



## **NEW 200 MG VIAL FOR ELOXATIN® (oxaliplatin injection) OFFERS GREATER CONVENIENCE AND EFFICIENCY OF PREPARATION**

**Bridgewater, NJ -- August 27, 2007 --** Sanofi-aventis U.S. launched today a new 200 mg single-use vial of its chemotherapy treatment Eloxatin® (oxaliplatin injection) for patients who have adjuvant stage III colon cancer and advanced colorectal cancer, which is expected to offer more convenience, efficiency and safety in the preparation of the injectable cancer drug. Previously, Eloxatin® had been available in 50 mg and 100 mg single-use vials. The 200 mg vial will be available for order by cancer treatment clinics and hospitals nationwide starting the last week of August 2007 (NDC number: [NDC 0024-0592-40](#)).

Eloxatin®, used in combination with two other chemotherapy medications, 5-fluorouracil and leucovorin (5-FU/LV), is indicated for adjuvant treatment of stage III colon cancer patients who have undergone complete resection of the primary tumor. The indication is based on an improvement in disease-free survival, with no demonstrated benefit in overall survival after a median follow-up of four years. In addition, Eloxatin® with 5-FU/LV is approved to treat advanced carcinoma of the colon or rectum. Studies have shown that Eloxatin® in combination with 5-FU/LV can prolong survival, shrink tumors, and delay the progression of cancer in some patients with advanced colorectal cancer.

“We developed the Eloxatin® 200 mg vial to provide even greater convenience, safety and flexibility,” said Frank Clyburn, Vice President and head of the U.S. Internal Medicine and Oncology Business Units at sanofi-aventis. “In 2005, we launched the aqueous formulation of Eloxatin®, a significant advance in preparation efficiency from the lyophilized powder formulation. Now, with this innovation, we are taking another step forward, demonstrating sanofi-aventis’ continued commitment to improving cancer care.”

The 200 mg vial provides more convenience because of a single vial use for the majority of patient types and efficiency of preparation by handling a wide range of doses in less time to oncology pharmacists and nurses. The drug dosage is individualized to each patient on the basis of their body surface area. This is particularly important in administering Eloxatin® to the nearly 70 percent of patients with a body surface area of  $>1.76\text{m}^2$  who require at least 150 mg dosage of Eloxatin®. In the past, pharmacists and nurses had to open two to four vials to prepare the necessary amount of Eloxatin® for these patients. However, with the introduction of the 200 mg vial, only one vial will be needed, not only saving time and effort, but also reducing the risk for mishandling, breakage and the volume of biohazardous waste disposal. With the same carton size as the 50 mg and 100 mg vials, the new 200 mg vial fits easily in pharmacy storage compartments without taking additional space.

“We will be using the new Eloxatin® 200 mg vial in our center in addition to the 50 mg and 100 mg vials because it offers increased efficiency and safety in preparing the most frequently needed doses,” commented Timothy Tyler, PharmD, FCSHP, Director of Pharmacy Services Comprehensive Cancer Center, Desert Regional Medical Center, Palm Springs, CA. “Also, fewer vials reduce the number of hazardous device adaptors needed, resulting in added cost savings.”

### **About Colorectal Cancer**

Strides have been made in the management of colorectal cancer but it is still the second leading cause of cancer-related deaths in the United States.<sup>i</sup> [[American Cancer Society/What Are the Key Statistics about Colorectal Cancer/page 1/line 11](#)] At stage II, the cancer has grown through the wall of the colon or rectum but has not yet spread to nearby lymph nodes. In stage III, the cancer has invaded one or more of the local lymph nodes but has not spread to distant sites. Metastatic (advanced) colorectal cancer means that the cancer has spread to other nodes and/or organs in the body.<sup>ii</sup> [[American Cancer Society/Colorectal Cancer Staging/page 3/lines 21 - 22, 25-26 and page 4/lines 3-4](#)] American Cancer Society estimates that in 2007 there will be about 112,340 new cases of colon cancer and 41,420 new cases of rectal cancer in the United States.<sup>i</sup> [[American Cancer Society/What Are the Key Statistics about Colorectal Cancer/page 1/lines 9-10](#)]

### **About Eloxatin<sup>®</sup>**

#### **Indications and Usage**

Eloxatin<sup>®</sup> (oxaliplatin injection), used in combination with infusional 5-FU/LV, is indicated for

- Adjuvant treatment of stage III colon cancer patients who have undergone complete resection of the primary tumor. The indication is based on an improvement in disease-free survival, with no demonstrated benefit in overall survival after a median follow-up of 4 years
- Treatment of advanced carcinoma of the colon or rectum

#### **Clinical Safety Considerations**

**Eloxatin<sup>®</sup> should be administered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.**

**Anaphylactic-like reactions to Eloxatin<sup>®</sup> have been reported and may occur within minutes of Eloxatin<sup>®</sup> administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms, and discontinuation of Eloxatin<sup>®</sup> therapy may be required.**

- Eloxatin<sup>®</sup> should not be administered to patients with a history of known allergy to Eloxatin<sup>®</sup> or other platinum compounds. Hypersensitivity and anaphylactic/anaphylactoid reactions to Eloxatin<sup>®</sup> have been reported and were similar in nature and severity to those reported with other platinum compounds (ie, rash, urticaria, erythema, pruritus, and, rarely, bronchospasm and hypotension). These reactions occur within minutes of administration and should be managed with appropriate supportive therapy. Drug-related deaths from this reaction have been reported

- Eloxatin<sup>®</sup> may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised not to become pregnant while receiving Eloxatin<sup>®</sup>. It is not known whether Eloxatin<sup>®</sup> or its derivatives are excreted in human milk
- Eloxatin<sup>®</sup> has been associated with pulmonary fibrosis (<1% of study patients), which may be fatal. The combined incidence of cough and dyspnea was 7.4% (<1% grade 3, no grade 4) in the Eloxatin<sup>®</sup> plus 5-FU/LV arm compared to 4.5% (no grade 3, 0.1% grade 4) in the 5-FU/LV alone arm in the adjuvant colon cancer study. In this study, one patient died from eosinophilic pneumonia in the Eloxatin<sup>®</sup> combination arm. The combined incidence of cough, dyspnea, and hypoxia was 43% (7% grade 3 and 4) in the Eloxatin<sup>®</sup> plus 5-FU/LV arm compared to 32% (5% grade 3 and 4) in the irinotecan plus 5-FU/LV arm in patients with previously untreated colorectal cancer. In case of unexplained respiratory symptoms, Eloxatin<sup>®</sup> should be discontinued until pulmonary investigation excludes interstitial lung disease or pulmonary fibrosis
- Eloxatin<sup>®</sup> is associated with two types of primarily peripheral sensory neuropathy: an acute, reversible type of early onset and a persistent type (>14 days). In patients with advanced colorectal cancer paresthesias occurred in 77% (all grades) and 18% (grade 3/4) of previously untreated patients. In previously treated patients, acute neuropathy occurred in 56% (all grades) and 2% (grade 3/4) of patients; persistent neuropathy occurred in 48% (all grades) and 6% (grade 3/4) of patients. In patients with stage II and III colon cancer, paresthesia was seen in 92% (all grades) and 13% (grade 3/4) of patients; 21% (all grades), 0.5% (grade 3/4) had residual paresthesia at 18-month follow-up
- Hepatotoxicity, as evidenced in the adjuvant study by increase in transaminases and alkaline phosphatase was observed more commonly in the Eloxatin<sup>®</sup> combination arm. The incidence of increased bilirubin was similar on both arms. Changes noted on liver biopsies include: peliosis, nodular regenerative hyperplasia or sinusoidal alterations, perisinusoidal fibrosis and veno-occlusive lesions. Hepatic vascular disorders should be considered and, if appropriate, investigated in case of abnormal liver function test results or portal hypertension not explained by liver metastases.
- Monitoring of white blood cell count with differential, hemoglobin, platelet count and blood chemistries (including ALT, AST, bilirubin and creatinine) is recommended before each Eloxatin<sup>®</sup> cycle
- The safety and effectiveness of Eloxatin<sup>®</sup> plus 5-FU/LV in patients with renal impairment have not been evaluated. Since the primary route of platinum elimination is renal, this combination should be used with caution in patients with preexisting renal impairment. Clearance of these products may be decreased by coadministration of potentially nephrotoxic compounds, although this has not been specifically studied
- The incidence of diarrhea, dehydration, hypokalemia, leukopenia, fatigue and syncope were higher in patients  $\geq 65$  years old
- Extravasation may result in local pain and inflammation that may be severe and lead to complications, including necrosis. Injection site reaction, including redness, swelling and pain, has been reported
- There have been reports of prolonged prothrombin time and INR occasionally associated with hemorrhage in patients receiving Eloxatin<sup>®</sup> plus 5-FU/LV while on anticoagulants.



Patients receiving Eloxatin<sup>®</sup> plus 5-FU/LV and requiring oral anticoagulants may require closer monitoring

- The most common adverse reactions in patients with stage II or III colon cancer receiving adjuvant therapy were peripheral sensory neuropathy, neutropenia, thrombocytopenia, anemia, nausea, increase in transaminases and alkaline phosphatase, diarrhea, emesis, fatigue, and stomatitis. The most common adverse reactions in patients with advanced colorectal cancer were peripheral sensory neuropathy, fatigue, neutropenia, nausea, emesis, and diarrhea

For more information about Eloxatin<sup>®</sup> or for full prescribing information, including BOXED WARNING, visit [www.eloxatin.com](http://www.eloxatin.com).

### **About sanofi-aventis**

Sanofi-aventis is one of the world leaders in the pharmaceutical industry, ranking number one in Europe. Backed by a world-class R&D organization, sanofi-aventis is developing leading positions in seven major therapeutic areas: cardiovascular, thrombosis, oncology, metabolic diseases, central nervous system, internal medicine and vaccines. Sanofi-aventis is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

### **Forward Looking Statements**

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include financial projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future events, operations, products and services, and statements regarding future performance. Forward-looking statements are generally identified by the words “expects,” “anticipates,” “believes,” “intends,” “estimates,” “plans” and similar expressions. Although sanofi-aventis’ management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of sanofi-aventis, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in sanofi-aventis’ annual report on Form 20-F for the year ended December 31, 2006. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.

### **Contact:**

Noelle Boyd  
(908) 981-6489

[Noelle.boyd@sanofi-aventis.com](mailto:Noelle.boyd@sanofi-aventis.com)

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<sup>i</sup> American Cancer Society. What are the key statistics for colorectal cancer? Available at: [http://www.cancer.org/docroot/CRI/content/CRI\\_2\\_4\\_1X\\_What\\_are\\_the\\_key\\_statistics\\_for\\_colon\\_and\\_rectum\\_cancer.asp?sitearea=](http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_are_the_key_statistics_for_colon_and_rectum_cancer.asp?sitearea=). Accessed 4.16.07.

<sup>ii</sup> American Cancer Society. How is colorectal cancer staged? Available at: [http://www.cancer.org/docroot/CRI/content/CRI\\_2\\_4\\_3X\\_How\\_is\\_colon\\_and\\_rectum\\_cancer\\_staged.asp](http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_How_is_colon_and_rectum_cancer_staged.asp). Accessed 4.16.07.

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