Genentech
*A Member of the Roche Group*

March 21, 2011

**Subject: Availability of Blister-Packaged XELODA® (capecitabine) Tablets**

Dear Healthcare Professional:

The purpose of this letter is to inform you of the temporary availability of an alternative packaging configuration for XELODA® (capecitabine) tablets due to the voluntary recall of 13 manufacturing lots of the customary 120-count bottle currently approved for use in the United States. XELODA is an orally administered prodrug of 5-fluorouracil that has been approved by the Food and Drug Administration (FDA) for the treatment of patients with Dukes' C colon cancer, metastatic colorectal carcinoma, and metastatic breast cancer.

Genentech, a member of the Roche group, has received reports of a mothball-like odor and/or taste due to low levels of naphthalene and 1,4-dichlorobenzene associated with XELODA tablets packaged in bottles. It has been determined in consultation with the FDA that the low levels of these contaminants are not likely to constitute a safety concern to patients. However, naphthalene toxicity, including hemolysis, has been reported in the literature in patients with hereditary deficiency of glucose-6-phosphate dehydrogenase (G6PD), sickle cell anemia, and sickle cell trait. Until the source of the contaminants is isolated and Genentech has completed its corrective action, exercise caution and schedule frequent monitoring when administering XELODA tablets packaged in bottles to patients with known G6PD deficiency, sickle cell anemia or trait. As a matter of product quality, lots associated with the complaints have been recalled from wholesalers and pharmacies. It is important to note that this product recall does not include product return for physicians or patients.

Genentech is working closely with the FDA to ensure that the US supply of XELODA tablets remains uninterrupted, and the FDA has utilized regulatory enforcement discretion for the temporary importation of blister-packaged XELODA from the United Kingdom to the United States. There have been no reports of mothball-like odor and/or taste associated with blister packs. In addition, the Consumer Product Safety Commission (CPSC) has granted a 3-month stay of enforcement to allow importation and distribution of blister-packaged XELODA that is not child-resistant. You may contact the Toll-free Consumer Hotline for CPSC at **1-800-638-2772** for further information.

**Please see the enclosed XELODA U.S. Prescribing Information for Boxed WARNING and Important Safety Information.**

Genentech will be temporarily supplying blister-packaged XELODA 500 mg tablets in addition to the customary 120-count bottles currently approved for use in the US. The blister-packaged XELODA 500 mg tablets are expected to be available by late March 2011. There may be an overlap of time when both configurations are available.

XELODA packaged in a blister configuration is approved and available in countries outside of the US, including countries of the European Union such as the United Kingdom (UK). XELODA tablets supplied in the blister packaged configuration are the same formulation, dosage, and pill shape as XELODA tablets supplied in bottles.

It is important to note that blister-packaged XELODA will include the UK Package Leaflet (intended for UK patients). In addition, unlike the current FDA-approved XELODA packaging (bottles with child-resistant closures), blister-packaged XELODA is NOT child-resistant.

If you are dispensing blister-packaged XELODA to patients:

- Please inform your patients that XELODA is being supplied temporarily as blister-packaged tablets due to the recall
- Please remove the UK leaflet and provide a copy of the US Patient Package Insert (USPPI). Genentech has provided copies of the USPPI, which are attached to this letter. You may also download the USPPI at **www.gene.com/gene/products/information/xeloda/pdf/ppi.pdf**
- A warning sticker has been applied to the carton to remind you that blister-packaged XELODA is not child-resistant
- Please notice that a new NDC number has been stickered on the blister-packaged XELODA carton in order to facilitate inventory management and distribution by wholesalers and dispensing by pharmacies

The images on Page 3 highlight the differences between the US packaged XELODA in bottles and UK packaged XELODA in blister packs.

If you or your patients have any further questions or require additional information, please contact the Genentech Resource Center at **1-877-GENENTECH.**

Additional information regarding this action can be found at **http://www.gene.com/gene/products/information/xeloda** and on the FDA website at **http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm**

**Please see the enclosed XELODA U.S. Prescribing Information for Boxed WARNING and Important Safety Information.**

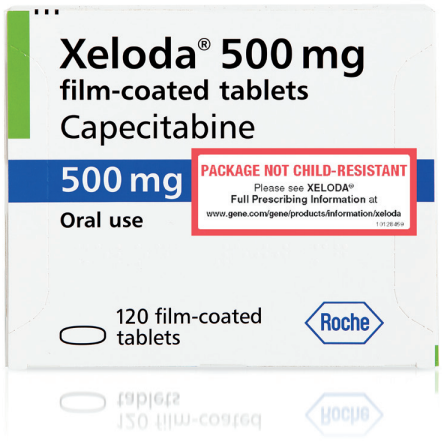
As always, you are encouraged to report side effects associated with the use of XELODA to Genentech at **1-888-835-2555.** Alternatively, such information may be reported to FDA's MedWatch Safety Information and Adverse Event Reporting Program, either online at **www.fda.gov/medwatch,** by telephone (**1-800-FDA-1088**), by facsimile (**1-800-FDA-0178**), or by mail using the MedWatch Form FDA 3500 (FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787).

Sincerely,

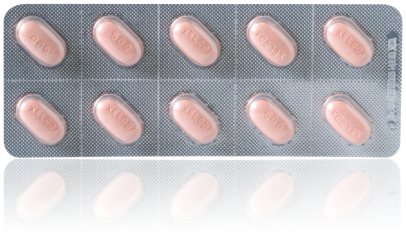
Chris Bowden
Vice President
Product Development Oncology
Genentech, Inc.

Enclosure


**Current Bottle**
**500 mg**
NDC Code:
0004-1101-50




**New Look**
**500 mg Box**
NDC Code:
0004-1101-75



**New**
**Blister Pack**
NDC Code:
0004-1101-75

**Please see the enclosed XELODA U.S. Prescribing Information for Boxed WARNING and Important Safety Information.**

The following safety information is excerpted from the XELODA Prescribing Information enclosed with this letter.

**INDICATIONS**

XELODA is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred. XELODA was non-inferior to 5-fluorouracil and leucovorin (5-FU/LV) for disease-free survival (DFS). Although neither XELODA nor combination chemotherapy prolongs overall survival (OS), combination chemotherapy has been demonstrated to improve disease-free survival compared to 5-FU/LV. Physicians should consider these results when prescribing single-agent XELODA in the adjuvant treatment of Dukes' C colon cancer.

XELODA is indicated as first-line treatment of patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred. Combination chemotherapy has shown a survival benefit compared to 5-FU/LV alone. A survival benefit over 5-FU/LV has not been demonstrated with XELODA monotherapy. Use of XELODA instead of 5-FU/LV in combinations has not been adequately studied to assure safety or preservation of the survival advantage.

XELODA monotherapy is indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, eg, patients who have received cumulative doses of 400 mg/$m^2$ of doxorubicin or doxorubicin equivalents. Resistance is defined as progressive disease while on treatment, with or without an initial response, or relapse within 6 months of completing treatment with an anthracycline-containing adjuvant regimen.

XELODA in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.

**Please see the enclosed XELODA U.S. Prescribing Information for Boxed WARNING and Important Safety Information.**

## BOXED Warning and Important Safety Information

**Boxed Warning**

**Warfarin Interaction - Coagulopathy**

- Patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulant therapy should have their anticoagulant response (INR or prothrombin time) monitored frequently in order to adjust the anticoagulant dose accordingly.
- A clinically important XELODA-Warfarin drug interaction was demonstrated in a clinical pharmacology trial.
- Altered coagulation parameters and/or bleeding, including death, have been reported in patients taking XELODA concomitantly with coumarin-derivative anticoagulants such as warfarin and phenprocoumon.
- Clinically significant increases in prothrombin time (PT) and INR have been observed in patients who were stabilized on anticoagulants at the time XELODA was introduced. These events occurred within several days and up to several months after initiating XELODA therapy, and infrequently within 1 month after stopping XELODA. These events occurred in patients with and without liver metastases.
- Age greater than 60 and a diagnosis of cancer independently predispose patients to an increased risk of coagulopathy.

### Contraindications

- XELODA is contraindicated in patients with known hypersensitivity to capecitabine or to any of its components or to 5-fluorouracil. XELODA is also contraindicated in patients with known dihydropyrimidine dehydrogenase (DPD) deficiency, or severe renal impairment.

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