CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Fam-Trastuzumab Deruxtecan-nxki (Enhertu®)

Version: 1.0

EFFECTIVE DATE: 5/5/2025

NantHealth® | Eviti®

Please note the following:

For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

Fam-Trastuzumab Deruxtecan-nxki (Enhertu®)

Discussion

Fam-trastuzumab deruxtecan-nxki is a human epidermal growth factor receptor (HER2)-directed antibody-drug conjugate. The antibody is a humanized anti-HER2 IgG1. The small molecule, DXd, is a topoisomerase I inhibitor attached to the antibody by a cleavable linker. When fam-trastuzumab deruxtecan-nxki binds to the HER2 protein on tumor cells, it is internalized into the cell. Inside the cell, the linker is cleaved by lysosomal enzymes, releasing DXd. Once released, DXd is membrane-permeable and causes DNA damage, ultimately leading to apoptotic cell death. This targeted mechanism allows the drug to kill HER2-positive cancer cells while sparing healthy cells specifically.[1]

Fam-trastuzumab deruxtecan-nxki is associated with the following most common adverse reactions: decreased white blood cell count, nausea, decreased hemoglobin, decreased neutrophil count, decreased lymphocyte count, fatigue, decreased platelet count, increased aspartate aminotransferase, increased alanine aminotransferase, increased blood alkaline phosphatase, vomiting, alopecia, constipation, decreased blood potassium, decreased appetite, diarrhea, and musculoskeletal pain.[2]

Fam-trastuzumab deruxtecan-nxki is approved by the Food and Drug Administration (FDA) for breast, non-small cell lung, gastric, gastroesophageal junction, and solid tumors.[1] The National Comprehensive Cancer Network (NCCN) endorses Fam-trastuzumab deruxtecan-nxki for the following cancer types: ampullary, biliary tract, bladder, breast, central nervous system, cervical, colon, esophageal and esophagogastric junction, gastric, head and neck, non-small cell lung, occult primary, ovarian and fallopian tube, pancreatic, rectal, small bowel, uterine, vaginal, and vulvar.[3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21]

Definitions

- **Amplified HER2 FISH** - A test that detects amplification of the HER2 gene via fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded breast cancer tissue specimens.[22]
- **Deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H)** - When the microsatellite DNA segments in cancer cells show changes (mutations), this indicates that the tumor cells are deficient in the repair of the mismatch errors. These cancers have microsatellite instability (MSI-High, MSI-H, or mismatch repair deficiency, dMMR).[23]
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.[24]
- **Human Epidermal Growth Factor Receptor (HER2)** - A targetable transmembrane glycoprotein receptor of the epidermal growth factor receptor (EGFR) family. It plays a crucial role in cell proliferation, survival, and differentiation.[25]
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN

consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.[26]

- **Topoisomerase I Inhibitors** - A class of anticancer agents that interrupt DNA replication in cancer cells, resulting in cell death.[27]

Policy

Coverage will be considered for FDA approved indications and for NCCN category 1, 2A, or 2B recommendations when the following criteria are met:

Ampullary Adenocarcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Therapy for disease progression as a single agent if human epidermal growth factor receptor (HER2) positive (IHC3+, or IHC2+ with FISH HER2 amplified), in patients with a good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake).[3]

Biliary Tract Cancer - Gallbladder/ Intrahepatic/ Extrahepatic Cholangiocarcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Subsequent treatment as a single agent for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease or metastatic disease that is human epidermal growth factor receptor (HER2) positive immunohistochemistry (IHC3+).[4]

Bladder Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line systemic therapy or subsequent-line systemic therapy (patients should have already received platinum and a checkpoint inhibitor, if eligible) as single agent for HER2 positive, IHC 3+ regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations) for one of the following:
   a) Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent bladder preserving chemoradiotherapy and maximal TURBT

b) Stage IIIB (cT1-T4a, N2,3) disease following progression after primary treatment with downstaging systemic therapy
c) Stage IVA (cT4b, any N, M0) disease if tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
d) Stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy
e) Metastatic stage IVB (any T, any N, M1b) disease
f) Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
g) Metastatic or local recurrence post cystectomy treated with curative intent; OR

4. Metastatic disease as a single agent for HER2-positive, IHC 3+ regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations) for second-line systemic therapy; OR

Upper GU Tract Tumors - Urothelial Carcinoma of the Prostate

For **NCCN** required criteria coverage:

5. Second-line therapy for metastatic disease as a single agent for HER2-positive, IHC 3+ regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations); OR
6. Subsequent-line systemic therapy for metastatic disease as a single agent for HER2-positive, IHC 3+ (patients should have already received platinum and a checkpoint inhibitor, if eligible) regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations); OR

Primary Carcinoma of the Urethra

For **NCCN** required criteria coverage:

7. Second-line systemic therapy for recurrent or metastatic disease as a single agent for HER2-positive, IHC 3+ regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations); OR
8. Subsequent-line systemic therapy for recurrent or metastatic disease as a single agent for HER2-positive, IHC 3+ (patients should have already received platinum and a checkpoint inhibitor, if eligible) regardless of previous therapy (pan-cancer tumor-agnostic treatments can be considered for patients with actionable mutations) for subsequent-line systemic therapy.[5]

Breast Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) disease who have received a prior anti-HER2-based regimen for either one of the following:

a) Metastatic setting
b) Neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy; OR

4. Unresectable or metastatic disease with one of the following:
   a) Hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) disease, that has progressed on one or more endocrine therapies in the metastatic setting
   b) HER2-low (IHC 1+ or IHC 2+/ISH-) disease, who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy; OR

Invasive Breast Cancer

For **NCCN** required criteria coverage:

5. First-line therapy as a single agent for recurrent unresectable (local or regional) or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative, hormone receptor positive with visceral crisis or endocrine therapy refractory disease if no germline BRCA 1/2 mutation and/or HER2 IHC 0+, 1+, or 2+/ISH negative (may be used for previously treated with at least one line of endocrine-based therapy in the metastatic setting); OR
6. Second-line therapy as a single-agent for recurrent unresectable (local or regional) or stage IV (M1) human epidermal growth factor receptor 2 (HER2) IHC 0+, 1+ or 2+/ISH negative disease for one of the following:
   a) Hormone receptor positive with visceral crisis or endocrine therapy refractory (may be used for previously treated disease with at least one line of endocrine-based therapy in the metastatic setting)
   b) Hormone receptor negative if no germline BRCA 1/2 mutation (may be considered in a later line if not used in second line or may be considered first-line therapy when disease has progressed during or within 6 months after completing adjuvant chemotherapy); OR
7. Single-agent for recurrent unresectable (local or regional) or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-positive disease that is hormone receptor-negative, or hormone receptor-positive with or without endocrine therapy
   a) Second-line therapy
   b) First-line therapy for select patients (i.e., those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens]); OR

Inflammatory Breast Cancer

For **NCCN** required criteria coverage:

8. First-line therapy as a single agent for patients with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-negative, hormone receptor positive with visceral crisis or endocrine therapy refractory disease if no germline BRCA 1/2 mutation and/or HER2 IHC 0+, 1+, or 2+/ISH negative (may be used for previously treated with at least one line of endocrine-based therapy in the metastatic setting); OR
9. Second-line therapy as a single-agent for patients with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) human

epidermal growth factor receptor 2 (HER2) IHC 1+ or 2+/ISH negative disease that is hormone receptor negative if no germline BRCA 1/2 mutation (may be considered in a later line if not used in second line or may be considered first-line therapy when disease has progressed during or within 6 months after completing adjuvant chemotherapy); OR

10. Single agent for patients with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is hormone receptor-negative, or hormone receptor-positive with or without endocrine therapy for one of the following:
    a) Second-line therapy
    b) First-line therapy for select patients (i.e. those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens]).[6]

Central Nervous System Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Limited Brain Metastases

For **NCCN** required criteria coverage:

3. Single-agent treatment for HER2 positive disease for one of the following:
    a) Initial treatment in select cases (eg, small asymptomatic brain metastases)
    b) Recurrent brain metastases
    c) Relapsed disease with either stable systemic disease or reasonable systemic treatment options; OR

Extensive Brain Metastases

For **NCCN** required criteria coverage:

4. Single-agent treatment for HER2 positive disease
    a) Primary treatment in select cases (e.g., small asymptomatic brain metastases)
    b) Recurrent disease with stable systemic disease or reasonable systemic treatment options.[7]

Cervical Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy as a single agent for HER2-positive tumors (IHC 3+ or 2+) tumors for one of the following:
    a) Locoregional recurrence
    b) Stage IVB or recurrence with distant metastases.[8]

Colon Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line and subsequent therapy (biomarker-directed) as a single agent, if not previously given, for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]) (HER2-amplified, IHC 3+); OR
4. Adjuvant treatment for unresectable metachronous metastases (HER2-amplified, IHC 3+) that converted to resectable disease after initial treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy. (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]); OR
5. Initial treatment as a single agent in patients (HER2-amplified, IHC 3+)(proficient mismatch repair/microsatellite-stable [pMMR/MSS]; deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb] and patient is not a candidate for immunotherapy) for patients with unresectable metachronous metastases and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPEOX (capecitabine and oxaliplatin) within the past 12 months; OR

Appendiceal Adenocarcinoma

6. Second-line and subsequent therapy (biomarker-driven) as a single agent, if not previously given, for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]) (HER2-amplified, IHC 3+).[9]

Esophageal and Esophagogastric Junction Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent palliative therapy as a single agent for patients with HER2 overexpression positive adenocarcinoma who are not surgical candidates or who have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score ≥60% or an ECOG performance score ≤2 as preferred second-line or subsequent therapy as a single agent.[10]

Gastric Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen; OR

For **NCCN** required criteria coverage:

4. Second-line or subsequent therapy as a single agent for palliative therapy for HER2 overexpression positive patients who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and Karnofsky performance score ≥60% or ECOG performance score ≤2.[11]

Head and Neck Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Very Advanced Head and Neck Cancer

For **NCCN** required criteria coverage:

3. Systemic therapy as an alternate single agent for subsequent-line option for non-nasopharyngeal cancer, if HER2+ (IHC 3+) and no satisfactory alternative treatment options, in patients with one of the following:
   a) Performance status (PS) 0-3 and persistent or progressive metastatic (M1) disease at initial presentation following first-line therapy
   b) PS 3 and unresectable locoregional recurrence without prior radiation therapy (RT) or unresectable persistent disease without prior RT
   c) PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent; OR

Salivary Gland Tumor

4. Single agent systemic therapy for human epidermal growth factor receptor 2 (HER2)-positive recurrent disease with one of the following:
   a) Distant metastases in patients with a performance status (PS) of 0-3
   b) Unresectable locoregional recurrence or second primary with prior radiation therapy.[12]

Non-Small Cell Lung Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Unresectable or metastatic disease whose tumors have activating HER2 (ERBB2) mutations and who have received a prior systemic therapy; OR

For **NCCN** required criteria coverage:

4. Single agent as subsequent therapy for ERBB2 (HER2) mutation positive recurrent, advanced, or metastatic disease

   Note: For agents with a similar mechanism of action, it is not recommended to switch between these drugs at the time of progression; OR
5. Subsequent systemic therapy as a single agent for recurrent, advanced, or metastatic disease in those with performance status 0-2 and HER2 overexpression (IHC 3+).[13]

Occult Primary

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent (in patients with HER2- positive [IHC 3+] tumors) in symptomatic patients with performance status (PS) 1-2 or asymptomatic patients with PS 0 and aggressive disease that is metastatic or where surgical resection is likely to result in severe morbidity, and that has progressed on or following prior systemic treatment and has no satisfactory alternative treatment options for one of the following:
   a) Axillary involvement in those with a prostate or post-prostatectomy if clinically indicated
   b) Lung nodules or breast marker-negative pleural effusion
   c) Resectable liver disease
   d) Peritoneal mass or ascites with non-ovarian histology
   e) Retroperitoneal mass of non-germ cell histology in selected patients
   f) Unresectable liver disease or disseminated metastases; OR
4. Single agent (in patients with HER2- positive [IHC 3+] tumors) in symptomatic patients with PS 1-2 or asymptomatic patients with PS 0 and aggressive disease for systemic therapy in patients with multiple lung nodules, pleural effusion, or disseminated metastases that progressed on or following prior systemic treatment and have no satisfactory alternative treatment options.[14]

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer, Carcinosarcoma (Malignant Mixed Müllerian Tumors), Clear Cell Carcinoma of the Ovary, Mucinous Neoplasms of the Ovary, and Grade 1 Endometrioid Carcinoma

For **NCCN** required criteria coverage:

3. Single-agent therapy for persistent disease or recurrence in HER2- positive tumors [IHC 3+ or 2+] for one of the following:
    a) Immediate treatment for serially rising CA-125 in patients who previously received chemotherapy
    b) Progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
    c) Stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
    d) Complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
    e) Radiographic and/or clinical relapse in patients with previous complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-sensitive disease).[15]

Pancreatic Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent if HER2 positive IHC3+, or IHC2+ with fluorescence in situ hybridization (FISH) HER2 amplified for locally advanced or metastatic disease and disease progression if good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake) or intermediate PS (ECOG 2); OR
4. Single agent, as alternate systemic therapy not previously used, if HER2 positive (IHC3+, or IHC2+ with FISH HER2 amplified) with a good performance status (ECOG PS 0-1) or intermediate PS (ECOG 2) for one of the following:
    a) Local recurrence in the pancreatic operative bed after resection
    b) Recurrent metastatic disease with or without local recurrence after resection.[16]

Rectal Cancers

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Initial treatment as a single agent in patients (HER2-amplified, IHC 3+) for patients with unresectable metachronous metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] and are not candidates for immunotherapy) and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPEOX (capecitabine and oxaliplatin) within the past 12 months; OR

4. Adjuvant treatment as a single agent for unresectable metachronous metastases (HER2-amplified, IHC 3+) pMMR/MSS or dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb] and who are not candidates for immunotherapy) that converted to resectable disease after initial treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy; OR
5. Second-line and subsequent therapy as a single agent, if not previously given, for progression of advanced or metastatic disease (HER2-amplified, IHC 3+) pMMR/MSS or is ineligible for, or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultra-hypermutated phenotype [eg, TMB >50 mut/Mb]).[17]

Small Bowel Adenocarcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line and subsequent therapy as a single agent for advanced or metastatic disease that is HER2-amplified (IHC 3+) (if not previously given).[18]

Solid Tumors

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Unresectable or metastatic HER2-positive (IHC 3+) disease patients who have received prior systemic treatment and have no satisfactory alternative treatment options.[1]

Uterine Neoplasms - Endometrial Carcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy as a single agent for a recurrent disease that is HER2-positive tumor (IHC 3+ or 2+) if not previously used for one of the following:
   a) Isolated metastases
   b) Disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
   c) Sequential EBRT and with or without brachytherapy for locoregional recurrence in patients with no prior RT to the site of recurrence, or previous vaginal brachytherapy only
   d) Surgical exploration, with sequential EBRT for locoregional recurrence in patients with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes

e) Surgical exploration, with or without sequential EBRT for locoregional recurrence in patients with upper abdominal or peritoneal disease
f) With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in patients who have received prior EBRT to site of recurrence.[19]

Vaginal Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy as a single agent for HER2-positive tumors (IHC 3+ or 2+) for one of the following:
   a) locoregional recurrence
   b) stage IVB or recurrent distant metastases.[20]

Vulvar Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Second-line or subsequent therapy for advanced or recurrent/metastatic disease as a single agent for HER-2 positive (IHC 3+ or 2+) tumors.[21]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Coding (CPT®, ICD-10, and HCPCS)

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C08.9	Malignant neoplasm of major salivary gland, unspecified
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C15	Malignant neoplasm of esophagus
C16	Malignant neoplasm of stomach
C17	Malignant neoplasm of small intestine
C18	Malignant neoplasm of colon
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C22.1	Intrahepatic bile duct carcinoma
C23	Malignant neoplasm of gallbladder
C24	Malignant neoplasm of other and unspecified parts of biliary tract
C25	Malignant neoplasm of pancreas
C34	Malignant neoplasm of bronchus and lung
C48.2	Malignant neoplasm of peritoneum, unspecified
C50	Malignant neoplasm of breast
C51	Malignant neoplasm of vulva
C52	Malignant neoplasm of vagina
C53	Malignant neoplasm of cervix uteri

C54	Malignant neoplasm of corpus uteri
C55	Malignant neoplasm of uterus, part unspecified
C56	Malignant neoplasm of ovary
C57	Malignant neoplasm of other and unspecified female genital organs
C61	Malignant neoplasm of prostate
C65	Malignant neoplasm of renal pelvis
C66	Malignant neoplasm of ureter
C67	Malignant neoplasm of bladder
C68	Malignant neoplasm of other and unspecified urinary organs
C72.9	Malignant neoplasm of central nervous system, unspecified
C79.31	Secondary malignant neoplasm of brain
C80.1	Malignant (primary) neoplasm, unspecified
J9358	Injection, fam-trastuzumab deruxtecan-nxki

Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	5/5/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	5/5/2025
6	Revision Changes:	

References

[1] Fam-Trastuzumab Deruxtecan-nxki (Enhertu) [Package Insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761139s032s035lbl.pdf. Accessed March 22, 2025.

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[16] National Comprehensive Cancer Network. NCCN Guidelines: Pancreatic Adenocarcinoma. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed March 22, 2025.

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