Reference number(s)
2626-A

STANDARD MEDICARE PART B MANAGEMENT

ERBITUX (cetuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
   Erbitux is indicated:
   a. In combination with radiation therapy for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).
   b. In combination with platinum-based therapy with fluorouracil for the first-line treatment of patients with recurrent locoregional disease or metastatic SCCHN.
   c. As a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.

2. K-Ras Wild-type, EGFR-expressing Colorectal Cancer (CRC)
   Erbitux is indicated for the treatment of *KRAS* wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by an FDA-approved test:
   a. In combination with FOLFIRI (irinotecan, fluorouracil, leucovorin) for first-line treatment,
   b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
   c. 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 treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

3. BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC)
   Erbitux is indicated 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.

B. Compendial Uses

1. Colorectal cancer
2. Squamous cell carcinoma of the head and neck
3. Occult primary head and neck cancer
4. Gastric and gastroesophageal cancer
5. Non-small cell lung cancer

6. Penile cancer
7. Squamous cell skin cancer

C. CMS Nationally Covered Uses

The following NCD policy applies to these criteria: Anti-cancer Chemotherapy for Colorectal Cancer (110.17).[6] CMS covers Erbitux for use in specific clinical trials (NCI-CMS Pilot Project). Refer to the Appendix for a list of these covered clinical trials.[7]

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following information must be available, upon request, for all submissions:

A. Documentation of RAS wild-type status, where applicable.
B. Documentation of BRAF mutation status, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 12 months may be granted for the treatment of colorectal cancer, including appendiceal carcinoma and anal adenocarcinoma, when all of the following criteria are met:

1. The member has RAS (*KRAS and NRAS*) negative (wild-type) tumors
2. If the tumor is positive for BRAF V600E mutation, the requested medication will be used in combination with encorafenib (Braftovi)

B. Head and Neck Cancer

Authorization of 12 months may be granted for the treatment of head and neck cancer.

C. Gastric and Gastroesophageal Cancer

Authorization of 12 months may be granted for the treatment of locally advanced or metastatic gastric or gastroesophageal cancer.

D. Penile Cancer

Authorization of 12 months may be granted as a single agent for subsequent treatment of metastatic penile cancer.

E. Squamous Cell Skin Cancer

Authorization of 12 months may be granted for the treatment of squamous cell skin cancer in unresectable/inoperable/incompletely resected, locally advanced, regional, recurrent, or distant metastatic disease.

F. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 12 months may be granted for the treatment of recurrent, advanced or metastatic NSCLC.

G. Nationally Covered Uses

Authorization of 12 months may be granted for the treatment of patients enrolled in any of the studies listed in the Appendix section.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with the requested medication.
B. The requested medication is being used to treat an indication enumerated in Section II.
C. The member is receiving benefit from therapy. Benefit is defined as:
   i. No evidence of unacceptable toxicity while on the current regimen and
   ii. No evidence of disease progression while on the current regimen.

V. APPENDIX: Erbitux NCI/CTEP-Sponsored Studies Selected for Inclusion in NCI-CMS Pilot Project (Studies in Various Stages of Development)[4,5]

Study ID #	Study Title	Phase
C80405	Phase III Trial of Irinotecan/5-FU/Leucovorin or Oxaliplatin/5FU/Leucovorin with Bevacizumab, or Cetuximab, or with the combination of Bevacizumab and Cetuximab for Patients with Untreated Metastatic Adenocarcinoma of the Colon or Rectum	Phase 3
E2204	An Intergroup Randomized Phase II Study of Bevacizumab or Cetuximab in Combination with Gemcitabine and in Combination with Chemoradiation (Capecitabine and Radiation) in Patients with Completely-Resected Pancreatic Carcinoma	Randomized Phase 2
RTOG-0522	Phase III Trial of Concurrent Accelerated Radiation & Cisplatin vs Concurrent Accelerated Radiation, Cisplatin, & Cetuximab (Followed by Surgery for Selected Patients) for Stage III & IV Head & Neck Carcinomas	Phase 3

Web page with links to the protocol summaries, eligibility and site locations:
https://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id90b.pdf

VI. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Erbitux.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology

3. NCCN Guideline: Penile cancer
4. NCCN Guideline: Squamous cell skin cancer
5. NCCN Guideline: Colon cancer
6. NCCN Guideline: Head and neck cancers
7. NCCN Guideline: Rectal cancer
8. National Coverage Determination (NCD) for Anti-cancer Chemotherapy for Colorectal Cancer (110.17)
9. NCI/CTEP-Sponsored Studies Selected for Inclusion in NCI-CMS Pilot Project

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Erbitux are covered in addition to the following:

1. Colorectal cancer
2. Head and neck cancer
3. Gastric and gastroesophageal cancer
4. Non-small cell lung cancer
5. Penile cancer
6. Squamous cell skin cancer

VII. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Erbitux to treat colorectal cancer, squamous cell carcinoma of the head and neck, occult primary head and neck cancer, non-small cell lung cancer, penile cancer, and squamous cell skin cancer can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Erbitux to treat gastric cancer can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Use of Erbitux in an NCI/CTE-sponsored study is covered according to the conditions outlined in National Coverage Determination Manual section 110.17 Anti-Cancer Chemotherapy for Colorectal Cancer.

VIII.REFERENCES

1. Erbitux [package insert]. Branchburg, NJ: ImClone LLC; September 2021.
2. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 12, 2022.
3. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. www.micromedexsolutions.com. Accessed July 14, 2022.
4. National Coverage Determination (NCD) for Anti-cancer Chemotherapy for Colorectal Cancer (110.17). Version 1. https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=291&ncdver=1&kc=dc634fd6-c&bc=AAAAAAgAAAAAAA%3d%3d&. Accessed July 13, 2022.

5. NCI/CTEP-Sponsored Studies Selected for Inclusion in NCI-CMS Pilot Project. https://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id90b.pdf. Accessed July 13, 2022.