ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Initial Request** ☐ **Renewal** ☐ **Appeal/Redetermination**[1]

☐ **Urgent**[2] ☐ **Non-Urgent**

Requested Drug Name: Erbitux® (cetuximab) – Medicare Part B

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Erbitux® (cetuximab)

Diagnosis (documentation supportive of diagnosis, intended regimen, and refractory therapy(s) is required)

☐ M**etastatic colorectal cancer (K-Ras mutation-negative; EGRF-expressing)**
- ☐ As monotherapy, in patients intolerant to irinotecan-based chemotherapy
- ☐ As monotherapy, in patients who failed both irinotecan- and oxaliplatin-based regimens
- ☐ In combination with irinotecan, in patients refractory to irinotecan-based chemotherapy
- ☐ 1st-line therapy, in combination with FOLFIRI (irinotecan, 5-fluorouracil, and leucovorin)

☐ **Head and neck cancer**
- ☐ Locally or regionally advanced squamous cell, in combination with radiation therapy
- ☐ Metastatic or recurrent squamous cell, as monotherapy, in patients who failed prior platinum-based therapy
- ☐ Squamous cell, metastatic or recurrent, 1st-line therapy, in combination with platinum-based chemotherapy with 5-fluorouracil

☐ **Other (please state):** _____

Physician Specialty

☐ Oncology
☐ Other (please state): _____

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

Dose:	Route:	Frequency:
Quantity:	Number of Refills:	

Product will be delivered to: ☐ Patient's Home ☐ Physician Office Other:

Prescriber or Authorized Signature: Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. Appeal/redetermination requests can be made for this medication within 60 calendar days from the date on the faxed/written denial notice you received at the time of the original request.

2. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request.

RMHP Formulary Coverage Policy

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

Erbitux® (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-alfa, 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-alpha, and following binding, the receptor-antibody complex is rapidly internalized, preventing further receptor exposure; down-regulation 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 (e.g. paclitaxel, cisplatin, and doxorubicin) and potentiation of irradiation responses have also been observed in human xenografts. Additive increases in growth inhibition of some cancer cell lines (e.g. 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-alpha (TGF-alpha); 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-alpha 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: Tier 6; Medical benefit
Commercial Formulary: Tier 6; Medical benefit
Medicare Part D coverage: Tier 3; Part B if incident to a physician's services

COVERAGE CRITERIA

Erbitux (cetuximab) meets the definition of **medical necessity** for all FDA approved indications not otherwise excluded from Part D, including the following (*documentation of diagnosis, mutation status, prior therapies, current regimen and other relevant information from the patient's medical record is required*):

- **HEAD and NECK Cancer:**
  - Locally or regionally advanced squamous cell, in combination with radiation therapy
  - Metastatic or recurrent squamous cell; as monotherapy in patients who failed prior platinum-based therapy
  - Squamous cell, metastatic or recurrent , first-line therapy, in combination with platinum-based chemotherapy with 5-fluorouracil

- **K-Ras Mutation-negative (wild-type), EGRF-expressing Metastatic Colorectal Cancer:**
  - as monotherapy, in patients intolerant to irinotecan-based chemotherapy
  - as monotherapy in patients who failed both irinotecan- and oxaliplatin-based regimens
  - in combination with irinotecan, in patients refractory to irinotecan-based chemotherapy
  - first-line therapy, in combination with FOLFIRI (irinotecan, 5-fluorouracil, and leucovorin)

The American Society of Clinical Oncology (ASCO) recommends all patients with metastatic colorectal carcinoma, who are candidates for anti-EGFR antibody treatment, have the tumor tested for KRAS mutations in a Clinical Laboratory Improvement Amendments (CLIA)-accredited laboratory. If KRAS mutation in codon 12 or 13 is identified, then the patient should not receive anti-EGFR antibody therapy. The manufacturer also recommends against the use in patients with the KRAS mutation in codon 12 or 13.

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

- Non-small cell lung cancer, Advanced or metastatic, with documented EGRF-expression when added to cisplatin and vinorelbine as first-line treatment for stage 4 patients. Evidence for use of Erbitux in NSCLC is inconclusive and requests will be reviewed on an individual basis.
- Head and neck cancer, Metastatic or recurrent squamous cell; refractory to platinum-based therapy; as combination therapy: Evidence favors efficacy and requests will be reviewed on an individual basis.
- Other cancers, EGFR-overexpressing
- Refractory metastatic colorectal cancer, non-EGFR expressing: Evidence is inconclusive
- **Ovarian cancer, EGRF-expressing**: use of Erbitux in ovarian cancer is ineffective and will not be a covered benefit for this indication
- Pancreatic cancer: use of Erbitux in pancreatic cancer is ineffective and will not be a covered benefit for this indication

Required Provider Specialty:

- Approval is limited to Oncology

DOSAGE/ADMINISTRATION:

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

- **Squamous Cell Carcinoma of the Head and Neck**
  - Erbitux in combination with radiation therapy or in combination with platinum-based therapy with 5-FU:
    - The recommended initial dose is 400 mg/m^2 administered one week prior to initiation of a course of radiation therapy or on the day of initiation of platinum-based therapy with 5-FU as a 120-minute intravenous infusion (maximum infusion rate 10 mg/min).
    - Complete Erbitux administration 1 hour prior to platinum-based therapy with 5-FU.
    - The recommended subsequent weekly dose (all other infusions) is 250 mg/m^2 infused over 60 minutes (maximum infusion rate 10 mg/min) for the duration of radiation therapy (6–7 weeks) or until disease progression or unacceptable toxicity when administered in combination with platinum-based therapy with 5-FU. Complete Erbitux administration 1 hour prior to radiation therapy or platinum-based therapy with 5-FU.
  - Erbitux monotherapy:
    - The recommended initial dose is 400 mg/m^2 administered as a 120-minute intravenous infusion (maximum infusion rate 10 mg/min).
    - The recommended subsequent weekly dose (all other infusions) is 250 mg/m^2 infused over 60 minutes (maximum infusion rate 10 mg/min) until disease progression or unacceptable toxicity.
- **Colorectal Cancer**
  - Determine *K-Ras* mutation and EGFR-expression status using FDA-approved tests prior to initiating treatment. Only patients whose tumors are *K-Ras* mutation-negative (wild-type) should receive Erbitux.
  - The recommended initial dose, either as monotherapy or in combination with irinotecan or FOLFIRI (irinotecan, 5-fluorouracil, leucovorin), is 400 mg/m^2 administered as a 120-minute intravenous infusion (maximum infusion rate 10 mg/min). Complete Erbitux administration 1 hour prior to FOLFIRI.
  - The recommended subsequent weekly dose, either as monotherapy or in combination with irinotecan or FOLFIRI, is 250 mg/m^2 infused over 60 minutes (maximum infusion rate 10 mg/min) until disease progression or unacceptable toxicity. Complete Erbitux administration 1 hour prior to FOLFIRI.

Notes:

- Do not administer Erbitux as an intravenous push or bolus. Administer via infusion pump or syringe pump. Do not exceed an infusion rate of 10 mg/min.
- **Premedicate** with an H1-antagonist (e.g. 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 (see package insert for complete information):

- Dermatologic toxicities (severe, grade 3 or 4 acneiform rash): delay for 1 to 2 weeks; if improved, restart at 250 mg/m^2 after the first occurrence, 200 mg/m^2 after the second occurrence, and 150 mg/m^2 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:

- **Black Box Warning:** Serious Infusion Reactions and Cardiopulmonary Arrest Infusion Reactions
  - Serious infusion reactions occurred with the administration of cetuximab in approximately 3% of patients in clinical trials, with fatal outcome reported in less than 1 in 1000. Immediately interrupt and permanently discontinue cetuximab infusion for serious infusion reactions.
  - Cardiopulmonary Arrest and/or sudden death occurred in 2% of patients with squamous cell carcinoma of the head and neck treated with cetuximab and radiation therapy in Study 1 and in 3% of patients with squamous cell carcinoma of the head and neck treated with European Union (EU)-approved cetuximab in combination with platinum-based therapy with 5-fluorouracil (5-FU) in Study 2. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after cetuximab administration.
- 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 acneiform rash, hypertrichosis and infectious sequelae (e.g. staphylococcus aureus sepsis, abscess formation, cellulitis) have been reported. Dose modifications are recommended for severe acneiform rash.
- Electrolyte abnormalities (e.g. 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	

COST

- AWP (April 2010): Erbitux 200mg/100ml vial: $1,152.00
- AWP (August 2012): Erivtux 200mg/100ml vial: $1,204.00
- AWP (January 2014): Erbitux 200mg/100ml vial: $1,222.80

COMMITTEE APPROVAL:

- March 2004

GUIDELINE UPDATE INFORMATION:

March 2004	Prior Authorization created
March 2006	Head and Neck Cancer indication added to PA
April 2010	Coverage Policy created
August 2012	Coverage Policy updated

REFERENCES:

DRUGDEX®, accessed 04/02/2010, 8/7/2012, 1/6/2014
Product Information: ERBITUX® IV injection, cetuximab IV injection. ImClone Systems Incorporated, Branchburg, NJ, 2009, 2012.