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# 5.21.084

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	September 23, 2016
<b>Subject:</b>	Erbix	<b>Page:</b>	1 of 7

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**Last Review Date:** September 6, 2024

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## Erbix

### Description

#### Erbix (cetuximab)

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#### Background

Erbix (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. Erbix 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. Erbix 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: Erbix (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 (CRC)
  - a. K-Ras wild-type, EGFR-expressing, as determined by FDA-approved tests
    - i. In combination with FOLFIRI for first-line treatment.

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbix	<b>Page:</b>	2 of 7

---

- 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.
- 3. Locally Advanced or Metastatic Colorectal Cancer (CRC)
  - a. Adult patients with KRAS G12C-mutated locally advanced or metastatic CRC, as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, in combination with adagrasib.

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)

Erbix 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).

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**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.*

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

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

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbitux	<b>Page:</b>	3 of 7

---

## 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 Braftovi (encorafenib)
      2. Patient must **NOT** have wild-type BRAF CRC
      3. **NOT** used as first-line therapy
3. Locally advanced or metastatic colorectal cancer (CRC)
  - a. Used in combination with Krazati (adagrasib)
  - b. Patient has received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbitux	<b>Page:</b>	4 of 7

---

- c. Presence of KRAS G12C mutation as determined by an FDA-approved test
- 4. Metastases of squamous cell skin cancer
- 5. Metastases of penile cancer
- 6. Non-small cell lung cancer (NSCLC)
  - a. EGFR mutation
  - b. Progressed after EGFR tyrosine kinase inhibitor therapy
  - c. Used in combination with Gilotrif (afatinib)

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

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

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## 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 Braftovi (encorafenib)
3. Locally advanced or metastatic colorectal cancer (CRC) **AND** the following:
  - a. Used in combination with Krazati (adagrasib)

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbixux	<b>Page:</b>	5 of 7

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4. Metastases of squamous cell skin cancer
5. Metastases of penile cancer
6. Non-small cell lung cancer (NSCLC)
  - a. Used in combination with Gilotrif (afatinib)

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

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

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Duration** 12 months

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### Prior – Approval *Renewal* Limits

Same as above

## Rationale

### Summary

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

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

### References

1. Erbixux [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2021.
2. Krazati [package insert]. San Diego, CA: Mirati Therapeutics, Inc.; June 2024.

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbitux	<b>Page:</b>	6 of 7

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3. NCCN Drugs & Biologics Compendium<sup>®</sup> Cetuximab 2024. National Comprehensive Cancer Network, Inc. Accessed on August 6, 2024.
4. NCCN Clinical Practice Guidelines in Oncology<sup>®</sup> Non-Small Cell Lung Cancer (Version 7.2024). National Comprehensive Cancer Network, Inc. June 2024. Accessed on August 6, 2024.
5. NCCN Clinical Practice Guidelines in Oncology<sup>®</sup> Colon Cancer (Version 4.2024). National Comprehensive Cancer Network, Inc. July 2024. Accessed on August 6, 2024.
6. NCCN Clinical Practice Guidelines in Oncology<sup>®</sup> Penile Cancer (Version 1.2024). National Comprehensive Cancer Network, Inc. December 2023. Accessed on August 6, 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
July 2024	Added indication of locally advanced or metastatic colorectal cancer in combination with Krazati. Also changed initiation approval duration to 12 months from 6 months
September 2024	Annual review and reference update

## Keywords

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# 5.21.084

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	October 1, 2024
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	June 16, 2017
<b>Subject:</b>	Erbitux	<b>Page:</b>	7 of 7

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 6, 2024 and is effective on October 1, 2024.**