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Budget impact of perampanel as adjunctive treatment of uncontrolled partial-onset and primary generalized tonic–clonic seizures in the United States

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ABSTRACT

Purpose: To evaluate the budget impact (BI) of adopting perampanel for adjunctive treatment of partial-onset seizures (POS), with or without secondarily generalized seizures, and the adjunctive treatment of primary generalized tonic–clonic seizures (PGTCS) in patients 12 years or older in the United States.
Methods: A BI model was developed to estimate the potential BI of adopting adjunctive perampanel from a US payer (direct costs only) and societal (direct and indirect costs) perspective over a 5-year period. Efficacy data for perampanel and antiepileptic drug (AED) maintenance therapy were obtained from perampanel phase III clinical trials. Drug, direct medical (healthcare provider, emergency room, and hospitalizations), and indirect (productivity loss) costs were obtained from appropriate sources (e.g., AnalySource® Online [wholesale acquisition costs], 2013 Optum Insight Clinformatics Database [market share percentages, direct medical costs per unit], and 2011–2013 National Health and Wellness Survey [NHWS; healthcare resource utilization, overall work impairment, and baseline distribution of patients across the 4 health states]). Mapping of seizure frequency to medical resource utilization and work impairment was obtained from Kantar Health's NHWS.
Results: In a hypothetical health plan of 1 million members, 660 (0.066%) members ≥12 years old had uncontrolled POS (395 [59.8%]) or PGTCS (265 [40.2%]). During the first 5 years of adoption of perampanel, absolute BI (including drug, direct medical, and indirect costs) was $852, $2124, $3855, $5318, and $6397, respectively, for a cumulative absolute BI of $18,545. Drug cost was estimated to increase by $13,888, $34,646, $62,863, $86,728, and $104,326, respectively; however, this cost would be mostly offset by decreases in direct medical ($5041, $12,576, $22,818, $31,481, and $37,869, respectively) and indirect ($7995, $19,946, $36,190, $49,929, and $60,060, respectively) costs. Total per-member-per-month cost (drug and direct medical costs) was estimated to increase by $0.0007, $0.0018, $0.0033, $0.0046, and $0.0055 from years 1 to 5.
Conclusions: Based on results of this BI model, increased cost of adopting perampanel in a health plan of 1 million members would be minimal for payers, and societal costs would be close to neutral.

1. Introduction

Epilepsy, the fourth most common neurological disorder after migraine, stroke, and Alzheimer's disease [1], varies in severity from individual to individual and is categorized as idiopathic or symptomatic and partial (focal [previously called partial-onset seizures [POS]], one hemisphere) or generalized (both hemispheres) [2]. Generalized tonic–clonic seizures (GTCS; grand-mal seizures) are the most dramatic type of idiopathic generalized epilepsy (IGE, also called primary or genetic generalized epilepsy) and account for more than half of newly diagnosed IGE [2,3].

Epilepsy extends well beyond seizures in many patients, imparting substantial lifestyle restrictions and financial burdens to patients, the healthcare system, and society at large [4–17]. Among patients with epilepsy, rates of comorbidity and mortality are increased, as is risk of sudden unexpected death in epilepsy (SUDEP), the most common cause of seizure-related mortality in those with chronic epilepsy [4,11–14]. Importantly, results of numerous studies indicate that seizure

Abbreviations: AE, adverse event; AED, antiepileptic drug; B, billion; BI, budget impact; BIM, budget impact model; IGE, idiopathic generalized epilepsy; GGE, genetic generalized epilepsy; GTCS, generalized tonic–clonic seizures; M, million; NHWS, National Health and Wellness Survey; PGTCS, primary generalized tonic–clonic seizures; PMPM, per member per month; POS, partial-onset seizure; SUDEP, sudden unexpected death in epilepsy.

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frequency is directly related to these and other outcomes [7,12–16]. In particular, risk of SUDEP increases with duration of epilepsy and increasing annual seizure frequency, especially of GTCS [13–16]. Having 3 or more seizures per year substantially increases risk for SUDEP, up to 20-fold compared with being seizure-free [11,16]. In addition, the incidence of SUDEP is inversely related to remission [13]. Further, results of an analysis of US data from the 2011–2013 National Health and Wellness Survey (NHWS) showed quality of life and utility scores worsen and activity impairment significantly increases with increasing seizure frequency among adults with primary GTCS (PGTCS) associated with IGE [7].

In addition to substantially affecting patients' lives, epilepsy poses a considerable economic burden. Using 1995 US population-based data, total lifetime costs for 181,000 people with epilepsy onset were estimated at $11.1 billion (B; direct, $1.8B; indirect, $9.3B), and total annual cost for 2.3 million prevalent cases was estimated at $12.5B (direct, $1.7B; indirect, $10.8B) [17]. In 2015 dollars, total lifetime and annual costs were estimated at $18.60B and $20.95B, respectively. Clearly, annual costs for patients with epilepsy are significantly higher than for those without epilepsy, in general and among the employed population [8–10]. In an analysis of data from a privately insured claims database (1999–2004), for example, direct annual costs for individuals with POS were significantly higher than for those without POS ($11,276 vs $4087, respectively; $p < 0.001$), and employees with POS incurred significantly higher annual costs than employed individuals without POS (total, $14,083 vs $5904; direct, $10,652 vs $4393; and indirect, $3431 vs $1511, respectively; $p < 0.001$) [9].

While costs associated with epilepsy are high in general, most are attributable to patients with uncontrolled seizures. Of the estimated $11.1B total lifetime costs from the 1995 US population-based study, $8.8B (direct, $1.1B; indirect, $7.7B) was attributable to those with intractable epilepsy, and of the estimated $12.5B total annual cost, $9.9B (direct, $0.6B; indirect, $9.3B) was attributable to those with intractable epilepsy [17]. Further, in a claims-based analysis (2007–2009), patients with uncontrolled epilepsy had significantly higher comorbidity rates, used more healthcare services (healthcare provider visits, emergency room visits, and hospitalizations), and had greater healthcare costs (overall: $23,238 vs $13,839; epilepsy-related: $12,399 vs $5511) than those with stable disease [8]. Also, in the aforementioned 2011–2013 NHWS analysis, patients with higher seizure frequencies (≥1 seizure/year) consistently had greater absenteeism, presenteeism, and overall work impairment; more health resource utilization (healthcare provider visits, emergency room visits, and hospitalizations); and higher direct and indirect costs than patients with <1 seizure/year [7].

The goals of epilepsy management are to achieve seizure control with minimal adverse events (AEs), reduce morbidity and mortality, and improve quality of life [4,18,19]. Antiepileptic drugs (AEDs) are the mainstay of treatment, which is tailored to the patient, taking into account AED- and patient-specific factors [4,18,20]. Despite advances in treatments, patient outcomes remain poor, and seizures in many patients are refractory to treatment [21,22]. Overall, AEDs fail to produce freedom from seizures in up to 30% of patients [23,24].

Perampanel, a selective, non-competitive α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antagonist, is approved in the US for adjunctive treatment of POS, with or without secondarily generalized seizures (since 2012), or PGTCS (since 2015) in patients 12 years or older with epilepsy [25,26]. Safety and efficacy of perampanel was demonstrated in patients with POS, with or without secondarily generalized seizures, in 3 phase III studies [27–29] and a subsequent open-label extension [30], as well as in patients with PGTCS in 1 phase III study [31] and subsequent open-label extension. Perampanel also has demonstrated safety and efficacy in several real-world clinical settings [32–38]. To estimate the economic impact of adding perampanel to US health plan formularies, a budget impact model (BIM) was developed focusing on costs associated with POS and PGTCS.

2. Methods

A BIM was developed to estimate the potential BI of adopting perampanel for the treatment of POS and PGTCS from a US payer (direct medical [physician visits, emergency room visits, hospitalizations] costs only) and societal (direct medical and indirect [productivity loss from absenteeism and presenteeism] costs) perspective. Time horizon was 5 years, with results calculated annually.

2.1. Model structure

Incremental BI of adopting perampanel was estimated by comparing direct and indirect costs of treating uncontrolled POS and PGTCS with and without perampanel (Fig. 1). Of note, the BI of perampanel as a tablet was investigated in this analysis. The BI of the recently approved oral suspension formulation will require an independent analysis.

2.2. Outcomes

Absolute BI of perampanel adoption in a hypothetical health plan of 1M members was evaluated using the following economic endpoints: annual plan costs (drug, direct medical, and indirect), expressed as cost per year and cost over 5 years, and per member per month (PMPM) cost (drug and direct medical) for each of the 5 years.

2.3. Data sources

2.3.1. Patient population

Target population comprised patients 12 years or older with uncontrolled POS or PGTCS. The proportion of these individuals in the population was based on 2012 US Census data [39]. Prevalence of epilepsy was based on literature [1], and prevalence of seizure types and patients with uncontrolled POS and PGTCS was based on data from the 2014 Optum Insight claims database (United Healthcare) (Eden Prairie, Minnesota, US) using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) codes 345.4 and 345.5 for POS, and 345.1 for PGTCS.

2.3.2. Clinical inputs

To estimate direct medical costs (physician visits, emergency room visits, hospitalizations) and indirect costs (productivity loss) associated with epilepsy, patients in 4 response rates were mapped to 4 health states representing different seizure frequencies corresponding to treatment efficacy (Fig. 1). Health states were 4 mutually exclusive categories of absolute seizure frequency: ≥1 seizure/week, 1–4 seizures/month, 1–12 seizures/year, and seizure-free. To determine the health state, 6 months of data were evaluated, and the average number of seizures per week, month, or year were calculated in such a manner that patients could not be in 2 health states at the same time. Response rates for perampanel plus standard of care (AED maintenance therapy) and standard of care alone were based on efficacy data from perampanel phase III clinical trials [28–31]. Baseline health state distribution was obtained from the 2011–2013 NHWS by Kantar Health.

2.3.3. Cost inputs

Drug, direct medical, and indirect costs were added to yield total costs of POS and PGTCS treatment. No administration costs were included because patients were assumed to self-administer oral therapies, and no monitoring costs were included because these costs were assumed to be similar across AEDs. Median wholesale acquisition cost per AED was identified from AnalySource® Online (AnalySource® Online, 2015). Weighted price of drugs was based on Optum Insights data (generic versus branded distribution for each drug). Median prices for generic and branded versions were applied to the proportion of patients taking the generic and branded versions, respectively, to generate average market prices for each AED.