Cost-effectiveness Analysis of Ublituximab for the Treatment of Relapsing-Remitting Multiple Sclerosis

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INTRODUCTION

- Multiple sclerosis (MS) affects ~1 million individuals in the U.S (85% Relapse Remitting MS), contributing to an estimated economic burden of $85 billion in 2019.
- Monoclonal antibodies including Ublituximab, Ofatumumab, Ocrelizumab, and Natalizumab represent some of the most efficacious first-line disease modifying therapies (DMTs) for RRMS. However, these therapies differ substantially in acquisition cost, administration setting, and monitoring requirements, creating important formulary and reimbursement challenges for U.S. payers.
- The Institute for Clinical and Economic Review (ICER)[1] 2023 report evaluated these agents using a lifetime QALY framework and a meta-analysis-derived outcomes intended to inform long-term policy decisions.
- However, no published study has directly compared all four agents using Phase III clinical trial efficacy data within a short-term, 1-year U.S. payer perspective.
- Given the limited post-approval real world evidence available for Ublituximab (FDA-approved 2022), annualized relapse rate (ARR), the primary endpoint across all four pivotal Phase III trials, represents the most appropriate outcome measure for a short-horizon comparative analysis.

OBJECTIVE

To compare the incremental cost per relapse avoided for Ublituximab (UBL) versus: (a) Ofatumumab (OFT), (b) Ocrelizumab (OCL), and (c) Natalizumab (NTZ), from a U.S. payer perspective over a 1-year time horizon using two economic models.

Model 1

Compare Ublituximab against Ofatumumab, Ocrelizumab, and Natalizumab using clinical trials data

Model 2

Compare Ublituximab and Ofatumumab as both clinical trials used the same comparator drug (Teriflunomide)

METHODS

MODEL TYPE	PERSPECTIVE	TIME HORIZON	POPULATION
Static decision analytic	U.S. payer (Direct medical costs)	One Year	Hypothetical RRMS patients

MODEL 1

- Ublituximab compared to Ofatumumab, Ocrelizumab, and Natalizumab
- Efficacy Input: Weighted baseline relapses sourced from pivotal Phase III clinical trials
- Accounts for different comparators across clinical trials (Teriflunomide, IFN-β, Placebo)

MODEL 2

- Ublituximab compared to Ofatumumab
- Efficacy Input: Weighted ARR from Teriflunomide comparator arms of Phase III clinical trials
- Reduces cross-trial heterogeneity; both clinical trials used identical double-blind, double-dummy design

COST

- Drug acquisition, administration, monitoring, neurologist visits, serious adverse event management, relapse management.

OUTCOME MEASURES

- Relative relapse reduction, Incremental cost per relapse avoided (ICER), Average Cost per relapse avoided (ACER)

SENSITIVITY ANALYSIS

- One-way sensitivity analysis (±20%) applied to drug acquisition costs and relapse management cost.

COST ADJUSTMENT

- All costs adjusted to 2025 USD using the Medical Care component of the Consumer Price Index.

- Weighted annualized relapse rate = Σ (Annual relapses × Number of patients in placebo group) ÷ Σ (Number of patients in placebo group)
- Number of relapses avoided per patient = Weighted annualized relapse rate × Relative rate reduction
- Number of relapses per patient = Weighted annualized relapse rate − Number of relapses avoided per patient
- Relative reduction in relapse (%) = [(Baseline relapse rate − Relapse rate at the end of trial) ÷ Baseline relapse rate] × 100

CLINICAL INPUT

Table 1: Number of relapses avoided per patient for Models 1 and 2

MODEL 1

DMTs	Relapses at Baseline	Number of Patients	Relapse per Patient	Relative Relapse Reduction (%)	Relapses Avoided per Patient
Ublituximab[8]	1.30	543	0.09	0.93	1.21
Ofatumumab[9]	1.25	946	0.10	0.92	1.15
Ocrelizumab[10]	1.32	827	0.16	0.87	1.16
Natalizumab[11]	1.53	627	0.23	0.85	1.31

MODEL 2

DMT	Relapse (Comparator)	Number of Patients	Relative Relapse Reduction (%)	Relapses Avoided per Patient	Relapses per Patient
Ublituximab[8]	0.19	546	54	0.117	0.0997
Ofatumumab[9]	0.24	936	55	0.118	0.0985
Weighted ARR for Teriflunomide = 0.22					

COST INPUT

Table 2: DMT administration, monitoring, and provider utilization for Models 1 and 2

	Ublituximab	Ofatumumab	Ocrelizumab	Natalizumab
Frequency of Drug Administration[2-6]	4	15	4	13
Monitoring During Treatment[2-6]				
Hepatitis B Virus Screening	1	1	1	Not recommended
Serum Immunoglobulins	2	2	2	Not recommended[2]
Liver Function Test	1	1	1	Not recommended[2]
Screening of JC virus (for PML)	N/A	N/A	N/A	2 (Cost not added; paid by manufacturer[1])
Monitoring with MRI	0	0	0	1
Neurologist Visit	3	2	3	4[7]
Annual Serious Adverse Event Probability[1]	2.2%	1.6%	0.7%	1.4%

ASSUMPTIONS

- Adherence was assumed to be 100%
- Patients took the assigned DMTs for a one-year period
- Clinical trial-based relapse inputs were assumed to represent short-term treatment effectiveness
- Disease severity did not change over a one-year period
- Neurologist visit frequency assumed for all except Natalizumab

RESULTS

Table 3: Total cost per patient, relapses avoided, cost per relapse avoided and ICERs for Models 1 and 2

Model 1: Ublituximab compared to Ofatumumab, Ocrelizumab, and Natalizumab

	Ublituximab	Ofatumumab	Ocrelizumab	Natalizumab
DMT Cost ($)	118,321.50	140,205.75	130,285.74	115,429.86
Administration + Monitoring + utilization+ Adverse Event Management Cost ($)	1,046.19	723.77	974.43	1,799.46
Relapse Management Cost ($)	253.09	312.36	476.36	684.76
Total Cost ($)	119,620.78	141,241.88	131,736.53	117,914.09
Relapse Avoided Per Patient	1.21	1.15	1.16	1.3
Cost ($) Per Relapse Avoided (ACER)	98,454.06	123,255.22	11,4053.42	90,703.14
ICER ($)	---	-313,074.51 UBL dominates OFT	-202,102.70 UBL dominates OCL	-20,076.57 NTZ dominates UBL

Model 2: Ublituximab compared to Ofatumumab

	Ublituximab	Ofatumumab
DMT Cost ($)	118,321.50	140,205.75
Administration + Monitoring + utilization+ Adverse Event Monitoring Cost ($)	1,046.19	723.77
Relapse Management Cost ($)	296.76	293.22
Total Cost ($)	119,664.45	141,222.75
Relapse Avoided Per Patient	0.1170	0.1182
Cost Per Relapse Avoided (ACER) ($)	1,022,495.03	1,194,593.54
ICER ($)	-	18,170,729.04

A= Ublituximab; B= Ofatumumab, Ocrelizumab and Natalizumab

Cost for relapse treatment was calculated as a product of number of relapses elapses after DMT treatment and cost of treating 1 relapse. Cost of treating relapse was extracted from literature[7]

ICER ($)= ($Cost^A$–$Cost^B$) ÷ (Number of relapses $avoided^A$–Number of relapses $avoided^B$)

SENSITIVITY ANALYSIS

Table: Univariate sensitivity analysis for ICER for Model 1 and 2

	Drug Acquisition Cost (Ublituximab) (±20%)		Cost for Relapse Treatment (±20%)	
	(+)	(-)	(+)	(-)
OFT	UBL vs OFT 27,584.80	UBL dominates OFT	UBL dominates OFT	UBL dominates OFT
OCL	UBL vs OCL 177,785.80	UBL dominates OCL	UBL dominates OCL	UBL dominates OCL
NTZ	NTZ dominates UBL	UBL vs NTZ $274,470.09	NTZ dominates UBL	NTZ dominates UBL

LIMITATIONS

- Trial-based efficacy inputs may not fully reflect real-world effectiveness.
- **Model 1** relied on indirect cross-trial comparisons, which may be affected by differences in trial design and baseline patient characteristics.
- Rebates, discounts, and payer-specific costs were not included.
- Only one-way sensitivity analysis was conducted.
- The 1-year time horizon did not capture long-term disability progression, treatment switching, or QALYs.

DISCUSSION

- Ublituximab demonstrated favorable short-term economic value in Model 1, dominating both Ofatumumab and Ocrelizumab.
- Natalizumab dominated Ublituximab primarily due to its lower annual drug acquisition cost.
- In Model 2, Ublituximab and Ofatumumab demonstrated nearly identical relapse reduction rates; therefore, the high ICER reflected minimal differences in clinical efficacy rather than poor economic value.
- The focused comparison in Model 2 reduced cross-trial heterogeneity because both pivotal trials used Teriflunomide as the common comparator.
- A 1-year time horizon was appropriate because short-term payer decisions often focus on trial-based outcomes, and relapse reduction can be directly measured within this period.

Key Takeaway

- Ublituximab may offer favorable 1-year economic value versus Ofatumumab and Ocrelizumab.
- Natalizumab's advantage was primarily driven by lower drug acquisition cost.
- In the focused comparison, Ublituximab and Ofatumumab showed near-equivalent short-term effectiveness

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