Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2021**
Policy Number: PA.CP.PHAR.317	**Effective Date: 01/2018** **Revision Date: 10/2021**
Policy Name: Cetuximab (Erbitux)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

4Q 2021 annual review: for CRC simplified requirements for prior and combination therapy; updated place in therapy for penile and squamous cell skin cancer per NCCN Compendium; for brand name requests added requirement for trial of generic equivalent if available; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Cetuximab (Erbitux)

Reference Number: PA.CP.PHAR.317
Effective Date: 01/18
Last Review Date: 10/2021

Coding Implications
Revision Log

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 (HNSCC)
  - 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 (CRC)
  - *K-Ras* wild-type, EGFR-expressing, metastatic CRC as determined by an FDA-approved test
    - 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 CRC or when the results of the *Ras* mutation tests are unknown.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness ® 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 HNSCC (*see Appendix D for subtypes by location*);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is advanced, recurrent, or metastatic;
5. Prescribed as one of the following (a or b)
   a. As a single agent;
   b. In combination with platinum-based therapy (e.g., cisplatin or carboplatin) with 5-FU;*
   **Prior authorization may be required for platinum-based therapies and 5-FU.*
6. For brand Erbitux requests, member must use generic cetuximab, if available, unless contraindicated or clinically significant adverse effects are experienced;

7. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed an initial dose of 400 mg/m^2 followed by 250 mg/m^2 weekly thereafter;
   b. Dose does not exceed 500 mg/m^2 every 2 weeks;
   c. 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

B. Colorectal Cancer (must meet all):
1. Diagnosis of colorectal cancer (CRC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is one of the following (a or b)
   a. Wild-type *RAS* (defined as wild-type in both *KRAS* and *NRAS*);
   b. BRAF wild-type;
5. One of the following (a or b):*
   a. Request for use as a single agent or in combination with FOLFIRI, FOLFOX, or irinotecan in the initial or subsequent line setting;
   b. Prescribed in combination with Braftovi® if BRAF V600E mutation positive (off-label);

   **Prior authorization may be required*
6. For brand Erbitux requests, member must use generic cetuximab, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed an initial dose of 400 mg/m^2 followed by 250 mg/m^2 weekly thereafter;
   b. Dose does not exceed 500 mg/m^2 every 2 weeks;
   c. 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

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of metastatic non-small cell lung cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Tumor is positive for a sensitizing EGFR mutation and T790M negative;
5. Disease has progressed on or after an EGFR tyrosine kinase inhibitor (TKI) therapy (e.g., Tarceva®, Gilotrif®, or Iressa®);

   **Prior authorization may be required for EGFR TKI therapies*
6. Prescribed in combination with Gilotrif as subsequent therapy;

   **Prior authorization is may be required for Gilotrif*
7. For brand Erbitux requests, member must use generic cetuximab, if available, unless contraindicated or clinically significant adverse effects are experienced;

8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Penile Cancer (off-label) (must meet all)**:**
1. Diagnosis of metastatic penile cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for use as a single agent as subsequent-line systemic therapy;
5. For brand Erbitux requests, member must use generic cetuximab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

E. Squamous Cell Skin Cancer (off-label) (must meet all)**:**
1. Diagnosis of basal cell carcinoma (non-melanoma), squamous cell skin cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is locally advanced, high-risk, very high-risk, inoperable or not fully resectable;
5. For brand Erbitux requests, member must use generic cetuximab, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

F. Other diagnoses/indications: Refer to PA.CP.PMN.53.

II. Continued Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is responding positively to therapy;
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 or 500 mg/m^2 every 2 weeks;
   b. 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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*); or
2. Refer to PA.CP.PMN.53

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 policies – PA.CP.PMN.53

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
FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin, irinotecan
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: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Modified FOLFOX 6	**CRC** Day 1: oxaliplatin 85 mg/m^2 IV Day 1: Folinic acid 400 mg/m^2 IV Days 1–3: 5-FU 400 mg/m^2 IV bolus on day 1, then 1,200 mg/m^2/day × 2 days (total 2,400 mg/m^2 over 46–48 hours) IV continuous infusion Repeat cycle every 2 weeks.	See dosing regimen
CapeOX	**CRC** Day 1: Oxaliplatin 130 mg/m^2 IV Days 1–14: Capecitabine 1,000 mg/m^2 PO BID Repeat cycle every 3 weeks.	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
FOLFIRI	**CRC** Day 1: Irinotecan 180 mg/m^2 IV Day 1: Leucovorin 400 mg/m^2 IV Day 1: Flurouracil 400 mg/m^2 IV followed by 2,400 mg/m^2 continuous IV over 46 hours Repeat cycle every 14 days.	See dosing regimen
FOLFOXIRI	**CRC** Day 1: Irinotecan 165 mg/m^2 IV, oxaliplatin 85 mg/m^2 IV, leucovorin 400 mg/m^2 IV, flurouracil 1,600 mg/m^2 continuous IV for 2 days (total 3,200 mg/m^2) Repeat cycle every 2 weeks.	See dosing regimen
Gilotrif (afatinib)	**Metastatic NSCLC** 40 mg PO QD	40 mg/day; 50 mg/day when on chronic concomitant therapy with a P-gp inducer
Iressa (gefitinib)	**Metastatic NSCLC** 250 mg PO QD	250 mg/day; 500 mg/day when used with a strong CYP3A4 inducer
Tarceva (erlotinib)	**Metastatic NSCLC** 150 mg PO QD	150 mg/day; 450 mg/day when used with a strong CYP3A4 inducer or 300 mg/day when used with a moderate CYP1A2 inducer
TIP (paclitaxel, ifosfamide, cisplatin)	**Penile Cancer** Paclitaxel 175 mg/m^2 IV on day 1; ifosfamide 1,200 mg/m^2 IV on day 1-3; cisplatin 25 mg/m^2 IV on day 1-3 Repeat every 3 to 4 weeks.	See dosing regimen
5-FU, cisplatin, carboplatin	**HNSCC** cisplatin 100 mg/m2 IV or carboplatin AUC 5 IV on day 1, plus 5-FU 1,000 mg/m^2 IV on days 1, 2, 3, and 4, repeated every 3 weeks **Penile Cancer** 5-FU 800 - 1,000 mg/m^2/day continuous IV on days 1-4 or 2-5; cisplatin 70-80 mg/m^2 IV on day 1 Repeat every 3 to 4 weeks.	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Braftovi (encorafenib)	**CRC** 300 mg PO once daily in combination with cetuximab (400 mg/m^2 IV over 120 minutes on day 1 followed by weekly infusions of cetuximab 250 mg/m^2 IV over 60 minutes) until disease progression or unacceptable toxicity.	450 mg/day.

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): infusions reactions, cardiopulmonary arrest

*Appendix D: 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	Weekly schedule: initial dose 400 mg/m^2 IV followed by 250 mg/m^2 IV weekly Biweekly schedule: initial and subsequent doses 500 mg/m^2 IV every 2 weeks	See dosing regimen

VI. Product Availability

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

VII. References

1. Erbitux Prescribing Information. Indianapolis, IN: Eli Lilly and Company; April 2021. Available at: http://uspl.lilly.com/erbitux/erbitux.html. Accessed July 20, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 20, 2021.
3. National Comprehensive Cancer Network. Colon Cancer Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed July 20, 2021.

4. National Comprehensive Cancer Network. Rectal Cancer Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed July 20, 2021.
5. National Comprehensive Cancer Network. Head and Neck Cancer Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed July 20, 2021.
6. National Comprehensive Cancer Network. Penile Cancer 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf. Accessed July 20, 2021.
7. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed July 20, 2021.
8. National Comprehensive Cancer Network. Squamous Cell Skin Cancer 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed July 20, 2021.
9. Cosyntropin Drug Monograph. Clinical Pharmacology. Tampa, FL: Gold Standard Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com. Accessed July 20, 2021.

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	Approval Date
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; references reviewed and updated	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
4Q 2020 annual review: added criteria to HNSCC indication for use as single agent or in combination with platinum based therapy with 5-FU; added BRAF disease wild-type and for treatment in combination with Braftovi if BRAF V600E mutation position to colorectal indication as per NCCN 2A or above off label indication; references reviewed and updated.	10/2020	
4Q 2021 annual review: for CRC simplified requirements for prior and combination therapy; updated place in therapy for penile and squamous cell skin cancer per NCCN Compendium; for brand name requests added requirement for trial of generic equivalent if available; references reviewed and updated.	10/2021	