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Cost effectiveness of Cladribine Tablets for treatment of RRMS in the Netherlands

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INTRODUCTION

- Multiple sclerosis (MS) is a chronic and degenerative neurological condition that is associated with neurological impairment, severe disability and premature mortality.[1]
- In the Netherlands, the overall age-sex-standardized incidence rate of MS was 4.8 per 100,000 person-years and prevalence was estimated to be 1 in 1000 people.[2]
- There are two broad categories for MS: relapsing disease and progressive disease. Relapsing disease is categorized in clinically isolated syndrome (CIS) and relapsing-remitting disease (RRMS). Over time, approximately 90% of patients with RRMS will develop Secondary Progressive disease (SPMS), a condition that bypasses the relapsing course of disease and is associated with fewer relapse events and a gradual progression in disability between relapses.[3] The RRMS phenotype is of primary interest for this poster, with special focus on the high disease activity (HDA) and rapidly evolving severe (RES) subpopulations.
- Recently, Cladribine Tablets have become available in the Netherlands for patients with RRMS, as a disease modifying drug (DMD) that reduces the frequency and severity of relapses and delays disability progression.

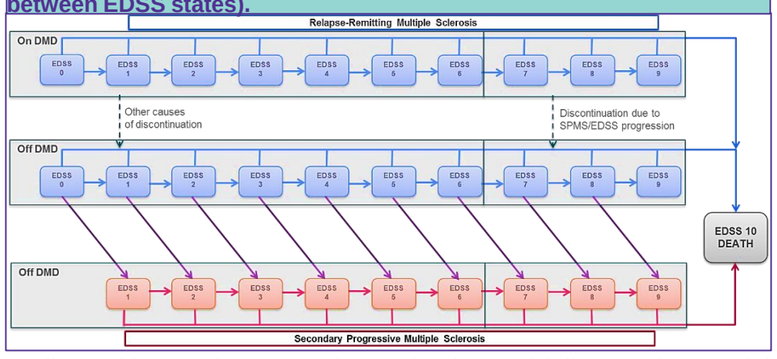
OBJECTIVE

This study aimed to evaluate the cost-effectiveness of Cladribine Tablets compared to alemtuzumab and fingolimod in the treatment of RRMS patients with HDA and natalizumab in the treatment of patients with RES MS in the Netherlands.

METHODS

A previously developed Markov model[4] was adapted to simulate costs and effects of RRMS treatment in the Netherlands. Disease progression was modelled using the Kurtzke's Expanded Disability Status Scale (EDSS) system, for RRMS, SPMS and general mortality (Figure 1).

Figure 1. Health state structure of the 21-state Markov model used to simulate progression within RRMS and to SPMS (incl. switching between EDSS states).



In line with Dutch economic evaluation guidelines[4], the model adopted a societal perspective, a lifetime horizon, and future costs and effects were discounted (1.5% and 4% respectively). Furthermore, a value-of-information (VOI) analysis was conducted. A VOI analysis quantifies the value of eliminating uncertainty around cost-effectiveness parameters. A VOI is mandatory in economic evaluations in the Netherlands.[4]

MODEL INPUTS

Table 1. Health state utilities

Health state	Utility	Health state	Utility
Relapse event:	-0.071	**SPMS conversion**	-0.045
Patient health utility:[6,7]			
EDSS 0	0.917	**EDSS 5**	0.623
EDSS 1	0.856	**EDSS 6**	0.548
EDSS 2	0.816	**EDSS 7**	0.422
EDSS 3	0.729	**EDSS 8**	0.234
EDSS 4	0.697	**EDSS 9**	0.005
Caregiver disutility:[8]			
EDSS 0	-0.002	**EDSS 5**	-0.160
EDSS 1	-0.002	**EDSS 6**	-0.173
EDSS 2	-0.002	**EDSS 7**	-0.030
EDSS 3	-0.045	**EDSS 8**	-0.095
EDSS 4	-0.142	**EDSS 9**	-0.095
Adverse events:			
Infusion site reaction[9]	-0.011	**Hypersensitivity[10]**	-1.000
Injection site reaction[9]	-0.011	**Autoimmune thyroid-related event[10]**	-0.110
PML[10]	-0.200	**Influenza-like symptoms[9]**	-0.210
Severe infection[11]	-0.190	**Malignancy[10]**	-0.116
Macular Oedema[10]	-0.040	**Immune thrombocytopenia purpura[10]**	-0.090
Gastrointestinal[9]	-0.240		

Table 2. Drug acquisition, administration and monitoring costs (€)

Therapy	Total cost year 1	Total cost year 2
Drug acquisition costs[13]		
Cladribine Tablets	33,988	33,988
Alemtuzumab	35,000	21,000
Fingolimod	22,112	22,112
Natalizumab	20,727	20,727
Drug administration costs[3]		
Cladribine Tablets	0	0
Alemtuzumab	1507	950
Fingolimod	278.49	0
Natalizumab	3620	0
Drug monitoring costs[3, 14]		
Cladribine Tablets	418	207
Alemtuzumab	580	562
Fingolimod	955	232
Natalizumab	458	483

Table 3. Costs by health state (€)

Health state	Direct medical costs[15]	Direct non-medical costs[15]	Indirect non-medical costs[15]
EDSS 0	12,071	5,301	15,754
EDSS 1	12,071	5,301	15,754
EDSS 2	12,071	5,301	15,754
EDSS 3	12,071	5,301	15,754
EDSS 4	14,634	16,025	24,006
EDSS 5	14,634	16,025	24,006
EDSS 6	14,634	16,025	24,006
EDSS 7	14,634	16,025	24,006
EDSS 8	14,966	56,001	36,605
EDSS 9	14,966	56,001	36,605

NB: costs for each relapse were estimated at € 1,024.

RESULTS

In the HDA sub-population, Cladribine Tablets is the dominant option compared to alemtuzumab and fingolimod. Cladribine Tablets was also the dominant option compared to natalizumab in the RES subpopulation.

Table 4. Results from the base case analysis

HDA population	Cladribine Tablets	Alemtuzumab	Fingolimod
Total costs	€1,365,355	€1,367,586	€1,467,097
Incremental costs (Cladribine Tablets vs comparator)	-	-€2,232	-€101,742
Total QALYs	9.314	9.276	8.332
Incremental QALY (Cladribine Tablets vs comparator)	-	0.038	0.982
ICER (Cladribine Tablets vs comparator)	-	Dominant	Dominant
Net Monetary Benefit (NMB)	-	€4,141	€150,858
RES population	**Cladribine Tablets**	**Natalizumab**	
Total costs	€1,436,253	€1,528,018	
Incremental costs (Cladribine Tablets vs comparator)	-	-€91,765	
Total QALYs	9.413	8.791	
Incremental QALY (Cladribine Tablets vs comparator)	-	0.622	
ICER (Cladribine Tablets vs comparator)	-	Dominant	
NMB	-	€122,862	

Deterministic sensitivity analysis

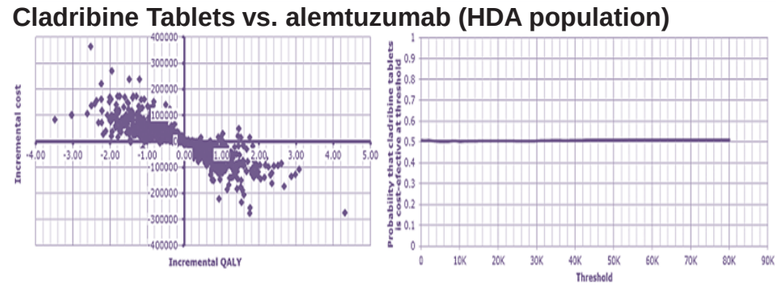
- A deterministic sensitivity analysis was performed with a threshold of €50,000 per QALY for both the HDA sub-population and the RES sub-population. Overall, the sensitivity analyses show robustness of the model, despite small parameter influences from disability progression.

Probabilistic sensitivity analysis

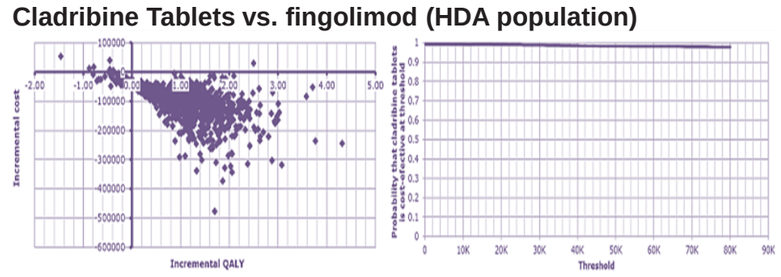
- For the HDA population, Cladribine Tablets was the dominant strategy when compared to alemtuzumab with a 50.9 % probability of being cost-effective at a threshold of €50,000 per QALY gained, and also when compared to fingolimod, with a 98.2% probability of being cost-effective at a threshold of €50,000 per QALY gained (Figure 2).
- For the RES population comparing against natalizumab, Cladribine Tablets was the dominant strategy with a 94.1% probability of being cost-effective at a threshold of €50,000 per QALY gained (Figure 2).
- The probabilistic sensitivity analyses showed significant overlap in the credible intervals for total lifetime QALY outcomes and costs of Cladribine Tablets and all relevant comparators.

Figure 2: Cost-effectiveness (CE) planes and CE acceptability curves

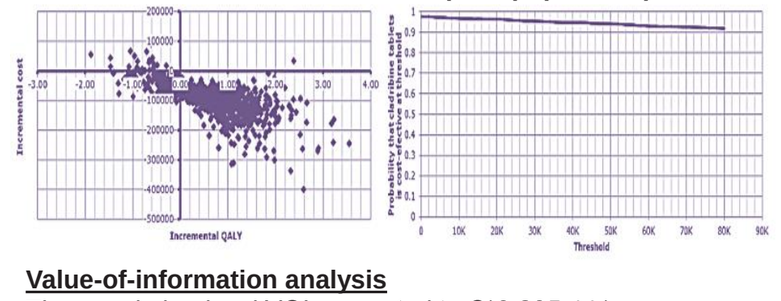
Cladribine Tablets vs. alemtuzumab (HDA population)



Cladribine Tablets vs. fingolimod (HDA population)



Cladribine Tablets vs. natalizumab (RES population)



Value-of-information analysis

The population-level VOI amounted to €19,295,441.

CONCLUSIONS

- **In the Netherlands, treatment of RRMS with Cladribine Tablets is cost-effective versus alemtuzumab and fingolimod in HDA patients, and cost-effective versus natalizumab in RES patients, at a threshold of €50,000.**
- **Cladribine Tablets was dominant in all base case analyses.**
- **Probabilistic sensitivity analysis showed that outcomes for Cladribine Tablets vs alemtuzumab are inconclusive, as roughly half are in the southeast quadrant (dominant) and half in the northwest quadrant (dominated).**
- **A key strength of this study is that the model considers cost-effectiveness across two important sub-populations of MS from a full societal perspective.**
- **The study included a VOI analysis quantifying the value of eliminating uncertainty in the model.**

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DISCLOSURES

Merck B.V., the Netherlands provided funding to IQVIA for data acquisition and analysis. **MK** is a former employee and **KS** is employee of Merck B.V., Schiphol-Rijk, the Netherlands, an affiliate of Merck KGaA, Darmstadt, Germany. **GH** is employee of EMD Serono, Boston. The authors report no further conflicts of interest.

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