

## Predictors of Duloxetine Treatment Persistence for Patients with Major Depressive Disorder

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### ABSTRACT

**OBJECTIVES:** Early discontinuation of antidepressant therapy is associated with relapse and increased costs. This exploratory study examined demographical and pretreatment clinical predictors of duloxetine (Eli Lilly and Company, Indianapolis, IN) treatment persistence in patients treated in real-world clinical settings.

**STUDY DESIGN:** Using a large US managed-care claims database (PharMetrics Integrated Outcomes Database; PharMetrics Inc., Watertown, MA), study subjects were individuals aged 18 to 64 years who initiated duloxetine treatment between April 2005 and March 2006, had  $\geq 1$  claim associated with major depressive disorder diagnosis, and had continuous insurance coverage 6 months before and 12 months after initiation of duloxetine therapy. Treatment persistence was defined as continuous duloxetine treatment without a 30-day gap for  $\geq 3$  months. Chi-squared tests and logistic regression analysis were used to examine predictors of persistence.

**RESULTS:** Among 9148 patients (74.1% female; mean age 45.6 years) who initiated duloxetine treatment, 63.5% stayed on the medication for  $\geq 3$  months. Logistic regression analysis showed that an initial dose  $\geq 60$  mg (odds ratio [OR] 1.43), older age groups (OR  $\geq 1.49$ ), and venlafaxine XR (OR 1.85) or selective serotonin reuptake inhibitor (OR 1.59) use in the prior 6 months were significantly associated with increased odds of treatment persistence, whereas prior benzodiazepine use (OR 0.86), comorbid alcohol dependence (OR 0.75), drug dependence (OR 0.76), and Parkinson disease (OR 0.36) were associated with decreased odds of treatment persistence. Findings were essentially unchanged with classification and regression tree analysis.

**CONCLUSION:** The results suggest that multiple demographic and clinical variables are associated with treatment persistence of duloxetine therapy. The findings may have important implications for clinicians to take actions to prevent early therapy discontinuation.

**KEYWORDS:** Depression; Medication non-adherence

**Major** depressive disorder (MDD) is a severe, recurring illness affecting about 121 million people worldwide.<sup>1</sup> People with MDD experience depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, poor concentration, and risk of suicide.<sup>1</sup> Depression frequently is treated with selective serotonin reuptake inhibitors (SSRIs). These medications have response rates of 50%-60% in daily practice as a first antidepressant.<sup>2</sup>

For antidepressant treatment to be successful, patients must continue medications long enough to produce optimal benefit and reduce the likelihood of relapse.<sup>3</sup> Adherence to treatment guidelines tends to prevent recurrence/relapse for at least 2 years after initiation of treatment.<sup>4</sup> Due to adverse events or insufficient efficacy, it is common for patients to discontinue medications and switch to other medications.<sup>2</sup> It has been reported that 42.4% of patients discontinued antidepressant treatment during the first 30 days, and only 27.6% continued antidepressant treatment for more than 90 days.<sup>5</sup> Way and colleagues<sup>6</sup> found that 10%-18% of patients taking fluoxetine, paroxetine, and sertraline switched to a second antidepressant, and of those who switched, 49%-52% switched to a drug of the same class. In a comparative study of second-generation antidepressants (SSRIs and serotonin-norepinephrine reuptake inhibitors), investigators found that adherence rates ranged from 37.2% (escitalopram) to 48.7% (duloxetine), and the average time of treatment persistence ranged from 95 days (escitalopram) to 107 days (duloxetine) in the 6 months after treatment initiation.<sup>7</sup>

Patient-related, disease-related, medication-related, physician-related, and psychosocial factors may influence a patient's adherence to drug therapy.<sup>8-10</sup> Not much is known about the factors that are related to antidepressant persistence or discontinuation. In one study, early antidepressant discontinuation was not significantly related to patient characteristics such as age, sex, race, education, or employment status.<sup>3</sup> In contrast, another study reported that antidepressant discontinuation during the first 30 days of treatment was more common among Hispanics, patients with fewer than 12 years of education, patients with low family incomes, and patients who lacked private health insurance.<sup>5</sup>

It has been shown that patients who switch antidepressant drug classes have higher all-cause health care costs and higher depression-related costs than patients who do not switch, but total costs decrease after switching to a different drug class.<sup>11</sup> A separate study<sup>12</sup> reported that medical costs—without pharmacy costs—were lower for patients remaining on antidepressant drugs for at least 90 continuous days. Considering the costs associated with switching antidepressant medications, information on factors that are associated with treatment persistence (and avoidance of switching) would be of value to those who make medical decisions.

Duloxetine is a serotonin-norepinephrine reuptake inhibitor approved for treating patients with MDD and is frequently chosen as a second-line agent, as well as a first-line agent for some patients.<sup>13</sup> Little is known about treatment patterns for duloxetine in the real-world clinical setting. Identifying differences in treatment history and characteristics of patients with MDD associated with persistence on duloxetine may help practitioners determine which patients are likely to maintain their prescribed treatment over time. The objective of this analysis was to use retrospective claims data to assess the impact of demographics, initial dose, prior medications, and comorbidities on duloxetine treatment persistence for patients with MDD. Treatment persistence was defined as at least 3 months of continuous duloxetine treatment after initiation.

## METHODS

### Database and Sample Selection

Data were extracted from the PharMetrics Integrated Outcomes Database (PharMetrics Inc., Watertown, MA), a private payer insurance claims database that includes medical and pharmacy claims for more than 58 million commercially insured patients and more than 70 different managed-care organizations across the US. Patients in the database are representative of the national commercially insured population on a variety of demographic measures. The database encompasses comprehensive records on members'

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