Winners and Losers: Patterns of Economic Analysis of AEDs

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ABSTRACT

Objectives: To examine patterns of published economic "value messages" for anti-epileptic drugs (AEDs).

Methods: Using literature review best practices, we identified, reviewed, and abstracted data from comparative economic analyses published in English and referenced in PubMed or presented at professional conferences. For each study, we documented:

- Comparators
- "Winners" and "losers"
- Explanation of economic advantage (if any)
- Study sponsor (if any)
- Year published
- Country of interest
- Study design

Results: We identified 26 studies containing at least one comparative economic value message for an AED. Fifty-seven percent (15) were published as manuscripts; 53% (14 of 26) were sponsored by a drug manufacturer (4 manuscripts and 10 conference abstracts); and 38% (10 of 26) were US-oriented. Of the 14 sponsored studies, Ortho-McNeil (topiramate) sponsored 6 (only 1 published; only 1 US-oriented); UCB (levetiracetam) 4; Novartis (carbamazepine, oxcarbazepine) 3; and GSK (lamotrigine) 1. With only one exception (Ortho-McNeil), sponsored studies generated positive messages for sponsors' products. The 26 studies generated 39 comparative messages. There was at least one winning message for 12 of the 13 AEDs studied. Topiramate was the most frequent winner (35% of all messages expressed economic superiority of topiramate over comparators). Lamotrigine was the most frequent loser (45% of all economic messages). For 7 of the 13 AEDs, at least one message showed economic superiority over lamotrigine. For generically available AEDs, the explanation for cost savings stemmed from lower drug price, with no evidence of clinical inferiority. For levetiracetam, the explanation for cost-effectiveness stemmed from reduced seizure frequency, a better side effect profile, and improved adherence. The rationale for topiramate's economic advantages was unclear from the conference abstracts.

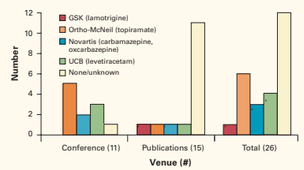
Conclusions: Several manufacturers of branded AEDs (Ortho-McNeil, UCB, Novartis) have produced studies describing their drug's economic value, while others have done very little work in this area. Patterns emerge in methods and comparators.

METHODS

- Searched articles with abstracts indexed in PubMed and published in English between 1990 and October 2005 to identify pharmacoeconomic value messages.
- Combined Medical Subject Heading (MeSH) terms "costs and cost analysis" and "economics, pharmaceutical" with the generic name of each of the 8 AEDs with the largest 2003 global market share (dollars), representing 95% of the market, plus phenytoin.
  - Conducted a supplementary search of the MeSH term "epilepsy" and the key words "resource utilization."
  - Of the 122 unique results, 26 studies contained comparative pharmacoeconomic messages and were included.
- Searched online repositories of abstracts presented during professional conferences and identified 9 ISPOR abstracts and 2 American Epilepsy Society abstracts.

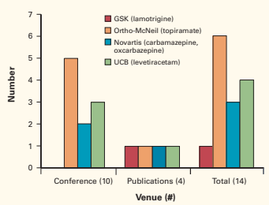
RESULTS

Figure 1. Frequency of Studies with Economic Value Messages in Epilepsy, by Sponsor and Venue



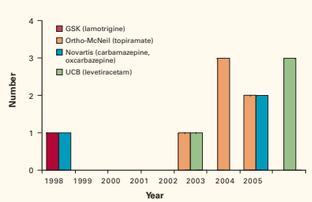
- Over half (14) were sponsored by a manufacturer of a drug treatment.
- Over half (15) of the studies were published manuscripts.
- Of the 11 studies presented at professional conferences, nearly all of them (10) were sponsored by a manufacturer.

Figure 2. Frequency of Studies with a Known Manufacturer-Sponsor, by Sponsor and Venue



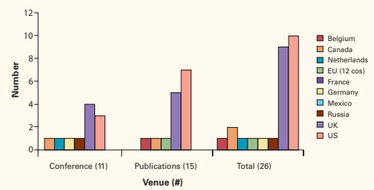
- Ortho-McNeil, manufacturer of topiramate, was responsible for nearly half (6).
- Of the studies sponsored by a manufacturer, UCB, manufacturer of levetiracetam, has sponsored 4 studies, 2 of which were presented at the joint annual meeting of the American Epilepsy Society and American Clinical Neurophysiology Society in December 2005.

Figure 3. Frequency of Manufacturer-Sponsored Studies, by Sponsor and Year



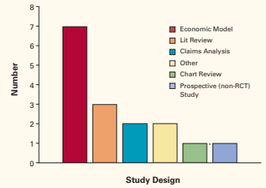
Manufacturers of branded AEDs, especially Ortho-McNeil, have been presenting research on a fairly consistent basis during the past 4 years.

Figure 4. Frequency of Studies, by Country and Venue



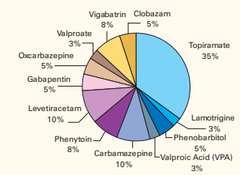
Fewer than half (38%) of the economics studies in epilepsy have been conducted in or for the US market (10 of 26 studies).

Figure 5. Frequency of Study Designs Resulting in Epilepsy Economic Value Messages



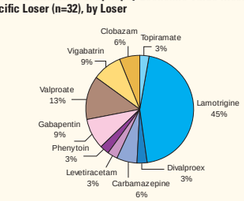
- Nearly half (7 of 16) of the economic research conveying drug-specific value messages in epilepsy employs some form of economic model.
- The models range from simple cost-minimization analyses looking at drug acquisition costs only to more sophisticated cost-utility models that rely on a variety of assumptions and data sources.

Figure 6. Distribution of Epilepsy Economic Value Messages with a Specific Winner (n=39), by Winner



- Of all studies that express a specific winner, topiramate has the highest number of winning value messages (14).
- Of the 39 drug-specific value messages put forward by pharmaceutical manufacturers and academic researchers, there is at least 1 published winning message for 12 of the 13 AEDs.

Figure 7. Distribution of Epilepsy Economic Value Messages with a Specific Loser (n=32), by Loser



Of the studies that express a specific loser (i.e., excluding standard therapy), lamotrigine is the most frequent loser in comparative value messages, losing in 45% of the economic comparisons.

Table 1. Number of Times Drug X Compared Favorably to Drug Y in Economic Studies in Epilepsy

DRUG Y		DRUG X														
Total Losses	Total Wins	14	1	2	0	1	4	3	4	2	2	1	3	2	0
		Topiramate	Lamotrigine	Phenobarbitol	Divalproex	VPA	Carbamazepine	Phenytoin	Levetiracetam	Gabapentin	Oxcarbazepine	Valproate	Vigabatrin	Clobazam	"Standard"
1	Topiramate			1											
14	Lamotrigine	5		1			3	2		1			1	1	
0	Phenobarbitol														
1	Divalproex					1									
0	Valproic Acid (VPA)														
2	Carbamazepine	2													
1	Phenytoin								1						
1	Levetiracetam	1													
3	Gabapentin	1							1				1		
0	Oxcarbazepine														
4	Valproate	2					1	1							
3	Vigabatrin	1								1				1	
2	Clobazam	1											1		
7	"Standard"	1	1						2		2	1			

- Lamotrigine is the most frequent loser in comparative value messages, losing in 45% of the economic comparisons.
- Topiramate is the winner in 35% of the economic comparisons, including 5 comparisons to lamotrigine.

EXPLANATIONS OF ECONOMIC SUPERIORITY

Economic studies of AEDs can be categorized by the explanation offered for economic superiority.

Lower Acquisition Price

- In Europe, because of its relatively higher acquisition price, lamotrigine is more costly than older AEDs (Heaney et al., 1998; Heaney et al., 2000; Levy, 1999), without sufficient evidence of superior effectiveness (Levy, 1999).
- Among the older AEDs, carbamazepine and phenytoin are "somewhat cheaper" than valproate (Levy, 1999).
- Guekht and colleagues (2002), from a study in Russia, suggest that valproate is a "cost-effective" monotherapy, although the explanation and study methods are unclear.

Cost-Effectiveness

- Lamotrigine is cost-effective due to cost offsets resulting from more seizure-free days (Markowitz et al., 1998).
- Carbamazepine costs less than lamotrigine, "even after accounting for costs associated with treating side effects and for therapeutic switching" (Shakespeare and Simeon, 1998).
- Adjunctive levetiracetam may be cost-effective (Blais et al., 2002) and may offer cost offsets resulting from more seizure-free days and fewer surgical evaluations and surgeries (Sheehy et al., 2005).
- Topiramate has been shown to be cost-effective relative to lamotrigine (van Hout et al., 2003; Remák et al., 2003a; Remák et al., 2003b; Remák et al., 2004), carbamazepine (Remák et al., 2003a; Remák and Steinhoff, 2004), and valproate (Remák et al., 2003a; Remák and Steinhoff, 2004).

Reduced Resource Utilization

- Oxcarbazepine reduces the occurrence of epilepsy-related hospitalizations (Erkens et al., 2004).
- Levetiracetam monotherapy may produce lower outpatient and inpatient resource utilization and cost compared to phenytoin (Grossman et al., 2005) and gabapentin (di Nicola et al., 2005).

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