

Title: cetuximab (Erbix)

Origination: 07/28/10	Revised:	Annual Review: 12/15/11
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Purpose:

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

Background Information:

Medication Summary

- Erbitux (cetuximab) is a recombinant, human/mouse chimeric monoclonal antibody that binds specifically to the extracellular domain of the human epidermal growth factor receptor (EGFR). Cetuximab is composed of the Fv regions of a murine anti-EGFR antibody with human IgG1 heavy and kappa light chain constant regions and has an approximate molecular weight of 152 kDa. Cetuximab is produced in mammalian (murine myeloma) cell culture.
- Cetuximab binds specifically to the EGFR on both normal and tumor cells, and competitively inhibits the binding of epidermal growth factor (EGF) and other ligands, such as transforming growth factor-alpha. *In vitro* assays and *in vivo* animal studies have shown that binding of cetuximab to the EGFR blocks phosphorylation and activation of receptor-associated kinases, resulting in inhibition of cell growth, induction of apoptosis, and decreased matrix metalloproteinase and vascular endothelial growth factor production.
- Signal transduction through the EGFR results in activation of wild-type KRAS protein. However, in cells with activating *KRAS* somatic mutations, the mutant KRAS protein is continuously active and appears independent of EGFR regulation.
- Indications for Erbitux include:
 - Squamous cell carcinoma of the head and neck (SCCHN):
 - In combination with radiation therapy for initial treatment;
 - As a single agent for recurrent or metastatic disease when prior platinum-based therapy has failed.
 - Colorectal cancer:
 - As a single agent for the treatment of EGFR expressing metastatic colorectal cancer after failure of both irinotecan- and oxaliplatin-based regimens;
 - In combination with irinotecan for the treatment of EGFR-expressing metastatic colorectal carcinoma in patients who are refractory to irinotecan-based chemotherapy.
- The recommended initial dose of Erbitux is 400mg/m² administered one (1) week prior to initiation of a course of radiation therapy as a 120 minute IV infusion (maximum infusion rate 10mg/min).
- The recommended subsequent weekly dose (all other infusions) is 250mg/m² infused over 60 minutes (maximum infusion rate 10mg/min) until disease progression or unacceptable toxicity.

Background Information, continued:

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Reference Statement

- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

Eligibility Criteria

- Member must be eligible and have applicable benefit coverage (i.e., self-injectable rider) within the specified date(s) of service.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

Procedure:

- 1.0 Request for *initial therapy* with Erbitux for **Colorectal cancer** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying all of the following:
 - 1.1 Member has undergone KRAS (Kirsten rat sarcoma viral oncogene) mutation analysis to assure response therapy;
 - 1.2 If criteria are met, Erbitux is approvable for six (6) months.
- 2.0 Request for *initial therapy* with Erbitux for **Non-small cell lung cancer (NSCLC)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying all of the following:
 - 2.1 First line therapy for recurrent or metastatic disease;
 - 2.2 Erbitux is approvable for six (6) months.
- 3.0 Request for *initial therapy* with Erbitux for **Squamous cell carcinoma of the head and neck (SCCHN)** requires documentation from the Member's medical; records maintained by the requesting independent practitioner:
 - 3.1 Erbitux is approvable for six (6) months.

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Procedure, continued:

- 4.0 Request for *continuation therapy* with Erbitux for **above indications** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **tumor response:**
- 4.1 Erbitux is approvable for six (6) months.

References:

1. Erbitux Prescribing Information. ImClone Systems Incorporated and Bristol Myers Squibb Company. Branchburg, NJ and Princeton, NJ. Rev March 2010.
2. Facts and Comparisons 4.0, St. Louis, MO. Walters Kluwer Health URL: www.factsandcomparisons.com Updated 2010.
3. National Comprehensive Cancer Network, Inc. (NCCN) Practice Guidelines in Oncology Version 2.2010, March 2010. Available at: www.nccn.org/professionals/physician_gls/f_guidelines.asp

Disclaimer Information:

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.