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Research paper

Cost-effectiveness of brexpiprazole adjunctive treatment for major depressive disorder

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ABSTRACT

Background: Major depressive disorder (MDD) is a debilitating psychiatric illness with a high cost burden. This analysis evaluates the cost-effectiveness of adjunctive brexpiprazole versus comparator branded adjunctive treatment for MDD and background antidepressant therapy (ADT) alone from a US payer perspective.

Methods: An economic model was developed to assess the cost-effectiveness of brexpiprazole versus comparator adjunctive treatment and ADT alone on total direct medical costs using a 6-week cycle time frame for a total of 48 weeks, with treatment response and remission as primary outcomes. The model consisted of 3 parts, 1 to represent the acute treatment phase and 2 to represent the maintenance stage.

Results: In the base-case analysis, brexpiprazole as reference treatment resulted in cost per additional responder ranging from $19,442–$48,745 and cost per additional remitter ranging from $27,196–$71,839 versus comparator treatments over 48 weeks. Sensitivity analyses showed treatment with brexpiprazole was more costly, but more clinically effective in all probabilistic simulations.

Limitations: This representation of disease natural history over 48 weeks may not account for all possible health states. Resource utilization on treatment was estimated using the resource use data from previous trials, and may overestimate medical costs compared to the real-world setting. Treatment comparators were limited to branded therapies, and head-to-head studies were not available to obtain data inputs.

Conclusion: Compared to other branded adjunctive therapies, brexpiprazole increases response and remission at 6 weeks; medical care cost savings were observed with the use of brexpiprazole. These findings may assist clinicians and formulary decision makers when selecting treatment for MDD.

1. Introduction

Major depressive disorder (MDD) is a widespread, debilitating psychiatric illness (Gelenberg et al., 2010) that has a lifetime prevalence of approximately 16% and annual prevalence of 6.6% in the US (Kessler et al., 2003, 2005). In a 2010 study, depressive disorders ranked second in global disability burden (Ferrari et al., 2013) and US cost burden of MDD for 2010 was estimated at $210.5 billion and increased by 21.5% from 2005 to 2010 (Greenberg et al., 2015; Kessler, 2012). There are a variety of monotherapy pharmacotherapies for treating MDD. These therapies fall into pharmacological classes which include tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRI), selective norepinephrine reuptake inhibitors (SNRI), selective serotonin and norepinephrine reuptake inhibitors, tetracyclic antidepressants (non-selective serotonin and norepinephrine reuptake inhibitors), monoamine oxidase inhibitors (irreversible and reversible inhibitors), agonists of the melatonin receptor, and other antidepressants (Zimovetz et al., 2012).

MDD therapy success is generally measured by response, although the ultimate goal of therapy is remission (Nierenberg and DeCecco, 2001; Gaynes et al., 2015). Approximately 50% of patients with MDD do not achieve adequate response to first-line antidepressant treatment (ADT) and nearly 30% do not benefit from trying a series of monotherapy treatments (Nierenberg et al., 2003; Han et al., 2013; Papakostas, 2009; Rush et al., 2006; Fava et al., 2006). In addition, only 27–39% of patients in a real-world setting achieve remission (Cuffel et al., 2003). Inadequate responses or increasing lines of therapies increases the overall

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burden for patients with MDD (Russell et al., 2004; Birnbaum et al., 2009; Simon et al., 2006; Mauskopf et al., 2009; Knoth et al., 2010).

Effective treatment for patients with MDD who do not respond adequately remains an important unmet need (Connolly and Thase, 2011; Han et al., 2013). Atypical antipsychotics (AAPs) are often used as adjunctive therapies for MDD. Following inadequate response to ADT, the current guidelines recommend switching ADT, adding a second ADT, or adding adjunctive therapy with a non-ADT (American Psychiatric Association, 2010; Patkar and Pae, 2013). Although AAPs can lead to adverse event (AE) risks, including extrapyramidal symptoms as well as metabolic syndrome and diabetes (Cha and McIntyre, 2012; Nelson and Papakostas, 2009; Gao et al., 2011), early adjunctive treatment with AAPs may reduce the cost burden for patients with MDD. Following the failure of initial trials with an ADT, early adjunctive treatment with an AAP lowered resource use and costs compared with patients who continued with monotherapy treatment trials (Legacy et al., 2015).

Brexpiprazole is an effective AAP-approved in the US by the FDA in July 2015 for adjunctive treatment of MDD (Thase et al., 2015a, 2015b; Otsuka Pharmaceutical Co., Ltd, 2015). Efficacy of brexpiprazole as an adjunct treatment of MDD was evaluated in two 6-week, placebo-controlled, fixed-dose pivotal trials of adult patients with MDD, with or without symptoms of anxiety, who had an inadequate response to 1–3 courses of a prior ADT in the current episode, as well as a demonstrated inadequate response throughout the 8 weeks of prospective ADTs (Thase et al., 2015a, 2015b). Adjunctive treatment with brexpiprazole significantly improved the mean Montgomery-Asberg Depression Rating Scale (MADRS) total scores of these patients. The incidence of activating treatment-emergent AEs (akathisia, insomnia, anxiety, and restlessness) was low, as was the incidence of sedating AEs (sedation, somnolence, and hypersomnia). A moderate weight increase was observed during treatment with adjunctive brexpiprazole, with small changes in metabolic parameters (Thase et al., 2015a, 2015b).

Evidence of efficacy and tolerability remain important in the evaluation and comparison of available therapies; however, it is also important to determine cost-effectiveness of these therapies, given limitations on healthcare spending. The objective of the present analysis was to evaluate the cost-effectiveness of adjunctive brexpiprazole versus comparator-branded adjunctive treatment for MDD, and background ADT alone, in the US healthcare setting, from a payer perspective. Specifically, MDD-related healthcare costs, as well as the number of patients achieving response and remission were estimated over a 48-week time horizon, and the results were used to estimate both the incremental cost per additional responder and per additional remitter. While a significant number of models evaluating the cost-effectiveness of alternative MDD strategies have been developed (Zimovetz et al., 2012), few models have assessed adjunctive AAPs for MDD treatment. Evaluating the cost-effectiveness of newly available branded treatments in MDD can shape policies concerning treatment coverage and reimbursement. In the case of oral antipsychotics, the majority of the treatments are available generically in the US. Given the cost pressures from payers, it is to be expected that generic drug utilization precedes the use of other available branded agents. Hence, for policy makers to evaluate new branded products for formulary placement, an appropriate analysis would involve comparisons of the newly available branded product with other available branded drugs.

2. Methods

2.1. Model description

An economic model was constructed to assess the impact of brexpiprazole versus comparator adjunctive treatment and ADT alone on total costs (direct medical plus pharmacy costs), focusing on treatment response and remission as primary outcomes. The model was programmed using Microsoft Excel 2010 and estimated cost-effectiveness from a US payer perspective. The model used a 6-week cycle time frame based on the length of treatment in the brexpiprazole pivotal trial and the minimum duration of comparator pivotal trials (Table 1). Clinical trials in MDD are often conducted over a period of 6–8 weeks, representing the acute phase of a depressive disorder (Zimovetz et al., 2012).

Table 1
Clinical event rates: response, remission, and all-cause treatment discontinuation.

Parameter and treatment	Relative rate (vs. respective placebo)	Derived rate (%)	PSA distribution	Source
MADRS response at 6 weeks				
Brexpiprazole 2 mg	1.49	48.45%	Beta	Thase, 2015a
Quetiapine XR 150 mg/day	1.16	37.82%	Beta	Bauer, 2009; El-Khalili, 2010
Quetiapine XR 300 mg/day	1.26	41.05%	Beta	Bauer, 2009; El-Khalili, 2010
Olanzapine/fluoxetine	1.28	41.77%	Beta	Shelton 2001; Shelton, 2005; Thase et al., 2007
Pooled ADT	N/A	32.53%	Beta	Shelton, 2001; Shelton 2005; Thase et al., 2007; Bauer, 2009; El-Khalili, 2010; Thase, 2015a
MADRS remission at 12 weeks[a]				
Brexpiprazole 2 mg	1.65	46.21%	Beta	Thase, 2015a
Quetiapine XR 150 mg/day	1.30	38.57%	Beta	Bauer, 2009; El-Khalili, 2010
Quetiapine XR 300 mg/day	1.44	41.65%	Beta	Bauer, 2009; El-Khalili, 2010
Olanzapine/fluoxetine	1.49	42.75%	Beta	Shelton, 2001; Shelton, 2005; Thase et al., 2007
Pooled ADT	N/A	31.91%	Beta	Shelton 2001, Shelton, 2005; Thase et al., 2007; Bauer, 2009; El-Khalili, 2010; Thase, 2015a
All-cause treatment discontinuation				
Brexpiprazole 2 mg	1.09	15.29%	Beta	Thase, 2015a
Quetiapine XR 150 mg/day	1.32	18.51%	Beta	Bauer, 2009; El-Khalili, 2010
Quetiapine XR 300 mg/day	1.82	25.41%	Beta	Bauer, 2009; El-Khalili, 2010
Olanzapine/fluoxetine	1.18	16.43%	Beta	Shelton, 2001; Shelton, 2005; Thase et al., 2007
Pooled ADT	N/A	13.98%	Beta	Shelton, 2001; Shelton, 2005; Thase et al., 2007; Bauer, 2009; El-Khalili, 2010; Thase, 2015a

ADT, antidepressant therapy; MADRS, Montgomery-Asberg Depression Rating Scale; PSA, probability sensitivity analysis.

[a] Based on clinical guidance, derived remission rates and then pooled ADT remission rates were given an additional 10%.