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Important Safety Information

Dear Healthcare Professional:

OSI Pharmaceuticals, Inc. and Genentech, Inc. would like to inform you of new safety information regarding the use of Tarceva® (erlotinib) in patients with hepatic impairment as well as other safety-related updates to the Tarceva prescribing information. Patients with hepatic impairment should be monitored closely during therapy with Tarceva, and dosing should be interrupted or discontinued if changes in liver function are severe.

Tarceva monotherapy is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen; Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable, or metastatic pancreatic cancer.

The new safety information comes from a pharmacokinetic (PK) study in patients with advanced solid tumors and moderate hepatic impairment according to the Child-Pugh criteria. In this study, 10 of the 15 patients died on treatment or within 30 days of the last Tarceva dose. Although 8 of these patients died from progressive disease, one patient died from hepatorenal syndrome and one patient died from rapidly progressing liver failure. Six out of the 10 patients who died had baseline total bilirubin > 3 x ULN suggesting severe, rather than moderate, hepatic impairment, highlighting the limitations of utilizing the Child-Pugh criteria in an oncology patient population. All patients had hepatic impairment due to advanced cancer with liver involvement such as hepatocellular carcinoma, cholangiocarcinoma, or liver metastases.

To communicate this important safety information, the following changes have been made to the labeling.

WARNINGS

- The previous **PRECAUTION** section, entitled **Patients with Hepatic Impairment,** has been updated and this section has been moved to the WARNINGS section. This section indicates that "Treatment with TARCEVA should be used with extra caution in patients with total bilirubin > 3 x ULN. Patients with hepatic impairment (total bilirubin > ULN or Child-Pugh A, B and C) should be closely monitored during therapy with TARCEVA. TARCEVA dosing should be interrupted or discontinued if changes in liver function are severe such as doubling of total bilirubin and/or tripling of transaminases in the setting of pretreatment values outside normal range."

- The previous **PRECAUTION** section, entitled **Hepatotoxicity,** has been updated and this section has been moved to the **WARNINGS** section. The section indicates that "TARCEVA dosing should be interrupted or discontinued if total bilirubin is greater than 3 x ULN and/or transaminases are greater than 5 x ULN in the setting of normal pretreatment values."

- The previous **PRECAUTION** section, entitled **Renal Failure,** has been updated to include the term "hepatorenal syndrome" and this section was moved to the **WARNINGS** section.

DOSAGE AND ADMINISTRATION

The **DOSAGE AND ADMINISTRATION** section of the labeling has been updated to reflect the dose interruption and/or discontinuation instructions included in the **WARNINGS** section, described above.

Our primary concern is the safety and well-being of patients who receive Tarceva treatment. For any questions, or to report adverse events suspected to be associated with the use of Tarceva, please call 1-877-TARCEVA (1-877-827-2382). Alternatively, adverse event information may be reported to the FDA's MedWatch reporting system by phone at **1-800-FDA-1088,** by facsimile at 1-800-FDA-0178, by mail to MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20857, or by the internet at http://www.fda.gov/medwatch/index.html.

The complete wording of these changes can be found in the enclosed copy of the full prescribing information for Tarceva.

Sincerely,

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and Clinical Development
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