcare auth durations (WCGCP.PHAR.70 to retire); references reviewed and updated.		
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
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; revised generic redirection language to "must use" per updated template; consolidated initial approval duration for Legacy WCG to align with standard Medicaid approach; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.29.22	11.22
4Q 2023 annual review: per NCCN, for breast cancer, updated lapatinib is prescribed in combination with "trastuzumab, and member has received at least 3 prior therapies" from previous criteria "trastuzumab, and member has received at least 2 prior therapies" to align with NCCN compendium and current invasive breast cancer guideline version 4.2023 as combination regimen is considered fourth-line currently; for initial approval criteria, added "advanced" to "disease is recurrent, advanced, or metastatic (stage IV)" to align with FDA approved indication language; references reviewed and updated.	07.03.23	11.23
4Q 2024 annual review: for bone cancer, added "conventional or chondroid" to criterion "diagnosis of recurrent **conventional or chondroid** chordoma" as supported by NCCN compendium; references reviewed and updated.	07.12.24	11.24

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.