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U.S. Department of Health & Human Services

U.S. Food and Drug Administration

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## News & Events

### FDA NEWS RELEASE

**For Immediate Release**: June 21, 2010
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**Consumer Inquiries**: 888-INFO-FDA

**FDA: Pfizer Voluntarily Withdraws Cancer Treatment Mylotarg from U.S. Market**

Pfizer Inc. today announced the voluntary withdrawal from the U.S. market of the drug Mylotarg (gemtuzumab ozogamicin) for patients with acute myeloid leukemia (AML), a bone marrow cancer. The company took the action at the request of the U.S. Food and Drug Administration after results from a recent clinical trial raised new concerns about the product's safety and the drug failed to demonstrate clinical benefit to patients enrolled in trials.

Mylotarg was approved in May 2000 under the FDA's accelerated approval program. This program allows the agency to approve a drug to treat serious diseases with an unmet medical need based on a surrogate endpoint – a laboratory measurement or a physical sign used as a substitute for a clinically meaningful endpoint that directly measures how a patient feels, functions, or survives.

Under accelerated approval, the company is required to conduct additional clinical trials after approval to confirm the drug's benefit. If those trials fail to confirm clinical benefit to patients, or if the company does not pursue the required confirmatory trials with due diligence, the FDA can withdraw the drug from the market using expedited procedures.

Mylotarg was approved to treat patients ages 60 years and older with recurrent AML who were not considered candidates for other chemotherapy. The initial approval was based on the surrogate endpoint of response rate (i.e., the percentage of patients whose leukemia decreased or disappeared in laboratory tests), observed in 142 patients with AML across three clinical trials.

A confirmatory, post approval clinical trial was begun by Wyeth (now Pfizer) in 2004. The trial was designed to determine whether adding Mylotarg to standard chemotherapy demonstrated an improvement in clinical benefit (survival time) to AML patients. The trial was stopped early when no improvement in clinical benefit was observed, and after a greater number of deaths occurred in the group of patients who received Mylotarg compared with those receiving chemotherapy alone.

At initial approval, Mylotarg was associated with a serious liver condition called veno-occlusive disease, which can be fatal. This rate has increased in the postmarket setting.

"Mylotarg was granted an accelerated approval to allow patient access to what was believed to be a promising new treatment for a devastating form of cancer," said Richard Pazdur, M.D., director, Office of Oncology Drug Products, part of FDA's Center for Drug Evaluation and Research. "However, a confirmatory clinical trial and years of postmarketing experience with the product have not shown evidence of clinical benefit in patients with AML."

As a result of the withdrawal, Mylotarg will not be commercially available to new patients. Patients who are currently receiving the drug may complete their therapy following consultation with their health care professional. Health care professionals should inform all patients receiving Mylotarg of the product's potential safety risks.

Following the withdrawal, any future use of Mylotarg in the United States will require submission of an investigational new drug application to FDA.

Mylotarg is manufactured by New York City-based Pfizer.

**For more information:**

- Pfizer: Mylotarg Withdrawal[1]
- FDA: Access to Investigational Drugs[2]
- FDA: Office of Oncology Drug Products[3]

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**Links on this page:**

1. http://www.pfizer.com
2. http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccesstoInvestigationalDrugs/default.htm
3. http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm091745.htm
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# Dear Healthcare Professional Letter

## Pfizer Prepares for Voluntary Withdrawal of U.S. New Drug Application and for Discontinuation of Commercial Availability of Mylotarg for Relapsed Acute Myeloid Leukemia

## IMPORTANT PRESCRIBING INFORMATION

June 21, 2010

Dear Healthcare Professional,

**Re: Mylotarg® (gemtuzumab ozogamicin for Injection) for patients with CD33+ acute myeloid leukemia (AML) in first relapse who are 60 years of age or older and who are not considered candidates for other cytotoxic chemotherapy.**

Pfizer would like to inform you of an important outcome for Mylotarg in the U.S. resulting from the failure of a required post-approval study to confirm the drug's clinical benefit. This study was stopped early based on interim results from the study showing no evidence of improved efficacy for patients treated with Mylotarg in addition to chemotherapy for previously untreated Acute Myeloid Leukemia (AML) (Southwest Oncology Group Web site. https://swog.org/Visitors/Spring10GpMtg/ROS1004.asp. Accessed June 17, 2010). The study also showed, in patients evaluable for induction toxicity, the fatal induction toxicity rate was significantly higher in the study arm containing Mylotarg combined with induction chemotherapy than the arm using chemotherapy alone (i.e. without Mylotarg).

After discussions with the U.S. Food and Drug Administration (FDA), Pfizer will be discontinuing commercial availability of Mylotarg and will be voluntarily withdrawing the New Drug Application (NDA) for Mylotarg in the United States effective October 15, 2010.

Patients who are currently taking Mylotarg and those patients who have been prescribed Mylotarg may continue their course of therapy, in consultation with their physicians. However, Pfizer recommends that no new patients in the U.S. be prescribed Mylotarg. Future use of Mylotarg for new patients in the U.S. will require physician submission of an Investigational New Drug (IND) application to the FDA.

Discussions are continuing with FDA to manage the orderly discontinuation of Mylotarg from commercial availability while ensuring continued access to the drug for your patients currently receiving the drug under the US labeled indication or through participation in approved clinical trials during this transition period up to October 15, 2010.

**Data Summary:**

PE MYT00006

Mylotarg® (gemtuzumab ozogamicin for Injection) was approved in the U.S. as a single agent treatment for patients with CD33 positive acute myeloid leukemia (AML) in first relapse who are 60 years of age or older and who are not considered candidates for other cytotoxic chemotherapy.

The approval of single agent Mylotarg in the U.S. was granted under FDA's accelerated approval regulations (Subpart H) based on overall response rate in three non-comparative studies. Accelerated approval is subject to the requirement to submit additional data to confirm clinical benefit. The required post approval study (SWOG Study S0106) combining Mylotarg with chemotherapeutic agents, daunorubicin and cytosine arabinoside, versus the same chemotherapy agent combination without Mylotarg in first-line AML patients under the age of 61 was conducted to confirm clinical benefit for Mylotarg. A total of 627 patients were enrolled in this study.

The decision to voluntarily withdraw the NDA is based on data from SWOG Study S0106 which failed to confirm clinical benefit. This study was stopped early based on interim results from the study showing no evidence of improved efficacy for patients treated with Mylotarg in addition to chemotherapy for previously untreated AML. Additionally, the fatal induction toxicity rate was significantly higher in the daunorubicin and cytosine arabinoside + Mylotarg arm (16/283=5.7% vs. 4/281=1.4%, P=0.01) (SWOG Update, April 15, 2010).

A second Phase 3 study (AML 15) enrolled over 1100 patients and evaluated the addition of Mylotarg to induction and/or consolidation chemotherapy in the first-line treatment of patients of ages 0-70 with AML. This study also failed to show improvement in relapse-free survival or overall survival in the intent to treat population with the addition of Mylotarg. Of note, the addition of Mylotarg to the induction chemotherapy treatment regimen did not add significant additional toxicity (Burnett et al., 2010, N. Engl. J. Med. submitted).

Although these studies did not confirm clinical benefit, it is Pfizer's view that the results do not directly impact the risk/benefit profile of Mylotarg in its approved indication as a single agent. While Pfizer is disappointed by the recent first line combination Phase 3 study results, we remain committed to provide Mylotarg in the near future to U.S. patients currently receiving the drug as agreed upon with the FDA.

For more information about Mylotarg, please contact Pfizer Medical Information at **1-800-438-1985 or www.pfizer.com**. We hope you find this information helpful in understanding this subject so you can continue to appropriately treat your patients.

Sincerely,

Signed

Pfizer Inc

PE MYT00006

For immediate release:
June 21, 2010

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**Pfizer Prepares For Voluntary Withdrawal Of U.S. New Drug Application And For Discontinuation Of Commercial Availability Of Mylotarg®**

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***Required Post-Marketing Study did not Confirm Clinical Benefit of Mylotarg***

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***Pfizer to Ensure Continued Access for Current Mylotarg Patients***

NEW YORK, N.Y., June 21 - Pfizer Inc. announced today that based on discussions with the U.S. Food and Drug Administration (FDA), it will be discontinuing commercial availability of Mylotarg® (gemtuzumab ozogamicin for Injection) (used for the treatment of relapsed acute myeloid leukemia (AML)) in the United States and that it will be voluntarily withdrawing the new drug application (NDA) for Mylotarg effective October 15, 2010.

The approval of single agent Mylotarg in the U.S. was granted under FDA's accelerated approval regulations based on overall response rate in three non-comparative studies and required submission of additional data to confirm clinical benefit. The required post-approval study (SWOG S0106) combining chemotherapy and Mylotarg did not demonstrate improved survival compared with chemotherapy alone in patients with previously untreated AML.

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Additionally, among all patients evaluable for early toxicity the fatal induction toxicity rate was significantly higher in subjects given the combination of standard induction chemotherapy and Mylotarg than in those treated with chemotherapy alone. After extensive discussions with the FDA, Pfizer has decided to withdraw the NDA effective October 15, 2010.

"We are disappointed that the study did not confirm the clinical benefit of Mylotarg. Our primary concern is for patients who suffer from AML, which remains a very serious and difficult-to-treat disease with limited treatment options. We advise patients to contact their physicians for further information," said Dr. Mace Rothenberg, senior vice president of clinical development and medical affairs for Pfizer Oncology Business Unit.

Patients who are currently taking Mylotarg and those patients who have been prescribed Mylotarg may continue their course of therapy, in consultation with their physicians. However, Pfizer recommends that no new patients in the U.S. be prescribed Mylotarg. Future use of Mylotarg for new patients in the U.S. will require physician submission of an Investigational New Drug (IND) application to the FDA.

The Company is also working with Health Authorities outside the U.S. and will keep patients, regulatory authorities, investigators and clinicians informed about FDA actions and appropriate next steps for Mylotarg.

For further information please contact Pfizer Medical Information at 1-800-438-1985 or at www.pfizer.com.

Mylotarg® (gemtuzumab ozogamicin for Injection) was approved in the U.S. as a single agent for patients with CD33 positive AML in first relapse who are 60 years of age or older and who are not considered candidates for other cytotoxic chemotherapy. Patients

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treated with Mylotarg receive one course of treatment that consists of two doses typically given 14 days apart.

AML is a relatively uncommon disease that affects approximately 13,000 new patients annually in the U.S. It is estimated that less than 2,500 patients receive Mylotarg annually in the U.S.

**SWOG S0106 Post Approval Study**

With the agreement of FDA, a Phase 3 randomized, comparative controlled trial (SWOG S0106) using Mylotarg in combination with other chemotherapeutic agents (daunorubicin and cytosine arabinoside) versus chemotherapy alone in first-line AML patients under the age of 61 was conducted to confirm clinical benefit for Mylotarg. A total of 627 patients were enrolled in this study. Although SWOG S0106 did not confirm the clinical benefit, the results do not directly impact the risk/benefit profile of Mylotarg in its approved indication as a single agent. Additionally, among all patients evaluable for early toxicity, the fatal induction toxicity rate was significantly higher in the daunorubicin and cytosine arabinoside + Mylotarg arm compared to the daunorubicin and cytosine arabinoside arm (16/283=5.7% vs. 4/281=1.4%, P=0.01).

**About Mylotarg® (gemtuzumab ozogamicin for Injection)**

Important safety information:

Mylotarg should be administered under the supervision of physicians experienced in the treatment of acute leukemia and in facilities equipped to monitor and treat leukemia patients.

There are no controlled trials demonstrating efficacy and safety using Mylotarg in combination with other chemotherapeutic agents. Therefore, Mylotarg should only be used as a single agent chemotherapy and not in combination chemotherapy regimens outside

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clinical trials. Severe myelosuppression occurs when Mylotarg is used at recommended doses.

Mylotarg administration can result in severe hypersensitivity reactions (including anaphylaxis), and other infusion-related reactions which may include severe pulmonary events. Infrequently, hypersensitivity reactions and pulmonary events have been fatal. In most cases, infusion-related symptoms occurred during the infusion or within 24 hours of administration of Mylotarg and resolved.

Mylotarg infusion should be interrupted for patients experiencing dyspnea or clinically significant hypotension. Patients should be monitored until signs and symptoms completely resolve. Discontinuation of Mylotarg (gemtuzumab ozogamicin for Injection) treatment should be strongly considered for patients who develop anaphylaxis, pulmonary edema, or acute respiratory distress syndrome. Since patients with high peripheral blast counts may be at greater risk for pulmonary events and tumor lysis syndrome, physicians should consider leukoreduction with hydroxyurea or leukapheresis to reduce the peripheral white count to below 30,000 per microliter prior to administration of Mylotarg.

Hepatotoxicity, including severe hepatic veno-occlusive disease (VOD), has been reported in association with the use of Mylotarg as a single agent, as part of a combination chemotherapy regimen, and in patients without a history of liver disease or hematopoietic stem-cell transplant (HSCT). (See WARNINGS and ADVERSE REACTIONS sections of the full Information.) Patients who receive Mylotarg either before or after HSCT, patients with underlying hepatic disease or abnormal liver function, and patients receiving Mylotarg in combinations with other chemotherapy may be at increased risk for developing severe VOD.

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Death from liver failure and from VOD has been reported in patients who receive Mylotarg (gemtuzumab ozogamicin for Injection). Physicians should monitor their patients carefully for symptoms of hepatotoxicity, particularly VOD. These symptoms can include: rapid weight gain, right upper quadrant pain, hepatomegaly, ascites, elevations in bilirubin and/or liver enzymes. However, careful monitoring may not identify all patients at risk or prevent the complications of hepatotoxicity.

Mylotarg may cause fetal harm when administered to a pregnant woman. The reported rates of Grades 3 and 4 thrombocytopenia, neutropenia, anemia, and bleeding were 99%, 98%, 47%, and 15%, respectively. Twenty-eight percent of patients experienced severe infections, including sepsis (16%) and pneumonia (7%).
The most common adverse events were fever (85%), chills (73%), nausea (70%), vomiting (63%), asthenia (44%), diarrhea (38%), abdominal pain (37%), headache (35%), stomatitis (32%), dyspnea (32%), epistaxis (31%), hypokalemia (31%), anorexia (29%), sepsis (25%), constipation (25%), local reaction (25%), nonspecific rash (22%), herpes simplex (22%), and neutropenic fever (21%).

Mylotarg can produce a postinfusion symptom complex of fever and chills and less commonly hypotension and dyspnea during the first 24 hours after administration. Patients should receive diphenhydramine 50 mg po and acetaminophen 650-1000 mg po one hour before Mylotarg (gemtuzumab ozogamicin for Injection) administration. Two additional doses of acetaminophen 650-1000 mg po every four hours may be given. Vital signs should be monitored during infusion and for four hours following infusion.

Please see full prescribing information at:
http://www.wyeth.com/content/showlabeling.asp?id=119.

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**About Pfizer Oncology**

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide. Our strong pipeline, one of the most robust in the industry, is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers, including breast, lung, prostate, sarcoma, melanoma, and various hematologic cancers. Pfizer Oncology has biologics and small molecules in clinical development and more than 200 clinical trials underway.

By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments, and licensing partners, Pfizer Oncology strives to cure or control cancer with breakthrough medicines, to deliver the right drug for each patient at the right time. For more information please visit www.Pfizer.com.

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