An Economic Evaluation of Brexpiprazole Treatment in Adult Patients with Schizophrenia in the United States

Poster # 169

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BACKGROUND

- Schizophrenia is a chronic, debilitating mental disorder impacting over 21 million people worldwide and 1.1% of US adults[1,2].
- While antipsychotic medications are used for the treatment of patients with schizophrenia, adherence to oral treatments is often poor. Major causes of antipsychotic treatment discontinuation are intolerable adverse events associated with commonly used treatments and lack of efficacy due to heterogeneous response, therefore additional treatment options are needed.
- Brexpiprazole, is a recently launched atypical antipsychotic indicated for adjunctive therapy to antidepressants for the treatment of major depressive disorder and treatment of schizophrenia in adults.
  - The efficacy of brexpiprazole in adults with schizophrenia was demonstrated in two 6-week, randomized, double-blind, placebo-controlled, fixed-dose clinical trials in patients with schizophrenia[3,4].
  - Brexpiprazole has demonstrated low incidence of sedating (e.g., sedation, somnolence, and hypersomnia) or activating adverse events (AEs) (e.g., akathisia, insomnia, anxiety, and restlessness), low rate of long-term metabolic effects, and moderate weight gain[3-5].
- Healthcare decision-makers such as health plans often evaluate new branded agents in contrast to existing branded treatment options; therefore, it is important to determine the cost-effectiveness of brexpiprazole compared with branded alternatives, including quetiapine XR and lurasidone.

OBJECTIVE

- This analysis aimed to examine the cost-effectiveness of brexpiprazole as monotherapy treatment of schizophrenia compared with quetiapine XR and lurasidone from a US payer perspective.

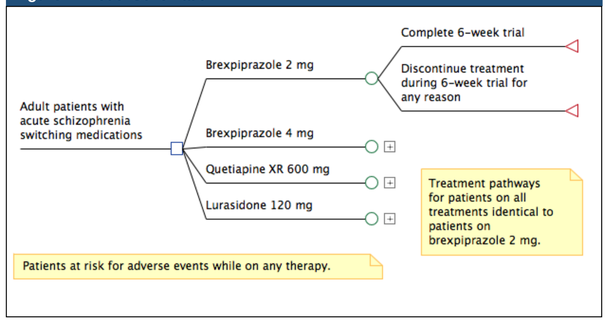
METHODS

Model Overview

- Type: Deterministic decision analysis model in Microsoft Excel 2011
- Population: Schizophrenia patients ages 18-65 switching treatment (2nd+ lines)
- Perspective: US Managed Care Payer
- Currency: 2014 US Dollars
- Time Horizon: 6 weeks
- Clinical Inputs: Adverse event (AE) rates, change in Positive and Negative Syndrome Scale (PANSS) score, change in Clinical Global Impressions-severity (CGI-S) score, rate of all-cause treatment discontinuation
- Cost Inputs: Product acquisition, adverse event treatment, patient monitoring
- Outcome Measures: Costs per patient, change in PANSS score, change in CGI-S score, $/CGI-S unit change, $/PANSS unit change

Patients entered the model after treatment with a previous antipsychotic, initiated treatment, and were simulated for 6 weeks reflecting clinical trial durations (**Figure 1**). While in the model, patients could discontinue therapy due to relapse, adverse events, or other causes. Changes in PANSS and CGI-S scores for patients on each treatment were incorporated after 6 weeks.

Figure 1. Model Schematic



Model Estimation (Inputs and Outcomes)

Clinical & Cost Inputs

- Clinical inputs were derived from 6-week clinical trials cited in products' prescribing information with comparable dosing and primary efficacy outcomes, including: brexpiprazole: two Phase 3 trials[3,4], quetiapine XR: three Phase 3 clinical trials[6-8], lurasidone: one Phase 3 trial[9] and one multicenter post-authorization trial[10].
- Clinical parameters included mean change in PANSS and CGI-S scores, and treatment discontinuation (**Table 1**).
- An adjusted relative-risk comparison using placebo as a common comparator used to obtain model input efficacy values.
- AE rates estimated based on unadjusted values in clinical trials (**Table 2**), and costs were based on published literature and expert opinion [11-13].

Table 1. Clinical Parameters Based on Indirect Comparisons

Parameter	Brexpiprazole 2mg[3,4]	Brexpiprazole 4mg[3,4]	Lurasidone [6-8]	Quetiapine XR[9,10]
PANSS Score Change	-19.65	-20.93	-18.69	-25.72
CGI-S Score Change	-1.09	-1.22	-1.03	-1.19
Treatment Discontinuation Rate	33.8%	33.6%	38.9%	34.9%

Table 2. Adverse Event Rates and Costs

Event	Brexpiprazole 2mg[3,4]	Brexpiprazole 4mg[3,4]	Lurasidone [6-8]	Quetiapine XR[9,10]	Cost ($ per event) [11-13]
Akathisia	4.6%	6.9%	23.6%	2.3%	220
Extrapyramidal Symptoms	5.4%	8.5%	17.9%	8.2%	228
Glucose Abnormalities	9.0%	14.5%	9.6%	5.6%	72
Lipid Abnormalities	8.2%	10.1%	6.9%	11.9%	163
Sedation	1.6%	2.7%	12.1%	16.1%	268
Weight Gain > 7%	10.5%	10.2%	6.5%	10.9%	781

Table 3. Product Acquisition and Medical Related Costs (2014 US dollars)

Parameter	Cost ($)[14,15]
Acquisition Costs (per pill)	29
Brexpiprazole 2mg	29
Brexpiprazole 4mg	29
Lurasidone 120mg	38
Quetiapine XR 600mg	39
Routine Office Visit (every 4 weeks)	45
Treatment Discontinuation (per event)	268

- Direct medical costs are presented in 2014 US dollars (**Table 3**).
- Product acquisition costs were based on wholesale acquisition costs, assuming 100% medication compliance[14].
- All patients attended one routine office visit per month; those discontinuing treatment required three psychiatrist visits[15].

Analyses:

- Average costs and changes in PANSS / CGI-S estimated for each therapy
- One-way sensitivity analyses (OWSA) were conducted, in which parameters were varied individually +/- 20% of the base case value.

RESULTS

Base Case Cost-Effectiveness:

- Brexpiprazole 2mg and 4mg resulted in lower 6-week per-patient total costs ($1,605 and $1,621, respectively) compared with lurasidone ($2,084) and quetiapine XR ($2,102).
- PANSS reduction for brexpiprazole 2mg and 4mg was -19.65 and -20.93, and for lurasidone and quetiapine XR were -18.69 and -25.72.
- CGI-S improvements were -1.09 for brexpiprazole 2mg, -1.22 for brexpiprazole 4mg, -1.03 for lurasidone, and -1.19 for quetiapine XR.
- The incremental cost-effectiveness ratio (in $/ unit PANSS improvement) for quetiapine XR was $82 compared to brexpiprazole 2mg, $101 compared to brexpiprazole 4mg. Lurasidone was dominated (i.e., more expensive and less efficacious) than either brexpiprazole dosing option (**Table 4**).
- Quetiapine XR had an incremental cost-effectiveness ratio of $4,996/CGI-S improvement compared with brexpiprazole 2mg, and was dominated by brexpiprazole 4mg; Lurasidone was dominated by both doses of brexpiprazole (**Table 5**).

Table 4. Base Case Results: $ / PANSS Reduction[a]

Treatment	Total cost per patient	Mean change in PANSS	ICER (incremental cost-effectiveness ratio)	
			vs. Brex 2mg	vs. Brex 4mg
Brexpiprazole 2mg	$1,605	-19.7	Reference	Cost Saving
Brexpiprazole 4mg	$1,621	-20.9	$12	Reference
Lurasidone 120mg	$2,084	-18.7	Dominated	Dominated
Quetiapine XR 600mg	$2,102	-25.7	$82	$101

Δ, change; Brex; brexpiprazole; CE, cost-effectiveness; mg, milligram; PANSS, positive and negative syndrome scale. [a]Results reported as 2014 US dollars per 1 unit reduction in PANSS total score.

Table 5. Base Case Results: $ / Change in CGI-S[a]

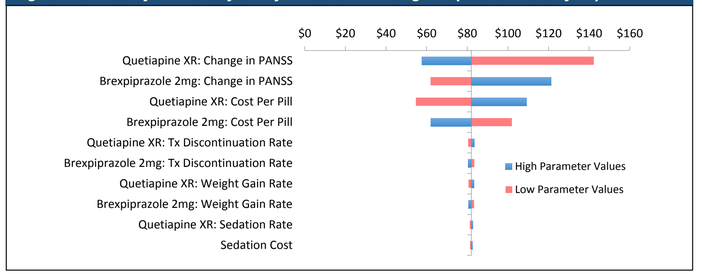
Treatment	Total cost per patient	Mean change in CGI-S	ICER (incremental cost-effectiveness ratio)	
			vs. Brex 2mg	vs. Brex 4mg
Brexpiprazole 2mg	$1,605	-1.09	Reference	Cost Saving
Brexpiprazole 4mg	$1,621	-1.22	$115	Reference
Lurasidone 120mg	$2,084	-1.03	Dominated	Dominated
Quetiapine XR 600mg	$2,102	-1.19	$4,996	Dominated

Δ, change; Brex; brexpiprazole; CE, cost-effectiveness; mg, milligram; CGI-S, clinical global impressions – severity. [a]Results reported as 2014 US dollars per 1 unit reduction in CGI-S score.

One-way Sensitivity Analyses (OWSA):

- Results of the OWSA indicated efficacy and product costs as the most influential variables.
- When comparing lurasidone and brexpiprazole 2mg, the only parameters that caused lurasidone to no longer be dominated were product costs.
- The tornado diagram (**Figure 2**) shows the impact on the base case cost-effectiveness ratio of varying all parameters +/- 10% when comparing quetiapine XR to brexpiprazole 2mg.

Figure 2. One-Way Sensitivity Analyses: Tornado Diagram ($/PANSS Analysis)



CONCLUSIONS

- Results of this analysis suggest that treating patients with brexpiprazole 2mg or 4mg would reduce costs compared to treatment with lurasidone or quetiapine XR.
- The model also found that use of brexpiprazole could improve performance in commonly used clinical rating scales such as the PANSS and CGI-S.
- While these rating scales are common in schizophrenia research, CGI-S may be more meaningful for non-research clinicians
- Results should be considered in light of limitations, including a limited 6-week time horizon and lack of head-to-head clinical trials to inform input parameters.
- Model results can assist in healthcare decision-making when evaluating the cost-effectiveness of treatments for schizophrenia.

References

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