

## 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 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](http://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](mailto:Pharmacyprecert@azblue.com).

#### Criteria:

- **Criteria for initial therapy:** Tukysa (tucatinib) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met:
1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with an Oncologist
  2. Individual is 18 years of age or older
  3. Individual has a confirmed diagnosis of **ONE** of the following:
    - a. In combination with trastuzumab and capecitabine for treatment of 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

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- b. 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
  - c. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A
4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
  - a. Negative pregnancy test in a woman of childbearing potential
  - b. Eastern Cooperative Oncology Group performance status of 0-2
  - c. Alanine transaminase (ALT), aspartate aminotransferase (AST), and bilirubin
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. When using Tukysa (tucatinib) and capecitabine combination, individual does not have severe renal impairment (CrCl less than 30 mL/min) due to capecitabine contraindication

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Tukysa (tucatinib) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):
1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist
  2. Individual's condition has responded while on therapy with response defined as there is no evidence of disease progression or unacceptable toxicity
  3. Dose is at least 150 mg twice a day
  4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
  5. For metastatic breast cancer: Agent will be used in combination with trastuzumab and capecitabine
  6. For unresectable or metastatic colorectal cancer: Agent will be used in combination with trastuzumab
  7. When using Tukysa (tucatinib) and capecitabine combination, individual does not have severe renal impairment (CrCl less than 30 mL/min) due to capecitabine contraindication
  8. Individual has been adherent with the medication

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9. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
  - a. Life-threatening diarrhea despite use of anti-diarrheal agents
  - b. Life-threatening hepatotoxicity
  - c. ALT or AST greater than 3 times ULN and bilirubin greater than 2 times ULN
  - d. Any other life-threatening adverse effect
10. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as:
  - a. Use with strong CYP3A inducers or a moderate CYP2C8 inducers (e.g., rifampin, others)
  - b. Use with strong CYP2C8 inhibitors (e.g., gemfibrozil, others)

**Renewal duration:** 12 months

- 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.

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#### **Definitions:**

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

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#### 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.

##### 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.

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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.

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