P281

# Cost-effectiveness Of Ofatumumab In Comparison With Other Disease Modifying Therapies And Best Supportive Care For The Treatment Of Relapsing-Remitting Multiple Sclerosis In Canada

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## Introduction

- Ofatumumab is the first fully human monoclonal anti-CD20 antibody approved in Canada for the initial treatment of relapsing-remitting multiple sclerosis (RRMS) with active disease
- 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 favourable safety profile that is similar to the widely used first-line disease modifying therapy (DMT), teriflunomide[2]
- Therefore, it is important to assess its cost effectiveness compared to currently available DMTs for RRMS

## Objective

- To evaluate the cost effectiveness of ofatumumab against other DMTs and best supportive care (BSC) for the treatment of adult patients with RRMS from a Canadian public healthcare system perspective

## Methods

### Model Overview

- A Markov cohort model with 10 total health states representing disability status defined by the Expanded Disability Status Scale (EDSS) levels 0 to 9 and a single state for death (EDSS 10) was constructed
  - Run over 65-years using annual cycle lengths
  - Costs and effects discounted at 1.5% per annum
  - 100% treatment discontinuation imposed at 10 years
  - Analyses conducted probabilistically using an incremental analysis considering dominance
- Baseline patient distribution was informed by a pooled analysis of the ASCLEPIOS trials[2]
- Each year, patients could transition between EDSS states, experience a relapse, discontinue therapy, or die (**Fig 1**)

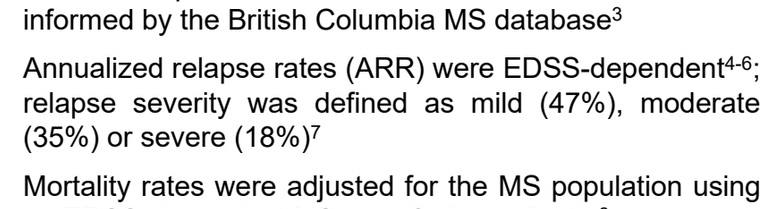
### Natural history data:

- Transition probabilities between EDSS states were informed by the British Columbia MS database[3]
- Annualized relapse rates (ARR) were EDSS-dependent[4-6]; relapse severity was defined as mild (47%), moderate (35%) or severe (18%)[7]
- Mortality rates were adjusted for the MS population using an EDSS-dependent MS-specific hazard ratio[8]

### Treatment-specific model inputs:

- Treatment effects for each DMT were modelled using hazard ratios for 6-month confirmed disability progression and ARR from an NMA[1]
- Discontinuation rates for each DMT were calculated using the relative effect estimates from the NMA using ofatumumab as a reference arm[1]
- Discontinuation rates for first-line DMTs were constant for 9 years, followed by 100% discontinuation at 10 years based on clinician opinion; discontinuation rate for cladribine was adjusted to 16% after 2 years[9]
- Adverse event (AE) probabilities were modelled as non-serious and serious, sourced from each of the treatments' pivotal trials, or from a pivotal trial where the treatment was a comparator

**Figure 1. Model Structure**




Rounded squares: health states; rounded rectangles: events that patients could experience at any time. Patients who reached an EDSS score of ≥ 7 while on treatment would discontinue and receive BSC. BSC: best supportive care; EDSS: Expanded Disability Status Scale.

## Methods – cont.

### Cost inputs:

- Direct medical costs for EDSS 1 to 6 were sourced from Grima et al.[10], while EDSS 7 to 9 costs were extrapolated based on Patwardhan et al.[11]
- Professional care costs were added to the total health state costs[12]
- Mild/moderate relapse costs ($7,275) were included[12]; severe ($17,459) relapse costs were extrapolated based on Patwardhan et al.[11]
- Drug acquisition costs (**Table 1**) were sourced from Ontario formularies[13,14] and manufacturer anticipated list price for ofatumumab
- Administration and monitoring costs (**Table 1**) were sourced from the Ontario Schedule of Benefits[15,16], Ontario Case Costing Initiative[17], formularies[13,14], published literature[18], and clinician opinion
- Costs for a physician visit and an MS Day Case admission were assumed for non-serious AEs ($84)[16] and serious AEs ($363)[17], respectively

### Utilities and Disutilities :

- Mean utility values were derived from normative utility data for the Canadian population (EDSS 0)[19] and a Canadian study of MS patients (EDSS 1 to 9)[20]
- Relapse disutilities distinguished between mild or moderate and severe relapses and have been used in previous economic models[21-23]
- Disutilities for AEs were derived based on assumptions and are aligned with previous MS economic models[4]

## Results

- Considering DMTs with a first-line indication in pair-wise analyses, ofatumumab was dominant (more efficacy, lower costs) vs. teriflunomide, interferons, dimethyl fumarate, and ocrelizumab; and resulted in incremental cost-effectiveness ratios (ICERs) of $24,177 CAD per quality-adjusted life-year (QALY) gained vs. glatiramer acetate and $28,034 vs. BSC (**Table 2**)
- Considering dominance in an incremental analysis resulted in only ofatumumab and BSC on the efficiency frontier; ofatumumab had an ICER of $28,034 vs. BSC
- At a WTP threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 63.3%
- Scenario analysis results against DMTs with a second-line indication are presented in Table 2; at a WTP threshold of $50,000/QALY gained, ofatumumab had the highest probability of being cost effective at 40.9%

**Table 1. Drug acquisition, administration, and monitoring (A&M) costs***

| Drug | Drug cost (Y1) | Drug cost (Y2) | A&M cost (Y1) | A&M cost (Y2+) |
|---|---|---|---|---|
| **Base case analysis (first-line therapies)** | | | | |
| Ofatumumab[a] | $30,917 | $26,500 | $1,136 | $38 |
| Ocrelizumab[14] | $32,600 | $32,600 | $3,374 | $1,581 |
| Teriflunomide[14] | $22,005 | $22,005 | $1,196 | $38 |
| Dimethyl fumarate[14] | $26,606 | $26,863 | $1,141 | $74 |
| Glatiramer acetate[13] | $11,834 | $11,834 | $1,125 | $38 |
| Avonex[14] | $24,886 | $24,886 | $1,261 | $84 |
| Rebif 22[14] | $23,610 | $23,610 | $1,261 | $84 |
| Rebif 44[14] | $28,743 | $28,743 | $1,261 | $84 |
| Betaseron[14] | $20,089 | $20,089 | $1,631 | $70 |
| Extavia[14] | $19,119 | $19,119 | $1,631 | $70 |
| BSC | $0 | $0 | $0 | $0 |
| **Scenario analysis (second-line therapies)** | | | | |
| Cladribine[b,14] | $44,968 | $44,968 | $1,158 | $82 |
| Natalizumab[14] | $46,911 | $46,911 | $6,397 | $3,681 |
| Fingolimod[13] | $26,996 | $26,996 | $1,682 | $84 |

*Canadian dollars. [a]Manufacturer's submitted price; [b]Cost for cladribine was only applied in Year 2 unless a patient was treated with a third dose, in which case the cost would also be applied to Year 3. BSC: best supportive care; Y1: year 1; Y2+: year 2 and beyond.

**Table 2. Results of the base case and scenario probabilistic analyses (pair-wise comparisons)***

| Drug | Total cost | QALY | Ofatumumab vs. Comparator: Incr. cost | Incr. QALY | ICER ($ per QALY) |
|---|---|---|---|---|---|
| **Base case analysis (first-line therapies)** | | | | | |
| Ofatumumab | $743,015 | 9.261 | - | - | - |
| Ocrelizumab | $784,832 | 9.131 | -$41,817 | 0.130 | Dominant† |
| Teriflunomide | $761,998 | 7.933 | -$18,983 | 1.328 | Dominant† |
| Dimethyl fumarate | $771,029 | 8.327 | -$28,014 | 0.934 | Dominant† |
| Glatiramer acetate | $713,474 | 8.039 | -$29,541 | 1.222 | $24,177 |
| Avonex | $770,188 | 8.102 | -$27,173 | 1.159 | Dominant† |
| Rebif 22 | $756,048 | 8.072 | -$13,033 | 1.189 | Dominant† |
| Rebif 44 | $781,810 | 7.978 | -$38,795 | 1.283 | Dominant† |
| Betaseron | $759,927 | 8.025 | -$16,911 | 1.236 | Dominant† |
| Extavia | $755,037 | 8.021 | -$12,022 | 1.240 | Dominant† |
| BSC | $689,506 | 7.352 | $53,509 | 1.909 | $28,034 |
| **Scenario analysis (second-line therapies)** | | | | | |
| Cladribine | $715,734 | 8.725 | $27,282 | 0.536 | $50,899 |
| Natalizumab | $869,833 | 9.123 | -$126,818 | 0.138 | Dominant† |
| Fingolimod | $772,790 | 8.410 | -$29,775 | 0.851 | Dominant† |

*Canadian dollars. †Ofatumumab dominant vs. comparator; BSC: best supportive care; ICER: incremental cost-effectiveness ratio; Incr: incremental; QALY: quality-adjusted life year.

## Conclusions:

- Ofatumumab is cost effective against all comparators and dominant compared to all currently approved and reimbursed DMTs with a first-line indication, except glatiramer acetate, from a Canadian public healthcare system perspective
- Cost savings associated with ofatumumab suggest greater disease management, reflected by increased QALYs gained, at a lower cost
- Ofatumumab's cost effectiveness, alongside its high-efficacy and favourable safety profile, demonstrate its value as an early treatment option in RRMS

### References

1. Samjoo IA, et al. *J Comp Eff Res.* 2021; 10(6):495-507.
2. Hauser SL, et al. *N Engl J Med.* 2020; 383(6):546-557.
3. Palace J, et al. *BMJ Open.* 2014; 4(1):e004073.
4. Mauskopf J, et al. *J Med Econ.* 2016; 19(4):432-42.
5. Patzold U and Pocklington PR, *Acta Neurol Scand.* 1982; 65(4):248-66.
6. Orme M, et al. *Value in health.* 2007; 10(1):54-60.
7. Mowry EM, et al. *PLoS One.* 2013; 8(10):e75416.
8. Pokorski RJ, *J Insur Med.* 1997; 29(2):101-6.
9. CADTH. CDR Pharmacoeconomic Review Report for Lemtrada. 2015.
10. Grima DT, et al. *Multiple sclerosis.* 2000; 6(2):91-8.
11. Patwardhan MB, et al. *Multiple sclerosis.* 2005; 11(2):232-9.
12. Karampampa K, et al. *J Popul Ther Clin Pharmacol.* 2012; 19(1):e11-25.
13. Government of Ontario. Ontario Drug Benefit Formulary. 2021.
14. Ontario Exceptional Access Program Formulary. 2021.
15. Ontario Ministry of Health. Schedule of Benefits, Lab Services. 2020.
16. Ontario Ministry of Health. Schedule of Benefits, Physician Services. 2021
17. Ontario Case Costing Initiative. 2018.
18. Tam VC, et al. *Curr Oncol.* 2013; 20(2):e90-e106.
19. Guertin JR, et al. *CMAJ.* 2018; 190(6):E155-E161.
20. Tappenden P, et al. *Value in health.* 2009; 12(5):657-65.
21. Chirikov V, et al. *Value in health.* 2019; 22(2):168-176.
22. CADTH therapeutic review. 2013.
23. Prosserr LA, et al. *Value in health.* 2004; 7(5):554-68.

### Disclosures

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