Data Request 1 – All years MTC adjusted for prior relapse rate

In line with the teriflunomide ACD, revised probabilistic analyses have been conducted with:

- All years MTC adjusted for baseline annualised relapse rates
- The ERGs preferred scenario:
    - Natural history progression data from placebo arms of TOWER and TEMSO
    - Baseline characteristics and initial EDSS distribution from TOWER and TEMSO
    - ERG amended calculation for SPMS conversion probabilities
    - Direct non-medical costs not included
    - Utilities observed in TEMSO, using increments from Orme for high EDSS states where trial data were not available
- Waning of treatment effect is 75% treatment effect after 2 years and 50% treatment effect after 5 years.

The results of the all years MTC adjusted for baseline annualized relapse rates are shown in Appendix 1 (DMTs versus placebo and teriflunomide versus other DMTs). In addition we have included a report outlining method used to carry out this adjustment. Finally, in Appendix 2 MTC results are shown using an alternative method for imputing 1 year prior ARR when only two year prior relapse rates are reported, to that used in the base case approach (the base case approach is outlined on page 3 of the methodological report).

The resulting probabilistic ICERs versus baseline and pairwise ICERs against teriflunomide for the preferred analysis are presented in Table 1.

Table 1 Probabilistic results of teriflunomide versus all comparators (using all years MTC adjusted for baseline ARR)

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER versus baseline (£)	ICER (£) teriflunomide versus comparator
Glatiramer acetate	[redacted]	[redacted]				13,234
Teriflunomide	[redacted]	[redacted]	2,638	0.199	13,234	
IFNβ-1a 44µg (Rebif)	[redacted]	[redacted]	7,999	-0.071	Dominated	Dominates
IFNβ-1a (Avonex)	[redacted]	[redacted]	14,202	-0.081	Dominated	Dominates
IFNβ-1a 22µg (Rebif)	[redacted]	[redacted]	14,684	-0.166	Dominated	Dominates
IFNβ-1b	[redacted]	[redacted]	15,964	-0.257	Dominated	Dominates

The results of the revised base case analysis indicate that teriflunomide dominated all comparators with the exception of glatiramer acetate, for which the ICER was £13,234 Since ICERs for teriflunomide are least preferential for teriflunomide vs glatiramer acetate , this is the comparator used in sensitivity analysis of the MTC. Like for like comparisons of teriflunomide versus glatiramer acetate are shown in Tables 2 and 3, with probabilistic and deterministic results respectively:

Table 2 Probabilistic ICERs of teriflunomide versus glatiramer acetate

Waning assumption	Post 2000 MTC	All years MTC (without meta-regression)	All years MTC (with meta-regression)
With 75% waning at 3-5 years, 50% after 5 years (in line additional information requested in ACD)	£9,216	£118,554	£13,234
No waning (preferred ERG analysis presented in ERG report)	£7,845	£107,148 (ERG report Table 70)	£10,143

Table 3: Deterministic ICERs of teriflunomide versus glatiramer acetate

Waning assumption	Post 2000 MTC	All years MTC (without meta-regression)	All years MTC (with meta-regression)
With 75% waning at 3-5 years, 50% after 5 years (in line additional information requested in ACD)	£10,396	£109,976	£15,866
No waning (preferred ERG analysis presented in ERG report)	£6,266 (ERG report Table 76)	£86,946 (ERG report Table 76)	£10,152

It was suggested in the ACD that the direct non-medical costs should be excluded from the base case to be conservative. However, it was recommended that the inclusion of these costs was tested in sensitivity analysis.

It is the belief of the manufacturer that direct non-medical costs as sourced from Tyas et al should be included within the model and ICERs are shown in Table 5 and 6 including these costs (Tyas et al. 2007). The justification for this is as follows:

- Although no details of what was meant by direct non-medical costs could be found in the Tyas paper the direct non-medical costs within this paper equate to those found in the Karampampa et al [1] paper which are also UK specific costs (see Table 4 below) where details of what is included in this category are provided. The table shows costs from Karampampa limited to professional non-medical support with and without the inclusion of investments / modifications. Investments / modifications were defined in a separate paper by Karampampa as home modifications, car modifications, walking stick, wheelchairs (Karampampa et al. 2012 [2])Professional non-medical support is split between home help (mean 37 hours a year) and professional help unspecified (mean 20 hours a year)
- The UK MS Survey carried out by the MS Society suggests that 50% of MS patients have their social care paid for entirely by the government and another 33% have their social care partly paid for by the government. Table 7 also shows the direct non-medical costs from Karampampa reduced by 33% to take into account that 17% of patients will pay for social care entirely from their own pocket and 33% partially from their own pocket (see Table 17 MS Society report 2013). These costs are still comparable to those in Tyas et al.
- The substantial increase in direct non-medical costs in higher EDSS states is supported by the results of the UK MS Survey which showed that 10% of patients requiring occasional assistance and 60% requiring constant assistance received social care (Table 15 MS Society report 2013). A report from the Work Foundation also identified high costs associated with the higher dependency states of MS; high dependency home care of £1345 per week, stay at a

residential home of £758 a week and maintenance of a special needs flat of £933 per week (see page 32 of Work Foundation report 2011)

Table 4: Comparing UK direct non-medical costs in Tyas et al to non-medical professional support and investments / modifications costs in Karampampa et al.

EDSS state	Tyas et (included in manufacturer basecase submission)	Karampampa et al (uplifted to 2013/14)	Karampampa et al - 66% (uplifted to 2013/14)
0	£5,335	£0-£53	£0-£35
1	£5,780	£0-£53	£0-£35
2	£6,735	£0-£53	£0-£35
3	£9,565	£0-£53	£0-£35
4	£6,462	£1055-£2671	£703-£1780
5	£9,489	£1055-£2671	£703-£1780
6	£9,811	£1055-£2671	£703-£1780
7	£15,761	£18241-£21558	£12160-£14371
8	£20,811	£18241-£21558	£12160-£14371
9	£12,915	£18241-£21558	£12160-£14371

Table 5: Sensitivity analysis: probabilistic results of teriflunomide versus all comparators including direct non-medical costs (not sorted by costs for comparison with Table 1)

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER versus baseline (£)	ICER (£) teriflunomide versus comparator
Glatiramer acetate	[redacted]	[redacted]				Dominated
Teriflunomide	[redacted]	[redacted]	-96	0.204	Dominates	
IFNβ-1a 44µg (Rebif)	[redacted]	[redacted]	8,064	-0.087	Dominated	Dominated
IFNβ-1a (Avonex)	[redacted]	[redacted]	15,344	-0.087	Dominated	Dominated
IFNβ-1a 22µg (Rebif)	[redacted]	[redacted]	16,399	-0.174	Dominated	Dominated
IFNβ-1b	[redacted]	[redacted]	20,363	-0.293	Dominated	Dominated

Table 6: Sensitivity analysis: probabilistic results of teriflunomide versus glatiramer acetate including direct non-medical costs

Waning assumption	Post 2000 MTC	All years MTC (without meta-regression)	All years MTC (with meta-regression)
With 75% waning at 3-5 years, 50% after 5 years (in line additional information requested in ACD)	Dominates	£121,910	Dominates
No waning (preferred ERG analysis presented in ERG report)	Dominates	£89,738	Dominates

As agreed in the teleconference between the manufacturer and the ERG and NICE on 24th September, a comparison between the outcomes from direct evidence for teriflunomide versus placebo and glatiramer acetate versus placebo compared to those obtained from the 3 MTCs is also provided as important contextual information (Table 7). The reason that this is thought to be important is because it is teriflunomide versus glatiramer which is not cost effective dependent on the choice of MTC to supply parameter values in the model; teriflunomide versus other comparators is cost effective irrespective of the choice of MTC.

Table 7: Comparison of MTC outputs to direct trial evidence for teriflunomide versus placebo and glatiramer acetate versus placebo

Comparison	Post-2000, 80% RRMS (MTC)	All Years with 80% RRMS	All Years with 80% RRMS adjusted for baseline	Direct Evidence	Trial Name and sample size	Author, Year
ARR						
GA vs. placebo	0.64 [0.53, 0.76]			0.72 [0.61, 0.87] 0.7 [0.57, 0.86] 0.67 [0.48, 0.93]	CONFIRM (n=713) Copolymer 1 MS Study (n=151) European/Canadian GA Study (n=139)	Fox, 2012 Johnson, 1995 Comi, 2001
Teriflunomide 14 vs. placebo	0.67 [0.57, 0.77]			0.68 [0.36, 1.27] 0.69 [0.58, 0.81] 0.64 [0.53, 0.77]	O'Connor, 2006 (n=118) TEMSO (n=722) TOWER (n=761)	O'Connor, 2006 O'Connor, 2011 Kappos, 2012
Three-month SAD						
GA vs. placebo	0.93 [0.59, 1.45]			0.93 [0.63, 1.37] 0.32 [0.09, 1.09] 0.86 [0.51, 1.45]	CONFIRM (n=713) Bornstein, 1987 (n=50) Copolymer 1 MS Study (n=151)	Fox, 2012 Bornstein, 1987 Johnson, 1995
Teriflunomide 14 vs. placebo	0.71 [0.53, 0.92]			0.7 [0.51, 0.96] 0.68 [0.47, 1]	TEMSO (n=722) TOWER (n=761)	O'Connor, 2011 Kappos, 2012
Discontinuation rate						
GA vs. placebo				0.59 [0.43, 0.81] 1.15 [0.57, 2.33] 1.01 [0.34, 2.97]	CONFIRM (n=713) Copolymer 1 MS Study (n=151) European/Canadian GA Study (n=139)	Fox, 2012 Johnson, 1995 Comi, 2001
Teriflunomide 14 vs. placebo				3.8 [1.15, 12.58] 0.9 [0.65, 1.25] 1.07 [0.79, 1.45]	O'Connor 2006 (n=118) TEMSO (n=722) TOWER (n=761)	O'Connor, 2006 O'Connor, 2011 Kappos, 2012

The following observations are thought to be of relevance in relation to Table 7:

- SAD HR 3 months data should be the primary focus of attention because the cost effectiveness results are substantially driven by this parameter value. For the two larger trials of glatiramer versus placebo, CONFIRM (0.93) and Johnson 1996 (0.86) the estimates of the SAD HR 3 months from the clinical trials are closest to post 2000 MTC output (0.93) followed by the adjusted all years MTC ([redacted]) and least close to the unadjusted all years MTC ([redacted]). The output from the small Bornstein study (0.32) is substantially different from the output from all three MTCs. The results of the Bornstein study are in fact an outlier in relation to all beta interferon studies vs placebbo (0.62-0.93) (Duquette 1993, Ebers 1998) as well as the other two glatiramer acetate studies. Teriflunomide versus placebo SAD HR direct evidence data is similar to the output from both the post 2000 years MTC and the unadjusted all years MTC and most dissimilar to that from that from the adjusted all years MTC.

- The HE model is to some extent sensitive to discontinuation rate (DR) although to a substantially less degree than to SAD HR. For glatiramer, all three MTCs provide similar DR output suggesting glatiramer has a lower discontinuation rate than placebo ([redacted]). The largest study CONFIRM (n=713) supports a lower than placebo discontinuation rate (0.59) closest to the output from the post 2000 MTC whilst the other two studies had higher than placebo discontinuation rates (1.01 and 1.15). For teriflunomide output from all three MTCS provide similar output ([redacted]); the TEMSO study direct evidence is closest to output from the post 2000 MTC (0.9 vs [redacted]) and the TOWER study closest to that from the adjusted all years MTC (1.07 vs [redacted]) with the smaller O'Connor et al study demonstrating substantially higher discontinuation rates than output from all three MTCs. Discontinuation rates are likely to be impacted substantially by trial protocols which have the potential to cause a substantial deviation between discontinuation seen within trials compared to those seen in clinical practice.

- The model is not sensitive to ARR RR results and these do not vary substantially across the three MTCs for glatiramer or teriflunomide versus placebo

Data Request 2 – Treatment sequencing impact

Cost-effectiveness analysis is presented for a number of treatment sequencing scenarios as recommended in the ACD. The following information gives a context / justification for the scenarios detailed in Table 8:

- Based on an interview of 30 neurologists and 15 MS nurses in the UK (all but 3 of the 45 were based in England and Wales) who see 30 or more MS patients a week, the following percentage use of MS treatments for mild / moderate patients as first and second line therapies was noted:
    - 1st line therapies: IFNβ-1a 44µg (Rebif) (27%), IFNβ-1a (Avonex) (25%), glatiramer acetate (22%), natalizumab (13%), IFNβ-1a 22µg (Rebif) (7%) and IFNβ-1b (5%)
    - 2nd line therapies: natalizumab (36%), fingolimod (21%), IFNβ-1a 44µg (Rebif) (16%), glatiramer acetate (12%), IFNβ-1a (Avonex) (10%), IFNβ-1b (2%), IFNβ-1a 22µg (Rebif) (2%)

Also of relevance in considering the treatment scenarios presented are the following conclusions from in depth interviews of 3 England based MS specialists (Genzyme KOL interview report, 2013):

- Teriflunomide would be used as a first line option, in patients with early, mild to moderate relapsing MS as an alternative to beta interferons or glatiramer acetate. It could be used at second line if a patient did not require a “stronger” therapy i.e. fingolimod or natalizumab.

- Teriflunomide is expected not to increase the number of lines of therapy before fingolimod or natalizumab; it gives another option but if a patient qualified for either fingolimod or natalizumab they would be used in preference.

- The following are existing therapies as second line alternatives: natalizumab, fingolimod, Rebif 44µg and glatiramer acetate (the interviewees were not asked to give a percentage split between treatment usage).

The approach to determining the most appropriate treatments sequences for cost effectiveness analysis was as follows:

- Scenarios 1 and 3 in Table 8 were specifically requested within the ACD.
- Scenario 2 is the equivalent of scenario 1 but assumes that teriflunomide does not add a line of therapy but substitutes for IFNβ-1a 44µg (Rebif) – in line with clinician interviews see above
- Scenario 4 is the equivalent of scenario 3 but assumes that teriflunomide does not add a line of therapy but substitutes for IFNβ-1a 44µg (Rebif) – in line with clinician interviews see above
- Scenarios 5 involves sequencing based on the most common 1st and 2nd line treatments assuming that teriflunomide does not add a line of treatment but substitutes for the most common first line treatment. Scenario 6 is the equivalent of scenario 5 but assumes that teriflunomide adds a line of therapy.
- Scenario 7 shows teriflunomide substituting as a 2nd line treatment for glatiramer acetate (this is consistent with the positioning as stated within the original submission of use in place of beta interferons or glatiramer acetate). The ERG, in the opinion of the manufacturer, has incorrectly interpreted the cost effectiveness analysis in the original submission as relating exclusively to treatment naïve patients when it is intended to relate to both treatment naïve and experienced patients. To illustrate this wider intentional positioning of teriflunomide, an analysis explicitly showing teriflunomide as a second line treatment is presented. The sequence of IFNβ-1a 44µg (Rebif) followed by glatiramer has been used as the comparator

since this is the most common sequencing of a beta interferon / glatiramer acetate followed by a beta interferon / glatiramer acetate.

The treatment sequencing analyses presented are using the preferred NICE base case scenario which uses the previously submitted all-years MTC adjusting for baseline ARR as in data request 1, as well as the previously submitted post 2000 MTC and all years MTC. The results in Table 9 shows probabilistic ICERS for each treatment sequence scenario for all three MTC options (using all other assumptions as run for Data request 1). The full pairwise comparison results in terms of costs and QALYs are given for the all-years MTC adjusted for baseline ARR treatment sequencing scenarios are given probabilistically in Table 10.

Table 8 Treatment sequences tested in scenario analyses

Scenario	Intervention sequence			Comparator sequence		
	1st	2nd	3rd	1st	2nd	3rd
1	Teriflunomide	IFNβ-1a 44µg (Rebif)	Fingolimod	IFNβ-1a 44µg (Rebif)	Fingolimod	BSC
2	Teriflunomide	Fingolimod	BSC	IFNβ-1a 44µg (Rebif)	Fingolimod	BSC
3	Teriflunomide	IFNβ-1a 44µg (Rebif)	Glatiramer acetate	IFNβ-1a 44µg (Rebif)	Glatiramer acetate	BSC
4	Teriflunomide	Glatiramer acetate	BSC	IFNβ-1a 44µg (Rebif)	Glatiramer acetate	BSC
5	Teriflunomide	Natalizumab	BSC	IFNβ-1a 44µg (Rebif)	Natalizumab	BSC
6	Teriflunomide	IFNβ-1a 44µg (Rebif)	Natalizumab	IFNβ-1a 44µg (Rebif)	Natalizumab	BSC
7	IFNβ-1a 44µg (Rebif)	Teriflunomide	BSC	IFNβ-1a 44µg (Rebif)	Glatiramer acetate	BSC

Table 9 Summary of resulting probabilistic ICERs of treatment sequencing scenario analysis

Scenario	ICERs		
	Post 2000 MTC	All years MTC not adjusted for baseline ARR	All years MTC adjusted for baseline ARR
1	Dominates	Dominates	Dominates
2	Dominates	Dominates	Dominates
3	£52,028	£90,164	£38,200
4	Dominates	Dominates	Dominates
5	Dominates	Dominates	Dominates
6	Dominates	Dominates	Dominates
7	£24,727	£122,104	£28,606

Table 10 Probabilistic treatment sequencing scenario analysis results using all years MTC adjusting for baseline annualized relapse rates

Scenario	Treatment sequence total costs (£)	Treatment sequence total QALYs	Inc costs (£)	Inc QALYs	ICER (£) Treatment versus Comparator
1	[redacted]	[redacted]	-4,298	0.207	Dominates
2	[redacted]	[redacted]	-5,052	0.272	Dominates
3	[redacted]	[redacted]	10,931	0.286	38,200
4	[redacted]	[redacted]	-5,131	0.269	Dominates
5	[redacted]	[redacted]	-4,956	0.278	Dominates
6	[redacted]	[redacted]	-10,091	0.192	Dominates
7	[redacted]	[redacted]	3,633	0.127	28,606

In scenarios 1, 2, 4, 5 and 6, sequences which begin with teriflunomide dominate the comparator sequences.

It is noted that the only treatment scenario that produces unacceptable ICER values (for the post 2000 or all years adjusted MTCs) is scenario 3 where teriflunomide adds a line of therapy. In this regard, it is noted that the conclusion from in depth interviews of 3 England based MS specialists (Genzyme KOL interview report, 2013) was that teriflunomide is expected not to increase the number of lines of therapy before fingolimod or natalizumab. Given this conclusion it is the belief of the manufacturer that where the comparator arms remain the same, the most appropriate assumption is that the number of lines of therapy between comparator and intervention arms is equal i.e. scenario 4 is more appropriate than scenario 3; scenario 2 is more appropriate than scenario 1; and scenario 5 is more appropriate than scenario 6.

Data Request 3 – external validation

Pairwise comparisons for the probabilistic cost-effectiveness estimates for the current active treatment (all beta interferons, glatiramer acetate) compared with no disease-modifying therapy are presented in Table 11 to externally validate the economic model for teriflunomide by showing how similar these cost-effectiveness estimates are to those in the NHS risk-sharing scheme for multiple sclerosis. The new base case teriflunomide model uses preferred analysis in the ACD report which contains waning of treatment effect; since waning of treatment effect was not considered in the risk-sharing scheme estimates, the comparisons of current active treatment and no disease-modifying therapy are also presented without waning of treatment effect in Table 12.

The results show that estimated total costs and QALYs are lower in the risk-sharing scheme estimates that from the teriflunomide model. One explanation for this is the difference in time horizon between the two models; the risk-sharing scheme estimates were over 20 years where as the teriflunomide model base case is over 50 years. The effect of reducing the time horizon of the teriflunomide analysis is explored in Table 13.

One issue of note in Table 13 is that total costs between TA 32 and those using the existing model are relatively similar when time horizons (and assumptions about waning are matched). What remains substantially different are the QALY results and the incremental QALYs between BSC and active treatments (beta interferons and glatiramer acetate. This may be explained by differences in the estimations of relative effectiveness in the present assessment and TA32 but there is a degree of opacity in the reported output from this earlier assessment which makes it difficult to determine how this was assessed.

To further externally validate the model, mean changes in EDSS score and utility score from interim risk-sharing scheme results are compared to equivalent model predictions for a blended comparator of DMTs included within the risk-sharing scheme. A comparison of teriflunomide with a bended comparator is shown in Table 14.

Table 11 Validation of output from teriflunomide model compared to TA 32 (with waning of treatment effect as recommended by the ERG in the existing assessment results)

				Existing assessment								
	TA 32 [NICE ERG report 2001]			Post 2000 MTC			All years MTC adjusted for baseline ARR			All years MTC not adjusted for baseline ARR		
	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)
BSC	68,453	8.93		[redacted]	[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	
IFN-β 1a (Avonex)	112,251	9.84	48,085	[redacted]	[redacted]	268,898	[redacted]	[redacted]	210,570	[redacted]	[redacted]	199,556
IFN-β 1b	102,133	9.57	52,523	[redacted]	[redacted]	1,449,050	[redacted]	[redacted]	1,915,664	[redacted]	[redacted]	270,317
IFN-β 1a (Rebif 22µg)	112,796	9.68	58,817	[redacted]	[redacted]	141,949	[redacted]	[redacted]	371,954	[redacted]	[redacted]	122,119
IFN-β 1a (Rebif 44µg)	131,455	9.73	78,556	[redacted]	[redacted]	186,012	[redacted]	[redacted]	170,893	[redacted]	[redacted]	139,840
Glatiramer acetate	101,831	9.27	97,690	[redacted]	[redacted]	178,557	[redacted]	[redacted]	98,785	[redacted]	[redacted]	75,584

Table 12 Validation of output from teriflunomide model compared to TA 32 (no waning of treatment effect in the existing assessment results)

				Existing assessment								
	TA 32 [NICE ERG report 2001]			Post 2000 MTC			All years MTC adjusted for baseline ARR			All years MTC not adjusted for baseline ARR		
	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)
BSC	68,453	8.93		[redacted]	[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	
IFN-β 1a (Avonex)	112,251	9.84	48,085	[redacted]	[redacted]	152,757	[redacted]	[redacted]	132,552	[redacted]	[redacted]	117,759
IFN-β 1b	102,133	9.57	52,523	[redacted]	[redacted]	204,675	[redacted]	[redacted]	445,215	[redacted]	[redacted]	131,825
IFN-β 1a (Rebif 22µg)	112,796	9.68	58,817	[redacted]	[redacted]	69,910	[redacted]	[redacted]	151,007	[redacted]	[redacted]	65,486
IFN-β 1a (Rebif 44µg)	131,455	9.73	78,556	[redacted]	[redacted]	101,604	[redacted]	[redacted]	98,794	[redacted]	[redacted]	79,027
Glatiramer acetate	101,831	9.27	97,690	[redacted]	[redacted]	86,194	[redacted]	[redacted]	57,141	[redacted]	[redacted]	46,473

Table 13 Validation of output from teriflunomide model compared to TA 32 (with time horizon of 20 years in the existing assessment results)

				Existing assessment								
	TA 32 [NICE ERG report 2001]			Post 2000 MTC			All years MTC adjusted for baseline ARR			All years MTC not adjusted for baseline ARR		
	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)	Total Costs (£)	Total QALYs	ICER versus BSC (£)
BSC	68,453	8.93		[redacted]	[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	
IFN-β 1a (Avonex)	112,251	9.84	48,085	[redacted]	[redacted]	379,367	[redacted]	[redacted]	309,143	[redacted]	[redacted]	261,260
IFN-β 1b	102,133	9.57	52,523	[redacted]	[redacted]	2,066,566	[redacted]	[redacted]	Dominates	[redacted]	[redacted]	379,845
IFN-β 1a (Rebif 22µg)	112,796	9.68	58,817	[redacted]	[redacted]	246,691	[redacted]	[redacted]	705,522	[redacted]	[redacted]	195,596
IFN-β 1a (Rebif 44µg)	131,455	9.73	78,556	[redacted]	[redacted]	328,169	[redacted]	[redacted]	295,995	[redacted]	[redacted]	217,300
Glatiramer acetate	101,831	9.27	97,690	[redacted]	[redacted]	253,137	[redacted]	[redacted]	139,930	[redacted]	[redacted]	108,866

Table 14 Validation of deterministic output from teriflunomide model compared to risk-sharing scheme 2 year results [Boggild et al. 2009]

				Existing assessment					
	Risk-sharing scheme [Boggild et al. 2009] per protocol analysis (n=3686)			Post 2000 MTC		All years MTC adjusted for baseline ARR		All years MTC not adjusted for baseline ARR	
	Predicted progression BSC	Predicted progression DMTs	Actual progression DMTs	Progression BSC	Progression blended comparator	Progression BSC	Progression blended comparator	Progression BSC	Progression blended comparator
EDSS	0.47	0.29	0.57	0.231	0.18	0.231	0.15	0.231	0.11
Utility score	-0.0254*	-0.0158*	-0.0266*	-0.0586	-0.0589	-0.0586	-0.0573	-0.0586	-0.0547

*assumed should be negative since relate to disease progression – unclear from publication

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