



Cetuximab (Erbix[®])

Revision: 2

Policy Number: M-0011

Last Update: 6/4/2014

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

When appropriate compendia references the use of one of the chemotherapeutic agents listed in this Article as part of a 'combination therapy', the drug is only approved for use in such 'combinations', and the documentation should reflect, and be specific about, the use of the additional 'combination therapy' drugs.

Coverage Guidelines:

FDA:

- 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
- Head and neck cancer, Squamous cell, metastatic or recurrent , first-line therapy, in combination with platinum-based chemotherapy with 5-fluorouracil
- 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:

- Gastric cancer



- Head and neck cancer, Metastatic or recurrent squamous cell; refractory to platinum-based therapy; as combination therapy
- Malignant neoplasm of cardio-esophageal junction of stomach
- Metastatic colorectal cancer, EGFR-expressing, in combination with irinotecan, in patients who failed both fluoropyrimidine- and oxaliplatin-based regimens
- Metastatic colorectal cancer, Epidermal growth factor receptor (EGFR) expressing, first-line therapy, in combination with irinotecan, 5-fluorouracil, and folinic acid

Coding Information:

HCPCS Code(s)

J9055	INJECTION, CETUXIMAB, 10 MG
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ICD-9 Code(s)

140.0 - 149.9	MALIGNANT NEOPLASM OF UPPER LIP VERMILION BORDER - MALIGNANT NEOPLASM OF ILL-DEFINED SITES WITHIN THE LIP AND ORAL CAVITY
153.0 - 153.9	MALIGNANT NEOPLASM OF HEPATIC FLEXURE - MALIGNANT NEOPLASM OF COLON UNSPECIFIED SITE
154.0 - 154.8	MALIGNANT NEOPLASM OF RECTOSIGMOID JUNCTION - MALIGNANT NEOPLASM OF OTHER SITES OF RECTUM RECTOSIGMOID JUNCTION AND ANUS
157.0 - 157.9	MALIGNANT NEOPLASM OF HEAD OF PANCREAS - MALIGNANT NEOPLASM OF PANCREAS PART UNSPECIFIED
160.0 - 160.9	MALIGNANT NEOPLASM OF NASAL CAVITIES - MALIGNANT NEOPLASM OF ACCESSORY SINUS UNSPECIFIED
161.0 - 161.9	MALIGNANT NEOPLASM OF GLOTTIS - MALIGNANT NEOPLASM OF LARYNX UNSPECIFIED
162.0 - 162.9	MALIGNANT NEOPLASM OF TRACHEA - MALIGNANT NEOPLASM OF BRONCHUS AND LUNG UNSPECIFIED
195.0	MALIGNANT NEOPLASM OF HEAD FACE AND NECK

Background:

Erbix is an epidermal growth factor receptor (EFR) antagonist indicated for the treatment of head and neck cancer and colorectal cancer. When growth factors bind to their receptors on the surface of the cell, the receptors give a signal that causes cells to divide. Some cancers are

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caused by mutated receptors that give a signal to divide even without growth factor. That causes the cells to divide uncontrollably. Cetuximab binds to receptors like that and turns off that signal.

The EGFR sends a signal down a pathway that includes another protein, KRAS. In some cancers, the EGFR is mutated. In other cancers, the KRAS protein is mutated, and KRAS sends a signal to divide uncontrollably instead.

Cetuximab binds to EGFR and turns off the uncontrolled growth in cancers with EGFR mutations. However, if the EGFR is normal, and the KRAS protein is mutated, cetuximab won't work, because the KRAS protein downstream is causing the problem, not the EGFR.

Therefore, before cetuximab is used, the KRAS protein in the cancer cells is tested. If KRAS is normal (wild), cetuximab might work. But if KRAS is mutated, cetuximab won't work, because KRAS will send a signal to divide even after cetuximab turns the EGFR signal off.

Black Box Warning:

WARNING: SERIOUS INFUSION REACTIONS and CARDIOPULMONARY ARREST

Infusion Reactions:

Serious infusion reactions occurred with the administration of Erbitux in approximately 3% of patients in clinical trials, with fatal outcome reports in less than 1 in 1000. Immediately interrupt and permanently discontinue Erbitux infusion for serious infusion reactions.

Cardiopulmonary Arrest:

Cardiopulmonary arrest and/or sudden death occurred in 2% of patients with squamous cell carcinoma of the head and neck treated with Erbitux and radiation in Study 1 and 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 Erbitux administration.



Definitions:

EGRF— epidermal growth factor receptor (EGFR; ErbB-1; HER1 in humans) is the cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands.¹

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

KRAS— V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog and KRAS, is a protein that in humans is encoded by the KRAS gene. The protein product of the normal KRAS gene performs an essential function in normal tissue signaling, and the mutation of a KRAS gene is an essential step in the development of many cancers.

References:

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2. The NCCN Drugs & Biologics Compendium™ © 2010 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 23, 2012.
3. Local Coverage Article for Drugs and Biologicals – Chemotherapeutic Agents (A48896) (R4). Available at: http://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=48896&ver=89&ContrlId=213&ContrVer=1&CntrctrSelected=213*1&Date=01%2f01%2f2013&DocID=A48896&bc=hAAAAAgEAAAAA%3d%3d&. Accessed August 30, 2013.
4. Micromedex ® 2.0. Erbitux. Available at: http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/A82F47/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/DC0AB5/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=erbitux. Accessed May 23, 2012.

Document History:



Date Written: 5/23/12

Effective Date: 4/1/13

Revision 1: 3/19/2013

Revision 2: 6/4/2014

Internal Review: 6/11/2014

External Review: 6/17/2014

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