# Cost-effectiveness of ofatumumab compared with other disease-modifying therapies for the treatment of relapsing multiple sclerosis in Greece

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## Introduction

- Ofatumumab (Kesimpta®) is the first fully human monoclonal anti-CD20 antibody approved in Greece for the initial treatment of relapsing multiple sclerosis (RMS). A network meta-analysis (NMA) demonstrated that ofatumumab has similar effectiveness to other highly efficacious monoclonal antibody therapies with respect to reducing relapse rates and disability progression.[1]
- Ofatumumab has a favorable safety profile that is similar to the widely used first-line disease-modifying therapy (DMT).[2]
- There are no published cost-effectiveness studies of OMB for RMS in Greece. Therefore, it is important to assess its cost effectiveness compared to other frequently used DMTs for RMS.

## Objective

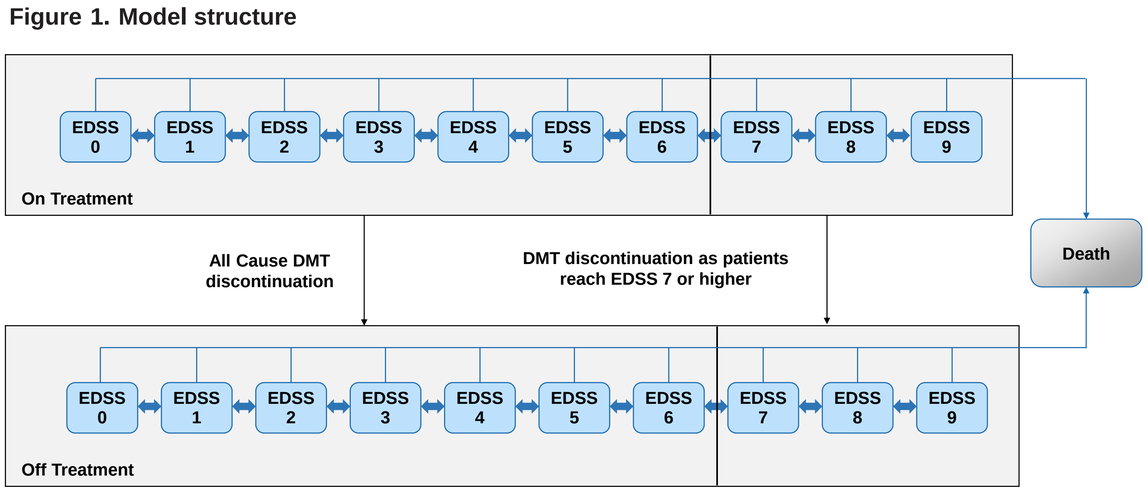
- The purpose of this study was to evaluate the cost-effectiveness of ofatumumab vs currently available and frequently used DMTs (interferon β-1a and -1b, dimethyl fumarate, teriflunomide, glatiramer acetate, ocrelizumab, natalizumab, and fingolimod) for RMS patients from the Greek payer perspective.

## Methods

### Model Structure and Inputs

- A discrete time Markov model based on expanded disability status scale (EDSS) health states (EDSS 0=neurologically normal; EDSS 10= death) was developed in Microsoft Excel® to simulate the natural history of disease progression in RMS patients.
- The baseline patient distribution considered in this model was aligned to the population included in the ASCLEPIOS I & II trials.[2] The mean age of the cohort was 38.2 years (standard error: 0.005) and had a baseline EDSS scores between 0–5.5.[2]
- During each cycle of the model, patients could remain at the same EDSS state or move to a higher/lower EDSS state or dead, as well as experience a relapse (**Figure 1**).
- Patients were assumed to discontinue treatment and move to best supportive care either when they reach EDSS 7 or higher or all cause discontinuation in line with ASCLEPIOS trials.[2]
- This analysis was conducted using a hypothetical cohort of RMS patients with cycle length of 1-year and for lifetime time horizon. Both the costs and effects were discounted at 3.5%.[3]
- In the absence of an officially defined willingness to pay (WTP) threshold in Greece, the WTP threshold was assumed to be €48,807/QALY (i.e., equal to three times the per capita gross domestic product in Greece, in line with the World Health Organization [WHO] cost-effectiveness definition).[4]

**Figure 1. Model structure**




DMT, disease modifying therapy; EDSS, expanded disability status scale.

- The transition probabilities between EDSS states of the untreated model were based on the British Colombia natural history dataset.[5] The annual relapse rate (ARR) by EDSS during the untreated course of the disease were based on a study of British MS patients and a prospective long-term study natural history data.[6,7]
- Treatment effects were applied in the model in the form of delaying disability progression and reducing the number of relapses.
- For the treatment-adjusted model, the hazards ratio (HR) for time to 6-month confirmed disability progression (CDP), rate ratio (RR) for ARR, were sourced from an NMA.[7] The annual discontinuation rates for ofatumumab and other DMTs were sourced from ASCLEPIOS trials and an NMA.[1,2]
- Mortality rates for the general population were derived from the age- and gender specific mortality rates for Greece,[8] adjusted for the MS population using the mortality multipliers reported in the literature.[9]
- Direct medical cost such as drug acquisition, monitoring and administration costs, relapse costs, EDSS-specific costs were sourced from the published sources.[10-13] Direct non-medical costs such as informal care and professional assistance costs was sourced from Yfantopoulos et al. study[12] (**Table 1**).

**Table 1. Drug acquisition*, administration, and monitoring costs**

| Drug Name | Drug acquisition costs | | Administration & monitoring costs | |
|---|---|---|---|---|
| | Year 1 | Year 2+ | Year 1 | Year 2+ |
| **Base case analysis** | | | | |
| Ofatumumab | €18,040 | €14,432 | €10 | €10 |
| Ocrelizumab | €16,805 | €16,805 | €274 | €177 |
| Interferon beta-1a | €5,961 | €5,961 | €347 | €126 |
| Teriflunomide | €6,977 | €6,977 | €877 | €390 |
| Glatiramer acetate | €6,268 | €6,268 | €10 | €10 |
| Dimethyl fumarate | €8,276 | €8,276 | €481 | €132 |
| Natalizumab | €12,861 | €12,861 | €1,787 | €1,552 |
| Fingolimod | €13,195 | €13,195 | €672 | €120 |
| Interferon β-1b | €5,469 | €5,469 | €243 | €126 |

*The drug acquisition costs are based on the officially reimbursed prices, and not the final net ones which are agreed following negotiations

- An additional scenario with indirect cost (salary reduction, early retirement, and productivity loss) was also considered to assess its impact on the results using Yfantopoulos et al. study[12] (**Table 1**). A probabilistic sensitivity analysis was also performed to address the underlying uncertainties due to the assumptions made as well as the inputs.
- Utility values as per the EDSS state and relapse disutility distinguished between mild, moderate, and severe states were also sourced from Orme et al. study.[6]

## Results

- Over a lifetime horizon, ofatumumab was predicted to yield more quality-adjusted life-years (QALYs) vs other DMTs (11.37 vs 10.17-11.21). Ofatumumab dominates ocrelizumab and fingolimod (i.e., cost-saving and more effective) (**Table 2**).
- Furthermore, ofatumumab was found to be cost-effective compared to other DMTs (natalizumab: €21,337/QALY; teriflunomide: €24,434/QALY; interferon β-1a: €26,756/QALY; glatiramer acetate: €30,788/QALY; interferon β-1b: €32,622 /QALY, and dimethyl fumarate: €32,659/QALY) at the WTP threshold of WHO-recommended three times gross domestic product per capita of Greece (i.e., €48,807/QALY) (**Table 2**).

**Table 2. Results of the base case analyses**

| Drug Name | Discounted Costs | Discounted QALYs | Incremental Costs (vs Referent) | Incremental QALYs (vs Referent) | ICER (vs Referent) | Inference |
|---|---|---|---|---|---|---|
| Ofatumumab | €387,027 | 11.37 | Referent | Referent | Referent | |
| Ocrelizumab | €400,667 | 11.21 | (€13,640) | 0.16 | (€87,455) | Ofatumumab dominates ocrelizumab |
| Interferon β-1a | €355,039 | 10.17 | €31,989 | 1.20 | €26,756 | Ofatumumab is cost-effective |
| Teriflunomide | €358,502 | 10.20 | €28,525 | 1.17 | €24,434 | Ofatumumab is cost-effective |
| Glatiramer acetate (Generic) | €354,212 | 10.30 | €32,815 | 1.07 | €30,788 | Ofatumumab is cost-effective |
| Dimethyl fumarate | €359,165 | 10.52 | €27,862 | 0.85 | €32,659 | Ofatumumab is cost-effective |
| Natalizumab | €383,339 | 11.20 | €3,689 | 0.17 | €21,337 | Ofatumumab is cost-effective |
| Fingolimod | €387,997 | 10.59 | (€970) | 0.78 | (€1,246) | Ofatumumab dominates fingolimod |
| Interferon β-1b | €352,329 | 10.31 | €34,698 | 1.06 | €32,622 | Ofatumumab is cost-effective |

ICER, incremental cost-effectiveness ratios; QALYs, quality adjusted life years
Value within parenthesis indicates negative value

- Additionally, the inclusion of indirect costs was projected to improve the cost-effectiveness of ofatumumab vs the other DMTs (**Table 3**).
- Probabilistic sensitivity analysis demonstrated that at a WTP threshold of €48,807/QALY, the probability of ofatumumab being a cost-effective treatment varied between 52% to 76% vs other DMTs.

**Table 3. Results of the scenario analyses**

| Drug Name | Discounted Costs | Discounted QALYs | Incremental Costs (vs Referent) | Incremental QALYs (vs Referent) | ICER (vs Referent) | Inference |
|---|---|---|---|---|---|---|
| Ofatumumab | €443,002 | 11.37 | Referent | Referent | Referent | |
| Ocrelizumab | €456,988 | 11.21 | - €13,986 | 0.16 | (€89,677) | Ofatumumab dominates Ocrelizumab |
| Interferon β-1a | €413,749 | 10.17 | €29,253 | 1.20 | €24,468 | Ofatumumab is cost-effective |
| Teriflunomide | €417,130 | 10.20 | €25,872 | 1.17 | €22,161 | Ofatumumab is cost-effective |
| Glatiramer acetate (Generic) | €412,591 | 10.30 | €30,411 | 1.07 | €28,532 | Ofatumumab is cost-effective |
| Dimethyl fumarate | €417,047 | 10.52 | €25,955 | 0.85 | €30,424 | Ofatumumab is cost-effective |
| Natalizumab | €439,661 | 11.20 | €3,340 | 0.17 | €19,322 | Ofatumumab is cost-effective |
| Fingolimod | €445,710 | 10.59 | - €2,708 | 0.78 | (€89,677) | Ofatumumab dominates fingolimod |
| Interferon β-1b | €410,687 | 10.31 | €32,315 | 1.06 | €30,381 | Ofatumumab is cost-effective |

ICER, incremental cost-effectiveness ratios; QALYs, quality-adjusted life years
Value within parenthesis indicates negative value

## Conclusions

- From a Greek payer perspective, ofatumumab was estimated to be cost-effective compared to the other frequently used DMTs for the treatment of RMS.
- Furthermore, the cost-effectiveness of high-efficacy therapy like ofatumumab coupled with its favorable safety profile demonstrates its value as an early treatment option for RMS patients having characteristics similar to those in ASCLEPIOS trials.

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## Disclosures

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