

**South African National Essential Medicines List
Adult Hospital Medication Review Process
Cost-effectiveness and budget impact analyses
Levetiracetam for the treatment of Epilepsy in the South African Public Sector**

Date: June 2019

Medicine: Levetiracetam

Indication: Newly diagnosed epilepsy in adults

Introduction

Epilepsy, a chronic neurological disorder has an estimated prevalence of 1% in South Africa and an estimated incidence of 0,2% (1)(2). Primary treatment of epilepsy in the South African public sector is through pharmacotherapy, with monotherapy being preferred to polytherapy. The current first-line epilepsy treatment in South Africa is lamotrigine, phenytoin or carbamazepine (3) (4). Levetiracetam is under consideration for use as first-line treatment due to the associated reported absence of serious side effects, its ease of use, linear pharmacokinetics and reduced interactions with other drugs(5).

Methods

The study was model-based and conducted from the providers' perspective, specifically the South African public health sector. The population used for the analysis was patients with newly diagnosed epilepsy who are expected to be serviced by the public sector. The analysis consisted of a cost-effectiveness analysis and a budget impact analysis. The budget impact analysis was conducted for the first year of treatment for each of the treatment strategies, while the cost-effectiveness analysis was conducted for a five-year period. Both a decision-tree and a Markov Model were used for the cost-effectiveness analysis. Costs were expressed as South African Rands, 2018 value and effects were expressed as QALYs. Results were expressed as Incremental Cost-Effectiveness Ratios and sensitivity analysis was performed to cater for uncertainty.

Results

The use of levetiracetam along with the use of phenytoin, valproate and carbamazepine in the treatment of newly diagnosed epilepsy was found to be dominated by treatment using lamotrigine. Treatment with lamotrigine over a five-year period was found to be the least costly treatment option and had the highest number of QALYs gained. The estimated cost of treating one case of epilepsy was R1 252 higher using levetiracetam compared to using lamotrigine. Levetiracetam had 0,02 QALYs lower than those of lamotrigine. Phenytoin, carbamazepine and valproate were found to have the same effect size of 3,97 QALYs.

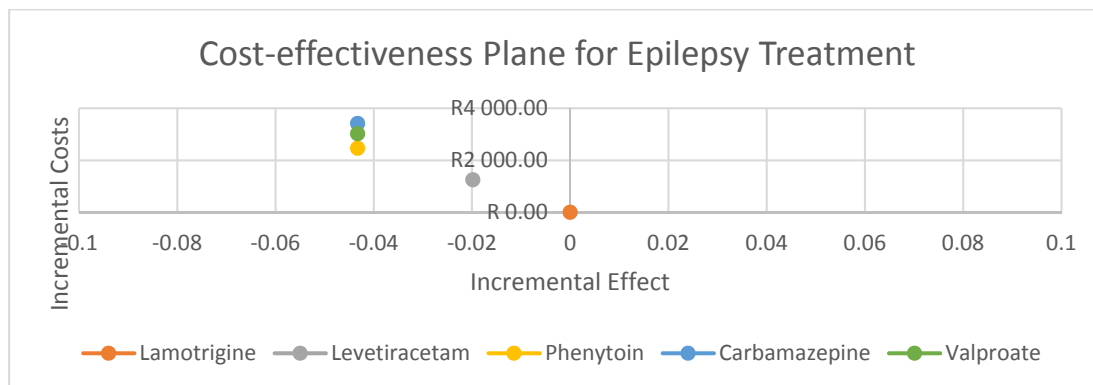


Figure 1: Cost-effectiveness plane for the treatment of epilepsy with levetiracetam.

Sensitivity analyses were conducted using some levetiracetam-related costs and some quality of life values. Both the levetiracetam-related costs used in the sensitivity analysis showed that levetiracetam became comparatively more cost-effective as the levetiracetam-related costs became lower. There were no trends observed regarding the impact of the quality of life measures on the ICER values obtained.

The pharmaceutical costs of treating newly diagnosed epilepsy with levetiracetam were found to be higher in comparison to those of comparators. For a 100% treatment coverage, the cost of treatment with lamotrigine was about R28,4 million cheaper compared to treatment with levetiracetam over a one-year period. Treatment with phenytoin was found to be the cheapest option, costing about R30,1 million less than treatment with levetiracetam.

Drug	8568 patients 100% coverage	6854 patients 80% coverage	4284 patients 50% coverage	857 patients 10% coverage
Levetiracetam	R35 352 047	R28 281 637	R17 676 023	R3 535 205
Carbamazepine	R5 281 576	R4 225 261	R2 640 788	R528 158
Lamotrigine	R6 976 368	R5 581 094	R3 488 184	R697 637
Phenytoin	R5 225 079	R4 180 063	R2 612 539	R522 508
Valproate	R8 127 900	R6 502 320	R4 063 950	R812 790

Table 1: BIA for pharmaceutical costs.

International Recommendations

International Organization	Recommendation for first-line treatment (Yes/No)	CEA study for LEV	Notes
NICE (United Kingdom)	No	Levetiracetam was not cost-effective	Levetiracetam only offered as adjunctive therapy to patients with generalized tonic-clonic seizures
CADTH (Canada)	No specification	Non-conclusive	–
SIGN (Scotland)	No	–	-Levetiracetam is recommended as first-line treatment in some instances, for example in women of reproductive age.

Table 2: International Recommendations

Discussion

The effect sizes of all the treatments under analysis were similar, with a difference of 0,04 QALYs between the most effective and the least effective treatment options. This led to costs being the main driver of the resulting ICER values. Although levetiracetam, together with phenytoin had the lowest values for non-pharmaceutical costs associated with the treatment of epilepsy, the high pharmaceutical costs of the drug led to its dominance by lamotrigine. Approximately a 93% price reduction is required for levetiracetam to be more cost-effective than lamotrigine. The model results agree with the study by Wilby et al 2005, which was conducted to inform the NICE treatment guidelines, which found that levetiracetam was not cost-effective.

Refer to the full report – available at: <http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/411-hospital-level-adults-costings>