Clinical Policy: Lapatinib (Tykerb)

Reference Number: CP.PHAR.79
Effective Date: 10.01.11
Last Review Date: 11.17
Line of Business: 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
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
  - Limitation(s) 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
  - Limitation(s) of use: 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 (which may include office chart notes and lab results) 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. Tykerb will be used in one of the following ways (a or b):
   a. FDA-approved use (i or ii):
      i. Diagnosis of advanced (stage III) or metastatic (stage IV) breast cancer and (a-d):
         a) Tykerb is prescribed in combination with capecitabine;
         b) Disease is HER2-positive;
         c) Member previously received trastuzumab, an anthracycline and a taxane (*see Appendix B*) AND disease progressed on trastuzumab;
      ii. Diagnosis of metastatic (stage IV) breast cancer and (a-d):
         a) Tykerb is prescribed in combination with letrozole;
         b) Disease is HER2-positive AND hormone receptor-positive*;

c) Member is postmenopausal;

b. Off-label NCCN recommended use (i or ii):
   i. Diagnosis of recurrent or metastatic (stage IV) breast cancer and (a-d);
      a) Tykerb is prescribed in combination with trastuzumab or capecitabine;
      b) Disease is HER2-positive and characterized by any of the following:
         1) Presence of symptomatic visceral disease or visceral crisis;
         2) Hormone receptor-negative*;
         3) Hormone receptor-positive* AND refractory to endocrine therapy (*see Appendix B*);
      c) Disease progressed on trastuzumab;
      d) Prescribed daily dose of Tykerb does not exceed the following:
         1) 1,250 mg if prescribed in combination with capecitabine;
         2) 1,000 mg if prescribed in combination with trastuzumab;
   ii. Diagnosis of recurrent or metastatic (stage IV) breast cancer and (a-d);
      a) Tykerb is prescribed in combination with an aromatase inhibitor (*see Appendix B*);
      b) Disease is estrogen receptor-positive AND HER2-positive;
      c) Member is postmenopausal or male;
      d) If male, an agent that suppresses testicular steroidogenesis is also prescribed;

2. Request meets one of the following (a or b):
   a. Dose does not exceed maximum indicated in section V;
   b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Hormone receptor-positive can indicate either estrogen receptor-positive (ER-positive) or progesterone receptor-positive (PR-positive)*

Approval duration: 6 months

B. Central Nervous System Cancer (off-label) (must meet all)**:**
1. Diagnosis of brain metastases with primary breast tumor sensitive to lapatinib;
2. Disease is recurrent;
3. If multiple (> 3) brain metastases, disease is stable;
4. Prescribed in combination with capecitabine;
5. Requested 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

C. Other diagnoses/indications
1. Refer to CP.PHAR.57 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 Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
3. If request is for a dose increase, meets one of the following (a or b):
   a. Dose does not exceed maximum indicated in section V;
   b. Requested 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 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 – CP.PHAR.57 evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
NCCN: National Comprehensive Cancer Network

Appendix B: Examples of Breast Cancer Antineoplastic Agents by Drug Class

Drug Class	Drug Class Subcategory	Drug: Generic (Brand)
Anthracyclines	Topoisomerase II inhibitors	Doxorubicin (Adriamycin) Epirubicin (Ellence)
Antimetabolites	Pyrimidine analogs	Capecitabine (Xeloda)
Antimicrotubulars	Taxane derivatives	Paclitaxel Docetaxel (Docefrez, Taxotere)
Endocrine agents	Nonsteroidal AIs	Anastrozole (Arimidex) Letrozole (Femara)
	Steroidal AIs	Exemestane (Aromasin)
	Serum ER modulators	Tamoxifen (Soltamox) Toremifene (Fareston)
	ER down-regulators	Fulvestrant (Fodex)
	Progestins	Megestrol acetate (Megace)
	Androgens	Fluoxymesterone (Androxy)
	High-dose estrogens	Ethinyl estradiol
Monoclonal antibodies	Anti-HER2s	Trastuzumab (Herceptin)

Drug Class	Drug Class Subcategory	Drug: Generic (Brand)
Tyrosine kinase inhibitors	Anti-HER2s; EGFR inhibitors	Lapatinib (Tykerb)

Abbreviations: aromatase inhibitor (AI); epidermal growth factor receptor (EGFR); estrogen receptor (ER); human epidermal receptor type 2 (HER2)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Advanced or metastatic breast cancer	1,250 mg (5 tablets) PO daily on Days 1-21 continuously in combination with capecitabine 2,000 mg/m^2/day (administered orally in 2 doses approximately 12 hours apart) on Days 1-14 in a repeating 21-day cycle. When co-administered with concomitant strong CYP3A4 inducers (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St. John's wort), the dose should be titrated gradually from 1,240 mg/day up to 4,500 mg/day based on tolerability.	4,500 mg/ day
Hormone receptor-positive, HER2-positive metastatic breast cancer	1,500 mg (6 tablets) given PO daily continuously in combination with letrozole. When Tykerb is coadminsitered with letrozole, the recommended dose of letrozole is 2.5 mg once daily. When co-administered with concomitant strong CYP3A4 inducers (e.g., dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital, St. John's wort), the dose should be titrated gradually from 1,500 mg/day up to 5,500 mg/day based on tolerability.	5,500 mg/day

VI. Product Availability

Tablets: 250 mg

VII. References

1. Tykerb Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2017. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/tykerb.pdf. Accessed August 30, 2017.
2. Lapatinib ditosylate. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed August 30, 2017.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted embedded SGM document into Centene policy	08.13	
Added Limitation of Use to Description Split algorithm into initial and reauthorization Added dosing adjustments to algorithm Added other adverse events to Appendix A Added Appendix B for dosing adjustments Updated Background information	12.13	12.13
Added question for LFT monitoring in Figure 2 Updated background information Updated references Added combination with trastuzumab indication	12.14	12.14
Policy converted to new template. Dose adjustment criteria removed; max dose limits added to criteria; lab test baselines removed but test result limits included in criteria. Contraindications limited to absolute indications only Appendices limited to abbreviations.	11.15	12.15
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

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.