Erbitux (cetuximab)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Erbitux (cetuximab)

APPROVAL CRITERIA:

Requests for Erbitux (cetuximab) may be approved if the following criteria are met:

I. Individual has a diagnosis of colon, rectal, colorectal, appendix or anal adenocarcinoma and the following criteria are met (NCCN 2A):
   A. Individual has advanced or metastatic disease; **AND**
   B. Extended RAS gene mutation testing is confirmed and the tumor is determined to be RAS wild-type[+]; **AND**
   C. Cetuximab is used as a single agent or as part of combination therapy; **AND**
   D. Individual has not received prior treatment with panitumumab*; **AND**
   E. Cetuximab is not being used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
   F. Cetuximab is used in a single line of therapy**;

   [+]**Note:** RAS wild-type means that the KRAS and NRAS genes are normal or lacking mutations.

OR

II. Individual has a diagnosis of colon, rectal, colorectal, appendix or anal adenocarcinoma and the following are met (NCCN 2A):
   A. Individual has advanced or metastatic disease; **AND**
   B. Gene mutation testing is confirmed, and the tumor is determined to be BRAF wild-type [++]; **AND**
   C. Individual is being treated for left-sided only tumors; **AND**
   D. Cetuximab is used as a single agent or as part of combination therapy; **AND**
   E. Individual has not received prior treatment with panitumumab*; **AND**
   F. Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
   G. Cetuximab is used in a single line of therapy **;

   ++**Note**: BRAF wild-type means that the BRAF gene is normal or lacking mutations.

OR

III. Individual has a diagnosis of unresectable, advanced, or metastatic colorectal cancer and the following are met (Label, NCCN 2A):
   A. Individual has BRAF V600E mutation with test results confirmed; **AND**
   B. Cetuximab is used in combination with encorafenib; **AND**

C. Individual has demonstrated disease progression after one or more prior lines of systemic therapy; **AND**
D. Individual has not received prior treatment with panitumumab*; **AND**
E. Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
F. Cetuximab is used in a single line of therapy **;

OR

IV. Individual has a diagnosis of squamous cell carcinoma of head and neck (SCCHN), and the following criteria are met:
A. Individual has not received prior treatment with panitumumab*; **AND**
B. Cetuximab is not being used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
C. Cetuximab is used in a single line of therapy**; **AND**
D. Cetuximab is used in one of the following indications:
1. In combination with radiation therapy, for the treatment of locally or regionally advanced disease; **OR**
2. As a single agent for the treatment of individuals with recurrent or metastatic disease for whom prior platinum-based therapy has failed **OR**
3. In combination with platinum-based therapy with 5-FU (fluorouracil) as first-line treatment for individuals with recurrent locoregional disease or metastatic SCCHN; **OR**
4. As a single agent or in combination therapy with or without radiation for **any** of the following indications (NCCN 2A):
a. Unresectable locoregional recurrence; **OR**
b. Second primary in individuals who have received prior radiation therapy; **OR**
c. Resectable locoregional recurrence in individuals who have not received prior radiation therapy; **OR**
d. Distant metastases;

OR

V. Individual has a diagnosis of squamous cell skin carcinoma, and the following criteria are met (NCCN 2A):
A. Individual has unresectable or locally advanced disease, regional recurrence, or distant metastatic disease; **AND**
B. Individual has not received prior treatment with panitumumab*; **AND**
C. Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
D. Cetuximab is used in a single line of therapy**

*__Note:__ A course of panitumumab discontinued because of adverse reaction, not progressive disease, is not considered prior treatment.
**__Note:__ If cetuximab is recommended as initial therapy, it should not be used in second or subsequent lines of therapy.

Requests for Erbitux (cetuximab) may **not** be approved for the following:

I. All other indications not included above; **OR**
II. In combination with other monoclonal antibodies; **OR**

III. Use as adjuvant therapy after resection for colon cancer; **OR**
IV. Treatment of squamous cell anal carcinoma; **OR**
V. Treatment of non-small cell lung cancer.

Note:
Erbitux has a black box warning for infusion reactions and cardiopulmonary arrest. Erbitux can cause serious and fatal infusion reactions; immediately interrupt and permanently discontinue for serious infusion reaction. Cardiopulmonary arrest or sudden death occurred in patients with SCCHN receiving Erbitux with radiation therapy or a cetuximab product with platinum-based therapy and fluorouracil. Monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after Erbitux administration.

Key References:

1. Alberts SR, Sargent DJ, Nair S, et al. Effect of oxaliplatin, fluorouracil, and leucovorin with or without cetuximab on survival among patients with resected stage III colon cancer. JAMA. 2012; 307(13):1383-1393.
2. Carthon BC, Ng CS, Pettaway CA, Pagliaro LC. Epidermal growth factor receptor-targeted therapy in locally advanced or metastatic squamous cell carcinoma of the penis. BJU Int. 2014; 113(6):871-877.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2021. URL: http://www.clinicalpharmacology.com. Updated periodically.
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: April 12, 2022.
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
6. Hecht JR, Mitchell E, Chidiac T, et al. A randomized phase IIIB trial of chemotherapy, bevacizumab, and panitumumab compared with chemotherapy and bevacizumab alone for metastatic colorectal cancer. J Clin Oncol. 2009; 27(5):672-680.
7. Janjigian YY, Smit EF, Groen HJ, et al. Dual inhibition of EGFR with afatinib and cetuximab in kinase inhibitor-resistant EGFR-mutant lung cancer with and without T790M mutations. Cancer Discov. 2014; 4(9):1036-1045.
8. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
9. Lynch TJ, Patel T, Dreisbach L, et al. Cetuximab and first-line taxane/carboplatin chemotherapy in advanced non-small-cell lung cancer: results of the randomized multicenter phase III trial BMS099. J Clin Oncol. 2010; 28(6):911-917.
10. Tol J, Koopman M, Cats A, et al. Chemotherapy, bevacizumab, and cetuximab in metastatic colorectal cancer. N Engl J Med. 2009; 360(6):563-572.
11. Pirker R, Pereira JR, von Pawel J, et al. EGFR expression as a predictor of survival for first-line chemotherapy plus cetuximab in patients with advanced non-small-cell lung cancer: analysis of data from the phase 3 FLEX study. Lancet Oncol. 2012; 13(1):33-42.
12. NCCN Clinical Practice Guidelines in Oncology™. © 2020 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed April 2022.
    a. Colon Cancer. V1.2022. Revised February 25, 2022.
    b. Head and Neck Cancers. V1.2022. Revised December 8, 2021.
    c. Non-Small Cell Lung Cancer. V3.2022. Revised March 16, 2022.
    d. Penile Cancer. V2. 2022. Revised January 26, 2022.
    e. Rectal Cancer. V1. 2022. Revised February 25, 2022.
    f. Squamous Cell Skin Cancer. V1.2022. Revised November 17, 2021.
    g. Small Bowel Adenocarcinoma. V1.2022. Revised March 9, 2022.