Cost-Effectiveness Analysis of Disease Modifiying Drugs (Interferons and Glatiramer Acetate) as First-Line Treatments in Remitting-Relapsing Multiple Sclerosis Patients

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Introduction

- Treatments used as first-line of Relapsing Remitting Multiple Sclerosis (RRMS) therapy are glatiramer acetate and the interferons β-1a and β-1b(1).
- In the current economical context, it is important to assess the cost-effectiveness ratio among the Disease Modifying Drugs (DMD), and provide reliable information that support clinicians and healthcare stakeholders.

Objective

To assess the cost-effectiveness of the different Disease Modifying Drugs used as first-line treatments (interferons IM IFNβ-1a, SC IFNβ-1a, SC IFNβ-1b and glatiramer acetate, GA) in Remitting-Relapsing Multiple Sclerosis (RRMS) in Spain.

Methods

- A Markov model was developed to simulate the progression of a cohort of patients with RRMS, during a period of 10 years.
- Seven health states, defined by the Expanded Disability Status Scale (EDSS), and death were considered in the model (Figure 1):
  - EDSS 0.0-2.5: no limitations or small mobility limitations
  - EDSS 3.0-5.5: moderate mobility limitations
  - EDSS 6.0-7.5: requiring some help to walk or a wheelchair
  - EDSS 8.0-9.5: incapable of getting out of bed
  - Death (natural causes or EDSS 10)
  - Relapse EDSS 0.0-2.5: a relapse with a change in disability within EDSS 0.0-2.5
  - Relapse EDSS 3.0-5.5: a relapse with a change in disability within EDSS 3.0-5.5
- In order to reflect current clinical practice for RRMS patients, patients with varying degrees of disability in terms of EDSS were included(2).
- The cycle length considered in this Markov Model was set to 1 month.
- Initial ditribution among EDSS health states was:
  - EDSS 0.0-2.5: 30.0%
  - EDSS 3.0-5.5: 31.7%
  - EDSS 6.0-7.5: 20.6%
  - EDSS 8.0-9.5: 17.7%
- DMD used as first-line RRMS treatment included in the model:
  - Intramuscular interferon β-1a (IM IFNβ-1a , Avonex®, Biogen Idec Ltd)
  - Subcutaneous interferon β-1a 44mcg (SC IFNβ-1a 44mcg, Rebif 44®, Serono Europe Ltd)
  - Subcutaneous interferon β-1b (SC IFNβ-1b, Betaferon®, Bayer Schering Pharma AG and Extavia®, Novartis Europharm Ltd)
  - Subcutaneous Glatiramer Acetate (SC GA; Copaxone®, Teva Pharmaceutical Ltd)
- In addition to treatment with a DMD, the model assumes that all patients receive symptomatic treatment for MS.
- An annual discount rate of 3% was applied to adjust clinical and economical results.
- Transition probabilities:
  - Transition probabilities for symptomatic treatment were obtained from the literature and represent the progression over time of patients with MS. One month probabilites were (3):
    - EDSS 0.0-2.5 to 3.0-5.5: 0.004438
    - EDSS 3.0-5.5 to 6.0-7.5: 0.009189
    - EDSS 6.0-7.5 to 8.0-9.5: 0.003583
    - EDSS 8.0-9.5 to 10 (death): 0.000952
    - Relapse Rate: 0.075500
  - It was assumed that DMD reduce the transition probabilities to health states with higher EDSS score (greater disability) and the probability of a relapse, i.e., a transition to a health state with a relapse (Relapse EDSS 0.0-2.5 or Relapse EDSS 3.0-5.5)
  - Effectiveness of each of the treatments was obtained from clinical trials
- Neutralizing antibodies
  - The current model assumes that the presence of NAbs modifies the probability of developing a relapse among patients who receive interferon- β as a DMD. Incidence rates were set to(4):
    - IM IFNβ-1a: 4.5%
    - SC IFNβ-1a: 23.5%
    - SC IFNβ-1b: 19.3%
    - SC GA: 0.0%
- Utilities:
  - Were obtained from an observational study performed in Spain using a sample of 1,626 patients with MS who responded to the EQ-5D questionnaire(5).
  - Utility weights were set to:
    - EDSS 0.0-2.5: 0.777
    - EDSS 3.0-5.5: 0.577
    - EDSS 6.0-7.5: 0.446
    - EDSS 8.0-9.5: 0.085
    - Relapse EDSS 0.0-2.5: 0.747
    - Relapse EDSS 3.0-5.5: 0.547
- All costs that were obtained from the literature, were confirmed by an expert panel and were updated to € 2010 through the annual data of the Consumer Price Index (CPI).
- Costs included in the model:
  - Pharmacological
  - Management of MS
  - Loss of productivity
- Unitary Costs are specified in Table 1.
- The life years gained (LYG), the quality-adjusted life years (QALY), during the time horizon considered were used as benefit measures.
- The efficiency of comparing the treatments in RRMS was established through the Incremental Cost-Effectiveness Ratio (ICER) and the Incremental Cost-Utility Ratio (ICUR). For each comparison, the reference treatment was the most effective of the treatments compared.
- For an appropriate interpretation of these ratios, it was used the commonly accepted efficiency threshold in Spain (€ 30,000 per QALY)(6).

Figure 1. Markov Model Structure

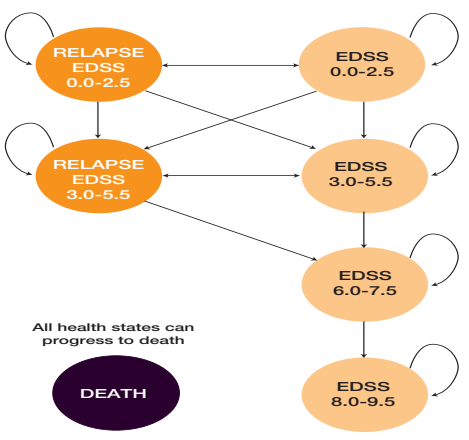

Table 1. Unitary Costs

Parameters	Reference Scenario
DMD- Drug costs	
IM IFNβ-1a	€ 907.96
SC IFNβ-1a	€ 1,267.95
SC IFNβ-1b	€ 942.59
SC GA	€ 848.68
MS management cost	
Health state-specific symptomatic treatment MS- costs	
EDSS 0.0-2.5	€ 135.04
EDSS 3.0-5.5	€ 159.08
EDSS 6.0-7.5	€ 168.06
EDSS 8.0-9.5	€ 202.43
Relapse EDSS 0.0-2.5	€ 135.04
Relapse EDSS 3.0-5.5	€ 159.08
Health state-specific MS-related costs	
EDSS 0.0-2.5	€ 936.72
EDSS 3.0-5.5	€ 1,683.79
EDSS 6.0-7.5	€ 2,898.13
EDSS 8.0-9.5	€ 4,350.83
Relapse EDSS 0.0-2.5	€ 1.856.56
Relapse EDSS 3.0-5.5	€ 2,603.13
Cost of lost worker productivity	
No treatment	€ 211.44
IM IFNβ-1a	€ 174.87
SC IFNβ-1a	€ 174.87
SC IFNβ-1b	€ 197.02
SC GA	€ 117.02

Results

- GA was the less costly strategy (€322,510), followed by IM IFNβ-1a (€ 329,595), SC IFNβ-1b (€ 333,925) and SC IFNβ-1a (€ 348,208).
- IM IFNβ-1a has shown the best efficacy results with 4,176 QALY, followed by SC IFNβ-1a (4.158 QALY), SC IFNβ-1b (4.157 QALY) and GA (4.117 QALY).
- Incremental costs per QALY gained with IM IFNβ-1a were €-1,005,194/QALY, €-223,397/QALY, and €117,914/QALY in comparison to SC IFNβ-1a, SC IFNβ-1b and GA, respectively.

Figure 2. Cost-efectiveness plane of IM IFNb-1a vs other DMDs (SC IFNβ-1a, SC IFNβ-1b,SC GA)

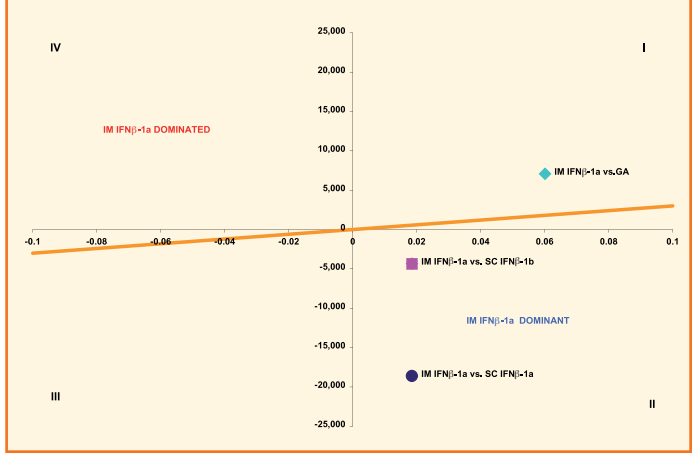

Table 2 Cost-effectiveness results

	IM IFNβ -1a	SC IFNβ -1a	SC IFNβ -1b	SC GA
MS Drug Costs per patient (€,2010)	€ 47,531.94	€ 65,474.67	€ 48,751.47	€ 42,453.89
Total Costs (€,2010)	€ 329,595.43	€ 348,208.20	€ 333,925.31	€ 322,509.96
Life Years Gained (LYG) per patient	8.580766998	8.580462928	8.580450005	8.579813781
Incremental cost-effectiveness ratio (cost/LYG) IM IFNβ-1a vs. (SC IFNβ-1a or SC IFNβ-1b or SC GA)	NA	Dominant	Dominant	7,433,218
Incremental cost-effectiveness ratio (cost/LYG) SC IFNβ-1a vs. (SC IFNβ-1b or SC GA)	NA	NA	1,105,230,210	39,587,705
Incremental cost-effectiveness ratio (cost/LYG) SC IFNβ-1b vs. SC GA	NA	NA	NA	17,942,344
Quality Adjusted Life Years (QALY) per patient	4.17699627	4.15847968	4.15761431	4.116906617
Incremental cost- utility ratio (cost/ QALY) IM IFNβ-1a vs. (SC IFNβ-1a or SC IFNβ-1b or SC GA)	NA	Dominant	Dominant	117,914
Incremental cost- utility ratio (cost/ QALY) SC IFNβ-1a vs.(or SC IFNβ-1b or SC GA)	NA	NA	16,504,952	618,146
Incremental cost- utility ratio (cost/ QALY) SC IFNβ-1b vs. SC GA	NA	NA	NA	280,422

Conclusions

- **First-line treatment with Glatiramer Acetate is the less costly strategy for the treatment of patients with Relapsing Remitting Multiple Sclerosis.**
- **Treatment with Intramuscular Interferon β-1a is a dominant strategy (lower cost and higher QALY) compared with Subcutaneous Interferon β-1a and Subcutaneous Interferon β-1b.**
- **Intramuscular Interferon β-1a is not a cost-effective strategy versus Glatiramer Acetate , because incremental cost per QALY gained with Intramuscular Interferon β-1a exceeds the € 30,000 per QALY threshold, commonly used in Spain.**

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