Erbitux (cetuximab)

Background
Erbitux is a medication used to treat patients with squamous cell carcinoma of the head and neck (SCCHN) and patients with epidermal growth factor receptor (EGFR)-expressing metastatic colorectal cancer, who also express the wild-type K-RAS gene. Metastatic colorectal cancer is an advanced form of cancer affecting the colon or rectum that has begun spreading to other parts of the body. 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
   b. In combination with FOLFIRI for first-line treatment
   c. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
   d. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

Limitation of Use:
Erbitux is not indicated for the treatment of *ras*-mutant colorectal cancer (1).

Off Label Uses: (2-5).
1. Head Neck cancer Stage III or IV – cancer has spread to nearby tissues and different parts of the body
2. Colorectal Cancer Stage IV – cancer has spread to distant parts of the body
   1. First progression
   2. Second progression
   3. Neoadjuvant therapy
   4. Adjuvant / postoperative, unresectable, or palliative therapy
3. Metastases of squamous cell skin cancer
4. Metastases of penile cancer
5. Non-small cell lung cancer (NSCLC)

Erbitux carries a boxed warning for serious infusion reactions and cardiopulmonary arrest. The reported incidence of serious infusion reactions was 3%, some of which were fatal. Cardiopulmonary arrest and/or sudden death occurred in 2% of patients with squamous cell carcinoma of the head and neck while being used in combination with radiation therapy, and 3% of patients with squamous cell carcinoma of the head and neck when used in combination with platinum-based therapy with 5-FU. 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
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 for patients 18 years of age or older with stage III squamous cell carcinoma of the head and neck in a non-nasopharyngeal site and concurrent therapy with radiation therapy is needed. Patients with stage IV squamous cell carcinoma of the head and neck with one of the following: non-nasopharyngeal site - concurrent therapy with radiation therapy and with one of the following: in combination with cisplatin therapy with or without 5-FU, docetaxel or paclitaxel, in combination with carboplatin and 5FU, or as a single agent: nasopharyngeal site - concurrent therapy with radiation therapy and carboplatin is needed. Patients with colorectal cancer and stage IV who have KRAS/NRAS wild-type gene expression as determined by FDA-approved tests; patient must have ONE of the following: first progression no previous treatment with Erbitux or Vectibix (panitumumab) and used as single agent or in combination with FOLFIRI or irinotecan, second progression no previous treatment with Erbitux or Vectibix (panitumumab) and used as single agent or in combination with irinotecan, neoadjuvant therapy used as single agent or in combination with FOLFIRI or FOLFOX, or adjuvant / postoperative, unresectable, or palliative therapy for patients who have received FOLFOX / CapeOX in the past 12 months – use in combination with FOLFIRI or irinotecan, or for patients who have not received FOLFOX / CapeOX in the past 12 months – use in combination with FOLFIRI or FOLFOX. Patients with metastases of squamous cell skin cancer or penile cancer; for non-small cell lung cancer (NSCLC) with EGFR mutation who have progressed after EGFR tyrosine kinase inhibitor therapy in combination with afatinib. The prescriber agrees to monitor serum electrolytes, magnesium, potassium, calcium levels and serious infusion reactions.

Erbitux is considered investigational in patients less than 18 years of age and 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. Colorectal cancer
   a. Stage IV
   b. KRAS/NRAS wild-type gene expression as determined by FDA-approved tests
   c. Patient must have ONE of the following:
      i. First progression
         1) NO previous treatment with Erbitux (cetuximab) or Vectibix (panitumumab)
         2) Used as single agent or in combination with FOLFIRI or irinotecan
      ii. Second progression
         3) NO previous treatment with Erbitux (cetuximab) or Vectibix (panitumumab)
         4) Used as single agent or in combination with irinotecan
      iii. Neoadjuvant therapy
         5) Used as single agent or in combination with FOLFIRI or FOLFOX
      iv. Adjuvant / postoperative, unresectable, or palliative therapy
         6) For patients who have received FOLFOX / CapeOX in the past 12 months – Use in combination with FOLFIRI or irinotecan
         7) For patients who have NOT received FOLFOX / CapeOX in the past 12 months – Use in combination with FOLFIRI or FOLFOX

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 ALL of the following:
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. Colorectal cancer
   a. Patient must have **ONE** of the following:
      i. First progression
         1) Used as single agent or in combination with FOLFIRI or irinotecan
      ii. Second progression
         1) Used as single agent or in combination with irinotecan
      iii. Neoadjuvant therapy
         1) Used as single agent or in combination with FOLFIRI or FOLFOX
      iv. Adjuvant / postoperative, unresectable, or palliative therapy
         1) For patients who have received FOLFOX / CapeOX in the past
            – Use in combination with FOLFIRI or irinotecan
         2) For patients who have **NOT** received FOLFOX / CapeOX in the past – Use in combination with FOLFIRI or FOLFOX

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:
   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 medically necessary for the treatment of head, neck and colorectal cancers. Erbitux should be used for head and neck cancers in combination with radiation therapy or platinum therapy with 5-FU. It may also be used as a single agent following disease progression after platinum-based therapy. Erbitux is also used for squamous cell skin cancer, penile cancer, or non-small cell lung cancer (NSCLC) Erbitux carries a boxed warning for serious infusion reactions and cardiopulmonary arrest. 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 (cetuximab) while maintaining optimal therapeutic outcomes.

References


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<tr>
<th>Date</th>
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<tbody>
<tr>
<td>September 2016</td>
<td>Addition to PA</td>
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<tr>
<td>December 2016</td>
<td>Annual review</td>
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<tr>
<td>June 2017</td>
<td>Annual review and reference update</td>
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<tr>
<td>June 2018</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>November 2018</td>
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<tr>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.