Enhertu (fam-trastuzumab deruxtecan-nxki)
PAM – 018

Iowa Medicaid Program	Prior Authorization	**Effective Date**	01/01/2021
Revision Number	5	**Last Reviewed**	10/18/2024
Reviewed By	Medicaid Medical Director	**Next Review**	10/17/2025
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	04/16/2021

Overview

Medication: [1]	fam-trastuzumab deruxtecan-nxki
Brand Name:	Enhertu®
Pharmacologic Category:	Antineoplastic; monoclonal antibody/antibody drug conjugate/ HER2-directed antibody and topoisomerase inhibitor conjugate
FDA-Approved Indication(s): 1. Adult patients with unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer who have received a prior anti-HER2-based regimen, either: • in the metastatic setting, or • in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy. 2. Adult patients with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. 3. Adult patients with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy. ➢ Accelerated Approval: This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. 4. Adult patients with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen. 5. Adult patients with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options. ➢ Accelerated Approval: This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. ➢ **NEW Indication** (FDA-approved April 5, 2024)	
How Supplied:	Single-dose vial: lyophilized powder, 100 mg
Dosage and Administration:	• IV: Breast Cancer, NSCLC, Solid Tumors: 5.4 mg/kg once every 3 weeks (21-day cycle) • Gastric Cancer: 6.4 mg/kg once every
Benefit Category:	Medical

BOXED WARNING: INTERSTITIAL LUNG DISEASE AND EMBRYO-FETAL TOXICITY
• Interstitial lung disease (ILD) and pneumonitis, including fatal cases, have been reported with Enhertu®. Monitor for and promptly investigate signs and symptoms including cough, dyspnea, fever, and other new or worsening respiratory symptoms. Permanently discontinue Enhertu® in all patients with Grade 2 or higher ILD/pneumonitis. Advise patients of the risk and to immediately report symptoms. • Exposure to Enhertu® during pregnancy can cause embryo-fetal harm. Advise patients of these risks and the need for effective contraception.

Patient Selection (Biomarkers and Testing)

Indication	Select patients for treatment with Enhertu® based on:
1. Unresectable or metastatic HER2-positive breast cancer	HER2 expression
2. Unresectable or Metastatic HER2-Low Breast Cancer	HER2 expression (IHC 1+ or IHC 2+/ISH-)
3. Unresectable or Metastatic HER2-Mutant NSCLC	The presence of activating *HER2 (ERBB2)* mutations in tumor or plasma specimens. If no mutation is detected in a plasma specimen, test tumor tissue.
4. Locally Advanced or Metastatic Gastric Cancer	HER2 protein overexpression or HER2 gene amplification. Reassess HER2 status if it is feasible to obtain a new tumor specimen after prior trastuzumab-based therapy and before treatment with Enhertu®.
5. HER2-positive (IHC 3+) Unresectable or Metastatic Solid Tumors	HER2-positive (IHC 3+) specimens

- American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) recommend that all newly diagnosed patients with breast cancer must have an HER2 test performed. Patients who then develop metastatic disease must have an HER2 test performed in a metastatic site, if tissue sample is available.[2]
- Information on FDA-approved tests for the detection of HER2 protein expression, HER2 gene amplification, and activating HER2 mutations is available at: www.fda.gov/CompanionDiagnostics.

Descriptive Narrative

Breast cancer is a heterogenous, phenotypically diverse disease composed of several biologic subtypes that have distinct behavior. Amplification or overexpression of the human epidermal growth factor receptor 2 *(HER2)* oncogene* is present in approximately 15 percent of primary invasive breast cancers. Women with both early-stage and metastatic** breast cancer that meet criteria for HER2 positivity are treated with regimens including HER2-directed therapy.[3]

Globally, breast cancer is the most frequently diagnosed malignancy, accounting for over two million cases each year. It is also the leading cause of cancer death in women worldwide. In the United States, breast cancer is the most common female cancer, and the second most common cause of cancer

death in women.[4] An estimated 3,010 new cases of breast cancer in females will be diagnosed in Iowa in 2024, making it the second most commonly diagnosed cancer in the state, and with an estimated 370 deaths, it is the fourth highest cause of cancer deaths in Iowa in 2024.[5]

Up to 5 percent of women diagnosed with breast cancer in the U.S. have metastatic disease at the time of first presentation, despite the gains in early detection, and up to 30 percent of women with early-stage non-metastatic breast cancer at diagnosis will develop distant metastatic disease.

Lung cancer is the leading cause of cancer death in the United States. In 2024, an estimated 234,580 new cases (116,310 in males and 118,270 in females) of lung and bronchial cancer will be diagnosed, and 125,070 deaths (65,790 in males and 59,280 in females) are estimated to occur because of the disease. Only 25.4 percent of patients with lung cancer are alive 5 years or more after diagnosis; this includes patients with non-small cell lung cancer (NSCLC) and those with small cell lung cancer (SCLC).

The availability of new treatments is associated with improved survival rates for patients with NSCLC. Five-year survival rates range from 15 percent to 50 percent, depending on the biomarker. Therefore, biomarker testing is critical to guide treatment selection and ensure optimal outcomes in patients with NSCLC, particularly for those with advanced or metastatic disease.[6]

* HER2 is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher-than-normal levels of HER2 are referred to as HER2-positive.

** Metastatic breast cancer (MBC). Also called stage IV, MBC is breast cancer that has spread to another part of the body, most commonly the liver, brain, bones, or lungs.

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.[7,8]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[9]

- Breast Cancer (v.4.2024 – July 3, 2024)
- Esophageal and Esophagogastric Junction Cancers (v.4.2024 – July 30, 2024)
- Gastric Cancer (v.4.2024 – August 12, 2024)
- Non-Small Cell Lung Cancer (Version 9.2024 – September 9, 2024)
- Cervical Cancer (v.3.2024 – May 6, 2024)
- Colon Cancer (v.5.2024 – August 22, 2024)
- Uterine Neoplasms (v.2.2024 – March 6, 2024)
- Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer (v.3.2024 – July 15, 2024)
- Head and Neck Cancers (v.4.2024 – May 1, 2024)
- Vaginal Cancer (v.2.2025 – August 8, 2024)

NCCN Guidelines® Recommendation(s) for Invasive Breast Cancer [recurrent unresectable (local or regional) or stage IV (M1) disease]
(1) HR-Positive and HER2-Negative with Visceral Crisis [a] or Endocrine Refractory a. Second-Line: HER2 IHC 1+ or 2+/ISH negative [b] i. Fam-trastuzumab deruxtecan-nxki [b]: Category 1, Preferred (2) HR-Negative and HER2-Negative (Triple-Negative Breast Cancer; TNBC) a. Second-Line: No germline *BRCA1/2* mutation and HER2 IHC 1+ or 2+/ISH negative [c] i. Fam-trastuzumab deruxtecan-nxki: Category 1, Preferred [d] (3) HR-Positive or -Negative and HER2-Positive a. Second Line [e] – Fam-trastuzumab deruxtecan-nxki [f]: Category 1, Preferred [a] According to the 5th ESO-ESMO international consensus guidelines (Cardoso F, et al. Ann Oncol 2020;31:1623-1649) for advanced breast cancer visceral crisis is defined as: "severe organ dysfunction, as assessed by signs and symptoms, laboratory studies and rapid progression of disease. Visceral crisis is not the mere presence of visceral metastases but implies important organ compromise leading to a clinical indication for the most rapidly efficacious therapy." [b] Fam-trastuzumab deruxtecan may be considered in a later line for HER2 IHC 1+ or 2+/ISH negative, if not used in second–line. Fam-trastuzumab deruxtecan-nxki is associated with interstitial lung disease (ILD)/pneumonitis. Regular monitoring for this serious side effect is recommended. For patients with a history of ILD/ pneumonitis, there are no data on managing safety or toxicity of this drug in a trial. [c] Assess for germline *BRCA1/2* mutations in all patients with recurrent or metastatic breast cancer to identify candidates for PARP inhibitor therapy. [d] Fam-trastuzumab deruxtecan may be considered in a later line for HER2 IHC 1+ or 2+/ISH negative, if not used in second–line. Fam-trastuzumab deruxtecan-nxki is associated with interstitial lung disease (ILD)/pneumonitis. Regular monitoring for this serious side effect is recommended. For patients with a history of ILD/ pneumonitis, there are no data on managing safety or toxicity of this drug in a trial. [e] Tucatinib + trastuzumab + capecitabine is preferred in patients with both systemic and CNS progression in the third-line setting and beyond; and it may be given in the second-line setting. [f] Fam-trastuzumab deruxtecan-nxki may be considered in the first-line setting as an option for select patients (i.e., those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens]). Fam-trastuzumab deruxtecan-nxki is associated with interstitial lung disease (ILD)/ pneumonitis. Regular monitoring for this serious side effect is recommended. For patients with a history of ILD/pneumonitis, there are no data on managing safety or toxicity of this drug in a trial.

NCCN Guidelines® Recommendation(s) for Esophageal and Esophagogastric Junction Cancers [unresectable locally advanced, recurrent, or metastatic disease (where local therapy is not indicated)]
(1) Adenocarcinoma a. Second-line or subsequent therapy (dependent on prior therapy and performance status [PS]) i. Fam-trastuzumab deruxtecan-nxki for HER2 overexpression positive: Category 2A, Preferred

NCCN Guidelines® Recommendation(s) for Gastric Cancer [unresectable locally advanced, recurrent, or metastatic disease (where local therapy is not indicated)]

(1) Adenocarcinoma
  a. Second-line or subsequent therapy (dependent on prior therapy and PS)
    i. Fam-trastuzumab deruxtecan-nxki for HER2 overexpression positive: Category 2A, Preferred

NCCN Guidelines® Recommendation(s) for Non-Small Cell Lung Cancer [advanced or metastatic disease – subsequent [a, b]]

(1) Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-2)
  a. Other Recommended Regimen (no previous IO or previous IO)
    i. Fam-trastuzumab deruxtecan-nxki: Category 2A [c]
(2) Squamous Cell Carcinoma (PS 0-2)
  a. Other Recommended Regimen (no previous IO or previous IO)
    i. Fam-trastuzumab deruxtecan-nxki: Category 2A [c]

[a] Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (i.e., EGFR exon 19 deletion or L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

[b] Monitoring During Subsequent Therapy or Maintenance Therapy: Response assessment with CT of known or high-risk sites of disease with or without contrast every 6–12 weeks. Timing of CT scans within Guidelines parameters is a clinical decision.

[c] Only in patients whose tumors have HER2 overexpression (IHC 3+). Smit EF, Felip E, Uprety D. et al. Trastuzumab deruxtecan in patients with metastatic non-small-cell lung cancer (DESTINY-Lung01): primary results of the HER2-overexpressing cohorts from a single-arm, phase 2 trial. Lancet Oncol 2024;25:439-454

NCCN Guidelines® Recommendation(s) for HER2-Positive (IHC 3+) Solid Tumors

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) lists fam-trastuzumab deruxtecan-nxki as a HER2-directed treatment option for previously treated patients with the following metastatic solid tumors:

(1) Cervical Cancer – Recurrent or Metastatic Disease, Second-Line or Subsequent Therapy
  a. HER2-positive tumors (IHC 3+ or 2+) – Fam-trastuzumab deruxtecan-nxki: Category 2A, Useful In Certain Circumstances
(2) Colorectal Cancer Continuum of Care – Advanced or Metastatic Disease
  a. [pMMR/MSS (or dMMR/MSI-H or POLE/POLD1 mutation that is ineligible for or progressed on checkpoint inhibitor immunotherapy)]
  b. Second-Line and Subsequent Therapy Options (if not previously given) [a]
    i. Biomarker-Directed Therapy – HER2-amplified (IHC 3+) – Fam-trastuzumab deruxtecan-nxki: Category 2A [b]
(3) Endometrial Cancer: Recurrent Disease – Second-Line or Subsequent Therapy
  a. Biomarker-Directed Therapy
    i. HER2-positive tumors (IHC 3+ or 2+) – fam-trastuzumab deruxtecan-nxki: Category 2A, Useful in Certain Circumstances
(4) Ovarian Cancer – Acceptable Recurrent Therapies for Epithelial Ovarian (including LOCC) Cancer
  a. Recurrence Therapy for Platinum-Resistant Disease: Targeted Therapy
    i. Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+]): Category 2A, Useful in Certain Circumstances
(5) Salivary Gland Tumors – Recurrent, Unresectable, or Metastatic (no surgery or RT option)
  a. The choice of systemic therapy should be individualized based on patient characteristics (e.g., PS, goals of therapy).
  b. HER2-targeted therapy for HER2+ tumors – Fam-trastuzumab deruxtecan-nxki: Category 2A, Useful in Certain Circumstances
(6) Primary Vaginal Cancer – Squamous Cell Carcinoma, Adenocarcinoma, Recurrent or Metastatic Disease
  a. Second-Line or Subsequent Therapy, HER2-positive tumors (IHC 3+ or 2+)
    i. Fam-trastuzumab deruxtecan-nxki: Category 2A, Useful in Certain Circumstances

[a] If patients had therapy stopped for reasons other than progression (e.g., cumulative toxicity, elective treatment break, patient preference), rechallenge is an option at time of progression

[b] Some activity was seen after a previous HER2-targeted regimen. May not be indicated in patients with underlying lung issues due to lung toxicity.

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
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.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale [10]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient, and to determine appropriate treatment and prognosis.

Grade	ECOG Performance Status [Synonyms: WHO/Zubrod score]
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 self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; 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.

Criteria

Prior authorization is required.

HER2-Positive Breast Cancer

Enhertu® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of recurrent, unresectable, or stage IV (M1) metastatic breast cancer that is human epidermal growth factor receptor 2 (HER2)-positive; **AND**
2. Member has received a prior anti-HER2-based regimen (either a *or* b):
    a. In the metastatic setting; or
    b. In the neoadjuvant or adjuvant setting and has rapid disease progression within 6 months of completing therapy (12 months for pertuzumab-containing regimens); **AND**
3. Member is 18 years of age or older; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5.4 mg/kg every 3 weeks (21-day cycle); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

HER2-Low (IHC 1+ or IHC 2+/ISH-) Breast Cancer

Enhertu® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of recurrent, unresectable, or stage IV (M1) metastatic breast cancer that is human epidermal growth factor receptor 2 (HER2)-low (IHC 1+ or IHC 2+/ISH-); **AND**
2. Member has received a prior chemotherapy:
    a. In either the metastatic setting, or in the adjuvant setting and member has disease recurrence within 6 months of completing therapy; **AND**
    b. If tumor is hormone-receptor (HR)-positive, disease is refractory to endocrine therapy; **AND**
3. Member is 18 years of age or older; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5.4 mg/kg every 3 weeks (21-day cycle); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Non-Small Cell Lung Cancer (NSCLC)

Enhertu® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of unresectable or metastatic non-small cell lung cancer (NSCLC); **AND**
2. Presence of activating human epidermal growth factor receptor 2 (HER2) (ERBB2) mutations in tumor or plasma specimens (if no mutation is detected in a plasma specimen, test tumor tissue); **AND**
3. Failure of one prior line of systemic therapy; **AND**
4. Member is 18 years of age or older; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5.4 mg/kg every 3 weeks (21-day cycle); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

HER2-Positive Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma

Enhertu® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of locally advanced or metastatic gastric or gastroesophageal junction (GEJ) cancer that has human epidermal growth factor receptor 2 (HER2)-protein overexpression or HER2 gene amplification; **AND**
2. Failure of a prior trastuzumab-based regimen; **AND**
3. Member is 18 years of age or older; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 6.4 mg/kg every 3 weeks (21-day cycle); or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

IHC 3+ Solid Tumors

Enhertu® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of HER2-positive, IHC 3+ solid tumor; **AND**
2. Disease is unresectable or metastatic; **AND**
3. Member is 18 years of age or older; **AND**
4. Failure of at least one prior line of standard therapy for disease, or there are no available standard treatments as a satisfactory alternative treatment option; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 5.4 mg/kg every 3 weeks; or
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Continuation Criteria (all indications)

Enhertu® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. The regimen prescribed meets one of the following (a, b, or c)
    a. Diagnosis of breast cancer, NSCLC, or IHC 3+ solid tumors, and dose does not exceed 5.4 mg/kg every 3 weeks; or
    b. Diagnosis of gastric or GEJ adenocarcinoma and dose does not exceed 6.4 mg/kg every 3 weeks; or
    c. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

Approval Duration	Initial Authorization: 6 months Subsequent Authorization(s): 12 months		
Quantity Limits	Metastatic breast cancer	5.4 mg/kg	once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity
	Unresectable or metastatic HER2-mutant NSCLC		
	IHC 3+ solid tumors		
	Locally advanced or metastatic gastric cancer	6.4 mg/kg	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9358	Injection, fam-trastuzumab deruxtecan-nxki, 1 mg

ICD-10	Description
C16.0 – C16.9	Gastric cancer: specific codes indicate primary site, e.g., C16.4 indicates malignant neoplasm of pylorus (additional ICD-10 codes apply identifying the location of the metastasis)
C34.10 – C34.92	Bronchus and lung cancer: specific codes indicate primary site, e.g., C34.10 indicates malignant neoplasm of upper lobe, unspecified bronchus or lung (additional ICD-10 codes apply identifying the location of the metastasis)
C50.011 – C50.929	Breast cancer: specific codes indicate primary site, e.g., C50.211 indicates malignant neoplasm of upper-inner quadrant of right female breast (additional ICD-10 codes apply identifying the location of the metastasis)

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
65597-0406-01 (100 mg single-dose vial)	Daiichi Sankyo, Inc. (65597)	1 mg	1	EA	100

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Enhertu prescribing information (04/2024). Daiichi Sankyo, Inc.: Basking Ridge, NJ. Available online: www.enhertuhcp.com. Accessed July 2, 2024.

[2] Wolff AC, 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. Epub 2018 May 30. PMID: 29846104.

[3] Yamauchi H, Bleiweiss IJ. HER2 and predicting response to therapy in breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 11, 2024.

[4] Joe BN. Clinical features, diagnosis, and staging of newly diagnosed breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 29, 2024.

[5] American Cancer Society: Cancer Statistics Center. State of Iowa. Available online at cancerstatisticscenter.cancer.org/states/iowa. Accessed July 29, 2024.

[6] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer (v.9.2024 – September 9, 2024). Accessed December 8, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

[7] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[8] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[9] NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Breast Cancer (v.4.2024 – July 3, 2024)
- Esophageal and Esophagogastric Junction Cancers (v.4.2024 – July 30, 2024)
- Gastric Cancer (v.4.2024 – August 12, 2024)
- Non-Small Cell Lung Cancer (v.9.2024 – September 9, 2024)
- Cervical Cancer (v.3.2024 – May 6, 2024)
- Colon Cancer (v.5.2024 – August 22, 2024)
- Uterine Neoplasms (v.2.2024 – March 6, 2024)
- Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer (v.3.2024 – July 15, 2024)
- Head and Neck Cancers (v.4.2024 – May 1, 2024)
- Vaginal Cancer (v.2.2025 – August 8, 2024)

[10] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Annual review (moved from January to October review to align with other policies for treatment of breast cancer). Updated Overview table and added criteria for new indication of IHC 3+ solid tumors (FDA-approved 4/5/2024). Reviewed and updated NCCN guidelines where applicable. Reviewed NCCN Guidelines for the 6 types of solid tumors listed on the labeler website at the time of this review.	5
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Annual review. Added overview of Lung Cancer to Descriptive Narrative. Updated NCCN Guidelines. Added dosing information into criteria.	4
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
01/20/2023	CAC	Added criteria for new indications: HER2-low metastatic breast cancer (FDA-approved 8/5/22); unresectable or metastatic HER2-Mutant NSCLC (FDA-approved via accelerated approval on 8/11/22). Updated HER2-positive breast cancer criteria to include rapid disease progression. Updated NCCN Guidelines® recommendations. Added section on patient selection.	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/15/2022	CAC	Annual review. Rewrite.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/16/2021	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee