Tukysa® (tucatinib)
(Oral)

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I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Tukysa 50 mg tablet – 4 tablets per day
- Tukysa 150 mg tablet – 4 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 600 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient has human epidermal growth factor receptor positive (HER2+)* disease; **AND**
- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
  - Coadministration with moderate CYP2C8 inducers (e.g., rifampin, etc.); **AND**
  - Coadministration with strong or moderate CYP2C8 inhibitors (e.g., gemfibrozil, clopidogrel, deferasirox, teriflunomide, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Breast Cancer † ‡ [1-3]

- Patient has recurrent unresectable (local or regional) or metastatic disease OR patient has inflammatory disease with no response to preoperative systemic therapy; **AND**
- Used as subsequent therapy in combination with trastuzumab and capecitabine

Colorectal Cancer (CRC) † ‡ Φ [1,2,7,9,10]

- Used in combination with trastuzumab; **AND**
    - Patient is both KRAS and NRAS mutation negative (wild-type) as determined by an FDA-approved or CLIA-compliant test§; **AND**
        - Patient has unresectable or metastatic disease; **AND**
        - Used as subsequent therapy following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy; **OR**
    - Patient has RAS and BRAF wild-type (WT) disease; **AND**
        - Used as initial treatment for unresectable metastatic disease and previous FOLFOX or CapeOX within the past 12 months; **AND**
            - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
        - Used as primary treatment for unresectable (or medically inoperable) or metastatic disease if intensive therapy is not recommended; **AND**
            - Patient has not previously received HER2-directed therapy; **AND**
                - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
                - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
                    - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; **OR**
        - Used as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable (or medically inoperable) rectal cancer if intensive therapy is not recommended; **AND**
            - Used if resection is contraindicated following total neoadjuvant therapy; **AND**
                - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
                - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
                    - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy; **OR**

- Used if resection is contraindicated following neoadjuvant/definitive immunotherapy; **AND**
  - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease; **OR**
- Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
  - Patient has not previously received HER2-directed therapy; **AND**
    - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
    - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta (POLE/POLD1) mutation; **AND**
      - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy

Central Nervous System (CNS) Cancers † ‡ Φ [1-3,6]

- Patient has brain metastases related to breast cancer previously treated with one or more lines of HER2-targeted therapy (e.g., trastuzumab, pertuzumab, ado-trastuzumab emtansine etc.); **AND**
- Patient does not have leptomeningeal disease; **AND**
- Used in combination with trastuzumab and capecitabine

Appendiceal Adenocarcinoma – Colon Cancer ‡ [2,9]

- Patient has RAS and BRAF wild-type (WT) disease; **AND**
- Used in combination with trastuzumab; **AND**
- Patient has not previously received HER2-targeted therapy; **AND**
- Used for one of the following:
  - Used as initial therapy for advanced or metastatic disease if intensive therapy is not recommended; **OR**
  - Used as subsequent therapy for progression of advanced or metastatic disease; **AND**
- Used in one of the following:
  - Patient has proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease; **OR**
  - Patient has deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) disease or polymerase epsilon/delta [POLE/POLD1] mutation; **AND**
    - Patient is not eligible for or has progressed on checkpoint inhibitor immunotherapy

Biliary Tract Cancers (Gallbladder Cancer or Intra-/Extra-Hepatic Cholangiocarcinoma) ‡ [2,11,12]

- Used as subsequent treatment for progression on or after systemic treatment for unresectable, resected gross residual (R2), or metastatic disease; **AND**
- Used in combination with trastuzumab

*HER2 overexpression criteria
Breast and CNS Cancer: [3,4,8]
• Immunohistochemistry (IHC) assay 3+; **OR** • Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; **OR** • Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following: o HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR** o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR** o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+
Colorectal Cancer and Appendiceal Adenocarcinoma: [9,10]
• Immunohistochemistry (IHC) assay 3+; **OR** • Fluorescence in situ hybridization (FISH) HER2/CEP17 ratio ≥ 2 AND concurrent IHC 2+; **OR** • Next-generation sequencing (NGS) panel HER2 (ERBB2) amplification
Biliary Tract Cancer:[3,8,12,13]
• Immunohistochemistry (IHC) assay 3+; **OR** • Dual-probe in situ hybridization (ISH) assay HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number ≥ 4.0 signals/cell; **OR** • Dual-probe in situ hybridization (ISH) assay AND concurrent IHC indicating one of the following: o HER2/CEP17 ratio ≥ 2.0 AND average HER2 copy number < 4.0 signals/cell AND concurrent IHC 3+; **OR** o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 6.0 signals/cell AND concurrent IHC 2+ or 3+; **OR** o HER2/CEP17 ratio < 2.0 AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell AND concurrent IHC 3+; **OR** • Next-generation sequencing (NGS) panel HER2 amplification

§*If confirmed using an FDA approved assay - http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hepatotoxicity (severe changes in liver function tests), severe diarrhea, etc.

V. Dosage/Administration [1,9,11]

Indication	Dose
Breast Cancer, CNS Cancers, Colorectal Cancer, Appendiceal Adenocarcinoma, Biliary Tract Cancers	Administer 300 mg (two 150 mg tablets), by mouth, twice daily until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code(s):

- J8999 - Prescription drug, oral, chemotherapeutic, nos
- C9399 - Unclassified drugs or biologicals

NDC(s):

- Tukysa 50 mg tablet – 51144-0001- xx
- Tukysa 150 mg tablet – 51144-0002- xx

VII. References

1. Tukysa [package insert]. Bothell, WA; Seagen Inc.; January 2023. Accessed April 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for tucatinib. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed April 2024.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 2.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2024.
4. Wolff AC, Hammond MEH, Allison KH, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. Arch Pathol Lab Med. 2018 Nov;142(11):1364-1382. doi: 10.5858/arpa.2018-0902-SA. Epub 2018 May 30. Arch Pathol Lab Med. 2018. PMID: 29846104.

5. Murthy RK, Loi S, Okines A, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2020 Feb 13;382(7):597-609. doi: 10.1056/NEJMoa1914609. Epub 2019 Dec 11. Erratum in: N Engl J Med. 2020 Feb 6;382(6):586.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers, Version 1.2023. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2024.
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8. Wolff AC, Hammond EH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105-2122.
9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer, Version 2.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2024.
10. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer, Version 2.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2024.
11. Nakamura Y, Mizuno N, Sunakawa Y, et al. Tucatinib and trastuzumab for previously treated human epidermal growth factor receptor 2-positive metastatic biliary tract cancer (SGNTUC-019): A phase II basket study. J Clin Oncol 2023;41:5569-5578.
12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Biliary Tract Cancers, Version 2.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed April 2024.
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basket study. Lancet Oncol. 2021 Sep;22(9):1290-1300. doi: 10.1016/S1470-2045(21)00336-3. Epub 2021 Jul 30.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tracts, unspecified
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast

ICD-10	ICD-10 Description
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast

ICD-10	ICD-10 Description
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31	Secondary malignant neoplasm of brain
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.3	Personal history of malignant neoplasm of breast

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC