NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology appraisals

Patient access scheme submission template

October 2009

1 Introduction

The 2009 Pharmaceutical Price Regulation Scheme (PPRS) (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS) is a non-contractual scheme between the Department of Health and the Association of the British Pharmaceutical Industry. The purpose of the 2009 PPRS is to ensure that safe and cost-effective medicines are available on reasonable terms to the NHS in England and Wales. One of the features of the 2009 PPRS is to improve patients' access to medicines at prices that better reflect their value through patient access schemes.

Patient access schemes are arrangements which may be used on an exceptional basis for the acquisition of medicines for the NHS in England and Wales. Patient access schemes propose either a discount or rebate that may be linked to the number, type or response of patients, or a change in the list price of a medicine linked to the collection of new evidence (outcomes). These schemes help to improve the cost effectiveness of a medicine and therefore allow the National Institute for Health and Care Excellence (NICE) to recommend treatments which it would otherwise not have found to be cost effective. More information on the framework for patient access schemes is provided in the 2009 PPRS (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS.

Patient access schemes are proposed by a pharmaceutical company and agreed with the Department of Health, with input from the Patient Access Schemes Liaison Unit (PASLU) within the Centre for Health Technology Evaluation at NICE.

2 Instructions for manufacturers and sponsors

This document is the patient access scheme submission template for technology appraisals. If manufacturers and sponsors want the National Institute for Health and Care Excellence (NICE) to consider a patient access scheme as part of a technology appraisal, they should use this template. NICE can only consider a patient access scheme after formal referral from the Department of Health.

The template contains the information NICE requires to assess the impact of a patient access scheme on the clinical and cost effectiveness of a technology, in the context of a technology appraisal, and explains the way in which background information (evidence) should be presented. If you are unable to follow this format, you must state your reasons clearly. You should insert 'N/A' against sections that you do not consider relevant, and give a reason for this response.

Please refer to the following documents when completing the template:

- 'Guide to the methods of technology appraisal' (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp)
- 'Specification for manufacturer/sponsor submission of evidence' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologyappraisalsubmissiontemplates.jsp) and
- Pharmaceutical Price Regulation Scheme 2009 (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS).

For further details on the technology appraisal process, please see NICE's 'Guide to the single technology appraisal (STA) process' and 'Guide to the multiple technology appraisal (MTA) process' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp). The

‘Specification for manufacturer/sponsor submission of evidence’ provides details on disclosure of information and equality issues.

Make the submission as brief and informative as possible. Only mark information as confidential when absolutely necessary. Sufficient information must be publicly available for stakeholders to comment on the full content of the technology appraisal, including details of the proposed patient access scheme. Send submissions electronically to NICE in Word or a compatible format, not as a PDF file.

Appendices may be used to include additional information that is considered relevant to the submission. Do not include information in the appendices that has been requested in the template. Appendices should be clearly referenced in the main submission.

When making a patient access scheme submission, include:

- an updated version of the checklist of confidential information, if necessary
- an economic model with the patient access scheme incorporated, in accordance with the ‘Guide to the methods of technology appraisal’ (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp).

If you are submitting the patient access scheme at the end of the appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

3 Details of the patient access scheme

3.1 Please give the name of the technology and the disease area to which the patient access scheme applies.

Technology: Teriflunomide (Aubagio ®).

Disease area: Relapsing remitting multiple sclerosis (RRMS).

3.2 Please outline the rationale for developing the patient access scheme.

The price of teriflunomide proposed within this application reflects the costs associated with prescribing the current standard of care in this indication; interferon-betas and glatiramer acetate.

Treatment for relapsing remitting multiple sclerosis (RRMS) is always initiated by a neurologist experienced in managing MS; this goes someway to ensuring that prescribing and monitoring is appropriate.

Teriflunomide will be the first oral agent to be licensed for use in RRMS; prior use of injectable agents such as interferon-beta or glatiramer acetate is not required. Prior to the availability of teriflunomide, patients with RRMS are likely to be prescribed an injectable disease-modifying treatment (interferon-beta or glatiramer acetate); in many cases this does not suit patients due to the route of administration. In other cases patients find it difficult to tolerate treatment with interferon-beta or glatiramer acetate; in such circumstances, teriflunomide provides an alternative option.

A simple discount patient access scheme (PAS) is in existence for fingolimod, an oral treatment prescribed for highly-active (HA) RRMS.

Teriflunomide would be suitable for provision to patients via the homecare route, if this suited the locality prescribing the treatment.

3.3 Please describe the type of patient access scheme, as defined by the PPRS.

This is a financially based scheme.

The proposed list price for teriflunomide 14mg per day is £13,529 per patient per year, however Genzyme propose offering a fixed price to NHS patients in England and Wales of [redacted] per patient, per year, representing [redacted] of the list price at this time.

Teriflunomide will be in tablet form with 28 tablets per pack. The anticipated list price will be £1,037.84 per 28 tab pack. The discounted PAS price would be [redacted] per 28 tab pack.

3.4 Please provide specific details of the patient population to which the patient access scheme applies. Does the scheme apply to the whole licensed population or only to a specific subgroup (for example, type of tumour, location of tumour)? If so:

- How is the subgroup defined?
- If certain criteria have been used to select patients, why have these have been chosen?
- How are the criteria measured and why have the measures been chosen?

Teriflunomide, Aubagio® is currently unlicensed, however, on 21 March 2013, the CHMP adopted a positive opinion, recommending the granting of a marketing authorisation for the Aubagio 14 mg film-coated tablet intended for the treatment of adult patients with relapsing remitting forms of multiple sclerosis.

As per the required criteria for a simple scheme the teriflunomide PAS will be valid for the whole licensed population.

Genzyme are unaware of clinical uses for teriflunomide outside of the proposed marketing authorisation and have no further clinical trials in progress in support of additional indications.

At this time Genzyme do not intend offering the NHS discount to non-NHS patients.

3.5 Please provide details of when the scheme will apply to the population specified in 3.4. Is the scheme dependent on certain criteria, for example, degree of response, response by a certain time point, number of injections? If so:

- Why have the criteria been chosen?
- How are the criteria measured and why have the measures been chosen.

The simple scheme will be operated as a reduction from the list price through a discount applied to all original invoices for the product and will apply from the point at which a Hospital Trust purchases a supply of teriflunomide for an NHS patient.

3.6 What proportion of the patient population (specified in 3.4) is expected to meet the scheme criteria (specified in 3.5)?

The scheme will apply to all relevant patients who are suitable for treatment with teriflunomide.

3.7 Please explain in detail the financial aspects of the scheme. How will any rebates be calculated and paid?

The simple scheme will be operated as a reduction from the list price through a discount applied to all original invoices for the product.

The fixed price will be offered on the original invoice to Hospital Trust purchasers of teriflunomide. Commissioners will be notified of this price and it is anticipated that this may be reflected in QIPP agreements at a local level.

3.8 Please provide details of how the scheme will be administered. Please specify whether any additional information will need to be collected, explaining when this will be done and by whom.

Not applicable. As per the requirements of a simple scheme, there is no additional administration required for the operation of the scheme.

3.9 Please provide a flow diagram that clearly shows how the scheme will operate. Any funding flows must be clearly demonstrated.

Not applicable. As per response 3.5 and 3.7, the scheme is operated as a reduction from the list price through a discount applied to all original invoices for the product.

3.10 Please provide details of the duration of the scheme.

Genzyme commit to continuing the scheme until NICE next reviews the product under the technology appraisals programme and a final decision has been published on the NICE website.

Should Genzyme receive new evidence on the effectiveness of teriflunomide before the NICE review is due, we will request that NICE bring forward the review.

This PAS is offered on condition that it is interpreted as the type of simple scheme where the fixed price offered is permitted by ministers to remain confidential. For the avoidance of doubt, if it is decided by ministers that the price offered may not be kept confidential then the scheme will be withdrawn. Genzyme understands that the existence of an adjusted price may be made public; it is just the subsequent fixed cost that we expect to be kept confidential.

Genzyme reserves the right to withdraw the scheme from a specific purchaser in the event that there is evidence of use of fixed price supplies of teriflunomide for patients outside the NHS (i.e. patients using private insurance or product being sold outside the NHS).

3.11 Are there any equity or equalities issues relating to the scheme, taking into account current legislation and, if applicable, any concerns identified during the course of the appraisal? If so, how have these been addressed?

Genzyme have no concerns regarding equality issues at this time however it should be noted that teriflunomide is not recommended for use in patients below 18 years of age since the safety and efficacy of teriflunomide in children and adolescents aged 0 to 18 years has not yet been established; no data are available.

3.12 If available, please list any scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians and patient information documents. Please include copies in the appendices.

NHS organisations will be required to sign an agreement to take part in the scheme. As per the requirements of a simple scheme there is no additional documentation required to be completed to receive the benefits of the scheme.

3.13 In the exceptional case that you are submitting an outcome-based scheme, as defined by the PPRS, please also refer to appendix B.

Not applicable.

4 Cost effectiveness

4.1 If the population to whom the scheme applies (as described in sections 3.4 and 3.5) has not been presented in the main manufacturer/sponsor submission of evidence for the technology appraisal (for example, the population is different as there has been a change in clinical outcomes or a new continuation rule), please (re-)submit the relevant sections from the 'Specification for manufacturer/sponsor submission of evidence' (particularly sections 5.5, 6.7 and 6.9). You should complete those sections both with and without the patient access scheme. You must also complete the rest of this template.

Not applicable.

4.2 If you are submitting the patient access scheme at the end of the technology appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

Not applicable.

4.3 Please provide details of how the patient access scheme has been incorporated into the economic model. If applicable, please also provide details of any changes made to the model to reflect the assumptions that the Appraisal Committee considered most plausible.

The price of teriflunomide has been reduced from £13,529 to [redacted] per year. The price remains the same for all EDSS health states in the model.

4.4 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic model which includes the patient access scheme.

The clinical effectiveness data used in the model does not change for the inclusion of the PAS and can be found in Section 7.3 of the main manufacturer/sponsor submission of evidence for the technology appraisal.

4.5 Please list any costs associated with the implementation and operation of the patient access scheme (for example, additional pharmacy time for stock management or rebate calculations). A suggested format is presented in table 1. Please give the reference source of these costs. Please refer to section 6.5 of the 'Specification for manufacturer/sponsor submission of evidence'.

Not applicable.

4.6 Please provide details of any additional treatment-related costs incurred by implementing the patient access scheme. A suggested format is presented in table 2. The costs should be provided for the intervention both with and without the patient access scheme. Please give the reference source of these costs.

Not applicable.

Summary results

Base-case analysis

4.7 Please present in separate tables the cost-effectiveness results as follows

- the results for the intervention without the patient access scheme
- the results for the intervention with the patient access scheme.

Table 1 Base-case probabilistic cost-effectiveness results without patient access scheme

	Teriflunomide	Blended comparator
Total costs (£)	[redacted]	[redacted]
Difference in total costs (£)	[redacted]	[redacted]
QALYs	[redacted]	[redacted]
QALY difference	[redacted]	[redacted]
ICER (£)	[redacted]	[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 2 Base-case probabilistic cost-effectiveness results with patient access scheme

	Teriflunomide	Blended comparator
Total costs (£)	[redacted]	[redacted]
Difference in total costs (£)	[redacted]	-5,491
QALYs	[redacted]	[redacted]
QALY difference	[redacted]	0.201
ICER (£)	[redacted]	Dominates

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 3 Base-case deterministic cost-effectiveness results without patient access scheme

	Teriflunomide	Blended comparator
Intervention cost (£)	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]
Difference in total costs (£)	[redacted]	[redacted]
LYG	[redacted]	[redacted]
LYG difference	[redacted]	[redacted]
QALYs	[redacted]	[redacted]
QALY difference	[redacted]	[redacted]
ICER (£)	[redacted]	[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 4 Base-case deterministic cost-effectiveness results with patient access scheme

	Teriflunomide	Blended comparator
Intervention cost (£)	[redacted]	[redacted]
Other costs (£)	[redacted]	[redacted]
Total costs (£)	[redacted]	[redacted]
Difference in total costs (£)	[redacted]	-6,724
LYG	[redacted]	[redacted]
LYG difference	[redacted]	[redacted]
QALYs	[redacted]	[redacted]
QALY difference	[redacted]	0.288
ICER (£)	[redacted]	Dominates

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

4.8 Please present in separate tables the incremental results as follows.

- the results for the intervention without the patient access scheme
- the results for the intervention with the patient access scheme.

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4.

Table 5 Base-case probabilistic incremental results of teriflunomide versus all comparators without patient access scheme

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)	ICER (£) INC (QALYs)
Glatiramer acetate	[redacted]	[redacted]				
Rebif 22µg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Rebif 44µg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Avonex	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Betaferon	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Aubagio	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio.

Table 6 Base-case probabilistic incremental results of teriflunomide versus all comparators with patient access scheme

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)	ICER (£) INC (QALYs)
Aubagio	[redacted]	[redacted]				
Copaxone	[redacted]	[redacted]	400	-0.184	Dominated	Dominated
Rebif 22µg	[redacted]	[redacted]	3,285	-0.034	Dominated	Dominated
Rebif 44µg	[redacted]	[redacted]	3,722	-0.133	Dominated	Dominated
Avonex	[redacted]	[redacted]	9,256	-0.221	Dominated	Dominated
Betaferon	[redacted]	[redacted]	12,881	-0.446	Dominated	Dominated

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 7 Base-case probabilistic incremental results of teriflunomide versus aggregated Rebif comparator with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	3,556	-0.095	Dominated

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 8 Base-case deterministic incremental results of teriflunomide versus all comparators without patient access scheme

Technologies	Total costs (£)	Total LYG	Total QALYs	INC costs (£)	INC LYG	INC QALYs	ICER (£) versus baseline (QALYs)	ICER (£) INC (QALYs)
Copaxone	[redacted]	[redacted]	[redacted]					
Rebif 44mcg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Rebif 22mcg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Avonex	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Betaferon	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Aubagio	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio.

Table 9 Base-case deterministic incremental results of teriflunomide versus all comparators with patient access scheme

Technologies	Total costs (£)	Total LYG	Total QALYs	INC costs (£)	INC LYG	INC QALYs	ICER (£) versus baseline (QALYs)	ICER (£) INC (QALYs)
Aubagio	[redacted]	[redacted]	[redacted]					
Copaxone	[redacted]	[redacted]	[redacted]	2,277	-0.057	-0.305	Dominated	Dominated
Rebif 44mcg	[redacted]	[redacted]	[redacted]	3,791	-0.029	-0.201	Dominated	Dominated
Rebif 22mcg*	[redacted]	[redacted]	[redacted]	4,796	-0.029	-0.196	Dominated	Dominated
Avonex	[redacted]	[redacted]	[redacted]	9,132	-0.054	-0.286	Dominated	Dominated
Betaferon	[redacted]	[redacted]	[redacted]	17,567	-0.133	-0.721	Dominated	Dominated

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

*see page 314 of main submission for discussion of the need to interpret Rebif 22 results with caution

Table 10 Base-case deterministic incremental results of teriflunomide versus aggregated Rebif comparator with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	4,219	-0.174	Dominated

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Sensitivity analyses

4.9 Please present deterministic sensitivity analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal. Consider using tornado diagrams.

As described in Section 7.6.2 of the main manufacturer/sponsor submission of evidence for the technology appraisal, deterministic one-way and parameter sensitivity analyses were run for the base case of teriflunomide versus a blended comparator with the PAS. The results of the one-way analysis are presented in a tornado diagram in Figure 1 and Table 11 in terms of incremental net monetary benefit at a willingness to pay of £30,000 per QALY. The results of the parameter uncertainty analysis are presented in Table 12.

Probabilistic and deterministic results are also presented in Tables 13-20 when using the all-years MTC (see Additional Appendix 2 of main submission) rather than the base case MTC with and without the Bornstein study (see Section B6.7.8 of main submission) [Bornstein et al, 1987].

Figure 1 Tornado diagram illustrating one-way sensitivity analysis results with the top ten most sensitive parameters

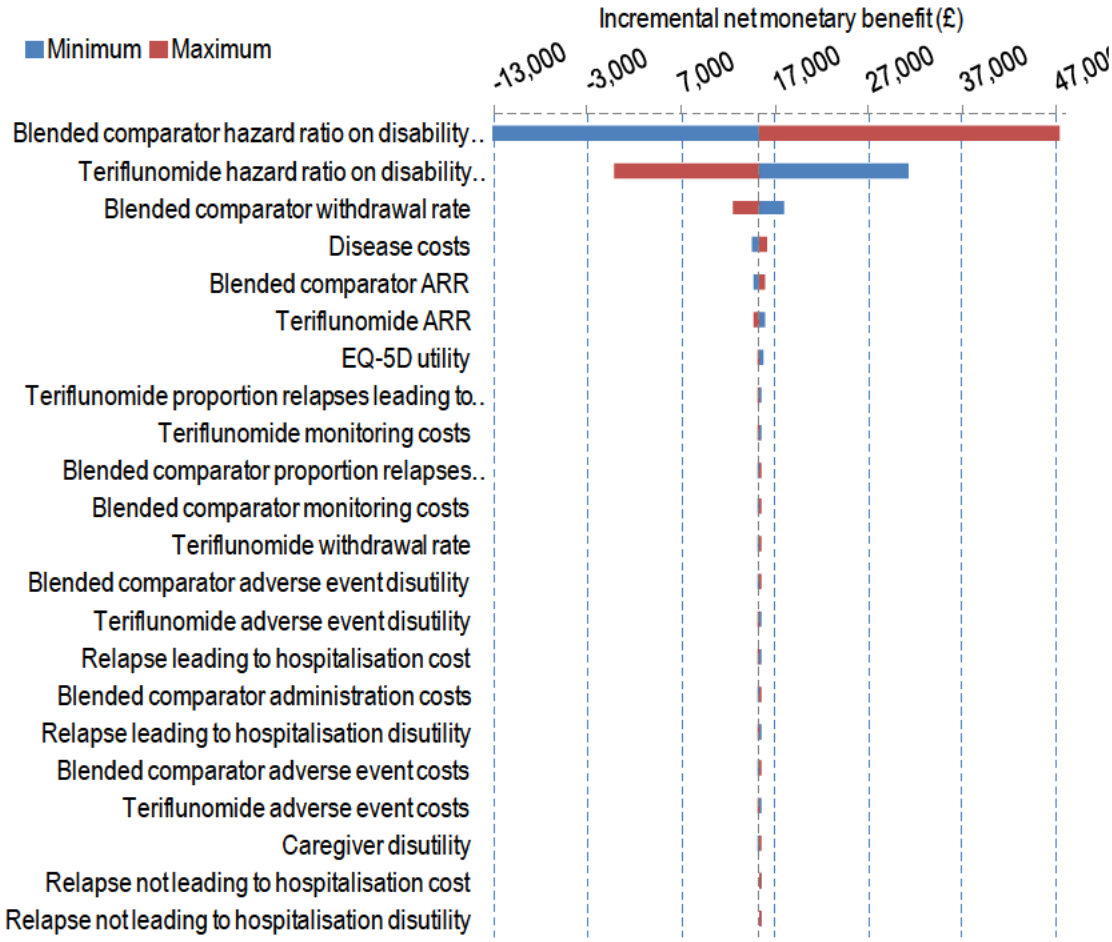


Table 11 One-way sensitivity analysis results

Parameter	Variation	Minimum				Maximum			
		Inc Cost	Inc QALY	ICER	INMB	Inc Cost	Inc QALY	ICER	INMB
Base case		-6,724	0.288	Dominates	15,355				
Blended comparator hazard ratio on disability progression	95% CI	4,745	-0.283	Dominated	-13,230	-19,551	0.925	Dominates	47,297
Teriflunomide hazard ratio on disability progression	95% CI	-13,094	0.603	Dominates	31,180	-459	-0.022	20,613	-209
Blended comparator withdrawal rate	95% CI	-10,076	0.267	Dominates	18,100	-3,300	0.309	Dominates	12,558
Disease costs	+/- 10%	-5,944	0.288	Dominates	14,575	-7,504	0.288	Dominates	16,136
Blended comparator ARR	95% CI	-6,278	0.284	Dominates	14,802	-7,261	0.292	Dominates	16,021
Teriflunomide ARR	95% CI	-7,138	0.291	Dominates	15,866	-6,310	0.284	Dominates	14,844
EQ-5D utility	95% CI	-6,724	0.304	Dominates	15,847	-6,724	0.281	Dominates	15,145
Teriflunomide proportion relapses leading to hospitalisation	+/- 10%	-6,840	0.288	Dominates	15,485	-6,608	0.287	Dominates	15,226
Teriflunomide monitoring costs	+/- 10%	-6,845	0.288	Dominates	15,477	-6,603	0.288	Dominates	15,234
Blended comparator proportion relapses leading to hospitalisation	+/- 10%	-6,624	0.287	Dominates	15,243	-6,824	0.288	Dominates	15,467
Blended comparator monitoring costs	+/- 10%	-6,614	0.288	Dominates	15,245	-6,834	0.288	Dominates	15,465
Teriflunomide withdrawal rate	95% CI	-5,891	0.313	Dominates	15,276	-7,536	0.263	Dominates	15,427
Blended comparator adverse event disutility	+/- 10%	-6,724	0.286	Dominates	15,295	-6,724	0.290	Dominates	15,416
Teriflunomide adverse event disutility	+/- 10%	-6,724	0.290	Dominates	15,412	-6,724	0.286	Dominates	15,298
Relapse leading to hospitalisation cost	+/- 10%	-6,746	0.288	Dominates	15,377	-6,702	0.288	Dominates	15,333
Blended comparator administration costs	+/- 10%	-6,711	0.288	Dominates	15,342	-6,737	0.288	Dominates	15,369
Relapse leading to hospitalisation disutility	+/- 10%	-6,724	0.288	Dominates	15,358	-6,724	0.288	Dominates	15,352
Blended comparator adverse event costs	+/- 10%	-6,722	0.288	Dominates	15,354	-6,726	0.288	Dominates	15,357
Teriflunomide adverse event costs	+/- 10%	-6,725	0.288	Dominates	15,357	-6,723	0.288	Dominates	15,354
Caregiver disutility	+/- 10%	-6,724	0.288	Dominates	15,355	-6,724	0.288	Dominates	15,356

Relapse not leading to hospitalisation cost	+/- 10%	-6,724	0.288	Dominates	15,355	-6,724	0.288	Dominates	15,355
Relapse not leading to hospitalisation disutility	+/- 10%	-6,724	0.288	Dominates	15,355	-6,724	0.288	Dominates	15,355

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio; INMB: incremental net monetary benefit.

Table 121 Parameter sensitivity analysis deterministic results

Scenario	Teri total costs (£)	Teri total QALYs	Blended comp costs (£)	Blended comp QALYs (£)	Inc costs (£)	Inc QALYs	ICER (£) inc (QALYs)
Base case	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.288	Dominates
Clinical data sourced from all-years, ≥80% RRMS MTC	[redacted]	[redacted]	[redacted]	[redacted]	-3,164	0.154	Dominates
Clinical data sourced from all-years, ≥80% RRMS MTC excluding Bornstein et al.	[redacted]	[redacted]	[redacted]	[redacted]	-3,233	0.158	Dominates
Natural history costs from Karampampa, 2012	[redacted]	[redacted]	[redacted]	[redacted]	-12,991	0.288	Dominates
Relapse costs from Tyas, 2007	[redacted]	[redacted]	[redacted]	[redacted]	-6,871	0.288	Dominates
Baseline EDSS utility score from TEMSO study	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.324	Dominates
Disutility of relapse from Orme, 2007	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.287	Dominates
Initial EDSS distribution from TOWER and TEMSO studies	[redacted]	[redacted]	[redacted]	[redacted]	-8,190	0.346	Dominates
Starting age and male: female ratio from TOWER and TEMSO studies	[redacted]	[redacted]	[redacted]	[redacted]	-6,811	0.289	Dominates
Natural history relapse rate from Patzold, 1982	[redacted]	[redacted]	[redacted]	[redacted]	-6,605	0.287	Dominates
Proportion of relapses leading to hospitalisation from placebo arms of TEMSO study	[redacted]	[redacted]	[redacted]	[redacted]	-6,623	0.287	Dominates
Probability of	[redacted]	[redacted]	[redacted]	[redacted]	-6,723	0.247	Dominates

adverse events in subsequent years equal to adverse events in year 1							

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

Tables 13-16 below relate to a sensitivity analysis carried out using the all years MTC (sensitivity analysis MTC) results in the model rather than the base case MTC. The rationale for having a base case MTC with a cut off of year of study / publication at ≥ 2000 is provided on pages 136 and 137 (and discussed on pages 184 and 185) of the main submission. The results of the all year (sensitivity analysis) MTC are presented in Additional Appendix 2 in which all relevant studies irrespective of year of study / publication were included in the MTC.

Table 13 Incremental probabilistic results of teriflunomide versus all comparators using sensitivity analysis MTC for 3-month SAD, ARR and withdrawal with patient access scheme

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Copaxone	[redacted]	[redacted]				
Aubagio	[redacted]	[redacted]	3,573	0.041	86,866	86,866
Rebif 44mcg	[redacted]	[redacted]	6,279	-0.093	Dominated	Dominated
Rebif 22mcg*	[redacted]	[redacted]	6,285	0.040	157,356	Dominated
Betaferon	[redacted]	[redacted]	10,787	-0.196	Dominated	Dominated
Avonex	[redacted]	[redacted]	11,948	-0.164	Dominated	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

*see page 314 of main submission for discussion of the need to interpret Rebif 22 results with caution

Table 14 Incremental probabilistic results of teriflunomide versus aggregated Rebif comparator using sensitivity analysis MTC for 3-month SAD, ARR and withdrawal with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	2,709	-0.084	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

Table 15 Incremental deterministic results of teriflunomide versus all comparators using sensitivity analysis MTC for 3-month SAD, ARR and withdrawal including with patient access scheme

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Copaxone	[redacted]	[redacted]				
Aubagio	[redacted]	[redacted]	3,599	0.074	48,635	48,635

Rebif 44µg	[redacted]	[redacted]	5,363	-0.061	Dominated	Dominated
Rebif 22µg*	[redacted]	[redacted]	5,851	-0.019	Dominated	Dominated
Betaferon	[redacted]	[redacted]	11,262	-0.238	Dominated	Dominated
Avonex	[redacted]	[redacted]	11,359	-0.178	Dominated	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

*see page 314 of main submission for discussion of the need to interpret Rebif 22 results with caution

Table 16 Incremental deterministic results of teriflunomide versus aggregated Rebif using sensitivity analysis MTC for 3-month SAD, ARR and withdrawal with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	2,014	-0.095	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

Tables 17-19 below relate to a sensitivity analysis carried out using the all years MTC (sensitivity analysis MTC) excluding Bornstein et al study results in the model rather than the base case MTC. The rationale for having a base case MTC with a cut off of year of study / publication at ≥ 2000 is provided on pages 136 and 137 (and discussed on pages 184 and 185) of the main submission. The results of the all year (sensitivity analysis) MTC are presented in Additional Appendix 2 in which all relevant studies irrespective of year of study / publication were included in the MTC with and without inclusion of the Bornstein et al study. The rationale for excluding Bornstein et al is discussed on pages 185 and 186 of the main submission.

Table 17 Incremental probabilistic results of teriflunomide versus all comparators using sensitivity analysis (all-years) MTC for ARR and withdrawal , and sensitivity analysis MTC excluding Bornstein et al for 3-month SAD a with patient access scheme

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Copaxone	[redacted]	[redacted]				
Aubagio	[redacted]	[redacted]	2,641	0.125	21,062	21,062
Rebif 22mcg*	[redacted]	[redacted]	4,130	0.130	31,685	301,857
Rebif 44mcg	[redacted]	[redacted]	4,233	0.002	1,884,941	Dominated
Betaferon	[redacted]	[redacted]	10,148	-0.167	Dominated	Dominated
Avonex	[redacted]	[redacted]	10,364	-0.110	Dominated	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

*see page 314 of main submission for discussion of the need to interpret Rebif 22 results with caution

Table 18 Incremental probabilistic results of teriflunomide versus all aggregated Rebif comparator using sensitivity analysis (all-years) MTC for ARR and withdrawal , and sensitivity analysis MTC excluding Bornstein et al for 3-month SAD a with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	1,552	-0.075	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

Table 19 Incremental deterministic results of teriflunomide versus all comparators using sensitivity analysis (all-years) MTC for ARR and withdrawal , and sensitivity analysis MTC excluding Bornstein et al for 3-month SAD a with patient access scheme

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Copaxone	[redacted]	[redacted]				
Aubagio	[redacted]	[redacted]	2,476	0.125	19,808	19,808
Rebif 44µg	[redacted]	[redacted]	3,627	0.02	181,350	Dominated
Rebif 22µg*	[redacted]	[redacted]	4,043	0.065	62,200	Dominated
Avonex	[redacted]	[redacted]	10,185	-0.125	Dominated	Dominated
Betaferon	[redacted]	[redacted]	11,059	-0.234	Dominated	Dominated

QALY: quality-adjusted life-year; INC: incremental; ICER: incremental cost-effectiveness ratio

*see page 314 of main submission for discussion of the need to interpret Rebif 22 results with caution

Table 20 Incremental deterministic results of teriflunomide versus all aggregated Rebif comparator using sensitivity analysis (all-years) MTC for ARR and withdrawal , and sensitivity analysis MTC excluding Bornstein et al for 3-month SAD a with patient access scheme (see p314 main submission for rationale for presenting aggregated Rebif results)

Technologies	Total costs (£)	Total QALYs	INC costs (£)	INC QALYs	ICER (£) versus baseline (QALYs)
Aubagio	[redacted]	[redacted]			
Rebif	[redacted]	[redacted]	1,376	-0.064	Dominated

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

4.10 Please present any probabilistic sensitivity analysis results, and include scatter plots and cost-effectiveness acceptability curves.

Mean results of the probabilistic sensitivity analysis with 10,000 simulations for teriflunomide with the PAS versus the blended comparator are given in Table 2 as the base case. Figure 2 shows the scatter plot of the base case PSA of teriflunomide versus the blended comparator. The uncertainty in the

probabilistic results is a consequence of the relatively wide confidence intervals in hazard ratios of 3 month disability progression obtained from the MTC, as discussed and investigated further in the main submission.

The corresponding cost-effectiveness acceptability curve is given in Figure 3 for teriflunomide versus the blended comparator. The probability of teriflunomide being cost-effective at willingness to pay threshold of £20,000 is 63%.

Figure 2 Scatter plot of probabilistic sensitivity analysis results of teriflunomide with the PAS versus the blended comparator

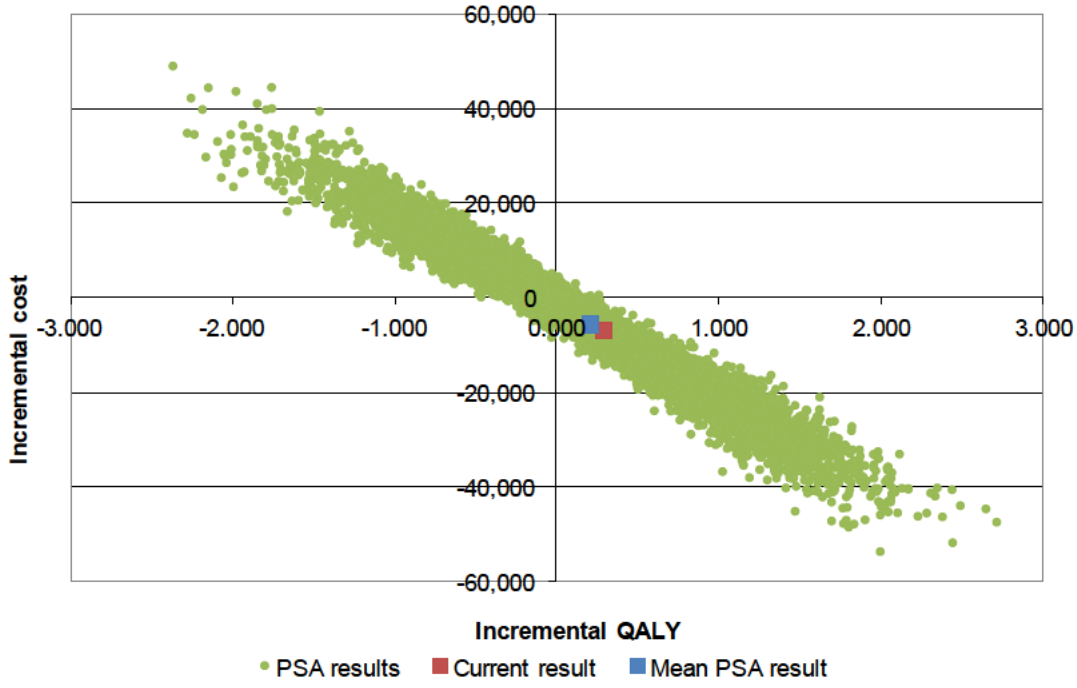
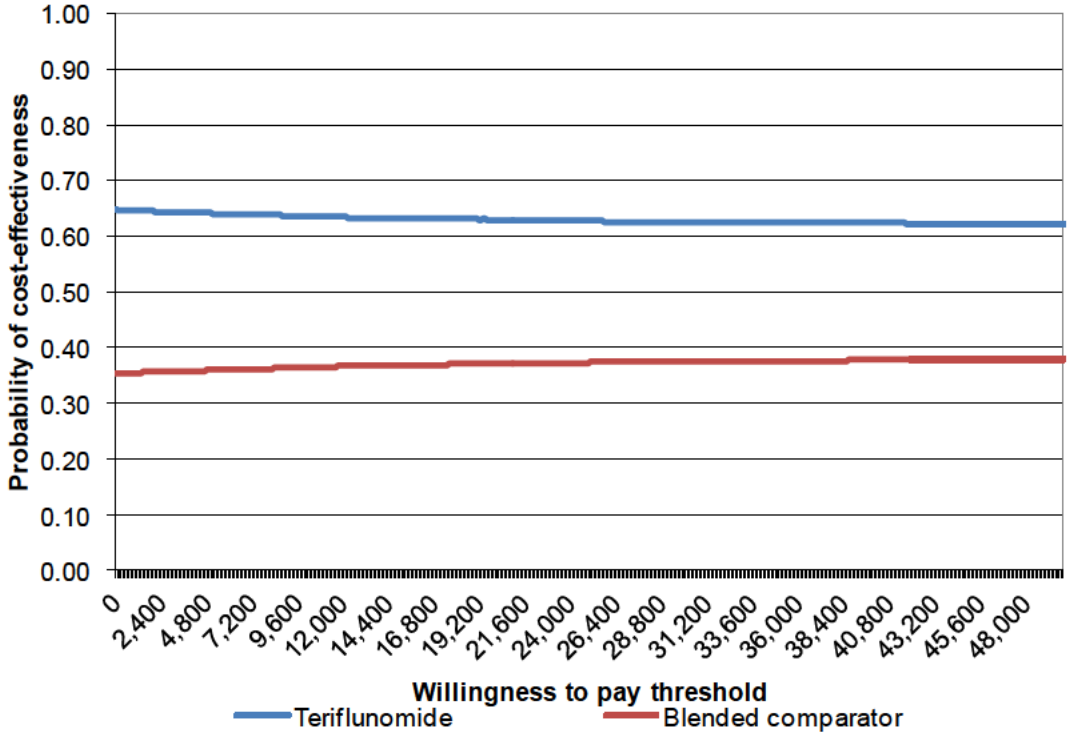


Figure 3 Cost-effectiveness acceptability curve of teriflunomide with the PAS versus the blended comparator



In addition, probabilistic analysis has been conducted on the incremental cost-effectiveness results of teriflunomide versus all beta-interferons and glatiramer acetate. The incremental probabilistic results are presented in Table 6. The corresponding multi-CEAC and CEAF are given in Figures 4 and 5. This shows that up to a willingness to pay threshold of at least £50,000 teriflunomide with the PAS had a greater probability of being cost-effective than all beta-interferons and glatiramer acetate.

Figure 4 Multi-CEAC for teriflunomide with the PAS versus all beta-interferons and glatiramer acetate

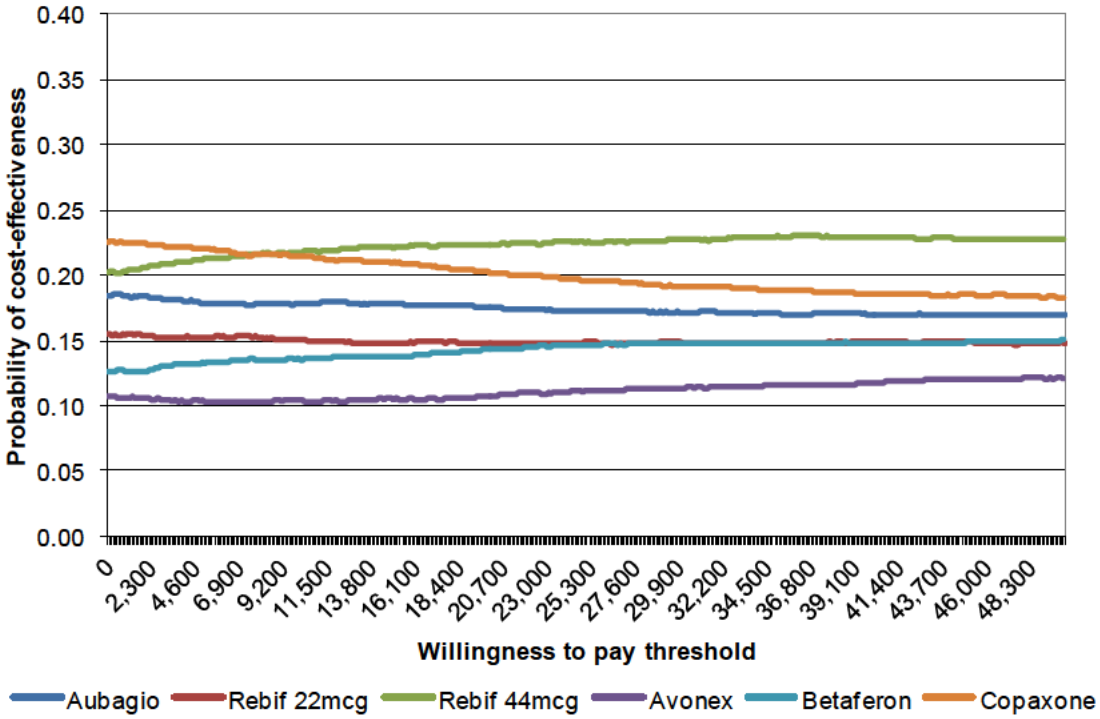
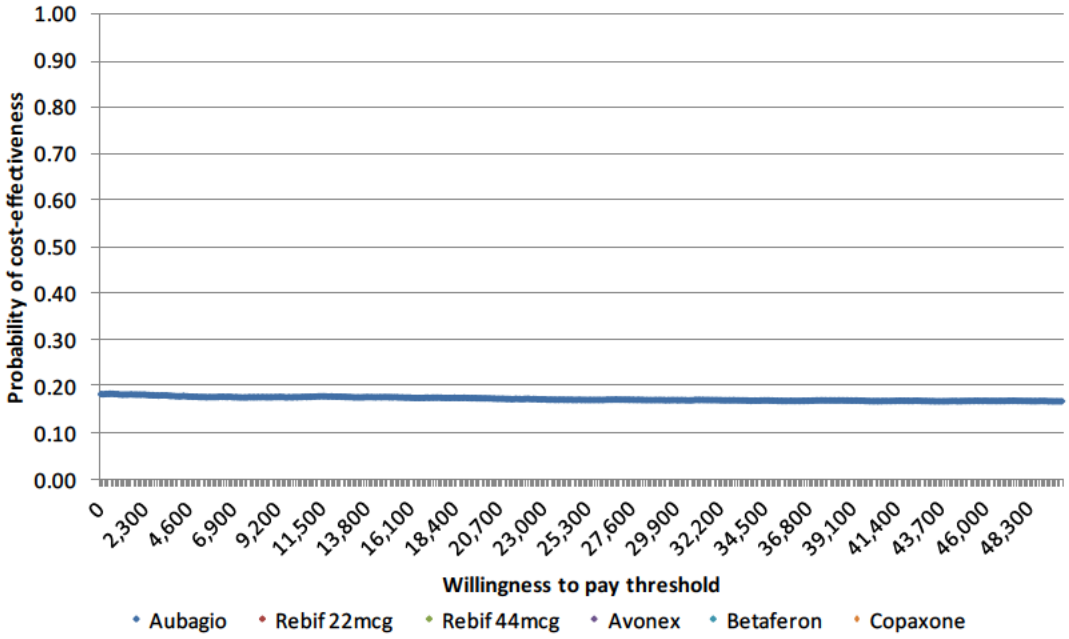


Figure 5 CEAF for teriflunomide with the PAS versus all beta-interferons and glatiramer acetate



4.11 Please present scenario analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal.

As discussed in Section 7.6.1 of the main manufacturer/sponsor submission of evidence for the technology appraisal, treatment sequencing scenarios were explored to more appropriately reflect current clinical practice. The cost-effectiveness results for the same sequences as discussed in the aforementioned section are presented in Table 21.

In addition, structural sensitivity analyses were performed to assess the impact of choice of sources of data, choice of MTC study inclusion criteria and structural assumptions within the model. The results of the deterministic structural sensitivity analysis are presented in Table 22; the results show sensitivity to the same parameters as the results without the PAS (presented in the main manufacturer/sponsor submission of evidence for the technology appraisal). Probabilistic results are presented for the scenario where treatment is received in SPMS (see Table 23 and 24). Finally, subgroup analyses are presented for HAD and RES as per the main manufacturer/sponsor submission (Table 25 -28).

Table 21 Treatment sequencing scenario analysis deterministic results with PAS

Sequencing scenario	Treatment sequence total costs (£)	Treatment sequence total QALYs	Comp sequence total costs (£)	Comp sequence total QALYs (£)	Inc costs (£)	Inc QALYs	ICER (£) inc (QALYs)
Base case	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.288	Dominates
1	[redacted]	[redacted]	[redacted]	[redacted]	-2,255	0.320	Dominates
1 with possible PAS price of £11,000	[redacted]	[redacted]	[redacted]	[redacted]	-4,571	0.320	Dominates
1 with possible PAS price of £13,000	[redacted]	[redacted]	[redacted]	[redacted]	-4,000	0.320	Dominates
2	[redacted]	[redacted]	[redacted]	[redacted]	-1,964	0.344	Dominates
3	[redacted]	[redacted]	[redacted]	[redacted]	-4,001	0.305	Dominates
3 with possible PAS price of £11,000	[redacted]	[redacted]	[redacted]	[redacted]	-4,584	0.305	Dominates
3 with possible PAS price of £13,000	[redacted]	[redacted]	[redacted]	[redacted]	-4,440	0.305	Dominates
4	[redacted]	[redacted]	[redacted]	[redacted]	-3,903	0.311	Dominates

Inc = Incremental, ICER = Incremental cost-effectiveness ratio, Comp = comparator

Table 22 Structural scenario analysis deterministic results

Scenario	Teri total costs (£)	Teri total QALYs	Blended comp costs (£)	Blended comp QALYs (£)	Inc costs (£)	Inc QALYs	ICER (£) inc (QALYs)
Base case	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.288	Dominates
Treatment effect reduction by 50% after 5 years	[redacted]	[redacted]	[redacted]	[redacted]	-5,971	0.247	Dominates
Treatment effect reduction by 25% after 5 years	[redacted]	[redacted]	[redacted]	[redacted]	-6,332	0.266	Dominates
No waning of discontinuation	[redacted]	[redacted]	[redacted]	[redacted]	-6,300	0.236	Dominates
Rate of discontinuation reduction by 75% after year 2	[redacted]	[redacted]	[redacted]	[redacted]	-6,845	0.327	Dominates
Natural history transition probabilities for Active RRMS	[redacted]	[redacted]	[redacted]	[redacted]	-6,749	0.290	Dominates
No treatment effect on relapses or proportion leading to hospitalisation	[redacted]	[redacted]	[redacted]	[redacted]	-6,809	0.288	Dominates
No discount rate costs	[redacted]	[redacted]	[redacted]	[redacted]	-8,470	0.288	Dominates
No discount rate outcomes	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.433	Dominates
6% discount rate costs	[redacted]	[redacted]	[redacted]	[redacted]	-5,601	0.288	Dominates
6% discount rate outcomes	[redacted]	[redacted]	[redacted]	[redacted]	-6,724	0.224	Dominates

Inc = Incremental, ICER = Incremental cost-effectiveness ratio, Teri = teriflunomide, Comp = comparator

Table 23 Probabilistic structural scenario analysis results of teriflunomide versus all comparators with treatment in SPMS of licensed beta-interferons

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Teriflunomide	[redacted]	[redacted]				
Rebif 44µg	[redacted]	[redacted]	10,619	-0.102	Dominated	Dominated
Rebif 22µg	[redacted]	[redacted]	11,709	0.111	105,604	105,604
Betaferon	[redacted]	[redacted]	25,402	-0.442	Dominated	Dominated
INC = Incremental, ICER = Incremental cost-effectiveness ratio, QALY = quality adjusted life year						

Table 24 Probabilistic structural scenario analysis results of teriflunomide versus aggregated Rebif with treatment in SPMS of licensed beta-interferons

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) versus baseline (QALYs)	ICER (£) Inc (QALYs)
Teriflunomide	[redacted]	[redacted]				
Rebif	[redacted]	[redacted]	11,031	-0.021	Dominated	Dominated
INC = Incremental, ICER = Incremental cost-effectiveness ratio, QALY = quality adjusted life year						

The results of the subgroup analysis are shown in Tables 25-28. In the HA population, teriflunomide is the most cost-effective treatment but in the rapidly-evolving severe (RES) population, natalizumab is the more cost-effective treatment.

Table 252 Probabilistic structural scenario analysis results of teriflunomide versus fingolimod in HAD population

Scenario	Teri costs (£)	Teri QALYs	Fing costs (£)	Fing QALYs	Inc costs (£)	Inc QALYs	ICER (£)
Fingolimod at £11,000 per year	[redacted]	[redacted]	[redacted]	[redacted]	-67,826	0.725	Dominates
Fingolimod at list price	[redacted]	[redacted]	[redacted]	[redacted]	-35,084	0.746	Dominates
Inc = Incremental, ICER = Incremental cost-effectiveness ratio, Teri = teriflunomide, QALY = quality adjusted life year, Fing = fingolimod							

Table 263 Probabilistic structural scenario analysis results of teriflunomide versus natalizumab in RES population

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) vs baseline (QALYs)
Teriflunomide	[redacted]	[redacted]			

Natalizumab	[redacted]	[redacted]	30,133	0.477	63,107
INC = Incremental, ICER = Incremental cost-effectiveness ratio, Teri = teriflunomide, QALY = quality adjusted life year					

Table 274 Deterministic structural scenario analysis results of teriflunomide versus fingolimod in HAD population

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) vs baseline (QALYs)	ICER (£) Inc (QALYs)
Teriflunomide	[redacted]	[redacted]				
Fingolimod at £11,000 per year	[redacted]	[redacted]	34,524	-0.828	Dominated	Dominated
Fingolimod at list price	[redacted]	[redacted]	64,403	-0.828	Dominated	Dominated
INC = Incremental, ICER = Incremental cost-effectiveness ratio, Teri = teriflunomide, QALY = quality adjusted life year						

Table 285 Deterministic structural scenario analysis results of teriflunomide versus natalizumab in RES population

Technologies	Total costs (£)	Total QALYs	Inc costs (£)	Inc QALYs	ICER (£) vs baseline (QALYs)
Teriflunomide	[redacted]	[redacted]			
Natalizumab	[redacted]	[redacted]	44,277	0.632	70,076
INC = Incremental, ICER = Incremental cost-effectiveness ratio, Teri = teriflunomide, QALY = quality adjusted life year					

4.12 If any of the criteria on which the patient access scheme depends are clinical variable (for example, choice of response measure, level of response, duration of treatment), sensitivity analyses around the individual criteria should be provided, so that the Appraisal Committee can determine which criteria are the most appropriate to use.

Not applicable.

Impact of patient access scheme on ICERs

4.13 For financially based schemes, please present the results showing the impact of the patient access scheme on the ICERs for the base-case and any scenario analyses. A suggested format is shown below (see table 5). If you are submitting the patient access scheme at the end of the appraisal process, you must include the scenario with the assumptions that the Appraisal Committee considered to be most plausible.

For all one-way probabilistic base case, deterministic base case and scenario analyses, teriflunomide dominated the blended comparator with the patient access scheme, as demonstrated in Table 27-29.

Table 27 Results showing the impact of patient access scheme on teriflunomide versus blended comparator ICERs

	Without PAS	With PAS
Base case probabilistic	[redacted]	Dominates
Base case deterministic	[redacted]	Dominates
Blended comparator hazard ratio on disability progression: LCI	[redacted]	Dominated
Blended comparator hazard ratio on disability progression: UCI	[redacted]	Dominates
Blended comparator ARR: LCI	[redacted]	Dominates
Blended comparator ARR: UCI	[redacted]	Dominates
Blended comparator withdrawal rate: LCI	[redacted]	Dominates
Blended comparator withdrawal rate: UCI	[redacted]	Dominates
Blended comparator proportion relapses leading to hospitalisation – 10%	[redacted]	Dominates
Blended comparator proportion relapses leading to hospitalisation + 10%	[redacted]	Dominates
Blended comparator administration costs – 10%	[redacted]	Dominates
Blended comparator administration costs + 10%	[redacted]	Dominates
Blended comparator monitoring costs – 10%	[redacted]	Dominates
Blended comparator monitoring costs + 10%	[redacted]	Dominates
Blended comparator adverse event costs – 10%	[redacted]	Dominates
Blended comparator adverse event costs + 10%	[redacted]	Dominates
Blended comparator adverse event disutility – 10%	[redacted]	Dominates
Blended comparator adverse event disutility + 10%	[redacted]	Dominates
Teriflunomide hazard ratio on disability progression: LCI	[redacted]	Dominates
Teriflunomide hazard ratio on disability progression: UCI	[redacted]	20,613
Teriflunomide ARR: LCI	[redacted]	Dominates
Teriflunomide ARR: UCI	[redacted]	Dominates
Teriflunomide withdrawal rate: LCI	[redacted]	Dominates
Teriflunomide withdrawal rate: UCI	[redacted]	Dominates
Teriflunomide proportion relapses leading to hospitalisation: LCI	[redacted]	Dominates
Teriflunomide proportion relapses leading to hospitalisation: UCI	[redacted]	Dominates

	Without PAS	With PAS
Teriflunomide monitoring costs – 10%	[redacted]	Dominates
Teriflunomide monitoring costs + 10%	[redacted]	Dominates
Teriflunomide adverse event costs – 10%	[redacted]	Dominates
Teriflunomide adverse event costs + 10%	[redacted]	Dominates
Teriflunomide adverse event disutility – 10%	[redacted]	Dominates
Teriflunomide adverse event disutility + 10%	[redacted]	Dominates
Disease costs – 10%	[redacted]	Dominates
Disease costs + 10%	[redacted]	Dominates
Relapse leading to hospitalisation cost - 10%	[redacted]	Dominates
Relapse leading to hospitalisation cost + 10%	[redacted]	Dominates
Relapse not leading to hospitalisation cost – 10%	[redacted]	Dominates
Relapse not leading to hospitalisation cost + 10%	[redacted]	Dominates
EQ-5D utility – 10%	[redacted]	Dominates
EQ-5D utility + 10%	[redacted]	Dominates
Relapse leading to hospitalisation disutility – 10%	[redacted]	Dominates
Relapse leading to hospitalisation disutility + 10%	[redacted]	Dominates
Relapse not leading to hospitalisation disutility – 10%	[redacted]	Dominates
Relapse not leading to hospitalisation disutility + 10%	[redacted]	Dominates
Caregiver disutility – 10%	[redacted]	Dominates
Caregiver disutility + 10%	[redacted]	Dominates

	Without PAS	With PAS
Treatment sequencing scenario 1	[redacted]	Dominates
Treatment sequencing scenario 1 with fingolimod price £11,000	[redacted]	Dominates
Treatment sequencing scenario 2	[redacted]	Dominates
Treatment sequencing scenario 3	[redacted]	Dominates
Treatment sequencing scenario 3 with fingolimod price £11,000	[redacted]	Dominates
Treatment sequencing scenario 4	[redacted]	Dominates
Clinical data sourced from all-years, ≥80% RRMS MTC	[redacted]	Dominates
Clinical data sourced from all-years, ≥80% RRMS MTC excluding Bornstein et al	[redacted]	Dominates
Natural history costs from Karampampa, 2012	[redacted]	Dominates
Relapse costs from Tyas, 2007	[redacted]	Dominates
Baseline EDSS utility score from TEMSO study	[redacted]	Dominates
Disutility of relapse from Orme, 2007	[redacted]	Dominates
Treatment effect reduction by 50% after 5 years	[redacted]	Dominates
Treatment effect reduction by 25% after 5 years	[redacted]	Dominates
No waning of discontinuation	[redacted]	Dominates
Rate of discontinuation reduction by 75% after year 2	[redacted]	Dominates
Initial EDSS distribution from TOWER and TEMSO studies	[redacted]	Dominates
Starting age and male: female ratio from TOWER and TEMSO studies	[redacted]	Dominates
Natural history relapse rate from Patzold, 1982	[redacted]	Dominates
Proportion of relapses leading to hospitalisation from placebo arms of TEMSO study	[redacted]	Dominates
Probability of adverse events in subsequent years equal to adverse events in year 1	[redacted]	Dominates
Natural history transition probabilities for Active RRMS	[redacted]	Dominates
No treatment effect on relapses or proportion leading to hospitalisation	[redacted]	Dominates
No discount rate on costs	[redacted]	Dominates
No discount rate on outcomes	[redacted]	Dominates
6% discount rate on costs	[redacted]	Dominates
6% discount rate on outcomes	[redacted]	Dominates

PAS: patient access scheme.

Table 28 Results showing the impact of patient access scheme on teriflunomide versus fingolimod in HAD

	Teriflunomide	
	Without PAS	**With PAS**
Deterministic Fingolimod at list price	[redacted]	Dominates
Deterministic Fingolimod at £11,000	[redacted]	Dominates

Table 29 Results showing the impact of patient access scheme on teriflunomide versus natalizumab in RES

	Teriflunomide (lower benefits, lower costs)	
	Without PAS	**With PAS**
Deterministic	[redacted]	70,076

5 Appendices

5.1 Appendix A: Additional documents

5.1.1 If available, please include copies of patient access scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians, patient information documents.

Not applicable.

5.2 Appendix B: Details of outcome-based schemes

5.2.1 If you are submitting a proven value: price increase scheme, as defined in the PPRS, please provide the following information:

- the current price of the intervention
- the proposed higher price of the intervention, which will be supported by the collection of new evidence
- a suggested date for when NICE should consider the additional evidence.

Not applicable.

5.2.2 If you are submitting an expected value: rebate scheme, as defined in the PPRS, please provide the following details:

- the current price of the intervention (the price that will be supported by the collection of new evidence)
- the planned lower price of the intervention in the event that the additional evidence does not support the current price
- a suggested date for when NICE should consider the additional evidence.

Not applicable.

5.2.3 If you are submitting a risk-sharing scheme, as defined in the PPRS, please provide the following details:

- the current price of the intervention (the price that will be supported by the collection of new evidence)
- the proposed relationship between future price changes and the evidence to be collected.

Not applicable.

5.2.4 For outcome-based schemes, as defined in the PPRS, please provide the full details of the new information (evidence) planned to be collected, who will collect it and who will carry the cost associated with this planned data collection. Details of the new information (evidence) may include:

- design of the new study
- patient population of the new study
- outcomes of the new study
- expected duration of data collection
- planned statistical analysis, definition of study groups and reporting (including uncertainty)
- expected results of the new study
- planned evidence synthesis/pooling of data (if applicable)
- expected results of the evidence synthesis/pooling of data (if applicable).

Not applicable.

5.2.5 If you are submitting a risk-sharing scheme, please specify the period between the time points when the additional evidence will be considered.

Not applicable.

5.2.6 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered.

Not applicable.

5.2.7 Please provide the other data used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered. These data could include cost/resource use, health-related quality of life and utilities.

Not applicable.

5.2.8 Please present the cost-effectiveness results as follows.

- For proven value: price increase schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the anticipated results based on the expected new evidence and the proposed higher price.
- For expected value: rebate schemes, please summarise in separate tables:
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming).
- For risk-sharing schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming)
  - the anticipated results based on the expected new evidence and the proposed higher price.

A suggested format is shown in table 3, section 4.7.

Not applicable.

5.2.9 Please present in separate tables the incremental results for the different scenarios as described above in section 5.2.8 for the type of outcome-based scheme being submitted.

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4, section 4.8.

Not applicable.