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ORIGINAL RESEARCH
Economic Evaulation

Cost-Effectiveness Evaluation in Sweden of Escitalopram Compared with Venlafaxine Extended-Release as First-Line Treatment in Major Depressive Disorder

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ABSTRACT

Objectives: Major depressive disorder (MDD) is a major public health concern associated with a high burden to society, the health-care system, and patients and an estimated cost of €3.5 billion in Sweden. The objective of this study was to assess the cost-effectiveness of escitalopram versus generic venlafaxine extended-release (XR) in MDD, accounting for the full clinical profile of each, adopting the Swedish societal perspective, and identifying major cost drivers. **Methods:** Cost-effectiveness of escitalopram versus venlafaxine XR was analyzed over a 6-month time frame, on the basis of a decision tree, for patients with MDD seeking primary care treatment in Sweden. Effectiveness outcomes for the model were quality-adjusted life-years and probability of sustained remission after acute treatment (first 8 weeks) and sustained for 6 months. Cost outcomes included direct treatment costs and indirect costs associated with sick leave. **Results:** Compared with generic venlafaxine XR, escitalopram was less costly and more effective in terms of quality-adjusted life-years (expected gain 0.00865) and expected 6-month sustained remission probability (incremental gain 0.0374). The better tolerability profile of escitalopram contributed to higher expected quality-adjusted life-years and lower health-care resource utilization in terms of pharmacological treatment of adverse events (though only a minor component of treatment costs). Expected per-patient saving was €169.15 for escitalopram versus venlafaxine. Cost from sick leave constituted about 85% of total costs. **Conclusions:** Escitalopram was estimated as more effective and cost saving than generic venlafaxine XR in first-line MDD treatment in Sweden, driven by the effectiveness and tolerability advantages of escitalopram. The study findings are robust and in line with similar pharmacoeconomic analyses.

Keywords: cost-effectiveness, first-line therapy, major depressive disorder (MDD), remission, selective norepinephrine reuptake inhibitor (SNRI), selective serotonin reuptake inhibitor (SSRI).

Background

Globally, major depressive disorder (MDD) is a major public health concern associated with a high burden to society, health-care system, and patients. In Sweden, the estimated cost of depression doubled between 1997 and 2005, from €1.7 to €3.5 billion [1]. This cost increase was primarily driven by an increase in indirect costs associated with sick leave and early retirement, over the past decade, whereas direct costs remained relatively stable over time [1].

The pharmacological treatment options in MDD include selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors. In a meta-analysis, venlafaxine, a serotonin norepinephrine reuptake inhibitor, has been shown to be more effective than traditional SSRIs [2]. Escitalopram, the S enantiomer of citalopram, is the most selective SSRI available [3]; in recent clinical studies, escitalopram was shown to be at least as efficacious as venlafaxine extended-release (XR), but with a better tolerability profile [4-7].

Clinical efficacy and tolerability are the first considerations when choosing an antidepressant drug (AD), but consideration of cost is also becoming increasingly important. Several cost-effectiveness (CE) studies of escitalopram versus venlafaxine XR have shown that the clinical advantages of escitalopram translate into benefits in real-life effectiveness: reduction in sick leave and health-care resource utilization (outpatient and inpatient care, pharmacological treatment, etc.) and associated costs [8-12]. These CE studies, however, tended to focus on efficacy without considering the impact of tolerability on quality of life. In addition, in countries such as Sweden, where a generic formulation of venlafaxine XR has recently become available, the CE of escitalopram versus venlafaxine XR needs to be re-evaluated.

In Sweden, with a single-payer health-care system and a strong health technology assessment outlook, adequate up-to-

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date evidence of CE is essential for decision making. The objective of the present analysis was to assess the CE of escitalopram versus generic venlafaxine XR in MDD, accounting for the full clinical profile (efficacy and tolerability) of the two ADs, adopting the societal perspective in Sweden, and identifying the major cost drivers associated with the management of depression.

Methods

A CE analysis of escitalopram versus venlafaxine XR was conducted over a 6-month time frame from the societal perspective, based on a decision tree. In this model, escitalopram was compared with generic venlafaxine XR, an AD of the serotonin norepinephrine reuptake inhibitor class. Both ADs are reimbursed for the treatment of depression in Sweden [13], and the market share of venlafaxine is expected to increase since it became generic in Sweden in 2009. The target population consisted of adult patients (aged 18–65 years) with moderate to severe MDD seeking treatment in a primary care setting in Sweden, consistently with underlying clinical data. The effectiveness outcomes for the model were quality-adjusted life-years (QALYs) and the probability of sustained remission, defined as a remission (Montgomery Åsberg Depression Rating Scale total score ≤12) achieved during acute treatment (first 8 weeks of treatment) and sustained until the end of the 6-month time frame. Cost outcomes included direct treatment costs (ambulatory care, hospitalizations, pharmacological therapy [AD use accounting for titration; treatment of adverse events, AEs]) and indirect costs associated with sick leave.

Model structure

A decision analytic model was created by using a previously published model of escitalopram versus sertraline [14], modified to reflect clinical practice patterns associated with the use of escitalopram and venlafaxine in the treatment of MDD in Sweden, based on newly available data, including long-term relapse data (i.e., relapse in patients who had achieved remission). The decision tree is presented in Figure 1. The 6-month time frame for the model, common for economic evaluations of ADs [15,16], was chosen to capture the largest proportion of clinical events within a given depressive episode (remission, AEs, relapses) but without being too long that extrapolations beyond the available clinical and real-life data would jeopardize the accuracy of the model. This time frame also limited the number of assumptions and the number of pathways (the overall structure) within the model. To populate the model, clinical trial data over 8 weeks were used, supplemented as much as possible by data from the country-specific real-life study HEADIS (a naturalistic longitudinal Swedish survey) [14]. The initial 2-month acute treatment was assumed to start with either 10 mg escitalopram or 75 mg venlafaxine XR, with a possible dose adjustment during the second month (to escitalopram 20 mg/d or venlafaxine 150 mg/d, respectively), in line with the dose recommendations for both products, according to the *Summary of Product Characteristics*. During this acute treatment period, patients could achieve remission of symptoms (Montgomery Åsberg Depression Rating Scale score ≤12). Patients who achieved remission during this period were assumed to continue medication for a 4-month maintenance period. During this maintenance treatment, patients could relapse or remain in remission (sustained remission). Patients who did not achieve remission during the 8 weeks of initial therapy either switched to another AD or stopped the treatment prematurely (based on real-life practice assessed as detailed below).

The results of the analysis were estimated on the basis of utilities and costs associated with different health states (as detailed below). The model was run as a Monte Carlo simulation comprising 10,000 iterations, resulting in 95% credibility intervals of point estimates of incremental costs and effectiveness (QALYs and probability of sustained remission) for escitalopram versus venlafaxine.

The model was developed by using Data 4.0 software (TreeAge Software, Inc., Williamstown, MA).

Data sources and model assumptions

Clinical inputs

The clinical inputs for remission, AEs, and relapse probabilities for each treatment arm are shown in Table 1. The 8-week remission probabilities were derived from a pooled analysis of two randomized controlled trials (RCTs) of venlafaxine and escitalopram [7].

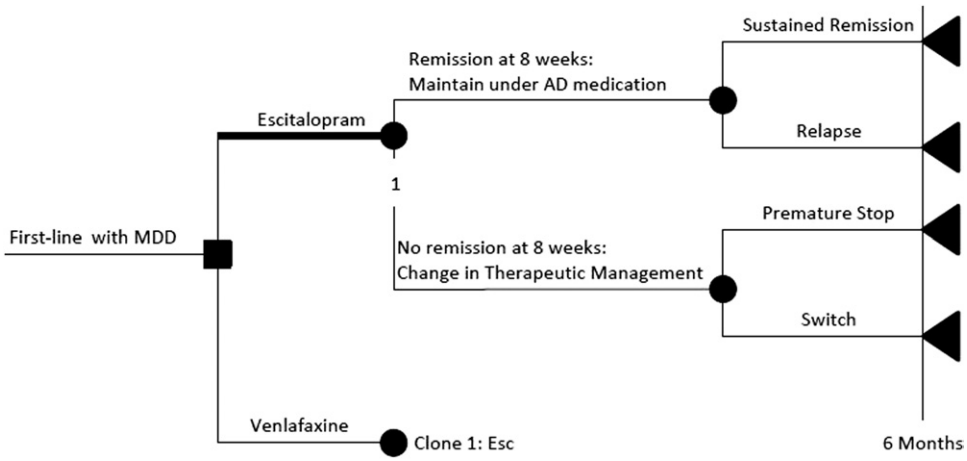

Fig. 1 – Cost-effectiveness model of escitalopram or venlafaxine extended-release for major depressive disorder in Sweden: 1) The venlafaxine arm is a clone of the escitalopram arm (implying the same structure). 2) Sustained remission at 6 mo: patients who achieved remission at week 8 since treatment initiation and remaining in remission by week 24. Patients were expected to continue on the same medication for another 4 mo (maintenance therapy). 3) Relapse at 6 mo: Patients who achieved remission at week 8 since treatment initiation but subsequently relapsed. 4) Premature stop at 8 wk: Patients who did not achieve remission during the first 8 wk of therapy and stopped medication. 5) Switch at 8 wk: Patients who did not achieve remission during the first 8 wk of therapy and switched to another medication. 6) The model was developed by using Data 4.0 software (TreeAge Software, Inc., Williamstown, MA). AD, antidepressant drug; Esc, escitalopram; MDD, major depressive disorder.