POLICY Document for CYRAMZA (ramucirumab)

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
Cyramza

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
Cyramza	ramucirumab

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]

Gastric Cancer: Cyramza as a single agent, or in combination with paclitaxel, is indicated for the treatment of patients with advanced or metastatic, gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine-or platinum-containing chemotherapy.

Non-Small Cell Lung Cancer (NSCLC):

Cyramza, in combination with docetaxel, is indicated for the treatment of patients with metastatic NSCLC with disease progression on or after platinum-based chemotherapy. Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza.

Cyramza, in combination with erlotinib, is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
Colorectal Cancer: Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and fluorouracil), is indicated for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.

Hepatocellular Carcinoma: Cyramza as a single agent, is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL and have been treated with sorafenib.

Compendial Uses[2,3]

Esophageal adenocarcinoma

Colorectal cancer, advanced, including anal adenocarcinoma and appendiceal adenocarcinoma

NSCLC, EGFR mutation positive, recurrent, advanced

Mesothelioma

Thymic carcinoma

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: EGFR mutation testing results and alpha fetoprotein (AFP) level results (where applicable).

Coverage Criteria

Gastric, Gastro-esophageal Junction (GEJ), Esophagogastric Junction (EGJ), and Esophageal Adenocarcinoma[1,2]

Authorization of 12 months may be granted for treatment of gastric, gastro-esophageal junction (GEJ), esophagogastric junction (EGJ), and esophageal adenocarcinoma for members who are not surgical candidates or who have unresectable locally advanced, recurrent or metastatic disease, when used as subsequent therapy as a single agent, in combination with paclitaxel, or in combination with irinotecan with or without fluorouracil.

Non-Small Cell Lung Cancer (NSCLC)[1,2]

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC when either of the following criteria is met:

Used in combination with docetaxel as subsequent therapy.
Used in combination with erlotinib for EGFR exon 19 deletion or exon 21 (L858R) substitution mutation positive disease.

Colorectal Cancer (CRC)[1-3]

Authorization of 12 months may be granted for treatment of advanced or metastatic colorectal cancer, including anal adenocarcinoma and appendiceal adenocarcinoma, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil) or irinotecan.

Hepatocellular Carcinoma (HCC)[1,2]

Authorization of 12 months may be granted for subsequent treatment of progressive hepatocellular carcinoma as a single agent in members who have an alpha fetoprotein (AFP) of greater than or equal to 400 ng/mL.

Mesothelioma[2]

Authorization of 12 months may be granted for the subsequent treatment of pleural mesothelioma, pericardial mesothelioma, or tunica vaginalis testis mesothelioma when used in combination with gemcitabine.

Thymic Carcinoma[2]

Authorization of 12 months may be granted for the treatment of thymic carcinoma when any of the following are met:
Member has recurrent, advanced, or metastatic disease and the requested medication will be used in combination with carboplatin and paclitaxel and continued as a single agent maintenance therapy, or
Member has had a R1 or R2 resection and the requested medication will be used in combination with carboplatin and paclitaxel as postoperative treatment, or
Member has surgically resectable disease, R0 resection is considered uncertain, and the requested medication will be used in combination with carboplatin and paclitaxel as preoperative treatment.

Continuation of Therapy

NSCLC

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NSCLC when either of the following criteria is met:

There is no evidence of unacceptable toxicity or disease progression while on the current regimen, or

Disease is T790M negative and there is no evidence of unacceptable toxicity

All other indications

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

1. Cyramza [package insert]. Indianapolis, IN: Eli Lilly and Company; March 2022.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed January 17, 2025.

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Anal Carcinoma. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. Accessed January 17, 2025.

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.)