1. Abstract

Title: Strattera patient exposures and adherence in the United Kingdom, Germany, the Netherlands, and Sweden: 2016 Bi-annual assessment report (B4Z-MC-B025)

Keywords: Atomoxetine, ADHD, drug utilisation, Europe

Rationale and background: In 2003, Eli Lilly and Company (Lilly) launched Strattera (atomoxetine), which was the first attention-deficit/hyperactivity disorder (ADHD) medication indicated for adult use. The adult indication was approved in the European Union (May 2013). The use of ADHD medications, including nonstimulant Strattera has been increasing over-time among children, adolescents and among adults (Castle et al. 2007; Habel et al. 2011; Zoega et al. 2011). There has also been a change in the duration of use in more recent years (Castle et al. 2007; Habel et al. 2011).

Research question and objectives: The main objective of this retrospective database study is to describe Strattera utilisation patterns for patients treated in the United Kingdom (UK), Germany, the Netherlands, and Sweden, by age group. This includes 1) estimating number of patients exposures to Strattera on years of available data, 2) estimating duration of exposure, medication possession ratio, and dose over the most recent 24 months of data available, 3) for those who stopped taking Strattera, estimating the number that restarted, gap time between, and duration of use in additional exposures over the most recent 24 months, and 4) describing the Strattera population in terms of common comorbidities and concomitant medications. This protocol describes the updated drug utilisation study for the studies previously conducted in Europe (B4Z-MC-B019, submitted November 2011 and B4Z-MC-B022, submitted April 2014).

Study design: Retrospective cohort study using secondary data.

Setting: This study included all patients, including children, adolescents, and adults, with prescriptions of Strattera for the longest available duration in each selected database from the UK, Germany, the Netherlands, and Sweden.

Subjects and study size, including dropouts: Patients needed at least two consecutive prescriptions to be eligible for inclusion.

Variables and data sources: The data sources for this study included: the longitudinal prescription (LRx) data in Germany and the Netherlands; the Disease Analyser (DA) and the Clinical Practice Research Datalink (CPRD) datasets in the UK; and the National Drug and Patient Register in Sweden. Variables drawn from these data sources included those related to Strattera exposure (dose, duration), outcomes related to patient counts and drug utilization measures of persistence, discontinuation and restarting patterns, mean daily dose (MDD), medication possession ratios, and length of therapy. Outcomes were assessed by various patient characteristics including country, age, and gender. Counts were also extracted for ADHD diagnoses, comorbidities, and concomitant medication usage.

Results: Among the prevalent cohort of Strattera users from 2008 to 2014, the majority of patients treated with Strattera in each of the countries were 13 to 17 years old. Use among

children 0 to 5 years old and adults 65+ years old continues to remain low (0 to 1%) across countries in each year. There was a trend towards increased use of Strattera among adults in recent years, as expected after EU approval of the ADHD indication in adults in 2013. While the majority of patients treated with Strattera were male, the proportion of use among females increased in Germany, Netherlands, and Sweden between 2008 and 2014. Among the incident user cohort, the majority of new users were male and <18 years old. However, new female users tended towards higher ages in all countries. This was most apparent in Sweden where among new female users, more than half were between 18 to 64 years old. The MDD ranged from approximately 27 mg (Germany) to 47 mg (UK). In all countries, as expected, the highest MDD was among patients ≥18 years old. The mean length of treatment supplied over 24 months ranged from approximately 262 days (Netherlands) to 405 days (UK) and the medication possession ratio (MPR) ranged from 40% (Netherlands) to 60% (UK). In all countries, over 80% of new user patients were treated with 1 episode over the 24-month follow-up period. The overall Strattera persistence patterns in these EU countries show that, on average, persistence beyond 1 year was low. The most frequent diagnoses and medications listed among Strattera-treated patients were not associated with comorbid cardiovascular conditions.

Discussion: This drug utilisation study found mean length of treatment episodes for Strattera patients in UK, Germany, the Netherlands, and Sweden varied, but were approximately 1 year and the majority of patients are treated with 1 episode. The overall Strattera persistence patterns in these EU countries are lower than those reported in the US. Patterns of usage show that, on average, persistence past 1 year is low. Taking into account MPR and mean days treated, even with persistence of more than 1 year, the patient is not necessarily being treated continuously during this period. Therefore, the utilisation patterns in the EU do not suggest any different potential risks of long-term severe cardiovascular outcomes related to Strattera treatment would be expected from those reported in large cohort studies conducted in the US.

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