



September 2010

Subject: Important Changes in the XENICAL[®] (orlistat) Prescribing Information – Severe liver injury with hepatocellular necrosis or acute hepatic failure has been reported in patients treated with XENICAL, with some of these cases resulting in liver transplant or death

Dear Healthcare Professional:

Genentech would like to inform you of updated and new important safety information about rare cases of severe liver injury that have been reported with the use of XENICAL (orlistat).

This new important safety information has been included in the XENICAL prescribing information under the **General** subsection of the **PRECAUTIONS** section and under the **Other Clinical Studies or Postmarketing Surveillance** subsection of the **ADVERSE REACTIONS** section. This important new safety information in the XENICAL prescribing information is described below.

REVISIONS TO PRODUCT LABELING REGARDING LIVER INJURY:

PRECAUTIONS

The **General** subsection of **PRECAUTIONS** includes the following information regarding hepatic safety:

There have been rare postmarketing reports of severe liver injury with hepatocellular necrosis or acute hepatic failure in patients treated with orlistat with some of these cases resulting in liver transplant or death. Patients should be instructed to report any symptoms of hepatic dysfunction (anorexia, pruritus, jaundice, dark urine, light colored stools, or right upper quadrant pain) while taking orlistat. When these symptoms occur, orlistat and other suspected medications should be discontinued immediately and liver function tests and ALT and AST levels obtained.

ADVERSE REACTIONS

The **Other Clinical Studies or Postmarketing Surveillance** subsection of **ADVERSE REACTIONS** includes the following updated and new text regarding hepatic safety:

There have been reports of hepatic failure observed with the use of XENICAL in post-marketing surveillance with some of these cases resulting in liver transplant or death.

Background

On August 24, 2009, the U.S. Food and Drug Administration (FDA) published information about an ongoing safety review of orlistat and hepatotoxicity. On May 26, 2010, the FDA notified healthcare professionals and patients that it had completed the review and approved a revised label for XENICAL to include this new safety information. Information related to the FDA review may be accessed via the following link:

<http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm180076.htm>

Important Information About XENICAL (orlistat)

Indications:

XENICAL is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet. XENICAL is also indicated to reduce the risk for weight regain after prior weight loss. XENICAL is indicated for obese patients with an initial body mass index (BMI) ≥ 30 kg/m² or ≥ 27 kg/m² in the presence of other risk factors (eg, hypertension, diabetes, dyslipidemia).

Important Safety Information:

The most commonly observed adverse events (incidence of ≥ 5 and twice that of placebo) were oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation and fecal incontinence, particularly after meals containing more fat than recommended. These and other commonly observed events were generally mild and transient, but for some people they may continue for 6 months or longer.

XENICAL is contraindicated in patients with chronic malabsorption syndrome or cholestasis. Organic causes of obesity, such as hypothyroidism, should be excluded before prescribing XENICAL. XENICAL is not recommended for use during pregnancy and should not be taken by nursing mothers.

To reduce the chance of a drug interaction resulting in reduced levels of cyclosporine, XENICAL and cyclosporine should not be taken within 2 hours of each other. More frequent monitoring of cyclosporine levels should be considered in patients taking both drugs (see **WARNINGS**).

Because XENICAL has been shown to reduce the absorption of some fat-soluble vitamins and beta-carotene, patients should be counseled to take a multivitamin supplement containing fat-soluble vitamins once a day at least 2 hours before or after taking XENICAL. There have been rare postmarketing reports of severe liver injury with hepatocellular necrosis or acute hepatic failure in patients treated with orlistat.

Please see the enclosed XENICAL complete Prescribing Information, which includes the updated and new information regarding the hepatic safety of orlistat.

If you have any questions or require additional information regarding the use of XENICAL, please contact our Medical Communications Group at 1-800-821-8590 from 5:30 AM to 4:00 PM Pacific Time, Monday through Friday.

Sincerely,



Hal Barron, MD
Executive Vice President
Head, Global Development
Chief Medical Officer

Enclosure: Complete Prescribing Information for XENICAL[®] (orlistat)