RXADVANCE
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Clinical Policy Title:	cetuximab
Policy Number:	RxA.266
Drug(s) Applied:	Erbitux®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cetuximab (Erbitux®)	HNSCC, CRC	Initial dose: 400 mg/m^2 IV followed by 250 mg/m^2 IV weekly	See dosing regimen

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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. 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).

   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

B. Colorectal Cancer (must meet all)**:**

1. Diagnosis of CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is KRAS or NRAS wild-type (i.e., not mutated);
5. One of the following (a, b, c, or d):
   a. Request is for first-line treatment: Prescribed in combination with FOLFOX (off-label) or FOLFIRI;
   b. Previous treatment with oxaliplatin- and irinotecan-based chemotherapy (e.g., FOLFOXIRI) or member is intolerant to irinotecan;
   c. Previous treatment with an oxaliplatin containing regimen (e.g., FOLFOX, CapeOx): Prescribed in combination with FOLFIRI, irinotecan, or irinotecan with Zelboraf® if BRAF V600E mutation positive (off-label);
   d. Previous treatment with FOLFIRI: Prescribed in combination with irinotecan, or irinotecan with Zelboraf if BRAF V600E mutation positive (off-label);
6. 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).

   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration
Commercial: 6 months
Medicaid: 6 months
HIM: 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 may be required for Gilotrif
7. 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
Commercial: 6 months
Medicaid: 6 months
HIM: 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. Member has received prior systemic chemotherapy (e.g., paclitaxel, ifosfamide, cisplatin, 5-FU);
5. 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
Commercial: 6 months
Medicaid: 6 months
HIM: 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. Member has regional recurrence or distant metastases;
5. 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
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Erbitux for a covered indication and has received this medication for at least 30 days;
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;
   b. New dose 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
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

III. Appendices

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
FOLFIRI	**CRC** Day 1: Irinotecan 180 mg/m^2 IV Day 1: Leucovorin 400 mg/m^2 IV	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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.	
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 once daily	40 mg/day; 50 mg/day when on chronic concomitant therapy with a P-gp inducer
Iressa (gefitinib)	**Metastatic NSCLC** 250 mg PO once daily	250 mg/day; 500 mg/day when used with a strong CYP3A4 inducer
Tarceva (erlotinib)	**Metastatic NSCLC** 150 mg PO once daily	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	**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

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.

References

1. Erbitux Prescribing Information. Indianapolis, IN: Eli Lilly and Company; April 2019. Available at: http://uspl.lilly.com/erbitux/erbitux.html. Accessed August 25, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 25, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Reference reviewed and updated	08/25/2020	09/14/2020