Draft Revised Policy: Do Not Implement

Panitumumab (Vectibix®)

DESCRIPTION

Panitumumab is a recombinant human IgG2 kappa monoclonal antibody which binds specifically to the human epidermal growth factor receptor (EGFR). EGFR is expressed in multiple cell lines including epithelial tissues and is over-expressed in certain cancers. EGFR functions in a complex cascade system that affects gene transcription involved with cellular growth, motility and proliferation. By binding to EGFR, panitumumab interrupts the cascade which ultimately leads to the development of cancer. This results in inhibition of excessive cell growth, induction of apoptosis, and decreased proinflammatory cytokine and vascular growth factor production.

In the EGFR cascade, certain proteins including the RAS proteins normally function as switches in the kinase pathway activated between cell surface EGFR and downstream signaling. The gene mapping normal, non-mutated gene is referred to as a wild-type gene. Mutations in one specific RAS protein, the KRAS gene, occur in 30% to 50% of colorectal cancers as well as other tumor types. These mutations in KRAS cause activation of the EGFR pathway beyond the point at which panitumumab would bind with EGFR and interrupt the cascade. This renders panitumumab and other anti-EGFR agents ineffective against those tumors expressing RAS mutations such as KRAS and, found more recently, those in another of the RAS proteins, NRAS.

Another common mutation is found in the BRAF gene, a serine/threonine kinase. BRAF encodes a component downstream of the RAS proteins in the EGFR cascade. The BRAF gene is important for transducing mitogenic signals from the cell surface. BRAF mutations have been found in thyroid, colorectal and lung cancers as well as in a majority of malignant melanomas, however specific targeting and treatment of BRAF-dependent tumors remains under investigation.

POLICY

- Panitumumab for the treatment of Colorectal Cancer is considered ***medically necessary*** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**
- Panitumumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age; **AND**

Universal Criteria

- Patient is both KRAS and NRAS mutation negative (wild-type) as determined by an FDA or CLIA-compliant test*; **AND**
- Patient has not been previously treated with cetuximab or panitumumab; **AND**
- Will not be used as part of an adjuvant treatment regimen; **AND**

Colorectal Cancer

- Patient has metastatic, unresectable (or medically inoperable), or advanced disease that is BRAF mutation negative (wild-type); **AND**
  - Used as ~~first-line or~~ primary treatment ~~therapy;~~ **AND**
    - Used in combination with FOLFOX; **OR**
    - Used in combination with FOLFIRI *(Note: Colon cancer patients must have left-sided tumor);* **OR**

  - Used in combination with an irinotecan-based regimen after previous adjuvant FOLFOX or CapeOX within the past 12 months ~~(*Note: Colon cancer patients must have left-sided tumors*)~~; **OR**
- Used as subsequent therapy; **AND**
  - ~~Used as single agent therapy after failure with fluoropyrimidine, oxaliplatin, and irinotecan-containing chemotherapy;~~ ~~**OR**~~
  - Used as a single agent for oxaliplatin- and/or irinotecan-refractory disease OR irinotecan-intolerant disease; **OR**
  - Used in combination with irinotecan for oxaliplatin- and/or irinotecan-refractory disease; **OR**
  - Used in combination with FOLFIRI for oxaliplatin-refractory disease; **OR**
  - Used in combination with FOLFOX for irinotecan-refractory disease; **OR**
- ~~Used in combination with FOLFOX or FOLFIRI for one of the following (*Note: Colon cancer patients must have left-sided tumors):*~~
  - ~~Disease that remains unresectable after primary therapy;~~ ~~**OR**~~
  - ~~Disease progression on non-intensive therapy with improvement in functional status *(excluding patients previously treated with fluoropyrimidine)*;~~ ~~**OR**~~
  - ~~Patients who have received adjuvant FOLFOX or CapeOX more than 12 months ago OR who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy;~~ ~~**OR**~~
- Patient has BRAF V600E mutation positive disease; **AND**
  - Used in combination with encorafenib; **AND**
    - Used as subsequent therapy for disease progression after at least one prior line of treatment in the advanced or metastatic disease setting; **OR**
    - Used as primary treatment for unresectable metastatic disease after previous adjuvant FOLFOX or CapeOX within the past 12 months

**If confirmed using an FDA approved assay - http://www.fda.gov/companiondiagnostics*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Disease response with treatment as defined by a stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: dermatologic/soft-tissue toxicity, electrolyte depletion, severe infusion-related reactions, acute renal failure, pulmonary fibrosis/interstitial lung disease (ILD), photosensitivity, keratitis, etc.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
Colorectal Cancer	Administer 6 mg/kg intravenously every 14 days until disease progression or unacceptable toxicity.

LENGTH OF AUTHORIZATION

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

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

- 70 units every 14 days

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Vectibix [package insert]. Thousand Oaks, CA; Amgen, Inc; June 2017. Accessed July 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) panitumumab. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
3. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
4. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
5. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dose vials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Colon Cancer. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
7. Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol. 2007 May 1;25(13):1658-64.

8. Price TJ, Peeters M, Kim TW, et al. Panitumumab versus cetuximab in patients with chemotherapy-refractory wild-type KRAS exon 2 metastatic colorectal cancer (ASPECCT): a randomised, multicentre, open-label, non-inferiority phase 3 study. Lancet Oncol. 2014 May;15(6):569-79. doi: 10.1016/S1470-2045(14)70118-4. Epub 2014 Apr 14.
9. Kim TW, Elme A, Kusic Z, et al. A phase 3 trial evaluating panitumumab plus best supportive care vs best supportive care in chemorefractory wild-type KRAS or RAS metastatic colorectal cancer. Br J Cancer. 2016 Nov 8;115(10):1206-1214. doi: 10.1038/bjc.2016.309. Epub 2016 Oct 13.
10. Douillard JY, Siena S, Cassidy J, et al. Final results from PRIME: randomized phase III study of panitumumab with FOLFOX4 for first-line treatment of metastatic colorectal cancer. Ann Oncol. 2014 Jul;25(7):1346-55. doi: 10.1093/annonc/mdu141. Epub 2014 Apr 8.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Rectal Cancer. Version 1.2021. National Comprehensive Cancer Network, 20201. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2021.
12. Lexi-Comp Online. (2021, February). AHFS DI. *Panitumumab*. Retrieved September 9, 2021 from Lexi-Comp Online with AHFS.
13. MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2020, December). *Panitumumab*. Retrieved September 9, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE

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