Drug Policy:

Erbitux™ (cetuximab)

POLICY NUMBER UM ONC_1133	SUBJECT Erbitux™ (cetuximab)		DEPT/PROGRAM UM Dept	PAGE 1 of 4
DATES COMMITTEE REVIEWED 07/22/11, 01/02/13, 03/13/13, 07/24/14, 12/16/15, 12/20/16, 12/14/17, 11/08/18, 09/30/19, 10/09/19, 12/11/19, 03/11/20, 05/13/20, 11/11/20, 12/09/20, 04/14/21, 11/15/21, 04/13/22, 05/11/22, 09/14/22, 03/08/23, 04/12/23, 10/11/23, 07/10/24, 01/08/25	**APPROVAL DATE** January 08, 2025	**EFFECTIVE DATE** January 31, 2025	**COMMITTEE APPROVAL DATES** 07/22/11, 01/02/13, 03/13/13, 07/24/14, 12/16/15, 12/20/16, 12/14/17, 11/08/18, 09/30/19, 10/09/19, 12/11/19, 03/11/20, 05/13/20, 11/11/20, 12/09/20, 04/14/21, 11/15/21, 04/13/22, 05/11/22, 09/14/22, 03/08/23, 04/12/23, 10/11/23, 07/10/24, 01/08/25	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Evolent Specialty Services Clinical Guideline Review Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses clinical guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this clinical guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their plan customer service representative for specific coverage information.

I. PURPOSE

To define and describe the accepted indications for Erbitux (cetuximab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. Colorectal Cancer

1. The member has stage IV, KRAS/NRAS/BRAF Wild-Type metastatic colorectal cancer and Erbitux (cetuximab) is being used as a single agent or in combination with FOLFIRI, FOLFOX, FOLFIRINOX, or irinotecan in the initial or subsequent line setting, except for members who have experienced disease progression on prior therapy with Erbitux (cetuximab) or Vectibix (panitumumab). Xeloda (capecitabine) may be substituted for 5-FU (5-fluorouracil) in the above mentioned 5-FU-based regimens.
2. Erbitux (cetuximab) may be used in combination with Braftovi (encorafenib) and FOLFOX in the initial line setting in members with stage IV, metastatic BRAF V600E mutation positive colorectal cancer, and KRAS/NRAS status is either Wild-Type or unknown.
    a. Members must also:
        i. Have not had prior treatment with any selective BRAF inhibitors or EGFR inhibitors
        ii. Have tumors that are not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) unless the member is ineligible to receive immune checkpoint inhibitors
3. The member has unresectable, advanced, or metastatic BRAF V600E mutation positive colorectal cancer, regardless of KRAS/NRAS status, and Erbitux (cetuximab) may be used in combination with Braftovi (encorafenib) after prior therapy in the metastatic setting. Mekinist (trametinib) use with the above combination is not supported by Evolent policy.
4. The member has KRAS G12C-mutated locally advanced or metastatic colorectal cancer and Erbitux (cetuximab) is being used in combination with adagrasib, AND the member has received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

C. Head and Neck Cancers

1. The member has squamous cell carcinoma of the head and neck Erbitux (cetuximab) may be used for locally advanced/recurrent/metastatic disease as a single agent or in combination with chemotherapy.
2. NOTE: [Erbitux (cetuximab) + Taxotere (docetaxel)], [Erbitux (cetuximab) + Keytruda (pembrolizumab)] are not supported by Evolent Policy for the treatment of head and neck cancers. This policy position is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with any of the above regimens compared to Evolent recommended regimens/agents, including but not limited to regimens available at https://www.evolent.com/pathways.

III. EXCLUSION CRITERIA

A. Disease progression on prior therapy (single agent or multiagent therapy) that included Erbitux (cetuximab) or Vectibix (panitumumab).

B. As a single agent or in combination with pre/post-operative chemotherapy for potentially resectable liver metastases from KRAS/NRAS wild-type colorectal cancer.

C. Absence of documented KRAS/NRAS testing and results of such testing.

D. Dosing exceeds single dose limit of Erbitux (cetuximab) as follows:

1. Loading dose of 400 mg/m^2 x 1 dose
2. Subsequent doses of 250 mg/m^2 weekly OR 500 mg/m^2 every 2 weeks.

E. Investigational use of Erbitux (cetuximab) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. CODING INFORMATION

HCPCS Code	Description
J9055	Injection, cetuximab, 10 mg

V. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

A. None

VIII. REFERENCES

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E. Tang et al. Concurrent cisplatin or cetuximab with radiotherapy in patients with locally advanced head and neck squamous cell carcinoma- A meta-analysis. Medicine: September 4, 2020- Volume 99-Issue 36-p e21785.

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M. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.

N. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

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