Essential Medicines List
Cost-Effectiveness Analysis

Interferon beta, fingolimod, teriflunomide

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Purpose/Objective (PICO):

-P (patient/population): Adults 30 years or older with diagnosis of RRMS
-I (intervention): Interferon Beta-1a
-C (comparators): Fingolimod and teriflunomide
-O (outcome): disability progression as measured by EDSS and quality adjusted life years

Introduction

This economic evaluation is undertaken alongside the review of for medications for use in neurology, specifically the use of Interferon Beta in patients with relapsing remitting multiple sclerosis (RRMS). The economic evaluation investigates the cost-effectiveness of interferon beta-1a compared to fingolomod and teriflunomide in the treatment of patients with RRMS, in the South African population.

Date: August 2019
Medicine (INN): Interferon Beta
Medicine (ATC): L03AB07/L03AB08
Indication (ICD10 code): Multiple Sclerosis (ICD -10: G35)
Patient population: Relapsing remitting multiple sclerosis
Prevalence of condition: 5-30 per 100 000. Two hundred cases in public sector
Level of Care: Tertiary
Prescriber Level: 4: Specialist neurologist
Current standard of Care: Supportive care
Efficacy estimates: (preferably NNT):

NNT to prevent one relapse per year:

IFN Beta 1a (Avonex 30 µg)	11
IFN Beta 1a (Rebif 22 µg)	8
IFN Beta 1b (Betaseron 250µg)	6
IFN Beta 1a (Rebif 44 µg)	6

NNT to prevent one disability progression:

IFN Beta 1a (Avonex 30 µg)	24
IFN Beta 1a (Rebif 22 µg)	20
IFN Beta 1b (Betaseron 250µg)	16
IFN Beta 1a (Rebif 44 µg)	19

Motivator/reviewer name(s): Anand Moodley and Selealo Mametja

Methodology

Perspective: The setting for this study is the South African public health sector and the evaluation takes the perspective of the payer (government). Only direct costs to the government are considered and indirect costs such as loss of productivity and worker absenteeism are not included.

The economic model

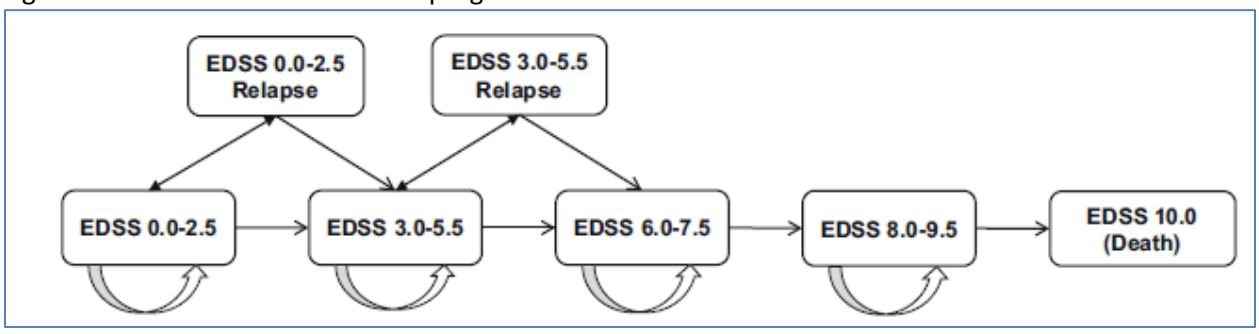
A Markov model was developed in Microsoft Excel, to simulate the natural history, treatment effects and costs of the three strategies beta interferon with fingolimod and teriflunomide, for treatment of patients with RRMS (Figure 1).

The model was adapted from similar analyses undertaken by Prosser et al (2004) and Melendez-Torres et al (2017). Taking a hypothetical cohort of adult men and women, the model includes the costs and health outcomes associated with treatment of relapses and accumulated disability, defined by the Expanded Disability Status Scale (EDSS) level. To model disease progression, EDSS levels are grouped into five health states: a) No/few limitations (EDSS 0–2.5), b) Moderate Limitations (EDSS 3–5.5), c) Walking Aid or Wheelchair (EDSS 6–7.5), d) Restricted to Bed (EDSS 8–9.5), and e) Death (EDSS 10). All patients were assumed to start from stage 1 (EDSS 0–2.5) and could only progress to a more severe health state or a relapse state.

Patients in EDSS 0.0–2.5 and 3.0–5.5 states would likely transition to a temporary state of relapse and stay for a cycle (1 month). Following a relapse, patients could transition back to the previous state or progress to a next more severe health state. Patients in EDSS 6.0–7.5 and EDSS 8.0–9.5 were assumed to have developed secondary progressive MS and would therefore not relapse.

Transition probabilities for disease progression, relapses, and discontinuation, as well as data on utilities were obtained from the literature. Costs of treatment were obtained from the National Department of Health Master Procurement Catalogue (Table 1).

Figure 1. Markov model for disease progression of MS



Note: All states can progress to death; EDSS=Expanded Disability Status Scale; model adapted from Zhang et al, 2014

Table 1. Model parameters

Parameters	Model value	Standard error	Distribution
Hazard rations for disease progression			
Fingolimod	0.7	0.09	Normal
Interferon B1a	1.353	0.17	Normal
Teriflunomide	0.7	0.09	Normal
Utility estimates			
Utility EDSS 0.0 – 0-2.5	0.899	0.08	Beta
Utility EDSS 3.0 – 0-5.5	0.821	0.09	Beta
Utility EDSS 6.0 – 0-7.5	0.769	0.1	Beta
Utility EDSS 8.0 – 0-9.5	0.491	0.06	Beta
Utility decreament Fingolimod	0.02	0.02	Beta
Utility decreament Interfron B1a	0.115	0.01	Beta
Utility decreament Teriflunomide	0.01	0.02	Beta
Cost estimates			
Cost Interferon B1a (ZAR)	4,548	4,548	Gamma
Cost Fingolimode (ZAR)	11,605	11,605	Gamma
Cost Teriflunomide (ZAR)	7,636	7,636	Gamma

We performed a probabilistic sensitivity analysis based on a second order Monte Carlo simulation, with 1,000 iterations. The distributions of hazard ratios were assumed to be normal, utilities followed a beta distribution, and costs were assumed to follow a gamma distribution.

Results

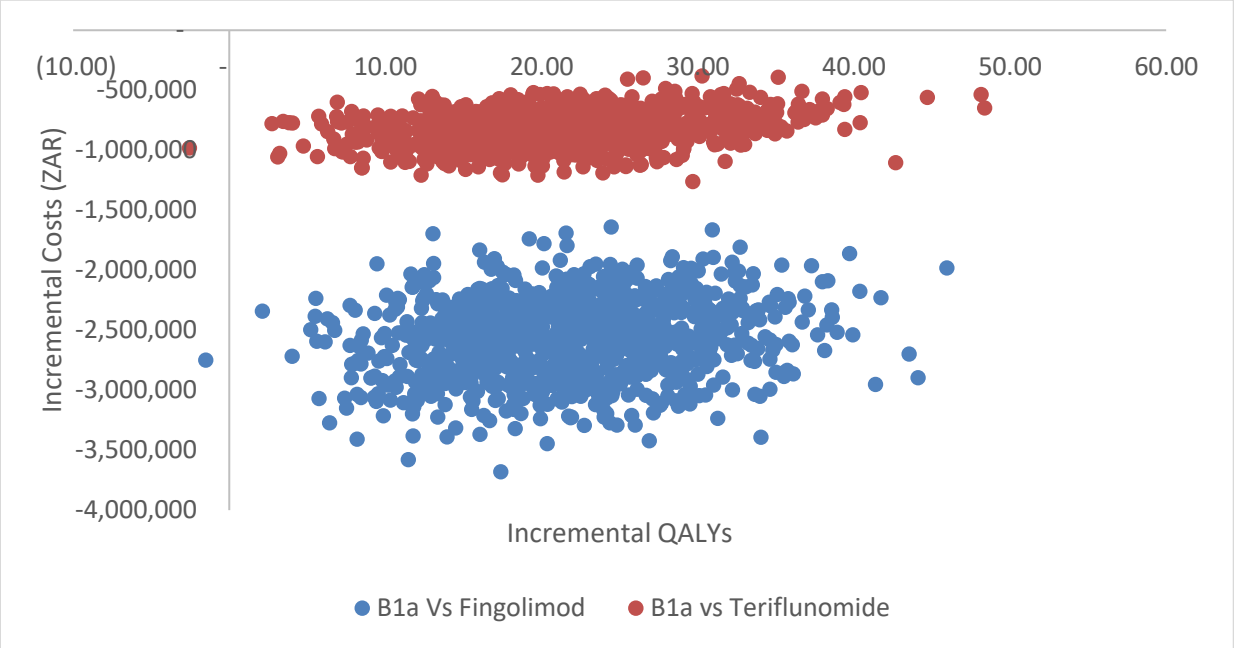
Table 2 shows the base case results of the cost-effectiveness analysis, giving the incremental costs and effects of interferon vs fingolimod and interferon vs teriflunomide. The incremental cost per QALY for interferon vs fingolimod is –R151,509 and that for interferon vs teriflunomide is –R47,911, i.e. both fingolimod and teriflunomide are dominated by interferon beta1a, which is both less costly and more effective.

Table 2. Base case results of the cost-effectiveness analysis

Drug	Costs (ZAR)	QALYs	Incremental Costs (ZAR)	Incremental QALYs	Incremental cost effectiveness ratio (ZAR/QALY)
Interferon B1a	400,076	69.72			
Fingolimod	2,967,487	52.78	-2,567,410	16.95	-151,509
Teriflunomide	1,211,954	52.78	-811,878	16.95	-47,911

The results of the probabilistic sensitivity analysis are presented in Figure 2. We used a scatter plot to show the results of the sensitivity analysis on the cost-effectiveness plane. Being more effective and less costly, interferon would be the favoured intervention even after running the analysis 1,000 times.

Figure 2. Cost-effectiveness scatterplot of interferon beta1a compared to fingolimod and teriflunomide



The choice to present the results in the form of a scatterplot was made because there is no known threshold for costs per QALY in SA. However, because the results of the analysis are that fingolimod and teriflunomide are dominated, interferon will be the most cost-effective drug at any given threshold. Therefore, no further presentations, e.g. of cost-effectiveness acceptability curves have been done.

Recommendation

The recommendation is made to use interferon for treatment of patients with RRMS.

References

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