Abnormal Bleeding—SSRIs and SNRIs, including duloxetine, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case series and case-controlled) have described a possible relationship between use of drugs that interfere with serotonin metabolism and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRIs and SNRIs have been reported from hemorrhages, hematomas, epistaxis, and postpartum hemorrhage.

Patients should be cautioned about the risk of bleeding associated with the concomitant use of NSAIDs, aspirin, or other drugs that affect coagulation.

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 rate at least twice the rate in placebo-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, fatigue, paresthesia, asthenia, irritability, anxiety, somnolence, hypomania, and vertigo. Discontinuation of other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), have been spontaneously reported despite adverse events occurring during discontinuation of these agents when abrupt discontinuation followed a dose reduction. No active substance is available after abrupt discontinuation of Cymbalta. Abrupt discontinuation of serotonin reuptake inhibitors may precipitate serotonin syndrome.

Patients should be monitored for these symptoms when discontinuing treatment with Cymbalta. A gradual reduction in the dose rather than abrupt cessation is recommended when discontinuing Cymbalta. When abrupt discontinuation of Cymbalta is required, the dose should be reduced by at least 30% per week. The dose should not be reduced by more than 50% per week. The dose should be tapered gradually to a level at which the patient can be tapered more slowly to the lowest possible dose.

Action of Mania/Hypomania—In placebo-controlled trials in patients with major depressive disorder, activation of mania or hypomania was reported in 0.1% (2/2125) of duloxetine-treated patients compared to 0.2% (1/708) of placebo-treated patients. No activation of mania or hypomania was reported in DPHD or GAQ placebo-controlled trials. Action of mania or hypomania has been reported in a small proportion of patients with mood disorders who were treated with other marketed drugs effective in the treatment of major depressive disorder. As with these other agents, Cymbalta should be used cautiously in patients with a history of a seizure disorder.

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