Genentech
A Member of the Roche Group
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South San Francisco, CA 94080

IMPORTANT DRUG WARNING

Subject: **Association of XELODA® (capecitabine) with Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)**

January 2014

Dear Healthcare Provider,

Genentech Inc., a Member of the Roche Group, in consultation with the United States Food and Drug Administration (FDA), would like to inform you of the risk of serious cutaneous adverse reactions in patients taking XELODA® (capecitabine):

Summary

- Serious cutaneous skin reactions such as Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported in patients treated with XELODA. Some of these reactions have been fatal.
- SJS and TEN must be distinguished from other dermatological conditions, including Hand-Foot Syndrome. If the diagnosis of SJS or TEN is confirmed, XELODA treatment should be permanently discontinued.

Further information on the safety concern and recommendations

SJS and TEN are considered to represent variants within a continuous spectrum of skin disorders characterized by generalized tender erythematous maculae progressing to blisters and denudation, and often preceded by photophobia, symptoms of upper respiratory tract infection and fever. There is significant morbidity and mortality associated with severe skin reactions, especially for SJS and TEN. Morbidity and mortality may be reduced in patients when the suspect drug is stopped early compared to continuation of the drug after the development of blisters.

- Healthcare providers should be aware that severe cutaneous adverse reactions can occur in patients receiving XELODA. XELODA should be permanently discontinued in patients who experience a severe skin reaction.
- Patients should be informed that XELODA treatment may cause severe skin reactions and be advised to discontinue XELODA and seek medical advice at the first sign of a serious skin reaction.

Genentech will work closely with the FDA to update the Prescribing Information (PI) for XELODA. Once approved by the FDA, the revised XELODA PI will be available on www.gene.com. Full prescribing and adverse event information for XELODA can be found in the currently authorized PI available via http://www.gene.com/download/pdf/xeloda_prescribing.pdf.

Therapeutic indications

Colorectal Cancer

- 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). Physicians should consider results of combination chemotherapy trials, which have shown improvement in DFS and OS, 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.

Breast Cancer

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

Boxed Warning and Contraindications

Patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulants such as warfarin and phenprocoumon should have their anticoagulant response (INR or prothrombin time) monitored frequently in order to adjust the anticoagulant dose accordingly. Altered coagulation parameters and/or bleeding, including death, have been reported during concomitant use.

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

Call for Reporting

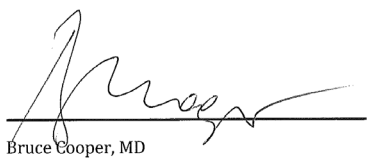
Healthcare providers should report any serious adverse events suspected to be associated with the use of XELODA to Genentech at 1-888-835-2555 or to the FDA's MedWatch reporting system by phone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), online (https://www.accessdata.fda.gov/scripts/medwatch/) or mailed, using the MedWatch form FDA 3500, to the FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville, MD 20852-9787.

Company Contact Point

Should you have any questions regarding the use of XELODA, please feel free to contact Genentech Medical Information/Communications Department at 1-800-821-8590.

Sincerely,

Genentech, a Member of the Roche Group



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