

SUPPLEMENTARY DOCUMENTS

Appendix 1: Markov model: data sources and key assumptions (the model is fully described in Piñol, 2016)

	Delayed treatment (Delayed treatment = no disease-modifying treatment before developing clinically definite multiple sclerosis)	Early treatment
Likelihood of transition to the next disability level every 6 months (Piñol, 2016) according to EDSS health state		
0	0.026	0.018
1-1.5	0.026	0.018
2-2.5	0.026	0.018
3-5.5	0.054	0.037
6-7.5	0.021	0.015
8-10	0.006	0.004
Likelihood of relapse at 6 months (Piñol, 2016; Prosser LA, et al. 2004)		
	0.453	0.282
Proportion still in CIS group (Prosser LA, et al. 2004)		
Year 1	0.72	0.86
Year 2	0.58	0.77
Year 3	0.50	0.72
Year 4	0.42	0.68
Year 5	0.38	0.61
Year 6	0.32	0.56
Year 7	0.28	0.50
Year 8	0.25	0.48
Year 9	0.22	0.42
Year 10	0.20	0.40
Year >10	We did not extrapolate data beyond the 10-year time frame. For cycles in the model after that time frame, we used the probability of conversion for the respective tenth year cycle.	
Yearly societal costs per patient (Ernstsson O, et al. 2016; Prosser LA, et al. 2004)	According to EDSS health state See table 1 (Italy, Spain and Sweden data)	
	Average early healthcare provider costs per person (euros, 2020 value)	
	<u>Italy</u> (Lazzaro C, et al. 2009): CIS = 8,288.68 ; CDMS = 8,252.57	
	<u>Spain</u> (Kobelt G, et al. 2006): CIS = 7,726.20 ; CDMS = 7,092.63	
	<u>Sweden</u> N/A	
	Average early societal costs per person (euros)	
	<u>Italy</u> (Lazzaro C, et al. 2009): CIS = 10,748.11; CDMS = 11,021.47	

	<u>Spain (Kobelt G, et al. 2006):</u> CIS = 13,619.28 ; CDMS = 13,828.08 <u>Sweden (Berg J, et al. 2006):</u> CIS = 21,346.35; CDMS = 22,092.64
QALY	<i>According to EDSS health state</i> See table 1 (Italy, Spain and Sweden data) Average early QALY <u>Italy (Lazzaro C, et al. 2009):</u> CIS = 0.314; CDMS = 0.300 <u>Spain (Kobelt G, et al. 2006):</u> CIS = 0.308; CDMS = 0.294 <u>Sweden (Berg J, et al. 2006):</u> CIS = 0.345; CDMS = 0.332

Note: The model included 2 types of relapses: conversion from CIS to CDMS and relapses after diagnosis of CDMS. Probability of relapse for CDMS patients in both treatment groups (early and delayed) was obtained from the literature. As with utility values, EDSS specific costs were assumed applicable to both CIS and MS patients. Patients could discontinue treatment at any time during the time horizon to reflect the real-world situation. Additionally, we assumed that IFN-1b treatment was suspended when a patient scored 7 on the EDSS, based on clinical expert opinion. In every cycle, patients who remained alive accrued 6 months of life which were later adjusted by the utility corresponding to their health state and occurrence of a relapse.

Appendix 2: sensitivity analyses

Healthcare provider and societal costs (euros) per person				QALYs per person		
Sensitivity 1 (cost)	Sensitivity 2 (cost)	Sensitivity 3 (cost)	Time horizon (years)	Sensitivity 1 (QALY)	Sensitivity 2 (QALY)	Sensitivity 3 (QALY)
relative increase in costs 10%	relative increase 20%	relative increase 30%	25-30	relative increase 10%	relative increase 15%	relative increase 20%
			31-40	relative increase 0%	relative increase 0%	relative increase 0%
			41-50	relative increase 15%	relative increase 20%	relative increase 25%