



FDA Grants Lilly's ALIMTA(R) (Pemetrexed for Injection) Third U.S. Approval

First-Line Chemotherapy Regimen Showed Clinically Relevant Survival Differences in Specific Histology Types of Advanced Non-Small Cell Lung Cancer

INDIANAPOLIS, Sept 29, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) announced today it received approval from the U.S. Food and Drug Administration (FDA) for the use of ALIMTA(R) (pemetrexed for injection), in combination with cisplatin, in the first-line treatment of locally-advanced and metastatic non-small cell lung cancer (NSCLC), for patients with nonsquamous histology. ALIMTA is not indicated for treatment of patients with squamous cell non-small cell lung cancer. NSCLC is the most common form of lung cancer, resulting in more than 180,000 new cases in the U.S. each year.(1,2)

NSCLC is defined as a group of histologies, that is, tumor types differentiated by cellular structure. Nonsquamous histology includes adenocarcinoma, large cell carcinoma and all other histologies except squamous cell carcinoma.

This marks the third U.S. indication for ALIMTA. In 2004, ALIMTA received consecutive approvals: first in combination with cisplatin as a treatment for patients with malignant pleural mesothelioma, whose disease is unresectable or who are otherwise not candidates for curative surgery, and then as a single agent for the second-line treatment of patients with locally-advanced or metastatic NSCLC after prior chemotherapy treatment.(3)

The ALIMTA approval in first-line advanced NSCLC for nonsquamous cell histology is based on a Phase III, open-label randomized study (1725 patients) that evaluated ALIMTA plus cisplatin (AC arm) versus GEMZAR(R) (gemcitabine HCl for injection) plus cisplatin (GC arm). The median survival was 10.3 months in the AC arm and 10.3 months in the GC arm [adjusted hazard ratio 0.94 (95% CI: 0.84, 1.05)]. The median progression-free survival was 4.8 and 5.1 months for the AC and GC arms, respectively [adjusted hazard ratio 1.04 (95% CI: 0.94, 1.15)]. The overall response rates were 27.1% and 24.7% for the AC and GC arms, respectively.

In a pre-specified analysis, the impact of NSCLC histology on overall survival was examined. Clinically relevant differences in survival according to histology were observed. In the nonsquamous cell NSCLC subgroup, the median survival was 11.0 and 10.1 months in the AC and GC groups, respectively [unadjusted hazard ratio 0.84 (95% CI: 0.74, 0.96)]. However, in the squamous cell histology subgroup, the median survival was 9.4 versus 10.8 months in the AC and GC groups, respectively [unadjusted hazard ratio 1.22 (95% CI: 0.99, 1.50)].(4) This unfavorable effect on overall survival associated with squamous cell histology observed with pemetrexed was also noted in a retrospective analysis of the single-agent trial of pemetrexed versus docetaxel in patients with stage III/IV NSCLC after prior chemotherapy.(5)

Patients treated with the ALIMTA regimen had less hematologic toxicity, fewer blood transfusions and decreased use of growth factors compared to those treated with the GEMZAR regimen. The most common adverse reactions (incidence greater than or equal to 20%) for ALIMTA in combination with cisplatin included vomiting, neutropenia, leukopenia, anemia, stomatitis/pharyngitis, thrombocytopenia and constipation.

Based on the same data, the FDA also approved a change to the second-line indication. ALIMTA is indicated as a single agent for the treatment of patients with locally-advanced or metastatic nonsquamous non-small cell lung cancer after prior chemotherapy. ALIMTA is not indicated for treatment of patients with squamous cell non-small cell lung cancer.

For full prescribing and safety information about ALIMTA, visit www.ALIMTA.com.

Notes to Editor

About Non-Small Cell Lung Cancer (NSCLC)

NSCLC is the most common type of lung cancer and represents 85 to 90 percent of all lung cancers.(6) NSCLC has five-tier staging, starting at 0 and rising to the severity of stage IV.(7) NSCLC can spread through the lymphatic system, penetrating the chest lining, ribs, and the nerves and blood vessels that lead to the arm. The liver, bones and brain are potential targets if the cancerous cells enter the bloodstream.

According to the World Health Organization (WHO) Cancer Report, lung cancer is the world's most common cancer and the

leading cause of cancer death for men and women. More than 1 million people die from lung cancer each year.(8)

NSCLC is defined as a group of histologies, that is, tumor types differentiated by cellular structure. The most common NSCLC histology types are squamous carcinoma, adenocarcinoma and large cell carcinoma.(9)

About Lilly Oncology, a Division of Eli Lilly and Company

For more than four decades, Lilly Oncology has been dedicated to delivering innovative solutions that improve the care of people living with cancer. Because no two cancer patients are alike, Lilly Oncology is committed to developing novel treatment approaches. Our quest is to develop a broad portfolio of tailored therapies that accelerate the pace and progress of cancer care. To learn more about Lilly's commitment to cancer, please visit www.LillyOncology.com.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs.

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ALIMTA(R) (pemetrexed for injection), Lilly
GEMZAR(R) (gemcitabine HCl for injection), Lilly

This press release contains forward-looking statements about the potential of ALIMTA and GEMZAR for the treatment of non-small cell lung cancer and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development, commercialization, and regulatory review. There is no guarantee that the products will receive additional regulatory approvals. There is also no guarantee that the products will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Important Safety Information for ALIMTA

ALIMTA is approved by the FDA in combination with cisplatin (another chemotherapy drug) for the initial treatment of advanced nonsquamous non-small cell lung cancer (NSCLC), a specific type of NSCLC. ALIMTA is not indicated for patients who have a different type of NSCLC called squamous cell.

ALIMTA is approved by the FDA as a single agent (used alone) for the treatment of patients with advanced nonsquamous non-small cell lung cancer (NSCLC), a specific type of NSCLC, after prior chemotherapy. ALIMTA is not indicated for patients who have a different type of NSCLC called squamous cell.

ALIMTA is a treatment for Malignant Pleural Mesothelioma (MPM), which is a cancer that affects the inside lining of the chest cavity. ALIMTA is given with cisplatin, another anti-cancer medicine (chemotherapy) when surgery is not an option.

Myelosuppression is usually the dose-limiting toxicity with ALIMTA therapy.

ALIMTA may not be appropriate for some patients. If you are allergic to ALIMTA, tell your doctor because you should not receive it. If you think you are pregnant, are planning to be pregnant, or are nursing, please tell your healthcare team. ALIMTA may harm your unborn or nursing baby. Your physician may advise you to use effective contraception (birth control) to prevent pregnancy while you are being treated with ALIMTA.

If you have liver or kidney problems, be sure to tell your doctor. Your dose of ALIMTA may have to be changed, or ALIMTA may not be right for you. There is a risk of side effects associated with ALIMTA therapy. ALIMTA can suppress bone marrow function. It is very important to take folic acid and vitamin B12 prior to and during your treatment with ALIMTA to lower your chances of harmful side effects.

Your healthcare professional will prescribe a medicine called a corticosteroid, which lowers your chances of getting skin reactions with ALIMTA. Ask your healthcare professional before taking medicines called NSAIDs (nonsteroidal anti-inflammatory drugs used to treat pain or swelling). Tell your doctor if you are taking other medicines, including prescription and non-prescription medicines, vitamins, and herbal supplements.

The most common side effects of ALIMTA when given alone or in combination with cisplatin, another chemotherapy drug, are low blood cell counts (red blood cells, white blood cells, and platelets); tiredness; stomach upset, including nausea, vomiting, and diarrhea; mouth, throat, or lip sores; loss of appetite; rash; and constipation.

Call your healthcare professional right away if you have a fever, chills, diarrhea, or mouth sores. These symptoms could mean you have an infection. These are not all of the side effects of ALIMTA. If you have any side effect that bothers you or that doesn't go away, be sure to talk with your healthcare professional.

You will have regular blood tests before and during your treatment with ALIMTA. Your doctor may adjust your dose of ALIMTA or delay your treatment based on the results of your blood test and on your general condition.

For more information about all of the side effects of ALIMTA, please talk with your healthcare team, see the complete Prescribing Information at www.ALIMTA.com, or call 1-800-545-5979.

Important Safety Information for GEMZAR

GEMZAR is indicated in combination with cisplatin (another type of chemotherapy) for the first-line treatment of patients with locally advanced (stage IIIA or stage IIIB) or metastatic (stage IV or cancer that has spread) non-small cell lung cancer for whom surgery is not possible.

Myelosuppression is usually the dose-limiting toxicity with GEMZAR therapy.

GEMZAR may not be appropriate for some patients. If you are allergic to GEMZAR, tell your doctor you should not receive it. GEMZAR can suppress bone marrow function. There have been rare reports of serious kidney or liver toxicity with GEMZAR treatment, sometimes fatal. Serious lung toxicity has also been reported, sometimes fatal. If you think you are pregnant, are planning to be pregnant, or are nursing, please tell your healthcare team. GEMZAR may harm your unborn or nursing baby.

If you have had prior kidney or liver problems or impairment, please tell your healthcare professional. GEMZAR may not be right for you. GEMZAR has not been shown to work in children. Tell your doctor if you are taking other medicines, including prescription and non-prescription medicines, vitamins, or herbal supplements.

There is a risk of side effects associated with GEMZAR therapy. The most common side effects are low blood cell counts (red blood cells, white blood cells, and platelets); fever; infection; hair loss; tiredness; nausea, vomiting, constipation, and diarrhea; rash; shortness of breath; muscle aches; and numbness or tingling in your toes or fingers. These are not all of the side effects of GEMZAR. If you have any side effect that bothers you or that doesn't go away, be sure to talk with your healthcare professional. Call your healthcare professional right away if you have fever or chills. These symptoms could mean you have an infection.

You will have regular blood tests before and during your treatment with GEMZAR. Your doctor may adjust your dose of GEMZAR or delay your treatment based on the results of your blood test and on your general condition.

For more information about all of the side effects of GEMZAR, please talk with your healthcare team, see the complete Prescribing Information at www.GEMZAR.com, or call 1-800-545-5979.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

(1) American Cancer Society, "What Is Non-Small Cell Lung Cancer?," October 15, 2007, American Cancer Society, http://www.cancer.org/docroot/CRI/content/CRI_2_4_1x_What_Is_Non-Small_Cell_Lung_Cancer.asp?rnav=crl, (February 21, 2008).

(2) American Cancer Society, "What Are the Key Statistics About Lung Cancer?," October 15, 2007, American Cancer Society, http://www.cancer.org/docroot/CRI/content/CRI_2_4_1x_What_Are_the_Key_Statistics_About_Lung_Cancer_15.asp?rnav=crl, (September 19, 2008).

(3) NOTE: The 2nd-line NSCLC indication was approved under 21 CFR 314.500 et seq (Subpart H - Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) using a surrogate endpoint.

(4) Scagliotti G, Vittorio P, et al. Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naive Patients With Advanced-Stage Non-Small-Cell Lung Cancer; *J Clin Oncol* 2008 26: 3543- 3551.

(5) Peterson P, Park K, et al. Is pemetrexed more effective in patients with non-squamous histology? A retrospective analysis of

a phase III trial of pemetrexed vs docetaxel in previously treated patients with advanced nonsmall cell lung cancer (NSCLC). Abstract P#6521, The European Cancer Conference 2007 (ECCO 14). European Journal of Cancer Supplements, Vol 5 No 4, Page 363.

(6) American Cancer Society, "What Is Non-Small Cell Lung Cancer?," October 15, 2007, American Cancer Society, http://www.cancer.org/docroot/CRI/content/CRI_2_4_1x_What_Is_Non-Small_Cell_Lung_Cancer.asp?rnav=cri, (February 21, 2008).

(7) American Cancer Society, "How Is Non-Small Cell Lung Cancer Staged?" October 15, 2007, American Cancer Society, www.cancer.org/docroot/CRI/content/CRI_2_4_3x_How_Is_Non-Small_Cell_Lung_Cancer_Staged.asp?rnav=cri, (February 21, 2008).

(8) World Health Organization, Gender in Lung Cancer and Smoking Research, Department of Gender, Women and Health, 2003, <http://www.who.int/gender/documents/en/lungcancerlow.pdf>.

(9) National Cancer Institute, "Non-Small Cell Lung Cancer Treatment (PDQ(R)) Health Professional Version," December 14, 2007, National Cancer Institute, www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/HealthProfessional/page2, (February 14, 2008).

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