POLICY Document for Enhertu

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 2: Oncology Clinical Policy
- Policy information specific to regimen review per NCCN Guidelines.

Section 1: Clinical Criteria

Specialty Guideline Management

Enhertu

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Enhertu	fam-trastuzumab deruxtecan-nxki

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

HER2-positive Breast Cancer

Enhertu is indicated for the treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-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.

HER2-low and HER2-ultralow Breast Cancer

- Enhertu is indicated for the treatment of adult patients with unresectable or metastatic HER2-low [immunohistochemistry score (IHC) 1+ or IHC 2+/ in situ hybridization test (ISH) negative] 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.
- Enhertu is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting.

Gastric or Gastroesophageal Junction Adenocarcinoma

Enhertu is indicated for the treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen.

Non-Small Cell Lung Cancer (NSCLC)

Enhertu is indicated for the treatment of 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.

Solid Tumors

Enhertu is indicated for the treatment of 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.

Compendial Uses[2-5]

- HER2-positive breast cancer, treatment of recurrent disease
- HER2-low and ultralow breast cancer, treatment of recurrent disease
- Non-small cell lung cancer with HER2 mutations, treatment of recurrent and advanced disease
- HER2-amplified colorectal cancer (including appendiceal and anal adenocarcinoma)
- HER2-positive esophageal, gastric or gastroesophageal junction cancer
- HER2-positive cervical cancer
- HER2-positive endometrial carcinoma
- HER2-positive salivary gland tumor
- HER2-positive ovarian cancer
- HER2-positive vaginal cancer
- HER2-positive biliary tract cancer
- HER2-positive solid tumors

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review: human epidermal growth factor receptor 2 (HER2) status (e.g., immunohistochemistry (IHC) score, in situ hybridization (ISH) test) and hormone receptor (HR) status.

Coverage Criteria

Breast cancer[1,2]

Authorization of 12 months may be granted for treatment of breast cancer when any of the following criteria are met:

- Member has HER2-positive breast cancer and meets all of the following criteria:
  - The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic, or unresectable
  - The requested medication will be used as a single agent.
- Member has HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer and meets all of the following criteria:
  - The disease had no response to preoperative systemic therapy, or the disease is recurrent, metastatic or unresectable
  - The requested medication will be used as a single agent
- Member has HER2-ultralow (IHC 0 with membrane staining) breast cancer and meets all of the following criteria:
  - The disease is recurrent metastatic or unresectable
  - The disease is hormone receptor positive with visceral crisis or endocrine therapy refractory or the disease is hormone receptor negative
  - The requested medication will be used as a single agent

Non-small cell lung cancer[1,2]

Authorization of 12 months may be granted for subsequent treatment of non-small cell lung cancer with HER2 (ERBB2) mutations when all of the following criteria are met:

- The disease is recurrent, advanced, metastatic or unresectable
- The requested medication will be used as a single agent
- The member has not experienced disease progression on a HER2 targeted drug (e.g., Enhertu, Kadycla)

Colorectal Cancer[2-4]

Authorization of 12 months may be granted for treatment of colorectal cancer (including appendiceal and anal adenocarcinoma) with HER2-amplified disease as a single agent when the requested medication will be used as subsequent therapy for progression of advanced or metastatic disease.

Esophageal, Gastric or Gastroesophageal Junction Adenocarcinoma[1,2]

Authorization of 12 months may be granted for members with HER2-positive disease who are not surgical candidates or for subsequent treatment of HER2-positive locally advanced, recurrent or metastatic esophageal, gastric or gastroesophageal junction adenocarcinoma as a single agent.

Cervical Cancer[2]

Authorization of 12 months may be granted for subsequent treatment of recurrent or metastatic HER2-positive (IHC 3+ or 2+) cervical cancer when used as a single agent.

Endometrial Carcinoma[2]

Authorization of 12 months may be granted for subsequent treatment of recurrent HER2-positive (IHC 3+ or 2+) endometrial carcinoma when used as a single agent.

Salivary Gland Tumor[2,5]

Authorization of 12 months may be granted for treatment of recurrent, unresectable or metastatic HER2-positive salivary gland tumor when used as a single agent.

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer[2]

Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer when all of the following criteria are met:

- The member has platinum-resistant persistent or recurrent disease
- The disease is HER2-positive (IHC 3+ or 2+)
- The requested medication will be used as a single agent

Solid Tumors[1,2]

Authorization of 12 months may be granted for treatment of solid tumors when all of the following criteria are met:

- The disease is unresectable, metastatic, advanced, recurrent or persistent
- The tumor is HER2-positive (IHC 3+ or 2+)
- The member received prior systemic treatment and has no satisfactory alternative treatment options
- The requested medication will be used as a single agent

Vaginal Cancer[2]

Authorization of 12 months may be granted for subsequent treatment of recurrent or metastatic HER2-positive (IHC 3+ or 2+) vaginal cancer when used as a single agent.

Biliary Tract Cancer[2]

Authorization of 12 months may be granted for subsequent treatment of unresectable or resected gross residual (R2) disease or metastatic HER2-positive (IHC 3+) biliary tract cancer (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer) when used as a single agent.

Continuation Of Therapy

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Section 2: Oncology Clinical Policy

PURPOSE

The purpose of this policy is to define the Novologix NCCN® Regimen Prior Authorization Program.

SCOPE

This policy applies to clients who have implemented the Novologix NCCN® Program as a part of their medical and/or pharmacy prior authorization solution.

PROGRAM DESCRIPTION

The National Comprehensive Care Network® (NCCN®) is an alliance of leading cancer centers devoted to patient care, research and education dedicated to improving the quality, effectiveness, and efficiency of cancer care so patients can live better lives.[1] It is comprised of oncology experts who convene regularly to establish the best treatments for patients. NCCN develops various resources for use by stakeholders in the health care delivery system. These resources include, but are not limited to, the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), the NCCN Drugs & Biologics Compendium (NCCN Compendium®) and the NCCN Chemotherapy Order Templates (NCCN Templates®).

NCCN Templates® are based on NCCN Guidelines® and NCCN Compendium®. The NCCN Compendium lists the appropriate drugs and biologics as treatment options for specific cancers using U.S. Food and Drug Administration (FDA)-approved disease indications and specific NCCN panel recommendations. Each recommendation is supported by a level of evidence category.

NCCN Categories of Evidence and Consensus[2]

- 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.

POLICY

Policy for Regimen Prior Authorization

A regimen prior authorization allows submission of a single prior authorization request for all oncology drugs or biologics within an NCCN template that require prior authorization.

PROCEDURE

This policy provides coverage of a regimen review when all of the following criteria are met:

1. Regimen prior authorization reviews, based on NCCN templates, are initiated through the provider portal.
   - If the prior authorization request is submitted via phone or fax, each drug or biologic will need to be submitted and reviewed as a separate prior authorization request for review with drug-specific criteria.
2. The prior authorization review is requested for an oncology drug or biologic.
3. The member is eligible for regimen review.
4. The indication is for a cancer that is eligible for regimen review. Currently, the cancer types in scope for regimen review include the following:
   - Ampullary Adenocarcinoma
   - Anal Carcinoma
   - B-Cell Lymphomas
   - Basal Cell Skin Cancer
   - Biliary Tract Cancers

- Bone Cancer
- Breast Cancer
- Bladder Cancer
- Central Nervous System Cancers
- Cervical Cancer
- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
- Chronic Myeloid leukemia
- Colon Cancer
- Dermatofibrosarcoma Protuberans
- Esophageal Cancer
- Gastric Cancer
- Gastrointestinal Stromal Tumors
- Gestational Trophoblastic Neoplasms
- Hairy Cell Leukemia
- Head and Neck Cancers
- Histiocytic Neoplasms
- Hodgkin Lymphoma
- Hepatocellular Carcinoma
- Kaposi Sarcoma
- Kidney Cancer
- Melanoma: Cutaneous
- Melanoma: Uveal
- Merkel Cell Carcinoma
- Mesothelioma: Peritoneal
- Mesothelioma: Pleural
- Multiple Myeloma
- Myelodysplastic Syndromes
- Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions
- Myeloproliferative Neoplasms
- Neuroendocrine and Adrenal Tumors
- Non-Small Cell Lung Cancer
- Occult Primary
- Ovarian Cancer
- Pancreatic Cancer
- Penile Cancer
- Primary Cutaneous Lymphomas
- Prostate Cancer
- Rectal Cancer
- Small Bowl Adenocarcinoma

- Small Cell Lung Cancer
- Soft Tissue Sarcoma
- Squamous Cell Skin Cancer
- Systemic Mastocytosis
- Systemic Light Chain Amyloidosis
- T-Cell Lymphomas
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Thyroid Carcinoma
- Uterine Neoplasms
- Vaginal Cancer
- Vulvar Cancer
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma
- Wilms Tumor (Nephroblastoma)

In addition, the following criteria must be met for approval:

1. The requested regimen for the drug(s) or biologic(s) and indication is consistent with an NCCN recommendation with a level of evidence category of 1 or 2A.
2. The NCCN template must be accepted by the provider without modification.

Further review may be indicated when the above criteria are not met.

Authorizations may be granted for 12 months or as medically required, based on the member's condition and provider's assessment.

Supportive Care: Myeloid Growth Factor Therapy

Granulocyte colony stimulating factors are recommended for primary prophylaxis based on the febrile neutropenia risk of the chemotherapy regimen. Febrile neutropenia risk levels vary by NCCN Chemotherapy Order template and are listed at the top of the template. Regimens associated with a high or intermediate risk of febrile neutropenia may include a granulocyte colony stimulating factor as part of the prior authorization.

Continuation of Therapy

To submit a request for continuation of therapy, a new regimen prior authorization review must be requested. Upon template selection, the template must be modified to include the appropriate therapies being used for maintenance treatment. The regimen request will be submitted for further review.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and evidence-based practice guidelines.

REFERENCES:

SECTION 1

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3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Anal Carcinoma. Version 1.2024. Accessed September 3, 2024. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer. Version 5.2024. Accessed September 3, 2024. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
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SECTION 2

1. National Comprehensive Cancer Network. About NCCN website. https://www.nccn.org/home/about, accessed September 9, 2024.
2. National Comprehensive Cancer Network. NCCN Categories of Evidence and Consensus website, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines, accessed September 9, 2024.
3. National Comprehensive Cancer Network. NCCN Guidelines website. https://www.nccn.org/guidelines/category_1, accessed September 9, 2024. (Note: An account may be required.)
4. National Comprehensive Cancer Network. NCCN Drugs and Biologics Compendium website https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia, accessed September 9, 2024. (Note: A subscription may be required.)
5. National Comprehensive Cancer Network. NCCN Chemotherapy Order Templates (NCCN Templates) website. https://www.nccn.org/compendia-templates/nccn-templates-main/browse-by-cancer-type, accessed September 9, 2024. (Note: A subscription may be required.)