

PHARMACY COVERAGE GUIDELINE

TUKYSA™ (tucatinib) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
 - This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
 - Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
 - The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
 - The “Description” section describes the Service.
 - The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
 - The “Resources” section lists the information and materials we considered in developing this PCG
 - **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
 - Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.
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Medical Necessity Requirements for TUKYSA (tucatinib)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by a physician specializing in the diagnosis or in consultation with an oncologist

Indication

- Advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer, including brain metastases, in combination with trastuzumab and capecitabine, after one or more prior anti-HER2-based regimens in the metastatic setting

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- RAS wild-type HER2-positive unresectable or metastatic colorectal cancer, in combination with trastuzumab, after progression following fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- Negative pregnancy test for women of childbearing potential
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
- Alanine transaminase (ALT), aspartate aminotransferase (AST), and bilirubin levels

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA)

Safety

- No severe renal impairment (creatinine clearance less than 30 mL/min) when used with capecitabine

Documentation Requirements

- A completed request form must be submitted, including:
 - Chart notes
 - Lab results (pregnancy test, ECOG status, ALT, AST, bilirubin)
 - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year
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Criteria for Continuation of Therapy (renewal therapy)

Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by a physician specializing in or is in consultation with an oncologist

Clinical Response

- No evidence of disease progression or unacceptable toxicity

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Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No significant adverse drug effects such as:
 - Life-threatening diarrhea despite anti-diarrheal agents
 - Life-threatening hepatotoxicity
 - ALT or AST greater than 3 times upper limit of normal and bilirubin greater than 2 times ULN
 - Any other life-threatening adverse effect
- No concomitant use with:
 - Strong cytochrome CYP3A inducers or moderate cytochrome CYP2C8 inducers (e.g., rifampin, etc.)
 - Strong cytochrome CYP2C8 inhibitors (e.g., gemfibrozil, etc.)
- No severe renal impairment (creatinine clearance less than 30 mL/min) when used with capecitabine

Additional Requirements

- Dose is at least 150 mg twice a day
- **For metastatic breast cancer:** Will be used in combination with trastuzumab and capecitabine
- **For unresectable or metastatic colorectal cancer:** Will be used in combination with trastuzumab

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year
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Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

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Description:

Tukysa (tucatinib) 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.

Tukysa (tucatinib) is also indicated 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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Tucatinib inhibits phosphorylation of HER2 and HER3, resulting in inhibition of downstream MAPK and AKT signaling and cell proliferation, and showed anti-tumor activity in HER2 expressing tumor cells. In vivo, tucatinib inhibited the growth of HER2 expressing tumors. The combination of tucatinib and trastuzumab showed increased anti-tumor activity in vitro and in vivo compared to either drug alone.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982

NCCN recommendation definitions:

Category 1:

Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:

Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:

Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

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Category 3:

Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Tukysa (tucatinib) product information, revised by Seagen, Inc. 01-2023. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer Version 4.2025 – Updated April 17, 2025. Available at <https://www.nccn.org>. Accessed April 17, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Colon Cancer Version 2.2025 – Updated March 31, 2025. Available at <https://www.nccn.org>. Accessed April 19, 2025.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.