POLICY Document for ERBITUX® (cetuximab)

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

ERBITUX® (cetuximab)

POLICY

I. 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.

A. FDA-Approved Indications

1. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
   Erbitux is indicated:
   a. In combination with radiation therapy for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).
   b. In combination with platinum-based therapy with fluorouracil for the first-line treatment of patients with recurrent locoregional disease or metastatic SCCHN.
   c. As a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.

2. K-Ras Wild-type, EGFR-expressing Colorectal Cancer (CRC)
   Erbitux is indicated for the treatment of K-Ras wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by an FDA-approved test:
   a. In combination with FOLFIRI (irinotecan, fluorouracil, leucovorin) for first-line treatment,
   b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
   c. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

   Limitations of Use:
   Erbitux is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

3. BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)
   Erbitux is indicated, in combination with encorafenib, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy.

B. Compendial Uses
1. Colorectal cancer
2. Squamous cell carcinoma of the head and neck
3. Occult primary head and neck cancer
4. Penile cancer
5. Squamous cell skin cancer
6. Non-small cell lung cancer

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

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Documentation of RAS wild-type status or KRAS G12C mutation, where applicable.
B. Documentation of BRAF mutation status, where applicable.
C. Documentation of EGFR expression, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including appendiceal adenocarcinoma and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease and the member has not previously experienced clinical failure on panitumumab when either of the following criteria are met:
1. The member meets all of the following criteria:
   i. The *RAS (KRAS* and *NRAS)* mutation status is negative (wild-type)
   ii. If the tumor is positive for BRAF V600E mutation, the requested medication will be used in combination with encorafenib (Braftovi)
   iii. For first-line treatment of colon cancer, the tumor is left-sided only, or
2. The member meets all of the following criteria:
   i. The disease is KRAS G12C mutation positive
   ii. The requested medication will be used in combination with sotorasib (Lumakras) or adagrasib (Krazati)
   iii. The member previously received treatment with chemotherapy

B. Squamous Cell Carcinoma of the Head and Neck

Authorization of 6 months may be granted for treatment of squamous cell carcinoma of the head and neck when any of the following criteria is met:
1. Disease is locally or regionally advanced, unresectable, recurrent, persistent, or metastatic.
2. Member is unfit for surgery.
3. The requested medication will be used in combination with radiation.

C. Occult Primary Head and Neck Cancer

Authorization of 6 months may be granted as a single agent for treatment of occult primary head and neck cancer for chemoradiation.

D. Penile Cancer

Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic penile cancer.

E. Squamous Cell Skin Cancer

Authorization of 6 months may be granted as a single agent for treatment of squamous cell skin cancer in unresectable/inoperable/incompletely resected, locally advanced, regional, recurrent, or distant metastatic disease.

F. Non-Small Cell Lung Cancer (NSCLC)
Authorization of 6 months may be granted for subsequent treatment of recurrent, advanced or metastatic NSCLC when all of the following criteria are met:
1. The requested medication will be used in combination with afatinib (Gilotrif).
2. The requested medication will be used in members with a known sensitizing EGFR mutation (e.g., EGFR exon 19 deletion or L858R mutation, or EGFR S768I, L861Q, and/or G719X mutation) following disease progression on EGFR tyrosine kinase inhibitor therapy.

IV. CONTINUATION OF THERAPY
Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III 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. Erbitux [package insert]. Branchburg, NJ: ImClone LLC; September 2021.
2. The NCCN Drugs & Biologics Compendium® © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 6, 2024.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer. Version 1.2024. Accessed February 6, 2024. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Anal Carcinoma. Version 3.2023. Accessed September 22, 2023. https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf

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. 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.)