Clinical Policy: Tucatinib (Tukysa)

Reference Number: CP.PHAR.497
Effective Date: 09.01.20
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Tucatinib (Tukysa™) is a tyrosine kinase inhibitor with anti-human epidermal growth factor receptor 2 (HER2) activity.

FDA Approved Indication(s)

Tukysa is indicated:

- In combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.
- In combination with trastuzumab for the treatment of adult patients with RAS wild-type, HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.*

**This indication is approved under accelerated approval based on tumor response rate and durability of response. Continue approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*

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 Tukysa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of advanced, unresectable, or metastatic breast cancer;
2. Confirmation of HER2 positive disease;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Failure of one or more anti-HER2 based regimens in the metastatic setting (*see Appendix* B), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for anti-HER2-based regimens*
6. Prescribed in combination with trastuzumab and capecitabine;*
   **Prior authorization may be required for trastuzumab and capecitabine*

7. For Tukysa requests, member must use tucatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 600 mg per day;
      ii. 4 tablets 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. Colon Cancer, Rectal Cancer, Appendiceal Adenocarcinoma (must meet all)**:**
1. Diagnosis of advanced, unresectable, or metastatic colon cancer, rectal cancer, or appendiceal adenocarcinoma;
2. Disease is both of the following (a and b):
   a. HER2 positive (amplified);
   b. RAS (i.e., both KRAS and NRAS) wild-type;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyla®, Tykerb®, Perjeta®);
6. Prescribed in combination with trastuzumab;*

   **Prior authorization may be required for trastuzumab*
7. One of the following (a or b):
   a. Disease has progressed following a fluoropyrimidine- (e.g., 5-fluorouracil, capecitabine), oxaliplatin-, or irinotecan-based regimen (*see Appendix B*);
   b. Both of the following (i and ii):
      i. Disease is BRAF wild-type;
      ii. Prescribed as initial systemic therapy when intensive therapy is not recommended;
8. For members with deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) cancer or POLE/POLD1 mutation, member is ineligible for, or disease has progressed on, checkpoint inhibitor immunotherapy *(see Appendix B)*;
9. For Tukysa requests, member must use tucatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
10. Request meets one of the following (a or b):*
    a. Dose does not exceed both of the following (i and ii):
       i. 600 mg per day;
       ii. 4 tablets 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

C. Biliary Tract Cancers (off-label) (must meet all)**:**
1. Diagnosis of biliary tract cancer (gallbladder cancer, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma) that is one of the following (a, b, or c):
   a. Unresectable;
   b. Resected gross residual (R2);
   c. Metastatic;
2. Disease is HER2 positive;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed in combination with trastuzumab;
   **Prior authorization may be required for trastuzumab*
6. Prescribed as subsequent therapy;
7. For Tukysa requests, member must use tucatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. 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 Tukysa 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, request meets one of the following (a or b):*
   a. New dose does not exceed both of the following (i or ii):
      i. 600 mg per day;
      ii. 4 tablets 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

dMMR/MSI-H: deficient mismatch repair/microsatellite instability-high
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
NCCN: National Comprehensive Cancer Network
NRAS: neuroblastoma rat sarcoma viral oncogene homologue

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Breast Cancer NCCN examples of systemic therapies for HER2-positive recurrent or metastatic disease • Perjeta® (pertuzumab) + Herceptin® (trastuzumab) + docetaxel • Perjeta + Herceptin + paclitaxel • Enhertu® (fam-trastuzumab deruxtecan-nxki) • Kadcyla® (ado-trastuzumab emtansine)	Varies	Varies
Colorectal Cancer NCCN examples of fluoropyrimidine-, oxaliplatin- and irinotecan-based regimens (not all inclusive): • FOLFOX (fluorouracil, leucovorin, and • oxaliplatin) ± bevacizumab (Avastin®, Mvasi®, Zirabev™, Alymsys®, Vegzelma™), Vectibix® (panitumumab), or Erbitux® (cetuximab) • CapeOX (capecitabine and oxaliplatin) ± bevacizumab • FOLFIRI (irinotecan, leucovorin, 5-FU) ± bevacizumab, Erbitux, Vectibix, Zaltrap® (ziv-aflibercept), or Cyramza® (ramucirumab) • FOLFOXIRI (irinotecan, oxaliplatin, leucovorin, fluorouracil) ± bevacizumab, Erbitux, or Vectibix • IROX (oxaliplatin, irinotecan) ± bevacizumab • Bolus or infusional 5-fluorouricil (5-FU) + leucovorin ± bevacizumab • Capecitabine ± bevacizumab • Irinotecan ± Erbitux, Vectibix, bevacizumab, Cyramza, or Zaltrap	Varies	Varies
dMMR/MSI-H Colorectal Cancer NCCN examples of checkpoint inhibitor immunotherapies: • Keytruda® (pembrolizumab) • Opdivo® (nivolumab) • Opdivo + Yervoy® (nivolumab + ipilimumab) • Jemperli® (dostarlimab)	Varies	Varies
Biliary Tract Cancer NCCN examples of systemic therapy for unresectable and metastatic disease: • Keytruda® (pembrolizumab) + gemcitabine + cisplatin • Imfinzi® (durvalumab) + gemcitabine + cisplatin	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• gemcitabine + cisplatin		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer, colorectal cancer	300 mg PO BID	600 mg/day

VI. Product Availability

Tablets: 50 mg, 150 mg

VII. References

1. Tukysa Prescribing Information. Bothell, WA: Seattle Genetics, Inc.; January 2023. Available at: www.Tukysa.com. Accessed May 6, 2024.
2. Murthy RK, Loi S, Okines A, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. N Engl J Med. 2020 Feb;382(7):597-609.
3. Tucatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 22, 2024.
4. National Comprehensive Cancer Network. Breast Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed May 22, 2024.
5. National Comprehensive Cancer Network. Colon Cancer Version 2.2024. Available at: www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed May 22, 2024.
6. National Comprehensive Cancer Network. Rectal Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed May 22, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.26.20	08.20
3Q 2021 annual review: no significant changes; added requirement for use in combination with trastuzumab and capecitabine per labeling; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.25.21	08.21
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
3Q 2022 annual review: no significant changes; revised redirection language to failure of one or more anti-HER2 based regimens; updated Appendix B with NCCN examples of systemic therapies for	04.08.22	08.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
HER2-positive recurrent or metastatic disease; added oral generic redirection language; references reviewed and updated.		
Template changes applied to other diagnoses/indications.	10.03.22	
RT4: added criteria for newly FDA-approved indication of colorectal cancer; updated Appendix B with NCCN examples of fluoropyrimidine-, oxaliplatin- and irinotecan-based regimens.	03.08.23	
3Q 2023 annual review: per NCCN recommendations added a requirement for checkpoint inhibitor immunotherapy for dMMR/MSI-H colorectal cancer; references reviewed and updated.	04.14.23	08.23
3Q 2024 annual review: added POLE/POLD1 mutation option if member is ineligible for, or disease has progressed on, checkpoint inhibitor immunotherapy in colorectal cancers; added off-label criteria for NCCN-supported biliary tract cancers; added note that prior authorization may be required for combination therapy for all indications; references reviewed and updated.	05.23.24	08.24

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.