SIDE BY SIDE COMPARISON OF U.S. AND EUROPEAN LABELS FOR CYMBALTA

European Medicines Agency Label (2006)	United States FDA Label (2009)
Discontinuation of treatment Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8). In clinical trials adverse events seen on abrupt treatment discontinuation occurred in approximately 45% of patients treated with Cymbalta and 23% of patients taking placebo. The risk of withdrawal symptoms seen with SSRI's and SNRI's may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. The most commonly reported reactions are listed in section 4.8. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that duloxetine should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks, according to the patient's needs (see section 4.2). *Section 4.8 states:* Discontinuation of duloxetine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia or electric shock-like sensations, particularly in the head), sleep disturbances (including insomnia and intense dreams), fatigue, somnolence, agitation or anxiety, nausea and/or vomiting, tremor, headache, myalgia, irritability, diarrhea, hyperhydrosis and vertigo are the most commonly reported reactions.	**Discontinuation of Treatment With Cymbalta** Discontinuation symptoms have been systematically evaluated in patients taking duloxetine. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at a rate greater than or equal to 1% and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis and vertigo. During marketing of other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, some have been reported to be severe. Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate [see Dosage and Administration (2.4)]

European Medicines Agency Label (2006) *[Section by Section Comparison]*	**United States FDA Label (2009)** *[Section by Section Comparison]*
"Withdrawal symptoms when treatment is discontinued **are common**, particularly if discontinuation is abrupt (see section 4.8). "Discontinuation of duloxetine (particularly when abrupt) **commonly leads to withdrawal symptoms**."	*Nothing about withdrawal being common.*
"In clinical trials adverse events seen on abrupt treatment discontinuation occurred **in approximately 45%** of patients treated with Cymbalta and 23% of patients taking placebo."	"Following abrupt or tapered discontinuation in placebo-controlled clinical trials, **the following symptoms occurred at a rate greater than or equal to 1%** and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, fatigue, paresthesia, vomiting, irritability, nightmares, insomnia, diarrhea, anxiety, hyperhidrosis and vertigo."
"The risk of withdrawal symptoms seen with SSRI's and SNRI's may be dependent on several factors including **the duration and dose of therapy and the rate of dose reduction.**"	*Nothing about dose or duration and its correlation with withdrawal.*
"Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They **usually occur within the first few days of discontinuing treatment**, but there have been very rare reports of such symptoms in patients who have **inadvertently missed a dose.**"	*Nothing about when withdrawal will likely occur upon discontinuation.* *Nothing about the risks of missing doses.*
"Generally these symptoms are self-limiting and usually resolve **within 2 weeks**, though in some individuals they **may be prolonged (2-3 months or more)**."	*Nothing about potential duration of withdrawal.*

"It is therefore advised that duloxetine should be gradually tapered when discontinuing treatment over a period of **no less than 2 weeks**, according to the patient's needs (see section 4.2)."	A gradual reduction in the dose rather than abrupt cessation **is recommended whenever possible.** If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then **resuming the previously prescribed dose may be considered.** Subsequently, the physician may continue decreasing the dose but at a more gradual rate [see Dosage and Administration (2.4)] *Nothing about a tapering regimen lasting no less than 2 weeks.*