I. Medication Description

The epidermal growth factor receptor, detected in many human cancers such as head and neck, colon and rectal cancer, is also found in many normal epithelial tissues. Erbitux® (cetuximab) is a monoclonal antibody that binds to the epidermal growth factor receptor (EGFR, HER1, c-ErbB-1) on both normal and tumor cells. Erbitux® competitively inhibits the binding of epidermal growth factor (EGF) and other ligands. Consequently, this action blocks phosphorylation and activation of receptor-associated kinases downstream, resulting in inhibition of cell growth, induction of apoptosis (cell death), and decreased matrix metalloproteinase and vascular endothelial growth factor production.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage will not be granted for treatment with Erbitux in combination with Avastin or Vectibix for any indication.

Coverage for Erbitux is provided for adult patients aged 18 years and older for treatment of the following conditions:

- Colorectal Cancer:
  - Patient must have wild-type, non-mutated KRAS/NRAS EGFR-expressing tumor AND
  - One of the following scenarios applies:
    - In combination with FOLFOX or FOLFIRI (applicable to left-sided only tumors for colon cancer):
      - As primary treatment for unresectable and/or metastatic disease
      - For unresectable metastases that remain unresectable after primary treatment
    - As primary treatment in combination with irinotecan or FOLFIRI for unresectable metastases and previous adjuvant FOLFOX or CapeOX within the past 12 months
    - As subsequent therapy for unresectable advanced or metastatic disease not previously treated with cetuximab or panitumumab
      - In combination with irinotecan or FOLFIRI after first progression for disease previously treated with irinotecan-based therapy without irinotecan
      - In combination with irinotecan after first progression for disease previously treated with irinotecan-based therapy without oxaliplatin
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- In combination with irinotecan after second or subsequent progression for disease previously treated with oxaliplatin- and irinotecan-based therapies
- In combination with irinotecan for disease previously treated with FOLFOXIRI

- **Non-Small Cell Lung Cancer:** In combination with afatinib as subsequent therapy for metastatic disease in patients with an EGFR mutation who are T790M negative and progressed on EGFR tyrosine kinase inhibitor therapy
- **Squamous Cell Carcinoma of the Head and Neck (SCCHN):**
  - Non-nasopharyngeal cancer:
    - For primary concurrent or sequential chemoradiation as a single agent **OR**
    - As a single-agent or in combination with cisplatin alone, or in combination with cisplatin or carboplatin and fluorouracil, docetaxel or paclitaxel for very advanced and recurrent/persistent disease
  - Nasopharyngeal cancer:
    - For primary treatment in combination with carboplatin
    - In combination with carboplatin for very advanced and recurrent/persistent disease
- **Squamous Cell skin cancers:** for regional recurrence or distant metastases
- **Penile Cancer:** as a single agent for subsequent-line therapy for metastatic disease

**IV. Quantity Limitations**

- No more than 125 billable units (1,250mg) in a single administration **AND**
- No more than 125 billable units (1,250mg) every 14 days

**V. Coverage Duration**

Coverage will be provided for 6 months and may be renewed.

**VI. Coverage Renewal Criteria**

Coverage can be renewed based upon the following criteria:

- Tumor response: documentation of disease stabilization, decrease in tumor size, decrease in metastases, lack of disease progression **AND**
- Absence of unacceptable toxicity from the drug

**VII. Billing/Coding Information**

- Available in 100mg/50ml and 200mg/100ml vials
- J9055: Injection, cetuximab, 1 unit=10 mg
- Relevant diagnoses:
  - Colorectal cancer: C17.0-C17.2, C17.8, C17.9, C18.0-C18.9, C19, C20, C21.8, C78.00-C78.02, C78.6, C78.7, Z85.038
  - Head and neck cancer: C00.0-C00.6, C00.8, C00.9, C01, C02.2,-C02.4, C02.8, C02.9, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C06.0, C05.0, C05.1, C06.2, C06.89, C06.9, C09.0, C09.1, C09.8,
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<td>o NSCLC: C33, C34.00-C34.02, C34.10-C34.12, C34.2, C34.30-C34.32, C34.80-C34.82, C34.90-C34.92, Z85.118</td>
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<td>o Penile cancer: C60.0-C60.2, C60.8, C60.9, C63.7, C63.8</td>
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<td>o Squamous cell skin cancers: C44.02, C44.121, C44.122, C44.129, C44.221, C44.222, C44.229, C44.320, C44.321, C44.329, C44.42, C44.520, C44.521, C44.529, C44.621, C44.622, C44.629, C44.721, C44.722, C44.729, C44.82, C44.92, Z85.828</td>
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VIII. Summary of Policy Changes

- 9/1/11: Chordoma indication added, renewal specifications added
- 6/15/12: No changes
- 3/15/13: Removed coverage for chordoma (per updated NCCN guidelines); Added coverage criteria for basal cell and squamous cell skin cancers; Updated pertinent ICD9 section.
- 3/15/14: Colorectal guidelines updated to include neoadjuvant treatment and to match current NCCN guidelines
- 3/15/15: Removed coverage criteria for basal cell skin cancer and updated CRC guideline to comply with current NCCN guidelines
- 6/15/15: Addition of penile cancer; colorectal cancer criteria minimized to correspond to NCCN guidelines; removal of coverage in NSCLC to correspond with updated NCCN guidelines
- 7/1/15: Formulary distinctions made
- 6/15/16: Updated coverage to coincide with current NCCN treatment guidelines, including addition of coverage in NSCLC
- 4/5/17: Updated coverage to coincide with current NCCN treatment guidelines

IX. References

1. UpToDate Online, retrieved March 2011
4. Facts and Comparisons Online, retrieved March 2011

*The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.*

*Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.*

*The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.*