



CLINICAL MEDICAL POLICY	
Policy Name:	Erbix (cetuximab)
Policy Number:	MP-034-MD-PA
Responsible Department(s):	Medical Management; Clinical Pharmacy
Provider Notice Date:	08/15/2017
Original Effective Date:	09/15/2017
Annual Approval Date:	07/15/2018
Revision Date:	N/A
Products:	Gateway Health SM Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 8

DISCLAIMER

Gateway HealthSM (Gateway) medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway HealthSM provides coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary intravenous infusions of Erbitux (cetuximab).

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

DEFINITIONS

Erbix (cetuximab) – A type of drug, called an EGFR inhibitor, used to treat cancer by blocking the activity of EGFR. Blocking EGFR may keep cancer cells from growing.

EGFR (Epidermal Growth Factor Receptor) – Spans the cell membrane so that one end of the protein remains inside the cell and the other end projects from the outer surface of the cell. This positioning allows the receptor to attach (bind) to other proteins, called ligands, outside the cell and to receive signals that help the cell respond to its environment. EGFR is found on both normal and tumor cells and is important for cell growth.

KRAS (wild-type) Gene – The KRAS gene provides instructions for making a protein called K-Ras that is involved primarily in regulating cell division. The KRAS gene belongs to a class of genes known as oncogenes. KRAS wild-type gene means the gene is normal or lacking mutations. When mutated, oncogenes have the potential to cause normal cells to become cancerous.

Squamous Cell – An epithelial cell. These cells make up the epidermis of the skin.

Squamous Cell Carcinoma of the Head and Neck (SCCHN) – A cancer that arises from particular cells called squamous cells. SCCHN develops in the mucous membranes of the mouth, nose, and throat.

PROCEDURES

1. Erbitux is considered medically necessary as an intravenous infusion when the member meets the following criteria:
 - A. Metastatic colorectal cancer (KRAS wild-type, EGFR-expressing)
 - 1) The member is at least 18 years of age; AND
 - 2) The prescribing physician is a Hematologist or Oncologist; AND
 - 3) The drug will not be used in combination with anti-VEGF agents (e.g. bevacizumab); AND
 - 4) The member was tested for and confirmed to not have KRAS or NRAS mutations (i.e. KRAS and NRAS wild-type gene only); AND
 - 5) The drug will be used as monotherapy when the member has failed irinotecan- and oxaliplatin-based chemotherapy or has intolerance to irinotecan; OR
 - 6) The drug will be used in combination with irinotecan when the member was refractory to irinotecan-based chemotherapy; AND
 - 7) Dosing is consistent with FDA-approved labeling:
 - a. Initial dose of 400 mg/m² IV one time
 - b. Maintenance dose of 250 mg/m² IV once weekly
 - B. Squamous cell carcinoma of the head and neck (SCCHN)
 - 1) The member is at least 18 years of age; AND
 - 2) The prescribing physician is a hematologist or oncologist; AND
 - 3) The drug will not be used in combination with anti-VEGF agents (e.g., bevacizumab); AND
 - 4) The drug will be used first-line in combination with platinum-based therapy with 5-fluorouracil AND disease is metastatic or recurrent; OR
 - 5) The drug will be used as monotherapy after disease progression with a platinum-based therapy AND The disease is metastatic or recurrent; OR
 - 6) The drug will be used in combination with radiation therapy for the initial treatment of locally or regionally advanced disease, AND the total treatment duration does not exceed 7 weeks; AND

- 7) Dosing is consistent with FDA-approved labeling:
- a) Initial dose of 400 mg/m² IV one time
 - b) Maintenance dose of 250 mg/m² IV once weekly

2. Contraindications

Serious infusion reactions may occur, and there have been fatal outcomes reported. If serious infusion reactions occur, immediately stop and permanently discontinue Erbitux.

3. When Erbitux services are not covered

Erbitux is not covered for conditions other than those listed above because the scientific evidence has not yet been established.

Coverage may be provided for any non-FDA labeled indication or a medically accepted indication that is supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis for which it is prescribed and will be reviewed on a case-by-case basis to determine medical necessity.

- It should be noted that some compendia identify Gastric Cancer as an off-label use, but at the time of this review, the NCCN 2.2016 Gastric Cancer guidelines do not have recommendations for cetuximab for gastric indications.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Post-payment Audit Statement

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway HealthSM at any time pursuant to the terms of your provider agreement.

5. Place of Service

The place of service for the administration of Erbitux is outpatient.

GOVERNING BODIES APPROVAL

On February 12, 2004, the FDA initially approved cetuximab (Erbitux) to treat patients with advanced colorectal cancer that has spread to other parts of the body. Drug is indicated to be used in combination with irinotecan. Erbitux is the first monoclonal antibody approved to treat colorectal cancer.

On August 20, 2005, the FDA approved cetuximab (Erbitux) to treat patients with squamous cell carcinoma of the head and neck (SCCHN). Drug is indicated to be used in combination with radiation therapy for locally or regionally advanced SCCHN.

On June 11, 2007, the FDA approved cetuximab (Erbitux) to treat patients with advanced colorectal cancer

On November 7, 2011, the FDA approved cetuximab (Erbitux) to treat patients with late stage (metastatic) head and neck cancer. Erbitux can be used in combination with chemotherapy

CODING REQUIREMENTS

Procedure Codes

CPT/HCPCS Code	Description
J9055	Injection, cetuximab, 10 mg (Erbix [®])
81275	KRAS gene analysis; variants in exon 2
88363	Examination and selection of retrieved archival (i.e., previously diagnosed) tissue(s) for molecular analysis (e.g., KRAS mutational analysis)

Diagnosis Codes

ICD-10 Codes	Description
Colorectal	
C17.0	Malignant neoplasm of duodenum
C17.1	Malignant neoplasm of jejunum
C17.2	Malignant neoplasm of ileum
C17.8	Malignant neoplasm of overlapping sites of small intestines
C17.9	Malignant neoplasm of small intestines, unspecified
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.8	Malignant neoplasm of overlapping sites of colon
C18.9	Malignant neoplasm of colon, unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and canal
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
C21.8	Malignant neoplasm of overlapping sites of the rectum, anus, and anus canal
C21.0	Malignant neoplasm of anus, unspecified
C21.1	Malignant neoplasm of anal canal
C21.2	Malignant neoplasm of cloacogenic zone
D01.0	Carcinoma in situ of colon
D01.1	Carcinoma in situ of rectosigmoid junction
D01.2	Carcinoma in situ of rectum
D01.3	Carcinoma in situ of anus and anal canal
D01.40	Carcinoma in situ of unspecified part of intestine
D01.49	Carcinoma in situ of other parts of intestine
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus
Squamous Cell Carcinoma Head & Neck	
C00.0	Malignant neoplasm of external upper lip

C00.1	Malignant neoplasm of external lower lip
C00.2	Malignant neoplasm of external lip, unspecified
C00.3	Malignant neoplasm of upper lip, inner aspect
C00.4	Malignant neoplasm of lower lip, inner aspect
C00.5	Malignant neoplasm of lip, unspecified, inner aspect
C00.6	Malignant neoplasm of commissure of lip, unspecified
C00.8	Malignant neoplasm of overlapping sites of lip
C00.9	Malignant neoplasm of lip, unspecified
C01	Malignant neoplasm of base of tongue
C02.0	Malignant neoplasm of other and unspecified parts of tongue
C02.1	Malignant neoplasm of border of tongue
C02.2	Malignant neoplasm of ventral surface of tongue
C02.3	Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4	Malignant neoplasm of lingual tonsil
C02.8	Malignant neoplasm of overlapping sites of tongue
C02.9	Malignant neoplasm of tongue, unspecified
C03.0	Malignant neoplasm of gum
C03.1	Malignant neoplasm of lower gum
C03.9	Malignant neoplasm of gum, unspecified
C04.0	Malignant neoplasm of anterior floor of mouth
C04.1	Malignant neoplasm of lateral floor of mouth
C04.8	Malignant neoplasm of overlapping sites of floor of mouth
C04.9	Malignant neoplasm of floor of mouth, unspecified
C05.0	Malignant neoplasm of hard palate
C05.1	Malignant neoplasm of soft palate
C06.0	Malignant neoplasm of cheek mucosa
C06.2	Malignant neoplasm of retromolar area
C06.80	Malignant neoplasm of overlapping sites of unspecified parts of mouth
C06.89	Malignant neoplasm of overlapping sites of other parts of mouth
C06.9	Malignant neoplasm of mouth, unspecified
C09.0	Malignant neoplasm of tonsillar fossa
C09.1	Malignant neoplasm of tonsillar pillar (anterior)(posterior)
C09.8	Malignant neoplasm of overlapping sites of oropharynx
C09.9	Malignant neoplasm of tonsil, unspecified
C10.3	Malignant neoplasm of posterior wall of oropharynx
C11.0	Malignant neoplasm of superior wall of nasopharynx
C11.1	Malignant neoplasm of posterior wall of nasopharynx
C11.2	Malignant neoplasm of lateral wall of nasopharynx
C11.3	Malignant neoplasm of anterior wall of nasopharynx
C11.8	Malignant neoplasm of overlapping sites of nasopharynx
C11.9	Malignant neoplasm of nasopharynx, unspecified
C12	Malignant neoplasm of pyriform sinus
C13.0	Malignant neoplasm of postcricoid region
C13.1	Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
C13.2	Malignant neoplasm of posterior wall of hypopharynx

C13.8	Malignant neoplasm of overlapping sites of hypopharynx
C13.9	Malignant neoplasm of hypopharynx, unspecified
C14.0	Malignant neoplasm of pharynx, unspecified
C14.2	Malignant neoplasm of Waldeyer's ring
C14.8	Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
C30.0	Malignant neoplasm of nasal cavity
C30.1	Malignant neoplasm of middle ear
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C31.2	Malignant neoplasm of frontal sinus
C31.3	Malignant neoplasm of sphenoid sinus
C31.8	Malignant neoplasm of overlapping sites of accessory sinuses
C31.9	Malignant neoplasm of accessory sinus, unspecified
C30.1	Malignant neoplasm of middle ear
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
C32	Malignant neoplasm of larynx
C32.0	Malignant neoplasm of glottis
C32.1	Malignant neoplasm of supraglottis
C32.2	Malignant neoplasm of subglottis
C32.3	Malignant neoplasm of laryngeal cartilage
C32.8	Malignant neoplasm of overlapping sites of larynx
C32.9	Malignant neoplasm of larynx, unspecified
C44.02	Squamous cell carcinoma of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.12	Squamous cell carcinoma of skin of eyelid, including canthus
C44.121	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.122	Squamous cell carcinoma of skin of right eyelid, including canthus
C44.129	Squamous cell carcinoma of skin of left eyelid, including canthus
C44.32	Squamous cell carcinoma of skin of other and unspecified parts of face
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.42	Squamous cell carcinoma of skin of scalp and neck
C76.0	Malignant neoplasm of head, face and neck [squamous cell]
C44.42	Squamous cell carcinoma of skin of scalp or neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face, and neck
D00.0	Carcinoma in situ of lip, oral cavity, and pharynx
D00.00	Carcinoma in situ of oral cavity, unspecified site
D00.01	Carcinoma in situ of labial mucosa and vermilion border
D00.02	Carcinoma in situ of buccal mucosa
D00.03	Carcinoma in situ of gingiva and edentulous alveolar ridge
D00.04	Carcinoma in situ of soft palate
D00.05	Carcinoma in situ of hard palate

D00.06	Carcinoma in situ of floor of mouth
D00.07	Carcinoma in situ of tongue
D00.08	Carcinoma in situ of pharynx
D02.0	Carcinoma in situ of larynx
Z85.810	Personal history of malignant neoplasm of the tongue
Z85.818	Personal history of malignant neoplasm of other sites of lip, oral cavity, and pharynx
Z85.819	Personal history of malignant neoplasm of unspecified site of lip, oral cavity, and pharynx
Z85.21	Personal history of malignant neoplasm of larynx
Z85.22	Personal history of malignant neoplasm of nasal cavities, middle ear, and accessory sinuses

REIMBURSEMENT

Participating facilities will be reimbursed per their Gateway HealthSM contract.

POLICY SOURCE(S)

Alberts SR, Sargent DJ, Nair S, et al. Effect of oxaliplatin, fluorouracil and leukovorin with or without cetuximab on survival among patients with resected stage III colon cancer: A randomized trial. JAMA 2012; 307:1383-1393. <http://www.ncbi.nlm.nih.gov/pubmed/22474202>.

Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for locoregionally advanced head and neck cancer: 5-year survival data from a phase 3 randomised trial, and relation between cetuximab-induced rash and survival. Lancet Oncol 2010; 11:21-28. <http://www.ncbi.nlm.nih.gov/pubmed/19897418>.

Erbix[®] (cetuximab) [package insert]. Indianapolis, Indiana: Lilly USA, LLC 2016. Accessed on January 4, 2017 and available at <http://erbitux.com/healthcare-professionals/index.html>.

Bouchahda M, Macarulla G, Lledo F, et al. Efficacy and safety of cetuximab (C) given with a simplified, every other week (q2w), schedule in patients (pts) with advanced colorectal cancer (aCRC): a multicenter, retrospective study. J Clin Oncol.

Cetuximab. In McEvoy GK, editor. AHFS drug information 2015 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2015 [cited 2015 June 18].

Cetuximab. In: Micromedex 2.0 online. Ann Arbor (MI): Truven Health Analytics; [2016; accessed December 13, 2016].

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version.2.2016. Head and Neck Cancers. Accessed on January 4, 2017 and available at: http://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf.

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version.1.2017. Colon Cancer. Accessed on January 4, 2017.

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 1.2015. Squamous Cell Skin Cancer. Available at: http://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed on December 28, 2016.

Venook AP, Niedzwiecki D, Lenz HJ, et al. CALGB/SWOG: Phase III trial of irinotecan/5-FU/leukovorin (FOLFIRI) or oxaliplatin/5-FU/leukovorin (FOLFOX) with bevacizumab or cetuximab for patients with KRAS wild-type untreated metastatic adenocarcinoma of the colon or rectum. ASCO Meeting Abstracts 2014: 32:LBA3. <http://meetinglibrary.asco.org/content/126013-144>.

Policy History

Date	Activity
06/30/2017	Initial policy developed
07/19/2017	QI/UM Committee approval
09/15/2017	Provider effective date