Cost-effectiveness and budget impact of adjunct quetiapine fumarate extended-release in patients with major depressive disorder with an inadequate response to previous therapy

Henrik Svedsäter,¹ Julie C Locklear,² Sukhvinder Johal,³ Ipek Özer-Stillman⁴

¹AstraZeneca R&D, Mölndal, Sweden; ²AstraZeneca Pharmaceuticals LP, Wilmington, Delaware, USA; ³RTI Health Solutions, Sheffield, UK; ⁴United BioSource Corporation, Lexington, Massachusetts, USA

Introduction

- ▶ MDD is highly prevalent, with estimates that more than 16% of adults will be affected at some point in their lives, leading to significant morbidity¹
- A primary goal of MDD treatment is remission, as patients failing to achieve remission have severely impaired functioning and increased risk of relapse²
- ▶ In the STAR*D study, depending on the definition of remission, 67.1% of patients failed to achieve remission in first-stage treatment with citalopram³
- ▶ Quetiapine XR and aripiprazole are atypical antipsychotics that have shown clinical efficacy in and are approved as adjunct therapy for patients with MDD⁴⁻⁷ with an inadequate response to previous antidepressant therapy

Objectives

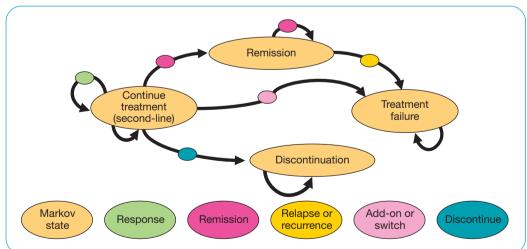
- ► To determine from a US managed care decision maker's perspective:
- The cost-effectiveness of adjunct quetiapine XR (150 or 300 mg/day) versus adjunct aripiprazole (15 mg/day) in MDD patients with an inadequate response to previous antidepressant therapy
- The budget impact of adding adjunct quetiapine XR in MDD patients with an inadequate response to previous antidepressant therapy

Methods

Cost-effectiveness model design

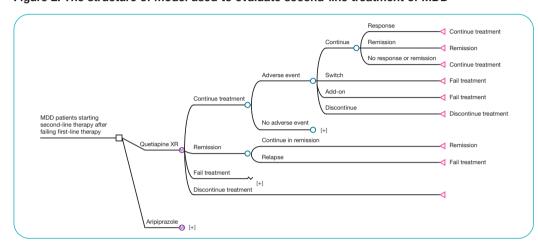
Cost-effectiveness was assessed using a Markov model. The cycle length was 1 week and the model was run over a time horizon of 52 weeks and included a population of 100,000 patients with MDD who had failed first-line treatment (**Figure 1**)

Figure 1. Markov mode



- ▶ The same model structure was utilized to separately and independently evaluate second- (Figure 2) and third-line treatment
- ► All costs were in 2008 USD
- ▶ Deterministic and probabilistic sensitivity analyses were performed
- The model outcomes were cost (in USD) per patient achieving remission with (or responding to) second- or third-line treatment
- Remission was defined as MADRS total score of ≤10
- Response was defined as ≥50% reduction in MADRS total score

Figure 2. The structure of model used to evaluate second-line treatment of MDD



Model assumptions and inputs

- ► Health effects were discounted at an annual rate of 3%
- The model assumed an average weekly cost of antidepressant therapy (USD32.98) in addition to the acquisition cost of quetiapine XR 150 or 300 mg or aripiprazole 15 mg
- The assumed daily cost of quetiapine XR 150 mg/day was USD6.50 and USD9.38 for quetiapine XR 300 mg/day
- The daily cost of aripiprazole 15 mg/day was USD11.20
- ► Efficacy parameters were weekly rates of remission, response, continuation, add-on, switch, discontinuation, and relapse
- Placebo-adjusted absolute weekly rates⁸ of remission and response were derived from clinical trials of quetiapine XR⁴ and aripiprazole⁵⁻⁷ among patients with an inadequate response to previous antidepressant therapy. These rates were assumed to be the same in second- and third-line therapy
- Continuation, add-on, switch, and discontinuation rates were derived from the PharMetrics database (January 2003 to March 2008: IMS Health, Watertown, MA. USA) and differed between second- and third-line therapy
- The weekly probability of relapse after remission was based on STAR*D data and was different for second- and third-line therapy⁹
- including post-treatment failure (add-on, switch, and relapse) costs and weekly post-discontinuation costs, were calculated from the PharMetrics database

Average weekly mental-health-related costs (inpatient and outpatient costs),

- Pharmacy costs (Wholesale Acquisition Costs) were obtained from the Red Book, 2008¹⁰ and calculated as 80% of the Average Wholesale Price
- An adverse event was included if it occurred at a frequency of 5% or more for either drug in the literature. The weekly costs of adverse events were calculated, assuming a physician visit if a drug was prescribed for an adverse event

Budget impact model

- The budget impact model assessed the impact of adding adjunct quetiapine XR to a hypothetical US managed care plan with a population of 185,000 patients, of whom 1.22% were being treated for MDD^{11,12}
- ▶ The composition of the current formulary allocation of the hypothetical managed care plan's formulary was based on the PharMetrics database
- ▶ In the revised formulary allocation, an increase in quetiapine XR use from 3.6% to 4.6% was assumed, with proportional reductions in the other treatments (Table 1)
- ▶ Default use of quetiapine XR was weighted as 100% adjunct therapy (150 mg: 50%, 300 mg: 50%) in both formulary allocations

- ▶ The average annual direct cost per treated population (pharmacy, inpatient, and outpatient costs) was calculated for all drugs as for the cost-effectiveness model
- Costs for each drug were weighted by the percentage of patients on second- and third-line therapy (61.35% and 38.65%, respectively) based on the PharMetrics

Table 1. Formulary allocations of MDD treatments in the budget impact model

Formulary allocation	Current overall allocation	Revised overall allocation		
Quetiapine XR	3.6%	4.6%		
Duloxetine	11.4%	11.3%		
Venlafaxine XR	25.2%	24.9%		
Aripiprazole	1.3%	1.2%		
Escitalopram	27.1%	26.8%		
Bupropion XL	31.4%	31.2%		
Total	100%	100%		

Results

Cost-effectiveness

- ► The main drivers of model outcomes were pharmacy costs and clinical efficacy
- Deterministic and probabilistic sensitivity analyses suggested that model outcomes were generally stable to varying assumptions

- Adjunct quetiapine XR 300 mg/day was more effective than adjunct aripiprazole in achieving remission. Compared with adjunct aripiprazole, it reduced total costs per remitting patient by USD1998 when used as second-line therapy (Table 2) and by USD2608 when used as third-line therapy (Table 2)
- Adjunct quetiapine XR 150 mg/day was associated with lower annual treatment costs than adjunct aripiprazole. It was less effective than adjunct aripiprazole in achieving remission, resulting in a higher cost per remitting patient when used as second- or third-line therapy (Table 2)

▶ Both adjunct quetiapine XR 150 and 300 mg/day were less effective than adjunct aripiprazole in achieving response, resulting in a higher cost per responding patient (Table 2)

- ▶ When used as a second- or third-line therapy for MDD, quetiapine XR had a limited and well-defined budget impact
- ▶ Increasing quetiapine XR use from 3.6% to 4.6%, assuming a proportional reduction in the use of other MDD treatments, increased overall annual health care costs by 0.14% (ie, from USD10,894,408 to USD10,909,591) (Figure 3)

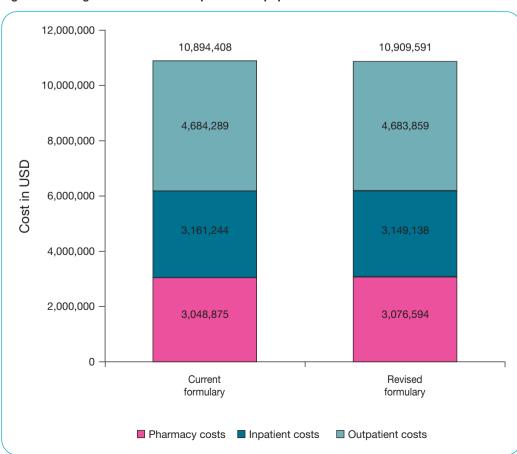
The details of the inclusion and remission criteria in the quetiapine XR⁴ and aripiprazole⁵ trials were different, which may have had influences on clinical inputs and model outcomes

Table 2. Comparison of the cost-effectiveness of adjunct quetiapine XR and adjunct aripiprazole in second- and third-line treatment of patients with MDD who had an inadequate

			Annual per patient costs (USD)				% patients who remit/	Cost (USD) per patient
			Hospital ^a	Pharmacy	Adverse events	Total ^b	respond in 1 year	who remits/responds
Remission	Second-line	Quetiapine XR 300 mg	3316	2075	20	5412	31.5	17,168
	treatment	Quetiapine XR 150 mg	3326	1574	26	4927	23.9	20,650
		Aripiprazole 15 mg	3319	2234	16	5570	29.1	19,166
	Third-line	Quetiapine XR 300 mg	3701	1755	16	5472	24.8	22,051
treatment	treatment	Quetiapine XR 150 mg	3742	1317	21	5080	18.3	27,766
		Aripiprazole 15 mg	3715	1864	13	5592	22.7	24,659
Response	Second-line	Quetiapine XR 300 mg	3316	2075	20	5412	20.4	26,586
	treatment	Quetiapine XR 150 mg	3326	1574	26	4927	15.2	32,502
		Aripiprazole 15 mg	3319	2234	16	5570	24.8	22,467
	Third-line	Quetiapine XR 300 mg	3701	1755	16	5472	16.9	32,296
	treatment	Quetiapine XR 150 mg	3742	1317	21	5080	12.1	42,011
		Aripiprazole 15 mg	3715	1864	13	5592	20.7	26,952

- ► The aripiprazole trials employed a flexible-dose design,^{5–7} while the quetiapine XR trials had a fixed-dose design. 4 The difference in trial design may impact on clinical efficacy comparisons as the former design provides a better opportunity to optimize
- ► The recommended aripiprazole dose range is 5–10 mg/day and the maximum dose is 15 mg/day. 13 An aripiprazole dose of 15 mg/day was used in the model as the mean doses in the aripiprazole trials, from which the clinical efficacy data were obtained, ranged from 10.8-11.8 mg/dav⁵⁻⁷

Figure 3. Average annual direct cost per treated population



Conclusions

- Quetiapine XR 300 mg/day, as adjunct therapy in patients with MDD who previously had an inadequate response to first- or second-line therapy, was cost-effective in achieving remission compared with adjunct aripiprazole 15 mg/day
- Increasing quetiapine XR use as second- or third-line therapy had a limited and well-defined budget impact
- alternatives, individual patient's history, needs, and characteristics should be considered when selecting therapy options

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MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; STAR*D, Sequenced Treatment Alternatives to Relieve Depression: XR, extended release

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