

Complete Patient and Physician information (PLEASE PRINT)

STEP 1	Member Name:	Physician Name:
	Address:	Address:
	Member ID:	Phone #:
	Member DOB:	Fax #:
		Tax ID or NPI Number:

If Applicable: Pharmacy Name: _____
Pharmacy Phone: _____

Complete the Clinical Assessment:

STEP 2	Diagnosis	<input type="checkbox"/> EGFR-expressing metastatic colorectal cancer <input type="checkbox"/> Locally or regionally advanced squamous cell carcinoma of the head & neck	<input type="checkbox"/> Recurrent or metastatic squamous cell carcinoma of the head & neck <input type="checkbox"/> Other (please state): _____
		<input type="checkbox"/> Patient intolerant to irinotecan, or cancer must be refractory to therapy with irinotecan. (required for colorectal cancer) <input type="checkbox"/> Erbitux is being given in combination with radiation therapy (head & neck cancer).	<input type="checkbox"/> If Erbitux is monotherapy for head & neck cancer, patient must be refractory to platinum based therapy. <input type="checkbox"/> Other (please state): _____
	Physician Specialty	<input type="checkbox"/> Oncology	<input type="checkbox"/> Other (please state): _____
	Supporting Documentation	Diagnosis: ICD-9 Code #/ Description / J Code (required):	
		Please attach a copy of the prescription or provide ALL of the information below: Erbitux [®] (cetuximab)	
		Strength _____ Sig _____ Qty _____ Refills _____	
		Please attach all relevant medical records and test results. Incomplete forms will not be processed.	

I certify that the above is correct and accurate to the best of my knowledge (please sign and date).

STEP 3 _____ Date _____
Prescriber Signature

**Fax completed form to the Rocky Mountain Health Plans Pharmacy Help Desk:
970-248-5034**

STEP 4

Name of Person filling out form: _____

Pharmacy Technician initials _____ Date Initiated _____

Confidentiality Notice:

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RMHP Formulary Coverage Policy

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

Erbix (cetuximab)

CLASSIFICATION

- Antineoplastic, monoclonal antibody

DESCRIPTION

- Cetuximab is a murine-human chimeric monoclonal antibody directed against EGFR.
- The proposed antitumor activity of cetuximab occurs through several proposed mechanisms: cell cycle inhibition (G1 phase; through the inhibition of p27(kip1) and a decrease in clear antigen expression), apoptosis (by altering the ratio of Bax to Bcl-2 expression and increasing apoptotic caspase expression), decreasing growth factors (TGF- α , amphiregulin, and cripto) and angiogenic factors associated with proliferation (VEGF, basic fibroblast growth factor, IL-8), and matrix metalloproteinase inhibition.
- Preclinical data suggest that complete saturation of EGFRs with antibody is necessary to achieve significant antitumor effects. Cetuximab binds specifically to the epidermal growth factor receptor (EGFR, HER1, c-ErbB-1) on both normal (including skin and hair follicle) and tumor cells.
- Cetuximab has greater in vitro affinity for EGFR than EGF or TGF- α , and following binding, the receptor-antibody complex is rapidly internalized, preventing further receptor exposure; downregulation of cell-surface binding sites and cetuximab competition for remaining sites reduces or prevents further ligand activation.
- Significant enhancement of the cytotoxic effects of chemotherapeutic agents (eg, paclitaxel, cisplatin, doxorubicin) and potentiation of irradiation responses have also been observed in human xenografts. Additive increases in growth inhibition of some cancer cell lines (eg, ovarian, colon, breast) were seen in vitro with a sequential schedule of topotecan plus cetuximab, and cetuximab enhanced apoptotic cell death induced by topotecan; near-complete tumor regression was observed with combined use of these agents in a xenograft model (colon cancer) compared to only minimal activity when each agent was given alone.
- Human epidermal growth factor receptor (EGFR), encoded by the c-erb-B proto-oncogene, is a transmembrane glycoprotein found primarily on cells of epithelial origin; it has been implicated in oncogenesis and progression of numerous tumor-types. EGFR is stimulated by several ligands, primarily epidermal growth factor (EGF) and transforming growth factor- α (TGF- α); ligand binding results in EGFR dimerization, activation of protein tyrosine kinase activity, and tyrosine autophosphorylation, and subsequent stimulation of a cascade of biochemical/physiologic responses involved in the mitogenic signal transduction of cells, supporting growth/survival of various human cancers. TGF- α is also produced by numerous tumor cells, and acts in an autocrine manner via EGFR activation. EGFR is expressed in many normal tissues, but at a lower magnitude than in overexpressing tumors; normal cells typically require higher amounts of exogenous growth factor than tumor cells for proliferation to occur.
- Overexpression of EGFR is seen in squamous cell carcinoma of the head and neck (nearly 100% of patients), non-small cell lung carcinoma (55%), melanoma, glioblastoma, and renal-cell, cervical, prostate, bladder, colorectal, pancreatic, and breast cancers. Overexpression has correlated with proliferation of many of these cancers, and its presence has served as a poor-prognosis marker.
- Murine antibodies against EGFR have been shown to compete with EGF binding and inhibit subsequent tyrosine kinase activity and cell proliferation/tumor growth

FORMULARY COVERAGE

Prior authorization: Required

Good Health Formulary: Medical benefit

Commercial Formulary: Medical benefit

Medicare Part D coverage: Part B

COVERAGE CRITERIA

Erbix (cetuximab) meets the definition of **medical necessity** for the following:

FDA Labeled indications include:

- Head and neck cancer, Locally or regionally advanced squamous cell, in combination with radiation therapy
- Head and neck cancer, Metastatic or recurrent squamous cell; as monotherapy in patients who failed prior platinum-based therapy
- Metastatic colorectal cancer, EGFR-expressing, as monotherapy, in patients intolerant to irinotecan-based chemotherapy
- Metastatic colorectal cancer, EGFR-expressing, as monotherapy in patients who failed both irinotecan- and oxaliplatin-based regimens
- Metastatic colorectal cancer, EGFR-expressing, in combination with irinotecan, in patients refractory to irinotecan-based chemotherapy

Off-label uses which have shown favorable efficacy include:

- Head and neck cancer, Metastatic or recurrent squamous cell; refractory to platinum-based therapy; as combination therapy
- Metastatic colorectal cancer, Epidermal growth factor receptor (EGFR) expressing, first-line therapy, in combination with irinotecan, 5-fluorouracil, and folinic acid
- Metastatic colorectal cancer, Refractory, non-epidermal growth factor receptor (EGFR) expressing
- Non-small cell lung cancer, Advanced or metastatic, with documented EGRF-expression

Erbix (cetuximab) is considered **experimental** for the following:

- Head and neck cancer, Squamous cell, metastatic or recurrent, first-line therapy, in combination with platinum-based chemotherapy
- Other cancers, EGFR-overexpressing
- Ovarian cancer, EGRF-expressing
- Pancreatic cancer

Required Provider Specialty:

- Approval is limited to Oncology

DOSAGE/ADMINISTRATION:

Adult Dosing (safety and efficacy in pediatric patients has not been established)

- Head and neck cancer, Locally or regionally advanced squamous cell, in combination with radiation therapy: 400 mg/m² initial IV loading dose over 120 min administered 1 week prior to the start of radiation therapy, followed by weekly doses of 250 mg/m² IV over 60 min for the duration of radiation therapy (6 to 7 weeks)
- Head and neck cancer, Metastatic or recurrent squamous cell; as monotherapy in patients who failed prior platinum-based therapy: 400 mg/m² initial IV loading dose over 120 min, followed by weekly doses of 250 mg/m² IV over 60 min until disease progression or unacceptable toxicity
- Metastatic colorectal cancer, EGFR-expressing, as monotherapy, in patients intolerant to irinotecan-based chemotherapy: 400 mg/m² initial IV loading dose over 120 min, followed by weekly doses of 250 mg/m² IV over 60 min until disease progression or unacceptable toxicity
- Metastatic colorectal cancer, EGFR-expressing, as monotherapy in patients who failed both irinotecan- and oxaliplatin-based regimens: 400 mg/m² initial IV loading dose over 120 min, followed by weekly doses of 250 mg/m² IV over 60 min until disease progression or unacceptable toxicity

- Metastatic colorectal cancer, EGFR-expressing, in combination with irinotecan, in patients refractory to irinotecan-based chemotherapy: 400 mg/m² initial IV loading dose over 120 min, followed by weekly doses of 250 mg/m² IV over 60 min until disease progression or unacceptable toxicity
- Non-small cell lung cancer, EGFR-expressing, advanced or metastatic: combination therapy, cetuximab 400 mg/m² IV over 2 hr loading dose on day 1, followed by 250 mg/m² over 1 hr per week on day 8, plus cisplatin 80 mg/m² on day 1 and vinorelbine 25 mg/m² on days 1 and 8, every 3 weeks up to 6 cycles has been used in a clinical trial

Notes:

- Premedicate with an H1-antagonist (diphenhydramine 50 mg IV) 30 to 60 min prior to the first dose; premedication should be administered prior to subsequent doses based upon the presence and severity of prior infusion reactions
- Ensure that appropriate medical resources are available for treatment of a severe infusion reaction; all patients should be observed for 1 hour following the completion of cetuximab

Dosing adjustments

- Dermatologic toxicities (severe, grade 3 or 4 acneform rash): delay for 1 to 2 weeks; if improved, restart at 250 mg/m² after the first occurrence, 200 mg/m² after the second occurrence, and 150 mg/m² after the third occurrence; cetuximab should be discontinued if a patient does not improve from a previous episode or has a fourth occurrence
- Infusion-related toxicities: decrease infusion rate by 50% for grade 1 or 2 (mild to moderate) infusion-related reactions and non-serious grade 3 or 4 infusion reactions; permanently discontinue cetuximab in patients experiencing a serious reaction that requires medical intervention and/or hospitalization
- Pulmonary toxicities: interrupt for acute onset or worsening of pulmonary symptoms; permanently discontinue cetuximab in patients if interstitial pulmonary lung disease (ILD) is confirmed

PRECAUTIONS:

- Premedicate with an H1-antagonist (diphenhydramine 50 mg IV) 30 to 60 min prior to the first dose; premedication should be administered prior to subsequent doses based upon the presence and severity of prior infusion reactions; ensure that appropriate medical resources are available for treatment of a severe infusion reaction; all patients should be observed for 1 hour following the completion of cetuximab
- Cardiopulmonary arrest and/or sudden death have been reported in patients with squamous cell carcinoma of the head and neck treated with concomitant radiation therapy; patients with a history of arrhythmias, congestive heart failure, or coronary artery disease may be at increased risk; monitoring of serum electrolytes recommended
- Infusion reactions, some serious (eg, bronchospasm, stridor, hypotension, shock, loss of consciousness, myocardial infarction, cardiac arrest) and fatal, have been reported; immediately and permanently discontinue for serious infusion reactions
- Concomitant use with radiation therapy and cisplatin (unapproved use); death and serious cardiotoxicity have been reported in patients with squamous cell carcinoma of the head and neck
- Dermatologic toxicities, including acneform rash, hypertrichosis, and infectious sequelae (eg, staphylococcus aureus sepsis, abscess formation, cellulitis) have been reported; dosage modifications recommended for severe acneform rash
- Electrolyte abnormalities (eg, hypomagnesemia, hypocalcemia, hypokalemia) have occurred; monitoring recommended
- Interstitial lung disease (ILD) has been reported; permanently discontinue for confirmed ILD
- Sun exposure; limit exposure for up to 2 months following the last cetuximab dose

Billing/Coding information

Associated HCPCS Codes:

J9055	Injection, cetuximab, 10 mg
J9206	Injection, irinotecan, 20 mg
J9303	Injection, panitumumab, 10 mg
Q0083 - Q0085	Chemotherapy administration

Associated CPT Coding:

83891	
83896	
83898	
83907	
83912	
96401 - 96450	

Associated ICD-9 Coding:

140.0 - 150.9	Malignant neoplasm of lip, tongue, salivary glands, gum, floor of mouth, other and unspecified parts of mouth, oropharynx, nasopharynx, hypopharynx, and esophagus [covered for squamous cell carcinoma of the head and neck only]
152.0 - 152.9	Malignant neoplasm of small intestine, including duodenum [covered for advanced or metastatic adenocarcinoma of the small bowel expressing the wild type KRAS mutation only]
153.0 - 154.8	Malignant neoplasm of colon, rectum, rectosigmoid junction and anus [covered for metastatic colorectal cancer expressing the wild type KRAS mutation only]
160.0 - 162.0	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses, larynx, and trachea [covered for squamous cell carcinoma of the head and neck only]
162.2 - 162.9	Malignant neoplasm of bronchus and lung [covered for metastatic or recurrent epidermal growth factor receptor (EGFR) positive non-small cell lung cancer only]
171.0	Malignant neoplasm of connective tissue and other soft tissue of head, face, and neck [covered for squamous cell carcinoma of the head and neck only]
173.0 - 173.4	Other malignant neoplasm of skin of lip, eyelid, including canthus, skin of ear and external auditory canal, skin of other and unspecified parts of face, and scalp and skin of neck [covered for squamous cell carcinoma of the head and neck only]
190.0 - 190.9	Malignant neoplasm of eye [covered for squamous cell carcinoma of the head and neck only]
195.0	Malignant neoplasm of the head, face, and neck [covered for squamous cell carcinoma of the head and neck only]
231.2	Carcinoma in situ of bronchus and lung [covered for metastatic or recurrent epidermal growth factor receptor (EGFR) positive non-small cell lung cancer only]
V10.05 - V10.06	Personal history of malignant neoplasm of large intestine, rectum, rectosigmoid junction, and anus [covered for advanced or metastatic adenocarcinoma of the small bowel expressing the wild type KRAS mutation only]

COST

- AWP (April 2010): Erbitux 200mg/100ml vial: \$1,152.00

COMMITTEE APPROVAL:

GUIDELINE UPDATE INFORMATION:

April 2010	Policy created

REFERENCES:

- DRUGDEX®, accessed 04/02/2010

Product Information: ERBITUX(R) IV injection, cetuximab IV injection. ImClone Systems Incorporated, Branchburg, NJ, 2009.