Clinical Policy: Cetuximab (Erbitux)

Reference Number: CP.PHAR.317
Effective Date: 02.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Cetuximab (Erbitux®) is an epidermal growth factor receptor (EGFR) antagonist.

FDA Approved Indication(s)
Erbitux is indicated for treatment of:

- Head and neck cancer
  - Locally or regionally advanced squamous cell carcinoma of the head and neck in combination with radiation therapy
  - Recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck in combination with platinum-based therapy with fluorouracil (5-FU)
  - Recurrent or metastatic squamous cell carcinoma of the head and neck progressing after platinum-based therapy
- Colorectal cancer
  - *K-Ras* wild-type, EGFR-expressing, metastatic colorectal cancer as determined by FDA-approved tests
    - In combination with FOLFIRI for first-line treatment
    - In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy
    - As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan

Limitation(s) of use: Erbitux is not indicated for treatment of *Ras*-mutant colorectal cancer.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Erbitux is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Head and Neck Squamous Cell Carcinoma (must meet all)**:**

1. Diagnosis of head and neck squamous cell carcinoma (HNSCC) (*see Appendix B for subtypes by location*);
2. Meets a or b:

a. FDA-approved use (i, ii, or iii):
   i. Locally or regionally advanced disease (stage III/IV) in combination with radiation therapy;
   ii. Recurrent locoregional or metastatic disease in combination with platinum-based therapy with 5-FU;
   iii. Recurrent or metastatic disease progressing after platinum-based therapy;
b. Off-label NCCN recommended use:
   i. For recurrent/persistent, unresectable or metastatic disease (a or b):
      a) In combination with carboplatin;
      b) As a single agent or in combination with either a) cisplatin or b) fluorouracil (with cisplatin or carboplatin) for any HNSCC subtype except nasopharyngeal cancer (*see Appendix B for subtypes by location*);

3. Request meets one of the following (a or b):
   a. Dose does not exceed an initial dose of 400 mg/m^2 followed by 250 mg/m^2 weekly thereafter;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 3 months

B. Colorectal Cancer (must meet all)**:**
1. Diagnosis of colorectal cancer (CRC);
2. Disease is KRAS or NRAS wild-type (i.e., not mutated);
3. Meets a or b:
   a. FDA-approved use:
      i. Prescribed for metastatic CRC (a, b, or c):
         a) As first-line therapy in combination with FOLFIRI*;
         b) As subsequent therapy in combination with irinotecan if refractory to irinotecan-based chemotherapy;
         c) As subsequent therapy as a single agent (1 or 2):
            1) After failing oxaliplatin- and irinotecan-based chemotherapy;
            2) If intolerant to irinotecan;
   b. Off-label NCCN recommended use (i or ii):
      i. Prescribed for unresectable, metastatic or inoperable CRC (a, b, or c):
         a) As primary therapy;
         b) As subsequent therapy (1, 2, or 3):
            1) If not previously treated with cetuximab or panitumumab;
            2) Following primary treatment with chemoradiation or local therapy;
            3) For unresectable metastatic disease;
      ii. Prescribed for rectal cancer in combination with FOLFOX* or FOLFIRI*:
         a) As primary therapy for disease characterized as (1, 2, 3, or 4):
            1) T3, N0, M0 (stage IIA)†;
            2) Any T, N1-2, M0 (stage III)†;
            3) T4 (stage IIB-C, stage IIIB-C, stage IV)†;
            4) Locally unresectable or inoperable disease with no metastases if resection is contraindicated following neoadjuvant** therapy;

4. Request meets one of the following (a or b):
   a. Dose does not exceed an initial dose of 400 mg/m^2 followed by 250 mg/m^2 weekly thereafter;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**FOLFIRI (fluorouracil, leucovorin, irinotecan); FOLFOX (fluorouracil, leucovorin, oxaliplatin).*
***Adjuvant therapy (therapy administered after the main treatment to help decrease the risk of cancer recurring); neoadjuvant therapy (therapy given as a first step to shrink a tumor before the main therapy).*
†T (primary tumor characteristics); N (regional lymph nodes); M (metastatic disease).

Approval duration: 6 months

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of metastatic non-small cell lung cancer;
2. Member has tumor with a sensitizing EGFR mutation and is T790M negative;
3. Disease progression on EGFR tyrosine kinase inhibitor therapy;
4. Presence of multiple symptomatic systemic lesions;
5. Erbitux will be used in combination with afatinib as subsequent therapy;
6. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Penile Cancer (off-label) (must meet all)**:**
1. Diagnosis of metastatic penile cancer;
2. Erbitux will be used as a single agent as subsequent-line therapy;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

E. Squamous Cell Skin Cancer (off-label) (must meet all)**:**
1. Diagnosis of non-melanoma, squamous cell skin cancer;
2. Member has regional recurrence or distance metastases;
3. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

F. Other diagnoses/indications
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
3. If request is for a dose increase, request meets one of the following (a or b):
   a. For HNSCC or CRC: New dose does not exceed 250 mg/m^2 weekly;
   b. For any indication: New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

5-FU: fluorouracil
CRC: colorectal cancer
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
FOLFIRI: fluorouracil, leucovorin, irinotecan
FOLFOX: fluorouracil, leucovorin, oxaliplatin
HER: human epidermal growth factor receptor
HNSCC: head and neck squamous cell carcinoma
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
NRAS: neuroblastoma RAS viral oncogene homologue

*Appendix B: Head and Neck Squamous Cell Cancers by Location**

- Paranasal sinuses (ethmoid, maxillary)
- Larynx (glottis, supraglottis)
- Pharynx (nasopharynx, oropharynx, hypopharynx)
- Lip and oral cavity
- Major salivary glands (parotid, submandibular, sublingual)
- Occult primary

**Squamous cell carcinoma, or a variant, is the histologic type in more than 90% of head and neck cancers.*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

HNSCC, CRC	Administer 400 mg/m^2 initial dose as a 120-minute intravenous infusion followed by 250 mg/m^2 weekly infused over 60 minutes.	See dosing regimen

VI. Product Availability

Single-use vials: 100 mg/50 mL, 200 mg/ 100 mL

VII. References

1. Erbitux prescribing information. Indianapolis, IN: Eli Lilly and Company; October 2016. Available at http://uspl.lilly.com/erbitux/erbitux.html. Accessed August 30, 2017.
2. Cetuximab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed August 30, 2017.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9055	Injection, cetuximab, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182 Excellus Oncology. NCCN off-label recommended uses added. HNSCC subtypes by location outlined at Appendix B. CRC: EGFR testing is removed from the FDA labeled criteria. NRAS wild type (i.e., not mutated) is added to KRAS wild type. Some NCCN colon cancer off-label recommendations are collapsed and combined into a colorectal section with some rectal cancer indications.	01/17	02/17
Policy converted to new template. Annual Review. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Criteria with NCCN 2B rating recommendations removed. Added criteria for NCCN 2A or above off-label indications for NSCLC, penile cancer, and squamous cell skin cancer. Authorization limits extended from 3 and 6 months to 6 and 12 months for initial and continued approval, respectively.	08.30.17	11.17

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.