

**Clinical Policy: Lapatinib (Tykerb)**

Reference Number: CP.PHAR.79

Effective Date: 10.01.11

Last Review Date: 05.20

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<sup>®</sup>) 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<sup>®</sup> 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  $\geq$  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;
  - 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);
6. 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** – Length of Benefit

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

1. Diagnosis of recurrent chordoma;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Disease is EGFR-positive;
5. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 1,500 mg per day;
  - b. 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** – Length of Benefit

**C. Colorectal Cancer (off-label) (must meet all):**

1. Diagnosis of advanced or metastatic colorectal cancer and both of the following (a and b):
    - a. Disease is HER2 positive;
    - b. Disease is wild-type *RAS* (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use);
  2. Prescribed by or in consultation with an oncologist;
  3. Age  $\geq$  18 years;
  4. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyla<sup>®</sup>, Tykerb, Perjeta<sup>®</sup>);
  5. Prescribed in combination with trastuzumab;\*
- \*Prior authorization may be required.*
6. 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** – Length of Benefit

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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. 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** – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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*

- 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: 1250 mg PO QD on Days 1-21 continuously in combination with capecitabine 2,000 mg/m <sup>2</sup> /day (administered PO in 2 doses approximately 12 hours apart) on Days 1-14 in a repeating 21-day cycle	1,500 mg/day
		5,500 mg/day if taking a strong CYP3A4 inducer
	HER2-positive: 1500 mg PO QD continuously in combination with letrozole 2.5 mg PO QD	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; December 2018. Available at: <https://www.tykerb.com>. Accessed February 10, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed February 10, 2020.
3. National Comprehensive Cancer Network. Bone Cancer Version 1.2020. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/bone.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf). Accessed August 13, 2019.
4. National Comprehensive Cancer Network Guidelines. Colon Cancer Version 1.2020. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.
5. National Comprehensive Cancer Network Guidelines. Rectal Cancer Version 1.2020. Available at [www.nccn.org](http://www.nccn.org). Accessed February 10, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy converted to new template. Removed prescriber and age requirements. Hormone receptor-positive and HER2-positive metastatic breast cancer (FDA approved use): Added that Tykerb must be prescribed in combination with letrozole. Normal baseline and follow-up LVEF added. Added max dose with CYP inducers under FDA indications. Added all NCCN recommended uses. Added appendix of breast cancer therapies by drug class.	11.16	12.16
Policy converted to new template. Annual Review. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Central nervous system cancer off-label use criteria added per NCCN 2A recommendation. Authorization limits extended from 3 and 6 months to 6 and 12 months for initial and continued approval, respectively.	08.17	11.17
4Q 2018 annual review: no significant changes; added commercial and HIM lines of business; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; added age; added COC; references reviewed and updated.	07.05.18	11.18
4Q 2019 annual review: added bone cancer off-label use criteria per NCCN 2A recommendation; 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

### **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.

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**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.

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