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5.21.084

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	September 23, 2016
Subject:	Erbitux	**Page:**	1 of 6

Last Review Date: March 8, 2024

Erbitux

Description

Erbitux (cetuximab)

Background
Erbitux (cetuximab) is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of squamous cell carcinoma of the head and neck and metastatic colorectal cancer. Erbitux is also used off-label for the treatment of squamous cell skin cancer, penile cancer, and non-small cell lung cancer. Epidermal growth factor receptor (EGFR) is a protein involved in the growth and spread of cancer cells that is detected in many human cancers, including those of the head, neck, colon and rectum. Erbitux competitively blocks the EGFR receptor and prevents the activation of kinases, resulting in inhibition of cell growth and induction of cell death (1).

Regulatory Status
FDA-approved indications: Erbitux (cetuximab) is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of (1):

1. Head and Neck Cancer
    a. Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy.
    b. Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with 5-FU.
    c. Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy.
2. Metastatic Colorectal Cancer
    a. K-Ras wild-type, EGFR-expressing, as determined by FDA-approved tests
        i. In combination with FOLFIRI for first-line treatment

ii. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
iii. 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 the treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

b. BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)
i. 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.

Off-Label Uses: (2-5).

1. Head and Neck cancer Stage III or IV
2. Metastases of squamous cell skin cancer
3. Metastases of penile cancer
4. Non-small cell lung cancer (NSCLC)

Erbitux carries a boxed warning for serious infusion reactions and cardiopulmonary arrest. Electrolytes including serum magnesium, potassium, and calcium should be closely monitored during and after Erbitux administration (1).

Safety and effectiveness of Erbitux in pediatric patients have not been established (1).

Related policies
Vectibix

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Erbitux may be considered **medically necessary** if the conditions indicated below are met.

Erbitux may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Squamous cell carcinoma of the head and neck
    a. Stage III
        i. If non-nasopharyngeal site- concurrent radiation therapy
    b. Stage IV
        i. If non-nasopharyngeal site- concurrent radiation therapy and **ONE** of the following:
            1. As a single agent
            2. In combination with carboplatin and fluorouracil
            3. In combination with cisplatin with or without fluorouracil, docetaxel or paclitaxel
        ii. If nasopharyngeal site- concurrent radiation and carboplatin
2. Metastatic colorectal cancer (CRC)
    a. Patient must have **ONE** of the following:
        i. *KRAS/NRAS* wild-type gene expression as determined by FDA-approved tests **AND ONE** of the following:
            1. Used as a single agent: patient has failed oxaliplatin- and irinotecan-based chemotherapy or is intolerant to irinotecan
            2. First-line treatment: used in combination with FOLFIRI
            3. Used in combination with irinotecan: patients is refractory to irinotecan-based chemotherapy
        ii. BRAF V600E mutation as detected by an FDA-approved test
            1. Used in combination with encorafenib
            2. Patient must **NOT** have wild-type BRAF CRC
            3. **NOT** used as first-line therapy
3. Metastases of squamous cell skin cancer
4. Metastases of penile cancer
5. Non-small cell lung cancer (NSCLC)
    a. EGFR mutation
    b. Progressed after EGFR tyrosine kinase inhibitor therapy
    c. Used in combination with afatinib

AND the following for **ALL** indications:

a. Prescriber agrees to monitor serum electrolytes, magnesium, potassium, calcium levels, and serious infusion reactions.

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Squamous cell carcinoma of the head and neck
    a. Stage III
        i. If non-nasopharyngeal site- concurrent radiation therapy
    b. Stage IV
        i. If non-nasopharyngeal site- concurrent radiation therapy and **ONE** of the following:
            1) As a single agent
            2) In combination with carboplatin and fluorouracil
            3) In combination with cisplatin with or without fluorouracil, docetaxel or paclitaxel
        ii. If nasopharyngeal site- concurrent radiation and carboplatin
2. Metastatic colorectal cancer (CRC) **AND ONE** of the following:
    a. Used as a single agent
    b. Used in combination with FOLFIRI
    c. Used in combination with irinotecan
    d. Used in combination with encorafenib
3. Metastases of squamous cell skin cancer
4. Metastases of penile cancer
5. Non-small cell lung cancer (NSCLC)
    a. Used in combination with afatinib

AND ALL of the following for **ALL** indications:

a. Prescriber agrees to monitor serum electrolytes, magnesium, potassium, and calcium levels
b. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Erbitux (cetuximab) is an epidermal growth factor receptor (EGFR) antagonist indicated for the treatment of head and neck cancer and colorectal cancer. Erbitux is also used off-label for the treatment of squamous cell skin cancer, penile cancer, and non-small cell lung cancer. Erbitux carries a boxed warning for serious infusion reactions and cardiopulmonary arrest. The safety and effectiveness of Erbitux in pediatric patients have not been established (1-5).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Erbitux while maintaining optimal therapeutic outcomes.

References

1. Erbitux [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2021.
2. NCCN Drugs & Biologics Compendium® Cetuximab 2024. National Comprehensive Cancer Network, Inc. Accessed on January 31, 2024.
3. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 1.2024). National Comprehensive Cancer Network, Inc. December 2023. Accessed on January 31, 2024.
4. NCCN Clinical Practice Guidelines in Oncology® Colon Cancer (Version 1.2024). National Comprehensive Cancer Network, Inc. December 2023. Accessed on January 31, 2024.
5. NCCN Clinical Practice Guidelines in Oncology® Penile Cancer (Version 1.2024). National Comprehensive Cancer Network, Inc. December 2023. Accessed on January 31, 2024.

Policy History

Date	Action
September 2016	Addition to PA
December 2016	Annual review

June 2017	Annual review and reference update
June 2018	Annual editorial review and reference update
November 2018	Annual review and reference update
June 2019	Annual review and reference update
April 2020	Revised requirements for metastatic colorectal cancer. Addition of indication for CRC in combination with encorafenib in patients with BRAF V600E mutation
June 2020	Annual review
March 2021	Annual editorial review and reference update
October 2021	Revised regulatory status per latest package insert
December 2021	Annual review and reference update
March 2022	Annual review and reference update
March 2023	Annual review and reference update. Changed policy number to 5.21.084
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.