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Ascension

Cetuximab

(Erbitux®) J9055 (10mg)

Covered with prior authorization

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

- Individual has a diagnosis of colon, rectal, colorectal, appendix or anal adenocarcinoma and the following are met (Label, NCCN 2A):
    - Individual has stage IV disease; **AND**
    - Extended RAS gene mutation testing is confirmed and the tumor is determined to be RAS wild-type**+**; **AND**
    - Cetuximab is used as a single agent or as part of combination therapy; **AND**
    - Individual has not received prior treatment with panitumumab*****; **AND**
    - Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
    - 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

- Individual has a diagnosis of colon, rectal, colorectal, appendix or anal adenocarcinoma and the following are met (NCCN 2A):
    - Individual has stage IV disease; **AND**
    - Gene mutation testing is confirmed, and the tumor is determined to be BRAF wild-type**++**; **AND**
    - Individual is being treated for left-sided only tumors; **AND**
    - Cetuximab is used as a single agent or as part of combination therapy; **AND**
    - Individual has not received prior treatment with panitumumab*****; **AND**
    - Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
    - Cetuximab is used in a single line of therapy******;
      ++Note: BRAF wild-type means that the BRAF gene is normal or lacking mutations

OR

- Individual has a diagnosis of unresectable, advanced, or metastatic colorectal cancer and the following are met (Label, NCCN 2A):
    - Individual has a BRAF V600E mutation with test results confirmed; **AND**
    - Cetuximab is used in combination with encorafenib; **AND**
    - Individual has demonstrated disease progression after one or more prior lines of systemic therapy; **AND**
    - Individual has not received prior treatment with panitumumab*****; **AND**

- Cetuximab is not used in combination with anti-VEGF agents (bevacizumab, ziv-aflibercept, or ramucirumab); **AND**
- Cetuximab is used in a single line of therapy**;

OR

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

OR

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

*A course of panitumumab discontinued because of adverse reaction (rather than progressive disease), is not considered prior treatment.
** If cetuximab is recommended as initial therapy, it should not be used in second or subsequent lines of therapy.
+Note: RAS wild-type means that the KRAS and NRAS genes are normal or lacking mutations.

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

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Requests for Erbitux® (Cetuximab) may **not** be approved if the above criteria are not met and for all other indications not included above.

Initial authorization and reauthorization are up to 12 months.

Annual reauthorizations will require medical chart documentation that the patient has been seen within the past 12 months and that markers of disease are improved by therapy.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Exclusion criteria:

- All other indications not included above
- In combination with other monoclonal antibodies
- Use as adjuvant therapy after resection for colon cancer
- Treatment of squamous cell anal carcinoma
- Treatment of non-small cell lung cancer
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk

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 reactions. 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.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage. Erbitux® is a recombinant human/mouse chimeric monoclonal antibody that targets and inhibits the biologic activity of the human epidermal growth factor receptor (EGFR). It is primarily used to treat colorectal cancer and squamous cell carcinoma of the head and neck (SCCHN). The FDA approved indications of Erbitux® for SCCHN include use in combination with radiation therapy for initial treatment; in combination with chemotherapy for first-line treatment of recurrent locoregional or metastatic disease; and as a single agent for recurrent or metastatic

disease in whom prior chemotherapy has failed. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Erbitux®. These recommendations include the use as a single agent or in combination therapy with or without radiation for: distant metastases; unresectable locoregional recurrence; resectable locoregional recurrence without prior radiation; and second primary after prior radiation therapy. Erbitux® is also FDA approved to treat metastatic colorectal cancer, in combination with chemotherapy or as a single agent. It is also FDA-approved for combination use with encorafenib for BRAF mutation positive colorectal cancer after prior therapy. Within the guidelines, NCCN recommends that appendiceal adenocarcinoma be treated with chemotherapy according to colon cancer guidelines. Similarly, it is recommended that anal adenocarcinoma, a rare histologic form of anal cancer, may be treated according to guidelines for rectal cancer. Guidelines for squamous cell anal cancer, the most common type of anal cancer, do not currently include Erbitux® among recommended treatments. Erbitux® has been studied in the adjuvant setting of colon cancer (Alberts 2012); but trial was halted when data from interim analysis did not demonstrate improved disease-free survival. NCCN notes that Erbitux® has no role in the adjuvant treatment of colon cancer at this time.

Key References Accessed 8/2022:

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. 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.
4. Janjigian YY, Smit EF, Groen HJ, et al. Dual inhibition of EGFR with afatinib and cetuximab in kinase inhibitor-resistant EGFRmutant lung cancer with and without T790M mutations. Cancer Discov. 2014; 4(9):1036-1045.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
6. 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.
7. 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.
8. 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.
    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.

Date	Summary of Changes
August 2022	Criteria for use summary developed by the Ascension Medical Specialty Prior Authorization Team.
September 2022	Criteria for use summary approved by the Ascension Ambulatory Care Expert Review Panel.
October 2022	Criteria for use summary approved by the Ascension Therapeutic Affinity Group.

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team, or email your questions to smarthealthspecialty@ascension.org.