



European Commission Approves Amgen's Vectibix® (panitumumab) As First-Line Treatment In Combination With FOLFIRI Chemotherapy For Metastatic Colorectal Cancer

April 6, 2015

Important Step Towards Increasing Treatment Options for Patients With This Serious Disease

THOUSAND OAKS, Calif., April 6, 2015 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced that the European Commission [approved](#) a new use of Vectibix® (panitumumab) as first-line treatment in combination with FOLFIRI for the treatment of adult patients with wild-type (WT) *RAS* metastatic colorectal cancer (mCRC). About half of the patients with mCRC have WT *RAS* tumors.¹ FOLFIRI, an irinotecan-based chemotherapy regimen, is frequently used in first-line colorectal cancer treatment in Europe.

"Colorectal cancer is the second most common cancer in Europe, and additional treatment options are important for patients and for physicians treating this serious disease," said Elliott M. Levy, M.D., senior vice president of Global Development at Amgen. "The European Commission approval of Vectibix as a first-line treatment in combination with FOLFIRI chemotherapy means physicians have another treatment option for adult patients with wild-type *RAS* metastatic colorectal cancer."

The new indication is based upon studies that evaluated Vectibix plus FOLFIRI in the first-line setting. Vectibix is now approved in the European Union (EU) for the treatment of adult patients with WT *RAS* mCRC: in first-line in combination with FOLFOX or FOLFIRI; in second-line in combination with FOLFIRI for patients who have received first-line fluoropyrimidine-based chemotherapy (excluding irinotecan); and as monotherapy after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.¹

Colorectal cancer is the third most common cancer worldwide, with approximately 1.2 million cases expected to occur globally.^{2,3} Colorectal cancer is the second most common cancer in Europe, with approximately 470,000 new cases each year;⁴ the highest incidence rate of colorectal cancer in the world. It is also the second greatest cause of cancer death in Europe following lung cancer, accounting for 12 percent of all cancer deaths.³

About Vectibix® (panitumumab)

In the EU, Vectibix is currently indicated for the treatment of adult patients with wild-type *RAS* mCRC:

- in first-line in combination with FOLFOX and FOLFIRI.
- in second-line in combination with FOLFIRI for patients who have received first-line fluoropyrimidine-based chemotherapy (excluding irinotecan).
- as monotherapy after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

Important EU Product Safety Information

Dermatologic related reactions, a pharmacologic effect observed with epidermal growth factor receptor (EGFr) inhibitors, are experienced with nearly all patients (approximately 90 percent) treated with Vectibix. The majority of dermatological reactions are mild to moderate in nature. In clinical studies, subsequent to the development of severe dermatological reactions (including stomatitis), infectious complications including sepsis, in rare cases leading to death, and local abscesses requiring incisions and drainage were reported. Patients who have severe dermatologic reactions or who develop worsening reactions whilst receiving Vectibix should be monitored for the development of inflammatory or infectious sequelae, and appropriate treatment promptly initiated.

Important U.S. Product Information

Vectibix is indicated for the treatment of patients with wild-type *KRAS* (exon 2 in codons 12 or 13) metastatic colorectal cancer (mCRC) as determined by an FDA-approved test for this use:

- As first-line therapy in combination with FOLFOX
- As monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy

Limitation of Use: Vectibix is not indicated for the treatment of patients with *RAS*-mutant mCRC or for whom *RAS* mutation status is unknown.

WARNING: DERMATOLOGIC TOXICITY

Dermatologic Toxicity: Dermatologic toxicities occurred in 90 percent of patients and were severe (NCI-CTC grade 3 or higher) in 15% of patients receiving Vectibix monotherapy.

Vectibix is not indicated for the treatment of patients with colorectal cancer that harbor somatic mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146) of either *KRAS* or *NRAS* and hereafter is referred to as "*RAS*".

Retrospective subset analyses across several randomized clinical trials were conducted to investigate the role of *RAS* mutations on the clinical effects of anti-EGFR-directed monoclonal antibodies (panitumumab or cetuximab). Anti-EGFR antibodies in patients with tumors containing *RAS* mutations resulted in exposing those patients to anti-EGFR related adverse reactions without clinical benefit from these agents.

Additionally, in Study 3, 272 patients with *RAS*-mutant mCRC tumors received Vectibix in combination with FOLFOX and 276 patients received FOLFOX alone. In an exploratory subgroup analysis, OS was shorter (HR = 1.21, 95% CI 1.01-1.45) in patients with *RAS*-mutant mCRC who received Vectibix and FOLFOX versus FOLFOX alone.

Progressively decreasing serum magnesium levels leading to severe (Grade 3-4) hypomagnesemia occurred in up to 7% (in Study 2) of patients

across clinical trials. Monitor patients for hypomagnesemia and hypocalcemia prior to initiating Vectibix treatment, periodically during Vectibix treatment, and for up to 8 weeks after the completion of treatment.

In Study 1, 4% of patients experienced infusion reactions and 1% of patients experienced severe infusion reactions (NCI-CTC grade 3-4).

Severe diarrhea and dehydration, leading to acute renal failure and other complications, have been observed in patients treated with Vectibix in combination with chemotherapy.

Fatal and non-fatal cases of interstitial lung disease (ILD) (1%) and pulmonary fibrosis have been observed in patients treated with Vectibix. Pulmonary fibrosis occurred in less than 1% (2/1467) of patients enrolled in clinical studies of Vectibix. In the event of acute onset or worsening of pulmonary symptoms, interrupt Vectibix therapy. Discontinue Vectibix therapy if ILD is confirmed.

Adverse Reactions

The most common adverse reactions (> 20%) of Vectibix are skin rash with variable presentations, paronychia, fatigue, nausea and diarrhea. The most frequently reported adverse reactions for Vectibix leading to withdrawal were general physical health deterioration and intestinal obstruction.

The most commonly reported adverse reactions (\geq 20%) in patients with wild-type *KRAS* mCRC receiving Vectibix (6 mg/kg every 2 weeks) and FOLFOX therapy (N = 322) in Study 3 were diarrhea, stomatitis, mucosal inflammation, asthenia, paronychia, anorexia, hypomagnesemia, hypokalemia, rash, acneiform dermatitis, pruritus, and dry skin. Serious adverse reactions (\geq 2% difference between treatment arms) in Vectibix-treated patients with wild-type *KRAS* mCRC were diarrhea and dehydration.

To see the full Vectibix Safety Information, visit www.vectibix.com.

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen, we or us) and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'s most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of April 6, 2015, and expressly disclaims any duty to update information contained in this news release.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us and our partners to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products (including products of our wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a

product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase common stock.

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