Medical Policy:

Erbitux® (cetuximab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.79	April 10, 2025	

Length of Authorization

Coverage will be provided for six months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

CRC, Head and Neck, Squamous Cell Skin, Penile: Weekly	NSCLC- Every two weeks
– Load: 100 billable units x 1 dose – Maintenance Dose: 60 billable units every 7 days	120 billable units every 14 days

Guideline

I. Initial Approval Criteria

Coverage is provided in the following conditions:

1. Patient is 18 years or older; **AND**

1. Colorectal Cancer (CRC) †

A. Patient meets ONE of the following (i, ii, **OR** iii):

i. Patient has advanced or metastatic disease and meets ONE of the following (a, b, c, **OR** d):

a. Patient meets ALL of the following [(1), (2), (3), **AND** (4)]:

1) Tumor or metastases are *KRAS*, *NRAS*, and *BRAF* wild-type; **AND**
Note: The tumor or metastases are KRAS/NRAS/BRAF mutation negative.

2) The primary tumor originated on the left side of the colon; **AND**
Note: Primary tumor originated from the splenic flexure to the rectum.

3) Medication is used for initial treatment; **AND**

4) Medication is used as a single agent or in combination with FOLFOX, CapeOX, or FOLFIRI; **OR**
Note: FOLFOX includes 5-fluorouracil; leucovorin, and oxaliplatin; CapeOX included capecitabine and oxaliplatin; and FOLFIRI includes 5-fluorouracil, leucovorin, and irinotecan.

b. Patient meets ALL of the following [(1), (2), **AND** (3):

1) Tumor or metastases are *KRAS/NRAS/BRAF* wild-type; **AND**
Note: The tumor or metastases are KRAS, NRAS, and BRAF mutation negative.

2) Medication is used for subsequent treatment; **AND**

3) Medication is used as a single agent or in combination with irinotecan, FOLFOX, CapeOX, or FOLFIRI; **OR**
Note: FOLFOX includes 5-fluorouracil; leucovorin, and oxaliplatin; CapeOX included capecitabine and oxaliplatin; and FOLFIRI includes 5-fluorouracil, leucovorin, and irinotecan.

c. Patient meets BOTH of the following [(1) **AND** (2)]:

1) Tumor or metastases are *BRAF V600E* mutation-positive; **AND**

2) Medication is used in combination with Braftovi (encorafenib capsules); **OR**

d. Patient meets ALL of the following [(1), (2), **AND** (3)]:

1) Tumor or metastases are *KRAS G12C* mutation positive; **AND**

2) Medication is used for subsequent therapy; **AND**
Note: This is subsequent therapy following the initial diagnosis of colon or rectal cancer.

3) Medication is used in combination with Lumakras (sotorasib tablets) or Krazati (adagrasib tablets); **OR**

ii. Patient has unresectable synchronous liver and/or lung metastases and meets ALL of the following [(1), (2), (3), **AND** (4)]:
Note: Synchronous metastases are metastases that are diagnosed at the same time as or within a few months of the initial diagnosis of colon or rectal cancer.

1) Metastases are *KRAS/NRAS/BRAF* wild-type; **AND**
Note: The metastases are KRAS, NRAS, and BRAF mutation negative.

2) The primary tumor originated on the left side of the colon; **AND**
Note: Primary tumor originated from the splenic flexure to the rectum.

3) Medication is used for primary treatment; **AND**

4) Medication is used in combination with FOLFOX or FOLFIRI; **OR**
Note: FOLFOX includes 5-fluorouracil, leucovorin, and oxaliplatin and FOLFIRI includes fluorouracil, leucovorin, and irinotecan.

iii. Patient has unresectable metachronous metastases and meets ONE of the following (a, b, **OR** c):
Note: Metachronous metastases are metastases that are diagnosed months to years after the initial diagnosis of colon or rectal cancer.

1) Patient meets ALL of the following [(1), (2), **AND** (3)]:
    i. Metastases are *KRAS*, *NRAS*, and *BRAF* wild-type; **AND**
    Note: The metastases are KRAS/NRAS/BRAF mutation negative.
    ii. Medication is used for initial treatment; **AND**
    iii. Medication is used in combination with irinotecan or FOLFIRI; **OR**
    Note: FOLFIRI includes fluorouracil, leucovorin, and irinotecan.
2) Patient meets ALL of the following [(1), (2), **AND** (3)]:
    i. Metastases are *BRAF V600E* mutation positive; **AND**
    ii. Medication is used for initial treatment; **AND**
    iii. Medication is used in combination with Braftovi; **OR**
3) Patient meets ALL of the following [(1), (2), **AND** (3)]:
    i. Metastases are *KRAS G12C* mutation positive; **AND**
    ii. Medication is used for initial treatment; **AND**
    iii. Medication is used in combination with Lumakras or Krazati

2. Squamous Cell Carcinoma of the Head and Neck (SCCHN) †

A. Patient meets **ONE** of the following (i, ii, iii, iv **OR** v):
    i. Erbitux will be used in combination with radiation therapy; **OR**
    ii. Erbitux will be used in combination with platinum-based therapy; **OR**
    Note: Examples of platinum chemotherapy include cisplatin and carboplatin.
    iii. Erbitux will be used in combination with paclitaxel or docetaxel; **OR**
    iv. Erbitux will be used in combination with Keytruda (pembrolizumab intravenous infusion) or Opdivo (nivolumab intravenous infusion); **OR**
    v. Erbitux will be used as a single agent.

3. Non-melanoma Skin Cancer (Basal Cell Skin Cancer and Squamous Cell Skin Cancer) ‡

A. Patient meets **ONE** of the following (i, ii, iii, or iv):
    i. Patient has locally advanced, high-risk, or very high-risk disease**; OR**
    ii. Patient has unresectable, inoperable, or incompletely resected regional disease; **OR**
    iii. Patient has local or regional recurrence; **OR**
    iv. Patient has distant metastases

4. Penile Cancer ‡

A. Patient must have metastatic disease; **AND**
B. Must be used for subsequent treatment; **AND**
C. Must be used as a single agent

5. Non-Small Cell Lung Cancer (NSCLC) ‡

A. Patient has recurrent, advanced, or metastatic non-small cell lung cancer; **AND**
B. Patient has a known sensitizing epidermal growth factor receptor *(EGFR)* mutation; **AND**
Note: Examples of EGFR mutations include EGFR exon 19 deletion, or exon 21 L858R, or EGFR S768I, L861Q, and/or G719X mutation positive.
C. Patient has received at least ONE tyrosine kinase inhibitor; **AND**
Note: Examples of tyrosine kinase inhibitors include erlotinib tablets, Iressa (gefitinib tablets), or Gilotrif (afatinib tablets)
D. Erbitux will be used in combination with Gilotrif (afatinib tablets)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

***May also be used for progression on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status (Note: Colon cancer patients must have left-sided tumors only).*

§ Colon cancer patients must have left-sided tumors only

II. Renewal Criteria

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet criteria identified above; **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe infusion reactions, cardiopulmonary arrest, pulmonary toxicity/interstitial lung disease, dermatologic toxicity, electrolyte abnormalities, etc.

III. Dosage/Administration

Indication	Dose
Colorectal Cancer	400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days until disease progression or unacceptable toxicity **OR** 500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity
NSCLC	500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity
Head and Neck Cancer	In combination with radiation therapy: 400 mg/m² loading dose intravenously 1 week prior to radiation therapy, then 250 mg/m² intravenously every 7 days for the duration of radiation therapy (up to 8 total weeks of therapy) Sequential systemic therapy/radiation: 400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days for up to 12 weeks of therapy Monotherapy, in combination with paclitaxel, or in combination with platinum-based therapy: 400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days until disease progression or unacceptable toxicity **OR** 500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity In combination with nivolumab: 500 mg/m² intravenously every 14 days until disease progression or unacceptable toxicity In combination with pembrolizumab: 400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days

	until disease progression or unacceptable toxicity
Squamous Cell Skin Cancer & Penile Cancer	400 mg/m² loading dose intravenously, then 250 mg/m² intravenously every 7 days until disease progression or unacceptable toxicity

Limitations/Exclusions

Erbitux® (cetuximab) is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

Applicable Procedure Codes

Code	Description
J9055	Injection, cetuximab, 10 mg

Applicable NDCs

Code	Description
66733-0948-xx	Erbitux 100 mg/50 mL single-use vial; solution for injection
66733-0958-xx	Erbitux 200 mg/100 mL single-use vial; solution for injection

ICD-10 Diagnoses

Code	Description
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 dorsal surface 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 upper 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
C05.8	Malignant neoplasm of overlapping sites of palate
C05.9	Malignant neoplasm of palate, unspecified
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 tonsil
C09.9	Malignant neoplasm of tonsil, unspecified
C10.0	Malignant neoplasm of vallecula
C10.1	Malignant neoplasm of anterior surface of epiglottis
C10.2	Malignant neoplasm of lateral wall of oropharynx
C10.3	Malignant neoplasm of posterior wall of oropharynx
C10.4	Malignant neoplasm of branchial cleft
C10.8	Malignant neoplasm of overlapping sites of oropharynx
C10.9	Malignant neoplasm of oropharynx, unspecified
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 foid, 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
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of large intestines
C18.9	Malignant neoplasm of colon, unspecified

C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21.8	Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C30.0	Malignant neoplasm of nasal cavity
C31.0	Malignant neoplasm of maxillary sinus
C31.1	Malignant neoplasm of ethmoidal sinus
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
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C44.00	Unspecified malignant neoplasm of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C44.1221	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.1222	Squamous cell carcinoma of skin of right eyelid, including canthus
C44.1292	Squamous cell carcinoma of skin of left eyelid, including canthus
C44.221	Squamous cell carcinoma of skin of unspecified ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
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
C44.520	Squamous cell carcinoma of anal skin
C44.521	Squamous cell carcinoma of skin of breast
C44.529	Squamous cell carcinoma of skin of other part of trunk
C44.621	Squamous cell carcinoma of skin of unspecified upper limb, including shoulder

C44.622	Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.629	Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.721	Squamous cell carcinoma of skin of unspecified lower limb, including hip
C44.722	Squamous cell carcinoma of skin of right lower limb, including hip
C44.729	Squamous cell carcinoma of skin of left lower limb, including hip
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.92	Squamous cell carcinoma of skin, unspecified
C60.0	Malignant neoplasm of prepuce
C60.1	Malignant neoplasm of glans penis
C60.2	Malignant neoplasm of body of penis
C60.8	Malignant neoplasm of overlapping sites of penis
C60.9	Malignant neoplasm of penis, unspecified
C63.7	Malignant neoplasm of other specified male genital organs
C63.8	Malignant neoplasm of overlapping sites of male genital organs
C76.0	Malignant neoplasm of head, face and neck
C77.0	Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
D37.01	Neoplasm of uncertain behavior of lip
D37.02	Neoplasm of uncertain behavior of tongue
D37.05	Neoplasm of uncertain behavior of pharynx
D37.09	Neoplasm of uncertain behavior of other specified sites of the oral cavity
D38.0	Neoplasm of uncertain behavior of larynx
D38.5	Neoplasm of uncertain behavior of other respiratory organs
D38.6	Neoplasm of uncertain behavior of respiratory organ, unspecified
Z85.038	Personal history of other malignant neoplasm of large intestine
Z85.118	Personal history of other malignant neoplasm of bronchus and lung

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	4/10/2025	Annual Review: Updated dosages/administration Colon and Rectal Cancer: Add new option for approval for patients with unresectable synchronous liver and/or lung metastases. Added new option for approval for patients with unresectable metachronous metastases. Removed criterion that the tumor or metastases are wild-type BRAF and criterion that the patient has previously received a chemotherapy regimen for colon or rectal cancer. Removed unresectable from criterion that the patient has advanced or metastatic disease and meets one of the following. Added BRAF to criterion that the tumor or metastases are KRAS/NRAS/BRAF mutation negative; and added medication is for initial therapy and medication is used in combination with FOLFOX, CapeOX, or FOLFIRI to condition of approval. Added condition of approval for the subsequent treatment of KRAS/NRAS/BRAF mutation negative disease. Added condition of approval for BRAF V600E mutation positive disease. Added condition of approval for KRAS G12C mutation positive disease. As a single

		agent added to the requirement that the medication is used as a single agent or in combination with FOLFOX, CapeOX, or FOLFIRI. Removed requirement that the medication is used for subsequent treatment. This is subsequent therapy following the initial diagnosis of colon or rectal cancer added as a Note. Added synchronous metastases are metastases that are diagnosed at the same time as or within a few months of the initial diagnosis of colon or rectal cancer as a Note. Added metachronous metastases are metastases that are diagnosed months to years after the initial diagnosis of colon or rectal cancer. Head and Neck Squamous Cell Carcinoma: Added new option of approval for Erbitux to be used in combination with paclitaxel or docetaxel. Added Keytruda (pembrolizumab intravenous infusion) to option of approval Erbitux will be used in combination with Keytruda (pembrolizumab intravenous infusion) or Opdivo (nivolumab intravenous infusion). Appendiceal Adenocarcinoma: Added new condition of approval. Penile Cancer: Added recurrent to requirement that the patient has recurrent or metastatic disease.
EmblemHealth & ConnectiCare	3/13/2024	Annual Review: Initial Criteria: Colorectal Cancer (CRC) † Removed and modified: "Will not be used as part of an adjuvant treatment regimen; AND Patient has not been previously treated with cetuximab or panitumumab; AND Patient must have progressive, metastatic, or unresectable advanced disease AND Used in combination with irinotecan- or oxaliplatin-based regimens‡; OR Used in combination with a vemurafenib-based regimen in patients with BRAF V600E mutations; OR Used as a single agent therapy for metastatic disease †; AND Patient has previously failed on an oxaliplatin- and irinotecan-based regimen; OR Patient is unable to tolerate irinotecan Used as primary treatment; AND Used in combination with FOLFIRI †; OR Used in combination with CapeOx or FOLFOX §; AND Used in combination with an irinotecan-based regimen after previous adjuvant FOLFOX or CapeOX within the past 12 months §; OR Used as subsequent therapy; AND Used in combination with irinotecan for irinotecan-refractory disease †; OR Used in combination with irinotecan for oxaliplatin-refractory disease §; OR Used in combination with FOLFIRI for oxaliplatin-refractory disease §**; OR Used in combination with FOLFOX for irinotecan-refractory disease §**; OR Used as a single agent for oxaliplatin- and/or irinotecan-refractory disease OR irinotecan-intolerant disease; OR Patient has BRAF V600E mutation positive disease as determined by an FDA-approved or CLIA-compliant test* †; AND Used in combination with encorafenib; AND Used as subsequent therapy for progression of advanced or metastatic disease after at least one prior line of treatment in the advanced or metastatic disease setting; ORUsed as primary treatment for unresectable metastatic disease after previous adjuvant FOLFOX or CapeOX within the past 12 months" To Read: "The primary tumor originated on the left side of the colon (from splenic flexure to rectum); AND Patient meets ONE of the following (i or ii): Patient's tumor or metastases are wild-type *BRAF* (that is, the tumor or metastases are *BRAF V600E* mutation-negative); OR Patient's tumor or metastases are *BRAF V600E* mutation-positive and the patient meets BOTH of the following (a and b): Patient has previously received a chemotherapy regimen for colon or rectal cancer; AND *Note: Examples of chemotherapy regimens include a fluoropyrimidine such as 5-fluorouracil (5-FU), capecitabine, oxaliplatin, irinotecan, or an adjunctive chemotherapy regimen such as FOLFOX (5-FU, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin).* Erbitux is prescribed in combination with Braftovi (encorafenib capsules); AND" Squamous Cell Carcinoma of the Head and Neck (SCCHN) † Modified: "Used in one of the following regimens: †" to read: "Patient meets ONE of the following (i, ii, iii, or iv):"

		Added: “Erbitux will be used in combination with Opdivo (nivolumab intravenous infusion); OR” Removed: “Patient has one of the following sub-types of SCCHN: ‡ Cancer of the Glottic Larynx, Cancer of the Hypopharynx, Cetuximab may also be used as a single agent for sequential chemoradiation ‡, Cancer of the Lip Cancer of the Oral Cavity (including mucosal lip), Cancer of the Nasopharynx, Cancer of the Oropharynx, Cetuximab may also be used as a single agent for sequential chemoradiation ‡, Cancer of the Supraglottic Larynx, Ethmoid Sinus Tumors, Maxillary Sinus Tumors, Very advanced and recurrent/persistent head and neck cancer, Cetuximab may also be used as a single agent for sequential chemoradiation ‡, Cetuximab may also be used as one of the following:– First-line or subsequent therapy as a single agent for non-nasopharyngeal cancer, – Subsequent therapy in combination with platinum-based therapy for nonnasopharyngeal cancer, – Sequential systemic therapy/radiation as a single agent in patients with non-nasopharyngeal cancer following induction or combination systemic therapy, – Subsequent therapy in combination with carboplatin for nasopharyngeal cancer, Occult Primary, Cetuximab may also be used as a single agent as sequential systemic therapy/radiation after induction chemotherapy for one of the following:– Poorly differentiated or nonkeratinizing squamous cell, anaplastic (not thyroid), squamous cell carcinoma, or not otherwise specified (NOS) histology ‡, – p16 (HPV)-positive disease” Non-melanoma Skin Cancer (Basal Cell Skin Cancer and Squamous Cell Skin Cancer) ‡Removed or modified: “For regional recurrence or distant metastases” To read: “Patient meets ONE of the following (i, ii, iii, or iv): Patient has locally advanced, high-risk, or very high-risk disease; OR Patient has unresectable, inoperable, or incompletely resected regional disease; OR Patient has local or regional recurrence; OR Patient has distant metastases” Non-Small Cell Lung Cancer (NSCLC) ‡ Removed or modified: “Patient must have metastatic disease; AND Must be used in combination with afatinib; AND Must be used as subsequent therapy for sensitizing EGFR mutation-positive tumors; AND Patient has progressed on EGFR tyrosine kinase inhibitor therapy (e.g. erlotinib, afatinib, or gefitinib, etc.); AND Patient has asymptomatic disease, symptomatic brain lesions, or isolated symptomatic systemic lesions; OR Patient has multiple symptomatic systemic lesions; AND Patient has T790M negative disease; OR Patient has T790M positive disease and progressed on osimertinib therapy” To Read: “Patient has recurrent, advanced, or metastatic non-small cell lung cancer; AND Patient has a known sensitizing epidermal growth factor receptor *(EGFR)* mutation; AND *Note: Examples of EGFR mutations include EGFR exon 19 deletion, or exon 21 L858R, or EGFR S768I, L861Q, and/or G719X mutation positive.* Patient has received at least ONE tyrosine kinase inhibitor; AND *Note: Examples of tyrosine kinase inhibitors include erlotinib tablets, Iressa (gefitinib tablets), or Gilotrif (afatinib tablets)* Erbitux will be used in combination with Gilotrif (afatinib tablets)” Updated dosage chart
EmblemHealth & ConnectiCare	7/5/2023	Annual Review: Colorectal Cancer (CRC) † Initial Criteria; Removed “Patient must have progressive, metastatic, or unresectable advanced disease; **AND** i. Used in combination with irinotecan- or oxaliplatin-based regimens**‡**; **OR** ii. Used in combination with a vemurafenib-based regimen in patients with BRAF V600E mutations; **OR** a. Used as a single agent therapy for metastatic disease **†**; **AND**

		i. Patient has previously failed on an oxaliplatin- and irinotecan-based regimen; **OR** A. Patient is unable to tolerate irinotecan" Added " Patient has metastatic, unresectable (or medically inoperable), or advanced disease that is BRAF mutation negative (wild-type); **AND** i. Used as primary treatment; **AND** a. Used in combination with FOLFIRI †; **OR** b. Used in combination with FOLFOX §; **OR** c. Used in combination with an irinotecan-based regimen after previous adjuvant FOLFOX or CapeOX within the past 12 months §; **OR** ii. Used as subsequent therapy; **AND** a. Used in combination with irinotecan for irinotecan-refractory disease †; **OR** b. Used in combination with irinotecan for oxaliplatin-refractory disease §; **OR** c. Used in combination with FOLFIRI for oxaliplatin-refractory disease §**; **OR** d. Used in combination with FOLFOX for irinotecan-refractory disease §**; **OR** e. Used as a single agent for oxaliplatin- and/or irinotecan-refractory disease **OR** irinotecan-intolerant disease; **OR** iii. Patient has BRAF V600E mutation positive disease as determined by an FDA-approved or CLIA-compliant test* †; **AND** a. Used in combination with encorafenib; **AND** 1) Used as subsequent therapy for progression of advanced or metastatic disease after at least one prior line of treatment in the advanced or metastatic disease setting; **OR** 2) Used as primary treatment for unresectable metastatic disease after previous adjuvant FOLFOX or CapeOX within the past 12 months" <u>Squamous Cell Carcinoma of the Head and Neck (SCCHN) † Initial Criteria:</u>Replaced "Cancer of the Lip" with " Cancer of the Oral Cavity (including mucosal lip)" a. Removed "Cetuximab may also be used as a single agent for sequential chemoradiation **‡"** and added " a. Cetuximab may also be used as one of the following: – First-line or subsequent therapy as a single agent for non-nasopharyngeal cancer – Subsequent therapy in combination with platinum-based therapy for nonnasopharyngeal cancer – Sequential systemic therapy/radiation as a single agent in patients with non-nasopharyngeal cancer following induction or combination systemic therapy – Subsequent therapy in combination with carboplatin for nasopharyngeal cancer 1. Occult Primary a. Cetuximab may also be used as a single agent as sequential systemic therapy/radiation after induction chemotherapy for one of the following: – Poorly differentiated or nonkeratinizing squamous cell, anaplastic (not thyroid), squamous cell

		carcinoma, or not otherwise specified (NOS) histology ‡ – p16 (HPV)-positive disease" Removed "Occult Primary Head and Neck Cancers ‡ 1. Must be used as initial treatment as a single agent with sequential chemoradiation " Non-Small Cell Lung Cancer (NSCLC) ‡ Removed "Patient is T790M negative and has multiple symptomatic systemic lesions" Added "Patient has multiple symptomatic systemic lesions; **AND** ▪ Patient has T790M negative disease; **OR** ▪ Patient has T790M positive disease and progressed on osimertinib therapy" Updated dosage chart
EmblemHealth & ConnectiCare	4/26/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	1/1/2020	Annual review

References

1. Erbitux [package insert]. Branchburg, NJ; ImClone LLC; June 2018; Accessed December 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) cetuximab. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2018.
3. 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. 2008; 26(15S): Abstract 15118. Presented at: The 44th American Society of Clinical Oncology Annual Meeting (ASCO). May 30–June 3, 2008. Chicago, Illinois.
4. Mrabti H, La Fouchardiere C, Desseigne F, Dussart S, Negrier S, Errihani H. Irinotecan associated with cetuximab given every 2 weeks versus cetuximab weekly in metastatic colorectal cancer. J Can Res Ther. 2009; 5:272-6.
5. Shitara K, Yuki S, Yoshida M, et al. Phase II study of combination chemotherapy with biweekly cetuximab and irinotecan for wild-type KRAS metastatic colorectal cancer refractory to irinotecan, oxaliplatin, and fluoropyrimidines World J Gastroenterol, 2011, April 14; 17(14): 1879-1888
6. Pfeiffer P, Bjerregarrd JK, Qvortrup C, et al, "Simplification of Cetuximab (Cet) Administration: Double Dose Every Second Week as a 60 Minute Infusion," J Clin Oncol, 2007, 25(18S):4133 [abstract 4133 from 2007 ASCO Annual Meeting Proceedings, Part I].
7. Pfeiffer P, Nielsen D, Bjerregaard J, et al, "Biweekly Cetuximab and Irinotecan as Third-Line Therapy in Patients with Advanced Colorectal Cancer after Failure to Irinotecan, Oxaliplatin and 5-Fluorouracil," *Ann Oncol*, 2008, 19(6):1141-5.
8. Carneiro BA, Ramanathan RK, Fakih MG, et al. Phase II study of irinotecan and cetuximab given every 2 weeks as second-line therapy for advanced colorectal cancer. Clin Colorectal Cancer. 2012 Mar; 11(1):53-9.
9. First Coast Service Options, Inc. Local Coverage Determination (LCD): Cetuximab (Erbitux®) (L33278). Centers for Medicare & Medicaid Services, Inc. Updated on 7/1/2014 with effective date 10/1/2015. Accessed March 2018Martins AM, Valadares ER, Porta G, et al. Recommendations on diagnosis, treatment, and monitoring for Gaucher disease. J Pediatr. 2009 Oct;155(4 Suppl):S10-8.
10. Kaplan P, Baris H, De Meirleir L, et al. Revised recommendations for the management of Gaucher disease in children. Eur J Pediatr. 2013 Apr;172(4):447-58: doi: 10.1007/s00431-012-1771-z. Epub 2012 Jul 8