

Corporate Medical Policy

Bevacizumab in Advanced Adenocarcinoma of the Pancreas

File Name: bevacizumab_in_advanced_adenocarcinoma_of_the_pancreas
Origination: 3/2010
Last CAP Review: 11/2018
Next CAP Review: 11/2019
Last Review: 2/2019

Description of Procedure or Service

Bevacizumab (Avastin®, Genentech BioOncology) is a humanized monoclonal antibody directed against vascular endothelial growth factor-A (VEGF-A). Vascular endothelial growth factors (VEGFs) and their receptors (VEGF-Rs) contribute to tumor growth and metastasis by promoting angiogenesis. This policy examines the available evidence for the off-label use of bevacizumab in patients with advanced adenocarcinoma of the pancreas.

In the U.S., pancreatic adenocarcinoma is the tenth most common cancer in men and the fourth leading cause of cancer deaths in men and women. Only 7% of cases are detected at an early stage, and more than 90% of patients develop metastases. The 1-year survival rate is 25%; the 5-year survival rate is 6% overall, and 22% for those diagnosed early with only local disease. For patients with advanced, unresectable disease, the standard of care is gemcitabine. Gemcitabine is approved by the U.S. Food and Drug Administration (FDA) as single-agent first-line treatment for patients with locally advanced (stage II or stage III when surgery is not an option) or metastatic (stage IV) adenocarcinoma of the pancreas, including patients previously treated with 5-fluorouracil. Gemcitabine is sometimes given as part of combination therapy with erlotinib (Tarceva®) which is approved by the FDA for first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

Vascular endothelial growth factors (VEGFs) and their receptors (VEGF-Rs) contribute to tumor growth and metastasis by promoting angiogenesis, the growth of new vasculature. Without angiogenesis, nutrients, oxygen and other essential molecules reach malignant cells only by passive diffusion from pre-existing blood vessels, which would limit most tumors to diameters of several millimeters. Certain normal physiologic processes (e.g., embryonic development, menstruation, wound healing) require angiogenesis, and some non-cancer pathologic processes are linked to angiogenesis (e.g., macular degeneration, atherosclerosis, psoriasis).

Approximately 89% to 93% of pancreatic cancer patients have a VEGF mutation, which is associated with early recurrence after surgery, liver metastases, and poor prognosis. A VEGF mutation in tumors also correlates with tumor size. Bevacizumab, a vascular endothelial growth factor-specific angiogenesis inhibitor, is used in the treatment of a variety of cancers. Because vascular endothelial growth factor (VEGF) appears to play a role in pancreatic cancer, bevacizumab was considered a promising therapy. The results of 2 phase 2 trials seemed to indicate potential benefit.

Regulatory Status

Bevacizumab for the treatment of advanced pancreatic adenocarcinoma is not a U.S. Food and Drug Administration (FDA)-labeled indication.

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****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.*

Policy

Bevacizumab in advanced adenocarcinoma of the pancreas is considered investigational for all applications.

BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Bevacizumab in Advanced Adenocarcinoma of the Pancreas is covered

Not applicable.

Use of bevacizumab may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**
- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Bevacizumab in Advanced Adenocarcinoma of the Pancreas is not covered

Bevacizumab is considered **investigational** for treatment of advanced adenocarcinoma of the pancreas.

BCBSNC does not provide coverage for investigational services or procedures.

Bevacizumab is considered investigational when criteria are not met regarding FDA labeling **OR** strong endorsement/support by nationally recognized compendia, as stated under "When Bevacizumab in Advanced Adenocarcinoma of the Pancreas is covered."

Policy Guidelines

Treatment of advanced adenocarcinoma of the pancreas with bevacizumab is not a U.S. Food and Drug Administration (FDA) approved indication.

For individuals who have advanced pancreatic cancer and who receive bevacizumab, the evidence includes phase 2, and 3 randomized controlled trials (RCTs) and a BCBSA TEC Assessment. Relevant outcomes are overall survival, disease-specific survival, symptoms, change in disease status, quality of

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life, and treatment-related morbidity. Studies have failed to demonstrate that bevacizumab, either alone or in combination with another therapy, improves overall survival; data for progression free survival have not been consistent. Therefore, the evidence is insufficient to determine the effects of the technology on health outcomes.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), “Investigational (Experimental) Services.”

Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: C9257, J9035, S0353, S0354

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual – 5.01.18, 10/6/2009

Senior Medical Director - 2/2010

Specialty Matched Consultant Advisory Panel – 11/2010

BCBSA Medical Policy Reference Manual – 5.01.18, 11/10/2011

Specialty Matched Consultant Advisory Panel 11/2011

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 9/13/2012

Specialty Matched Consultant Advisory Panel – 12/2012

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 10/15/2013

Specialty Matched Consultant Advisory Panel – 11/2013

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 10/9/2014

Specialty Matched Consultant Advisory Panel – 11/2014

Medical Director review 3/2015

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 10/15/2015

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Specialty Matched Consultant Advisory Panel – 11/2015

Medical Director review 8/2016

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 10/13/2016

Specialty Matched Consultant Advisory Panel – 11/2016

Specialty Matched Consultant Advisory Panel – 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 11/9/2017

BCBSA Medical Policy Reference Manual [Electronic Version]– 5.01.18, 10/10/2018

Specialty Matched Consultant Advisory Panel – 11/2018

Policy Implementation/Update Information

- 3/2/10 New Evidence Based Guideline implemented. “Bevacizumab for patients with advanced adenocarcinoma of the pancreas is not recommended.” Senior Medical Director review 2/1/2010. (btw)

- 6/22/10 Policy Guideline Number(s) removed (amw)

- 12/21/10 Specialty Matched Consultant Advisory Panel review 11/29/2010. No changes to the intent of the guideline. (btw)

- 2/7/12 Added 6th bullet to Description section to indicate; “November 2011: FDA approval withdrawn for breast cancer.” Specialty Matched Consultant Advisory Panel review 11/30/2011. Reference added. (btw)

- 1/15/13 Specialty Matched Consultant Advisory Panel review 12/4/12. No change to policy intent. Reference added. (btw)

- 12/10/13 Specialty Matched Consultant Advisory Panel review 11/20/13. No change to policy. Reference added. (btw)

- 1/28/14 Description section updated. (btw)

- 12/9/14 Reference added. Specialty Matched Consultant Advisory Panel review 11/24/2014. No change to policy intent. (lpr)

- 7/28/15 Evidence based guideline converted to corporate medical policy. Medical Director review. Notification given 7/28/15 for effective date 10/1/15. (lpr)

- 12/30/15 Updated Policy Guidelines section. Reference added. Specialty Matched Consultant Advisory Panel review 11/18/2015. No change to policy statement. (lpr)

- 12/30/16 Updated Description and Policy Guidelines section. Specialty Matched Consultant Advisory Panel review 11/30/2016. Medical Director review 11/2016. Added HCPCS codes S0353 and S0354 to Billing/Coding section. No change to policy statement. Notification given 12/30/16 for effective date 4/1/17. (lpr)

- 12/8/17 Specialty Matched Consultant Advisory Panel review 11/29/2017. No change to policy statement. Reference added. (lpr)

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- 1/15/19 Minor changes made to Description section for clarity. Added code C9257 to Billing/Coding section. References added. Specialty Matched Consultant Advisory Panel review 11/28/2018. (krc)
- 2/12/19 Added the following statement to “When Covered” section: “Use of bevacizumab may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either: In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); OR In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.” Under “When Not Covered” section, added the statement “Bevacizumab is considered investigational when criteria are not met regarding FDA labeling **OR** strong endorsement/ support by nationally recognized compendia, as stated under “When Bevacizumab in Advanced Adenocarcinoma of the Pancreas is covered.” Added the following statements under “Policy Guidelines” section: “1) Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy, Investigational (Experimental) Services. 2) Please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia.” (krc)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.