RXADVANCE
2 Park Central Drive
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Clinical Policy Title:	lapatinib
Policy Number:	RxA.525
Drug(s) Applied:	Tykerb®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Lapatinib (Tykerb®) is a kinase inhibitor. It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lapatinib (Tykerb®)	Breast cancer	Advanced or metastatic: 1250 mg orally once 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. HER2-positive metastatic: 1500 mg orally once daily continuously in combination with letrozole (recommended dose of letrozole is 2.5 mg PO once daily).	1500 mg/day 5500 mg/day if taking a strong CYP3A4 inducer 500 mg/day if taking a strong CYP3A4 inhibitor

Dosage Forms

- Tablets: 250 mg

Clinical Policy

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

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;
   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
Commercial: 6 months
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. 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 offlabel use (prescriber must submit supporting evidence).

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

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Colon Cancer or Rectal Cancer (off-label) (must meet all):

1. Diagnosis of advanced or metastatic colorectal cancer and member meets both of the following (a and b):
   a. Disease is HER-2 positive;
   b. Disease is RAS and BRAF wild-type;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member had no previous treatment with a HER-2 inhibitor (e.g., trastuzumab, Kadcyla®, Perjeta®)
5. Prescribed in combination with trastuzumab;
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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving the medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;, 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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.
- KRAS, NRAS, and BRAF mutation testing:
  - All patients with metastatic colorectal cancer should have tumor tissue genotyped for RAS (KRAS and NRAS) and BRAF mutations individually or as part of an NGS panel.
  - Testing for KRAS, NRAS and BRAF mutations should be performed only in laboratories that are certified under the clinical laboratory improvement amendments of 1988 (CLIA-88) as qualified to perform high-complexity clinical laboratory (molecular pathology) testing. No specific methodology is recommended (e.g., sequencing, hybridization).

References

1. Tykerb Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018. Available at: https://www.us.tykerb.com/ . Accessed September 2, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed September 20, 2020.
3. National Comprehensive Cancer Network. Breast Cancer Version 6.2020 -September 8,2020.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed September 23, 2020.
4. National Comprehensive Cancer Network. Bone Cancer Version 1.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed September 20, 2020.
5. National Comprehensive Cancer Network. Colon Cancer Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed October 07, 2020.
6. National Comprehensive Cancer Network. Rectal Cancer Version 6.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed October 07, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. "Line of Business Policy Applies" to was updated to All lines of business. 3. Dosing Regimen QD is replaced with once daily. 4. Approval duration was updated for Commercial and removed HIM . 5. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized	10/07/2020	12/07/2020

by RxAdvance". 6. Added initial therapy criteria for colon and rectal cancer 7. Appendix D updated to include information on gene mutation testing 8. References was reviewed and updated.		