NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology appraisals

Patient access scheme submission

TA313: Ustekinumab for treating active psoriatic arthritis

August 2014

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' (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9)
- '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' (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9).

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.

Ustekinumab (Stelara®) for the treatment of active psoriatic arthritis (PsA) in adult patients when the response to previous non-biological disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate

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

Ustekinumab is already recommended by NICE for moderate to severe psoriasis, contingent upon a patient access scheme (PAS). The NICE TA180 (ustekinumab for the treatment of adults with moderate to severe psoriasis), issued in September 2009, states that: “The manufacturer provides the 90 mg dose (two 45 mg vials) for people who weigh more than 100 kg at the same total cost as for a single 45 mg vial.”(1)

Janssen proposed that the same PAS be extended to also cover the PsA indication.

We believe that having the same PAS across two closely associated conditions will support NHS frontline staff by avoiding the need to manage two different pricing schemes for ustekinumab between the psoriasis and PsA indications.

Furthermore, we believe that the introduction of this scheme improves the cost-effectiveness of ustekinumab for PsA to a level that is acceptable to secure a positive recommendation by NICE, facilitating patient access to this important new treatment option.

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

Financially-based scheme (under the 2009 PPRS terminology)

Complex scheme (under the 2014 PPRS terminology)

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?**

Under the PAS, Janssen will provide the 90 mg dose (2×45 mg as pre-filled syringes) for patients who weigh more than 100 kg at the same total cost as for a single 45 mg pre-filled syringe. The cut-off based on patient weight is consistent with the posology of ustekinumab ('weight-based dosing') for both the original plaque psoriasis indication and the new PsA indication.

Posology as described in SmPC(2)

Plaque psoriasis

The recommended posology of STELARA is an initial dose of 45 mg administered subcutaneously, followed by a 45 mg dose 4 weeks later, and then every 12 weeks thereafter.

Patients with body weight > 100 kg

For patients with a body weight > 100 kg the initial dose is 90 mg administered subcutaneously, followed by a 90 mg dose 4 weeks later, and then every 12 weeks thereafter. In these patients, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy. (see section 5.1, Table 2).

Psoriatic arthritis (PsA)

The recommended posology of STELARA is an initial dose of 45 mg administered subcutaneously, followed by a 45 mg dose 4 weeks later, and then every 12 weeks thereafter. Alternatively, 90 mg may be used in patients with a body weight > 100 kg.

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 PAS will apply to the entire subgroup of adults with active PsA, i.e. those with a body weight > 100kg. There is no other criterion a patient needs to satisfy for the PAS to be applied.

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

The PAS will apply to the entire subgroup of adults with active PsA, i.e. those with a body weight > 100kg.

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

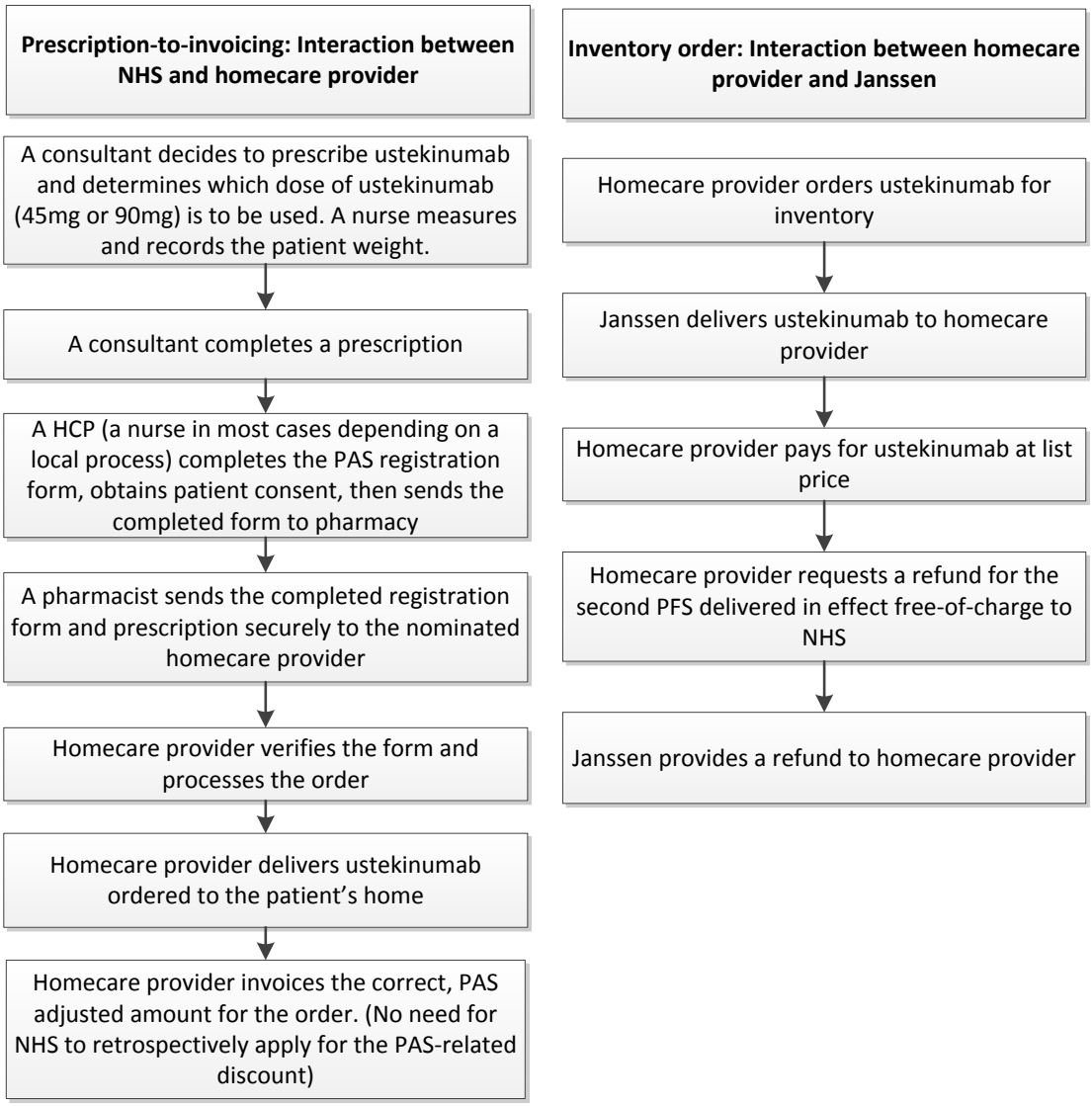
Orders for ustekinumab are handled by a homecare provider (Bupa Home Healthcare in most cases) who acts on behalf of Janssen for the NHS. Since the homecare provider facilitates the processing of the PAS at the point of ordering, there is no need for the NHS to retrospectively request discounts/refunds. When an order for ustekinumab is placed with the homecare provider, the patient's weight is provided alongside the prescription, allowing the homecare provider to identify patients for whom the PAS applies. The homecare provider is then able to charge the correct, PAS-adjusted amounts to the relevant NHS bodies immediately.

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.

Please refer to the flow charts in Section 3.9 below for the details of how the PAS will be administered. The only additional information that will need to be collected to administer the PAS (which would not be necessary in the absence of the PAS) is patient weight. Typically, a nurse will measure and record the patient weight.

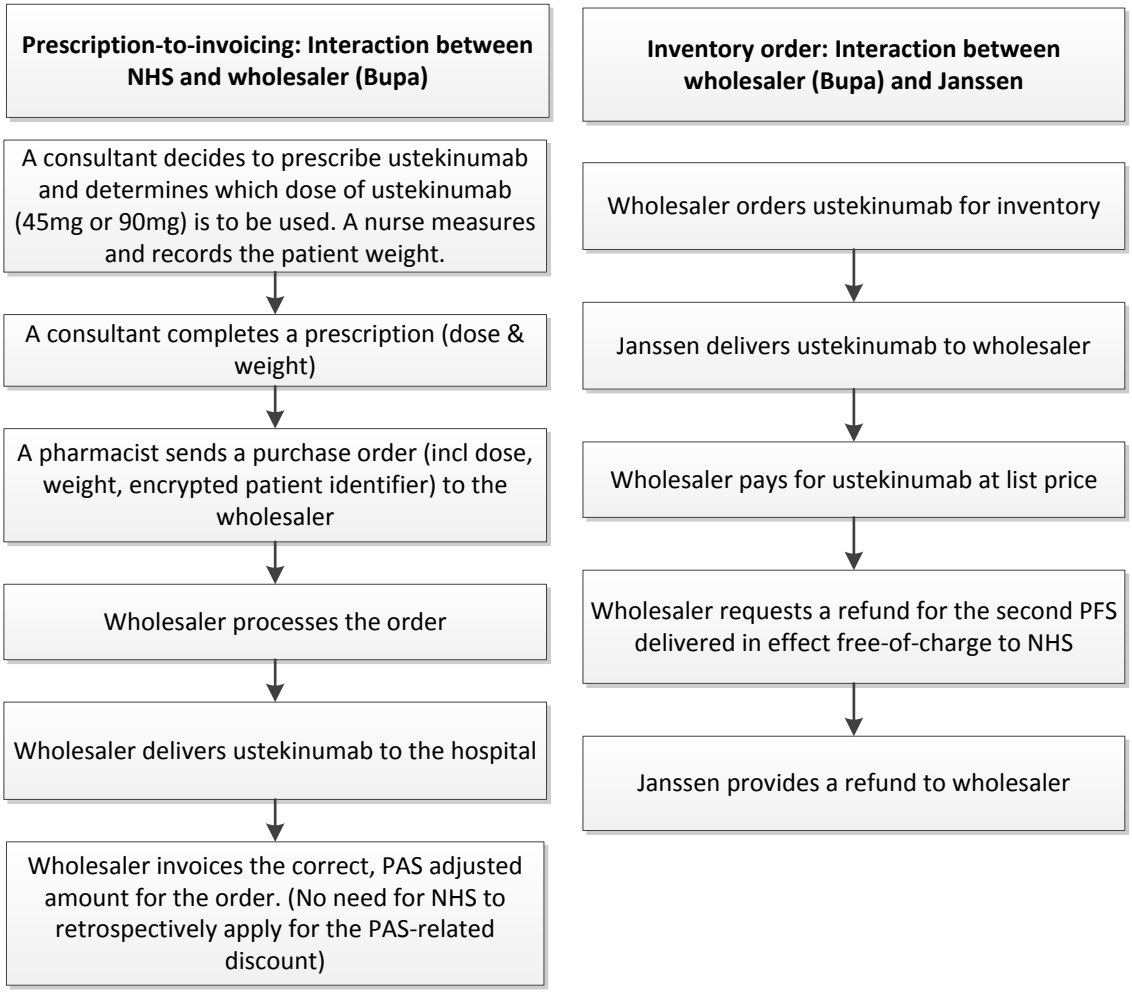
3.9 Please provide a flow diagram that clearly shows how the scheme will operate. Any funding flows must be clearly demonstrated.

Home delivery



HCP, healthcare professional; PAS, patient access scheme; PFS, pre-filled syringe

Hospital delivery



HCP, healthcare professional; PAS, patient access scheme; PFS, pre-filled syringe

3.10 Please provide details of the duration of the scheme.

Until further notice. Janssen is committed to maintaining the availability of ustekinumab for patients with plaque psoriasis and PsA.

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?

The PAS ensures that the drug acquisition cost is equal among all patients regardless of the dose of ustekinumab they receive, avoiding any potential inequality issues. Without the PAS, ustekinumab 90mg for psoriasis (for patients weighing more than 100kg) would not have been recommended by NICE.

The PAS for the PsA indication would prevent a similar potential inequality issue among PsA patients, and between psoriasis and PsA patients.

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.

The following forms are displayed in Appendix A.

- Patient registration form (to be used when Bupa Home Healthcare is chosen by a NHS trust as a homecare provider)
- Patient registration form (to be used when another homecare provider is chosen by a NHS trust)
- Patient referral guide
- Patient information guide

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.

N/A

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.

The cost effectiveness analysis in our original submission already incorporated the weight-based dosing. As discussed in Sections 3.5 and 3.6 of this template, the PAS will apply to the entire subgroup of adults with active PsA, i.e. those with a body weight > 100kg. There is no other criterion a patient needs to satisfy for the PAS to be applied.

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.

The following three economic models are submitted along with this document;

- TNF alpha inhibitor-naïve population
- TNF alpha inhibitor-exposed population: sequencing analysis
- TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

The changes made to the models are described in Section 4.3 below.

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.

We have incorporated the PAS into the economic model by simply reducing the unit cost of ustekinumab 90mg by 50% from £4,294 to £2,147 (worksheet 'Inp_Costs' cell 'E15').

We have also incorporated the effect of conventional management on skin symptoms into the economic model as suggested in the NICE technology appraisal guidance 313. TA Guidance 313 stated; "The Committee noted that it would have liked to have seen an exploration of the effect of conventional management on skin symptoms" (para 4.13).(3)

To fully capture the effect of conventional management on skin symptoms, additional inputs were added to the economic models; PASI 50, PASI 75 and PASI 90 response rates at Week 12-16 and at Week 24 (Table 1, Table 2 and Table 3).

Table 1: PASI response rates for conventional management - TNF alpha inhibitor-naïve model

Outcome	Time-point	Mean	Lower bound (95% CI)	Upper bound (95% CI)	Reference
PASI 50	Week 12-16	19.4%	14.7%	24.5%	PSUMMIT 1 and PSUMMIT 2
	Week 24	25.4%	20.2%	31.0%	PSUMMIT 1 and PSUMMIT 2
PASI 75	Week 12-16	4.2%	[redacted]%	[redacted]%	MTC (2013)
	Week 24	3.5%	[redacted]%	[redacted]%	MTC (2013)
PASI 90	Week 12-16	0.6%	[redacted]%	[redacted]%	MTC (2013)
	Week 24	1.1%	[redacted]%	[redacted]%	MTC (2013)
CI, credible interval					

Table 2: PASI response rates for conventional management – sequencing analysis

Outcome	Time-point	Mean	Lower bound (95% CI)	Upper bound (95% CI)	Reference
PASI 50	Week 12-16	19.4%	14.7%	24.5%	PSUMMIT 1 and PSUMMIT 2
	Week 24	25.4%	20.2%	31.0%	PSUMMIT 1 and PSUMMIT 2
PASI 75	Week 12-16	4.2%	[redacted]%	[redacted]%	MTC (2013)
	Week 24	3.5%	[redacted]%	[redacted]%	MTC (2013)
PASI 90	Week 12-16	0.6%	[redacted]%	[redacted]%	MTC (2013)
	Week 24	1.1%	[redacted]%	[redacted]%	MTC (2013)
CI, credible interval					

Table 3: PASI response rates for conventional management - TNF alpha inhibitor-experienced model (ustekinumab vs. conventional management)

Outcome	Time-point	Mean	Lower bound (95% CI)	Upper bound (95% CI)	Reference
PASI 50	Week 12-16	6.5%	1.82%	13.71%	PSUMMIT 2
	Week 24	8.1%	2.72%	15.95%	PSUMMIT 2
PASI 75	Week 12-16	1.61%	0.04%	5.87%	PSUMMIT 2
	Week 24	3.23%	0.40%	8.80%	PSUMMIT 2
PASI 90	Week 12-16	1.6%	0.04%	5.87%	PSUMMIT 2
	Week 24	3.2%	0.40%	8.80%	PSUMMIT 2
CI, credible interval					

The PASI 50, PASI 75 and PASI 90 response rates with conventional management were used to calculate the change in PASI score for 'PASI 75 responders' and for 'PASI 75 non-responders'. These calculations are consistent with those included in the original model for the PASI score change with ustekinumab or with TNF alpha inhibitors.

The calculations for conventional management were then updated to allow patients to fall into any of the following health states based on PsARC and PASI 75 responses:

- Neither PsARC or PASI 75 response
- PsARC and PASI 75 response
- PsARC response only
- PASI 75 response only
- Dead (absorbing state)

These health states are consistent with those for ustekinumab and TNF alpha inhibitors, with the exception that there is no opportunity to withdraw from conventional management. In line with all previous economic models for psoriatic arthritis, it is assumed that once patients are receiving conventional management, they will do so until death (or for the remainder of the model time horizon). All other calculations for conventional management which were affected by the addition of these states were then updated. These included the average Health Assessment Questionnaire (HAQ) and PASI scores, the HAQ and PASI related costs, quality-adjusted life years (QALYs) and life years (LYs).

The assumption around the long-term impact of treatment on the PASI score was also updated throughout the model. Previously, it was assumed that patients receiving conventional management received no improvement in PASI score, and

that, for patients who withdrew to conventional management, their PASI score rebounded back to its baseline value and subsequently remained constant. In the updated model, patients initially receiving conventional management are assumed to have a constant PASI score, which is lower than the baseline score and which is dependent on whether the patient is a PASI 75 responder or not. For patients initially receiving ustekinumab or TNF alpha inhibitor, it is assumed that, upon withdrawal to conventional management, their PASI score rebounds to a level which is equal to the expected PASI score for patients receiving conventional management, and subsequently remains constant. The expected PASI score for patients receiving conventional management is calculated as follows:

$$\begin{aligned} Baseline\ PASI\ score - [\%\ PASI\ 75\ responders\ \times PASI\ change\ (PASI\ 75\ responder) \\ +\ \%\ PASI\ 75\ non\ responders \\ \times PASI\ change\ (PASI\ 75\ non\ responder)] \end{aligned}$$

Finally, it was assumed in the ERG sequencing analysis that only the Psoriatic Arthritis Response Criteria (PsARC) response would be affected by sequential use of TNF alpha inhibitors, i.e. sequential use of TNF alpha inhibitors has no impact on PASI response rates. The same assumption has therefore been made for conventional management within the updated model; the data used for PASI response with conventional management in the sequencing analysis is equal to that used in the TNF alpha inhibitor naïve model. It is worth noting that this set of assumptions (i.e. only PsARC response is affected by sequential use of treatment) is in fact conservative for ustekinumab's cost-effectiveness compared against TNF alpha inhibitors or conventional management. While the data is limited, it is plausible that PASI response rates for TNF alpha inhibitors and conventional management in the sequencing analysis should be lower than those in the TNF alpha inhibitor naïve model. If so, the ICER for ustekinumab would be lower since the incremental benefit of ustekinumab would be higher.

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.

Since the PAS only affects the drug acquisition cost of ustekinumab 90mg, there is no change to the clinical effectiveness data, with the exception of the effect of conventional management on skin symptoms as discussed in Section 4.3 above.

For the clinical effectiveness data used in the economic model, please refer to Sections 6.7.6 and 7.3.6 from our original submission and our response to clarification question A18.

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'.

Table 4: Costs associated with the implementation and operation of the patient access scheme (PAS)

	Calculation of cost	Reference source
Stock management	£0	No additional cost incurred due to the patient access scheme
Administration of claim forms	£4	PSSRU, Unit Costs of Health and Social Care 2012 (page 218). Hourly wage for hospital pharmacist £24 * 10 additional minutes to administer the patient access scheme
Staff training	£0	The relevant staff are likely to be already familiar with the patient access scheme for the psoriasis indication
Tracking of supplies	£0	This activity is conducted by the homecare provider
Other costs	£15	PSSRU, Unit Costs of Health and Social Care 2012 (page 235). Hourly wage for consultant (medical) £91 * 10 additional minutes to obtain patient consent and to administer the patient access scheme
Audit	£12	PSSRU, Unit Costs of Health and Social Care 2012 (page 218). Hourly wage for hospital pharmacist £24 * 30 minutes to audit (if needed)
Total implementation and operation costs	£31	Total cost per psoriatic arthritis patient who receives ustekinumab
PSSRU: Personal and Social Services Research Unit		

Due to its immateriality, the cost associated with the implementation and operation of the PAS (£31 per patient) is not incorporated in the cost-effectiveness analyses presented below.

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.

Table 5: Additional treatment-related costs for the intervention both with and without the patient access scheme (PAS)

	Calculation of cost	Reference source
Providing intervention	£0	N/A
Monitoring tests	£0	N/A
Diagnostic tests	£0	N/A
Appointments	£0	N/A
Other costs	£2	PSSRU, Unit Costs of Health and Social Care 2012 (page 225). Hourly wage for hospital nurse £20 * 5 additional minutes to administer the patient access scheme per patient
Other [add more rows as necessary]	£0	N/A
Total treatment-related costs	£2	
PSSRU: Personal and Social Services Research Unit		

Due to its immateriality, the treatment-related cost associated with the PAS (£2 per patient) is not incorporated in the cost-effectiveness analyses presented below.

Summary results

Base-case analysis

4.7 Please present in separate tables the cost-effectiveness results as follows.[1]

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

TNF alpha inhibitor-naïve population

Table 6: Breakdown of costs TNF alpha inhibitor-naïve population – *without* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£13,329	£13,329	£9,576	£26,107
Adalimumab	£29,872	£0	£10,652	£10,353	£9,308	£60,185
Ustekinumab	**£35,256**	**£0**	**£10,652**	**£10,445**	**£9,505**	**£65,857**
Etanercept	£36,789	£0	£10,652	£10,083	£9,652	£67,175
Golimumab	£37,792	£0	£10,652	£10,122	£9,189	£67,755
Infliximab	£61,957	£37,700	£10,652	£10,017	£8,767	£129,092
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

Table 7: Breakdown of costs TNF alpha inhibitor-naïve population – *with* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£13,329	£13,329	£9,576	£26,107
Adalimumab	£29,872	£0	£10,652	£10,353	£9,308	£60,185
Ustekinumab	**£28,379**	**£0**	**£10,652**	**£10,445**	**£9,505**	**£58,981**
Etanercept	£36,789	£0	£10,652	£10,083	£9,652	£67,175
Golimumab	£37,792	£0	£10,652	£10,122	£9,189	£67,755
Infliximab	£61,957	£37,700	£10,652	£10,017	£8,767	£129,092
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

[1] For outcome-based schemes, please see section 5.2.8 in appendix B.

TNF alpha inhibitor-exposed population: sequencing analysis

Table 8: Breakdown of costs TNF alpha inhibitor-exposed population – *without* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£14,092	£14,092	£11,177	£28,947
Adalimumab	£8,872	£0	£10,758	£11,805	£11,497	£42,932
Etanercept	£10,580	£0	£10,758	£11,728	£11,593	£44,659
Golimumab	£10,780	£0	£10,758	£11,750	£11,453	£44,742
Ustekinumab	**£28,444**	**£0**	**£10,759**	**£11,472**	**£11,361**	**£62,037**
Infliximab	£20,135	£51,303	£10,758	£11,709	£11,344	£105,250
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

Table 9: Breakdown of costs TNF alpha inhibitor- exposed population – *with* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£14,092	£14,092	£11,177	£28,947
Adalimumab	£8,872	£0	£10,758	£11,805	£11,497	£42,932
Etanercept	£10,580	£0	£10,758	£11,728	£11,593	£44,659
Golimumab	£10,780	£0	£10,758	£11,750	£11,453	£44,742
Ustekinumab	**£20,984**	**£0**	**£10,759**	**£11,472**	**£11,361**	**£54,576**
Infliximab	£20,135	£51,303	£10,758	£11,709	£11,344	£105,250
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

Table 10: Breakdown of costs TNF alpha inhibitor-exposed population – *without* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£14,085	£14,085	£12,538	£29,998
Ustekinumab	**£38,803**	**£0**	**£10,759**	**£11,313**	**£11,743**	**£72,618**
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

Table 11: Breakdown of costs TNF alpha inhibitor- exposed population – *with* the PAS for ustekinumab

Technologies	Drug acquisition costs	Treatment administration costs	MRU costs	HAQ related costs	PASI related costs	Total costs
Conv. mgmt.	£0	£0	£14,085	£14,085	£12,538	£29,998
Ustekinumab	**£28,625**	**£0**	**£10,759**	**£11,313**	**£11,743**	**£62,440**
HAQ = Health Assessment Questionnaire, MRU = Medical Resource Use, PASI = Psoriasis Area and Severity Index						

4.8 Please present in separate tables the incremental results as follows.[2]

- **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.

TNF alpha inhibitor-naïve population

Since the extension of the PAS to the new PsA indication reduces the drug acquisition cost of ustekinumab 90mg by 50%, the PAS has a substantial impact on the total cost, and thus the cost-effectiveness, of ustekinumab. Whilst ustekinumab is dominated by adalimumab in the absence of the PAS (Table 12), it becomes the lowest-cost biologic treatment option if the PAS is applied (Table 13).

Table 12: Deterministic analysis, TNF alpha inhibitor-naïve population – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Adalimumab	£60,185	30.32	6.04	£34,077	1.67	£20,450	£20,450
Ustekinumab	**£65,857**	**30.32**	**5.89**	**£5,673**	**-0.15**	**Dominated**	**£26,230**
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	6.48	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 13: Deterministic analysis, TNF alpha inhibitor-naïve population – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Ustekinumab	**£58,981**	**30.32**	**5.89**	**£32,874**	**1.52**	**£21,692**	**£21,692**
Adalimumab	£60,185	30.32	6.04	£1,204	0.15	£7,979	£20,450
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	6.48	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

[2] For outcome-based schemes, please see section 5.2.9 in appendix B.

TA Guidance 313 noted that “conventional management is the most appropriate comparator” for a subgroup of patients “for whom TNF alpha inhibitors are inappropriate because of contraindications” (para 4.19). As can be observed in Table 13 above, the ICER for ustekinumab vs. conventional management is £21,692 when the PAS is applied, a cost-effective result.

As noted in TA Guidance 313, there is a considerable unmet need in patients for whom TNF alpha inhibitors are unsuitable. This could be due to contraindication to TNF alpha inhibitors such as patient or family history of demyelination or congestive heart failure. There are also patients who are hepatitis B surface antigen positive, patients with a history of haematological abnormalities, and patients who have received a TNF alpha inhibitor and developed lupus like syndrome and are positive for antibodies against double stranded DNA. Moreover, there are patients who are needlephobic and thus a more frequent dosing regimen with a TNF alpha inhibitor is not suitable; these patients may benefit from ustekinumab’s infrequent 12 weekly regimen. Furthermore, the homecare service provided free-of-charge to the NHS ensures that any nervous or concerned patients can receive treatment safely, and support their adherence to ustekinumab treatment.

To conclude, the base case results shown in Table 13 demonstrate that, with the PAS, ustekinumab is a cost-effective treatment option for anti-TNFα naïve patients, especially for those whom TNF alpha inhibitors are inappropriate.

TNF alpha inhibitor-exposed population: sequencing analysis

According to the TA Guidance 313, the Committee considered that the exploratory sequencing analysis by the ERG "provided useful information for establishing a full picture of the cost effectiveness of ustekinumab", and that "the most informative scenario was the one in which the first-line TNF alpha inhibitor failed because of lack of efficacy and clinical effectiveness data for ustekinumab were taken directly from PSUMMIT 2" (para. 4.20).(3)

We have used the sequencing analysis in order to assess the impact of the PAS on ustekinumab's cost-effectiveness compared with TNF alpha inhibitors. In line with the Committee's comment, Janssen's analysis focused on the scenario where the first anti-TNFα failed due to lack of efficacy.

The results of the sequencing analysis are shown in Table 14, Table 15, Table 16 and Table 17 below.

Table 14: Deterministic analysis, TNF alpha inhibitor-exposed population (sequencing analysis) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	3.08	£83	-0.02	Dominated	£31,509
Ustekinumab	**£62,037**	**30.83**	**3.57**	**£17,378**	**0.47**	**£37,222**	**£33,467**
Infliximab	£105,250	30.83	3.15	£43,213	-0.42	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 15: Deterministic analysis, TNF alpha inhibitor- exposed population (sequencing analysis) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	3.08	£83	-0.02	Dominated	£31,509
Ustekinumab	**£54,576**	**30.83**	**3.57**	**£9,917**	**0.47**	**£21,241**	**£25,921**
Infliximab	£105,250	30.83	3.15	£50,674	-0.42	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 16: Deterministic, incremental analysis by first-line biologic drug, TNF alpha inhibitor-exposed population (sequencing analysis) – *without* the PAS for ustekinumab

	Costs	QALY	First-line biologic drug				
			Adalimumab	Etanercept	Golimumab	Ustekinumab	Infliximab
Conv. mgmt.	£28,947	2.58					
Adalimumab	£42,932	2.98	N/A	£14,385	ED	ED	ED
Etanercept	£44,659	3.10	£30,107	N/A	£30,107	£30,107	£30,107
Golimumab	£44,742	3.08	Dominated	Dominated	N/A	Dominated	Dominated
Ustekinumab	**£62,037**	**3.57**	**£37,222**	**£33,467**	**£37,222**	**N/A**	**£37,222**
Infliximab	£105,250	3.15	Dominated	Dominated	Dominated	£1,356,063	N/A
ED, extendedly dominated							

Table 17: Deterministic, incremental analysis by first-line biologic drug, TNF alpha inhibitor-exposed population (sequencing analysis) – *with* the PAS for ustekinumab

	Costs	QALY	First-line biologic drug				
			Adalimumab	Etanercept	Golimumab	Ustekinumab	Infliximab
Conv. mgmt.	£28,947	2.58					
Adalimumab	£42,932	2.98	N/A	ED	ED	ED	ED
Etanercept	£44,659	3.10	£30,107	N/A	£30,107	£30,107	£30,107
Golimumab	£44,742	3.08	Dominated	Dominated	N/A	Dominated	Dominated
Ustekinumab	**£54,576**	**3.57**	**£21,241**	**£25,921**	**£21,241**	**N/A**	**£21,241**
Infliximab	£105,250	3.15	Dominated	Dominated	Dominated	£1,356,063	N/A
ED, extendedly dominated							

Applying the PAS for ustekinumab reduces the ICER substantially from above £33k/QALY to £21-26k/QALY.

In the sequencing analysis, the odds of achieving a PsARC response on the second line TNF alpha inhibitor is reduced 2.7 fold compared with the first line treatment (as explained fully in the ERG report(4)). This lowers QALYs for TNF alpha inhibitors compared with those in the TNF alpha inhibitor-naïve model. Their total costs are also lower because, in the sequencing model, higher proportions of patients discontinue TNF alpha inhibitors at week 12 compared with those in the TNF alpha inhibitor-naïve model. For this reason, the total cost for ustekinumab is higher than those for adalimumab, etanercept or golimumab even with the PAS; however, this is counterbalanced by substantially higher QALY for ustekinumab (3.57) compared with TNF alpha inhibitors' (2.98-3.15).

According to recent market research of biologic drugs for PsA, adalimumab has the highest market share, followed by etanercept and golimumab (Table 18). By applying the relative market shares of TNF alpha inhibitors to ustekinumab's ICERs (Table 17), it can be estimated that, with the PAS, the weighted-average ICER for ustekinumab is £[redacted]/QALY.

Table 18: Market share of biologic drugs used to treat PsA

Treatment option	Market share
Adalimumab	[redacted]
Etanercept	[redacted]
Golimumab	[redacted]
Infliximab	[redacted]
Others (including ustekinumab)	[redacted]
Source: Market research commissioned by Janssen (May 2014)	

The sequencing analysis of the TNF alpha inhibitor exposed population demonstrates that, with the PAS, ustekinumab is a cost effective treatment option when compared against TNF alpha inhibitors.

TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

The PAS substantially reduces ustekinumab's ICER vs. conventional management from £32.2k/QALY to £24.5k/QALY (Table 19 and Table 20).

Table 19: Deterministic analysis, TNF alpha inhibitor-exposed population (vs. conventional management only) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£29,998	30.83	2.54				
Ustekinumab	**£72,618**	**30.83**	**3.86**	**£42,620**	**1.32**	**£32,215**	**£32,215**
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 20: Deterministic analysis, TNF alpha inhibitor- exposed population (vs. conventional management only) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£29,998	30.83	2.54				
Ustekinumab	**£62,440**	**30.83**	**3.86**	**£32,442**	**1.32**	**£24,522**	**£24,522**
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

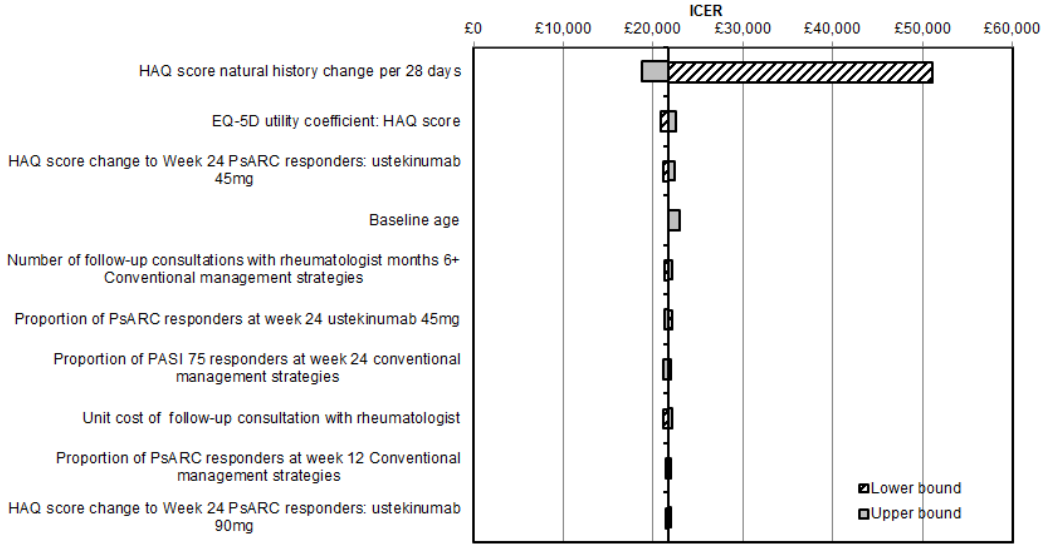
Sensitivity analyses

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.

The results of deterministic sensitivity analyses are shown below in Figure 1 and Figure 2. Consistent with previous analyses, the ICER is most sensitive to the change in HAQ-DI score over time associated with the natural history of PsA.

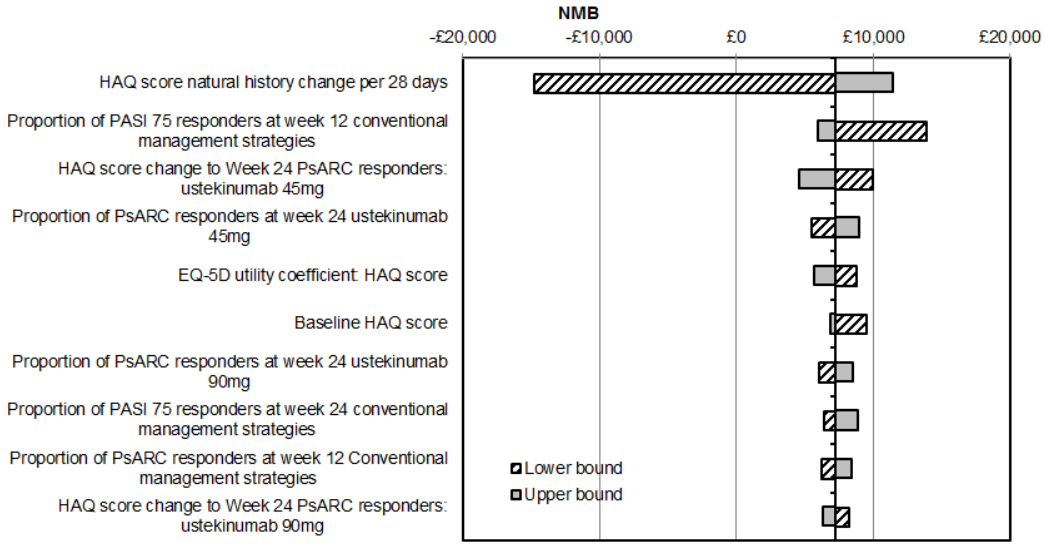
TNF alpha inhibitor-naïve population

Figure 1: Tornado diagram, TNF alpha inhibitor-naïve population, ustekinumab vs. conventional management – *with* the PAS for ustekinumab



TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

Figure 2: Tornado diagram, TNF alpha inhibitor-experienced population, ustekinumab vs. conventional management – *with* the PAS for ustekinumab



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

TNF alpha inhibitor-naïve population

The PSA result demonstrates that ustekinumab has the lowest cost among biologic treatment options, and demonstrates an ICER of £23k/QALY vs. conventional management (Table 21). The overall result is consistent with those from the deterministic analysis (Table 13).

Table 21: Probabilistic sensitivity analysis, TNF alpha inhibitor-naïve population – *with* the PAS for ustekinumab

Technologies	Total		Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	QALYs	Costs	QALYs		
Conv. mgmt.	£25,970	4.66				
Ustekinumab	**£59,105**	**6.09**	**£33,135**	**1.43**	**£23,164**	**£23,164**
Adalimumab	£60,311	6.24	£1,206	0.15	£8,182	£21,765
Etanercept	£67,324	6.72	£7,013	0.48	£14,580	£20,086
Golimumab	£67,933	6.65	£610	-0.08	Dominated	£21,162
Infliximab	£128,345	6.90	£61,021	0.18	£344,064	£45,781
ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years						

Figure 3: Scatter plot, TNF alpha inhibitor-naïve population – *with* the PAS for ustekinumab

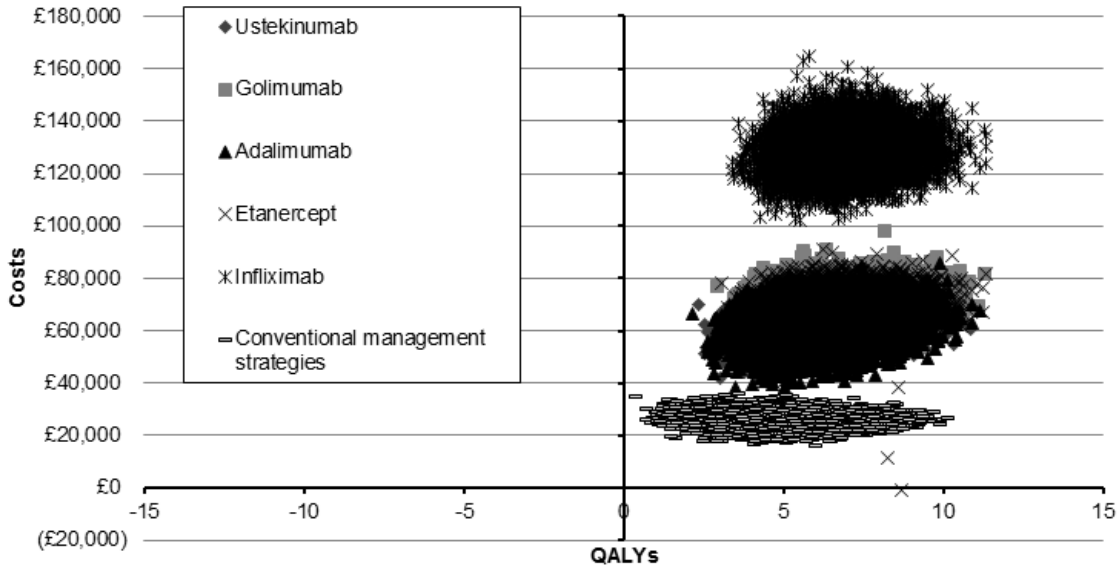
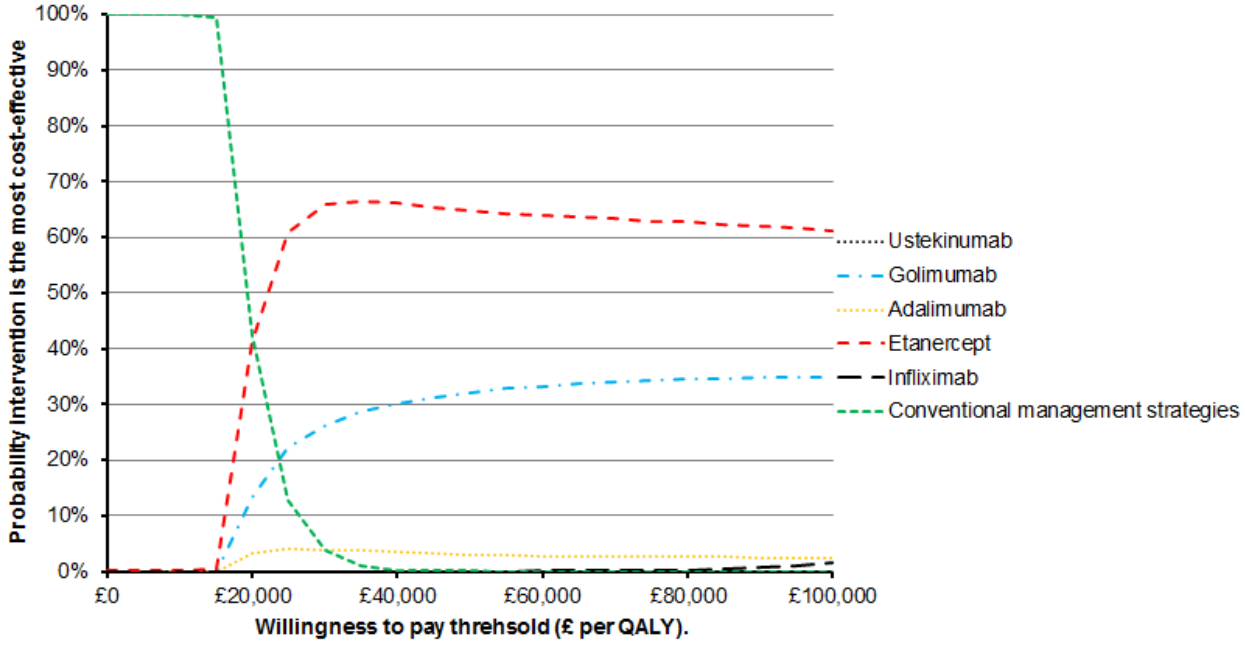


Figure 4: Cost-effectiveness acceptability curves, TNF alpha inhibitor-naïve population – *with* the PAS for ustekinumab



TNF alpha inhibitor-exposed population: sequencing analysis

In line with the ERG report (Section 6.3.10), only deterministic results are presented due to a lack of appropriate data.

TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

The PSA result indicates that ustekinumab's ICER vs. conventional management is £25.7k/QALY, which is similar to the deterministic result (£24.5k/QALY).

Table 22: Probabilistic sensitivity analysis, TNF alpha inhibitor-exposed population (vs. conventional management only) – *with* the PAS for ustekinumab

Technologies	Total		Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	QALYs	Costs	QALYs		
Conv. mgmt.	£30,024	2.81				
Ustekinumab	**£62,724**	**4.08**	**£32,700**	**1.27**	**£25,675**	**£25,675**
ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years						

Figure 5: Scatter plot, TNF alpha inhibitor-exposed population – *with* the PAS for ustekinumab

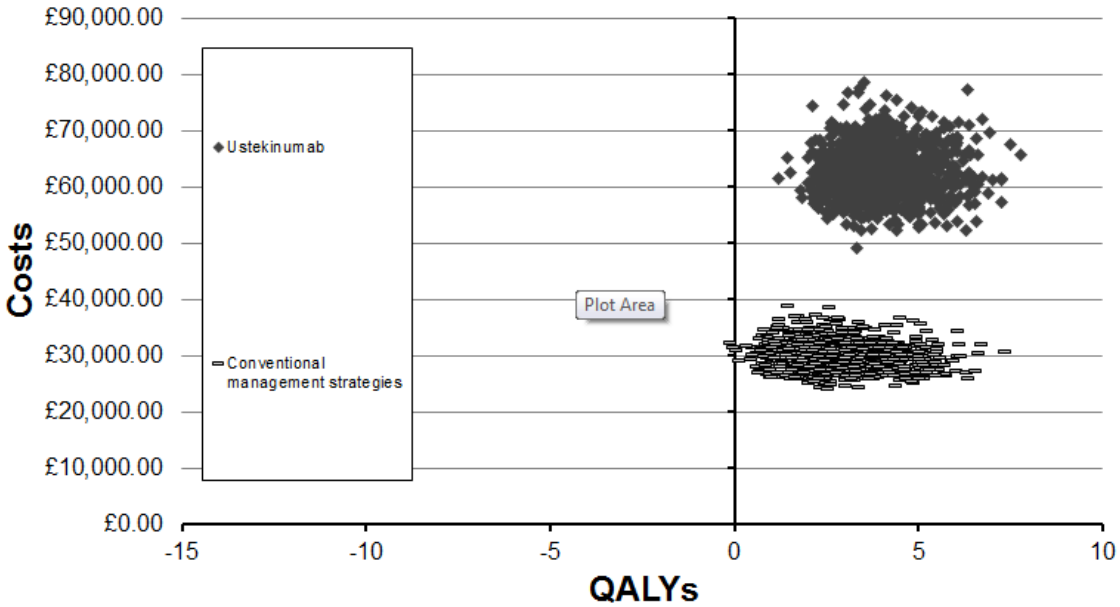
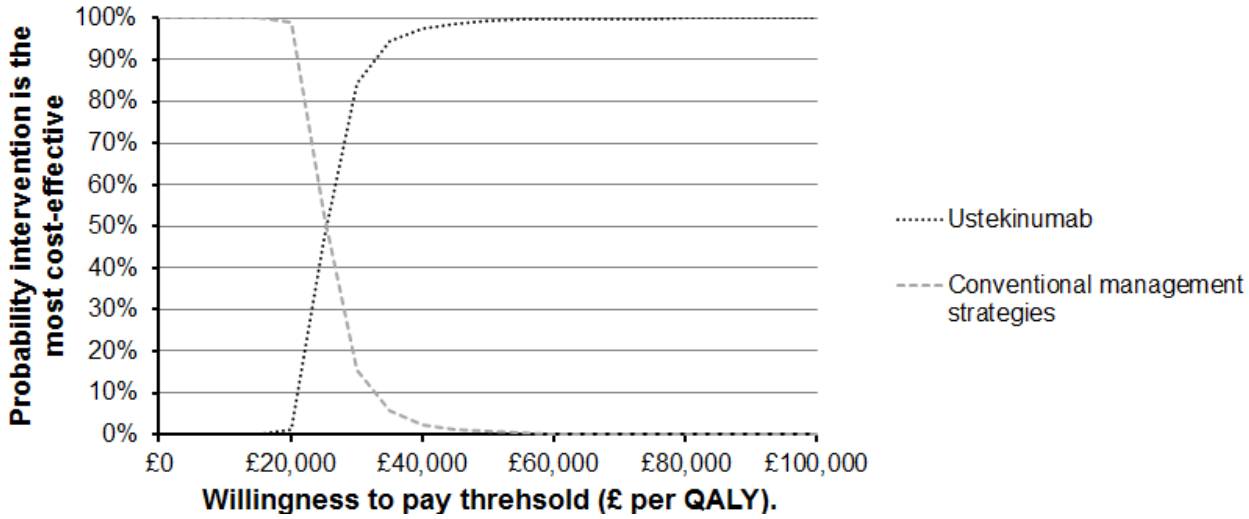


Figure 6: Cost-effectiveness acceptability curves, TNF alpha inhibitor-exposed population – *with* the PAS for ustekinumab



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

Scenario analysis results are shown on the series of tables below. Please refer to Section 4.13 below for commentaries on the results.

TNF alpha inhibitor-naïve population

Table 23: Scenario analysis 1: All treatments assessed for initial response at week 12 – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Adalimumab	£60,185	30.32	6.04	£34,077	1.67	£20,450	£20,450
Ustekinumab	**£64,445**	**30.32**	**5.65**	**£4,260**	**-0.39**	**Dominated**	**£29,962**
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	6.48	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 24: Scenario analysis 1: All treatments assessed for initial response at week 12 – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Ustekinumab	**£57,874**	**30.32**	**5.65**	**£31,766**	**1.28**	**£24,826**	**£24,826**
Adalimumab	£60,185	30.32	6.04	£2,311	0.39	£5,975	£20,450
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	6.48	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 25: Scenario analysis 2: All treatments assessed for initial response at week 24 – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,079	30.32	4.75				
Adalimumab	£64,649	30.32	6.45	£38,570	1.70	£22,634	£22,634
Ustekinumab	**£65,536**	**30.32**	**5.91**	**£888**	**-0.54**	**Dominated**	**£33,806**
Etanercept	£66,852	30.32	6.54	£2,203	0.09	£23,798	£22,694
Golimumab	£69,378	30.32	6.76	£2,527	0.22	£11,454	£21,465
Infliximab	£126,571	30.32	6.61	£57,193	-0.16	Dominated	£54,010
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 26: Scenario analysis 2: All treatments assessed for initial response at week 24 – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,079	30.32	4.75				
Ustekinumab	**£58,660**	**30.32**	**5.91**	**£32,581**	**1.17**	**£27,914**	**£27,914**
Adalimumab	£64,649	30.32	6.45	£5,989	0.54	£11,155	£22,634
Etanercept	£66,852	30.32	6.54	£2,203	0.09	£23,798	£22,694
Golimumab	£69,378	30.32	6.76	£2,527	0.22	£11,454	£21,465
Infliximab	£126,571	30.32	6.61	£57,193	-0.16	Dominated	£54,010
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 27: Scenario analysis 3: PsARC or PASI 75 responders continue treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Adalimumab	£67,830	30.32	6.46	£41,723	2.09	£19,969	£19,969
Etanercept	£69,805	30.32	6.69	£1,975	0.22	£8,844	£18,895
Golimumab	£72,671	30.32	6.73	£2,866	0.04	£64,285	£19,754
Ustekinumab	**£74,529**	**30.32**	**6.22**	**£1,858**	**-0.51**	**Dominated**	**£26,202**
Infliximab	£136,874	30.32	7.08	£64,203	0.35	£185,294	£40,968
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 28: Scenario analysis 3: PsARC or PASI 75 responders continue treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Ustekinumab	**£65,862**	**30.32**	**6.22**	**£39,755**	**1.85**	**£21,512**	**£21,512**
Adalimumab	£67,830	30.32	6.46	£1,968	0.24	£8,155	£19,969
Etanercept	£69,805	30.32	6.69	£1,975	0.22	£8,844	£18,895
Golimumab	£72,671	30.32	6.73	£2,866	0.04	£64,285	£19,754
Infliximab	£136,874	30.32	7.08	£64,203	0.35	£185,294	£40,968
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 29: Scenario analysis 4: PsARC and PASI 75 responders continue treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Etanercept	£42,003	30.32	4.95	£15,896	0.58	£27,469	£27,469
Adalimumab	£46,049	30.32	5.18	£4,046	0.23	£17,856	£24,764
Ustekinumab	**£47,723**	**30.32**	**5.11**	**£1,674**	**-0.07**	**Dominated**	**£29,290**
Golimumab	£52,386	30.32	5.57	£6,337	0.39	£16,110	£21,924
Infliximab	£116,574	30.32	6.06	£64,188	0.48	£132,891	£53,797
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 30: Scenario analysis 4: PsARC and PASI 75 responders continue treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Etanercept	£42,003	30.32	4.95	£15,896	0.58	£27,469	£27,469
Ustekinumab	**£44,505**	**30.32**	**5.11**	**£2,502**	**0.16**	**£15,704**	**£24,929**
Adalimumab	£46,049	30.32	5.18	£1,545	0.07	£22,948	£24,764
Golimumab	£52,386	30.32	5.57	£6,337	0.39	£16,110	£21,924
Infliximab	£116,574	30.32	6.06	£64,188	0.48	£132,891	£53,797
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 31: Scenario analysis 5: PASI score related costs include phototherapy – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£46,706	30.32	4.38				
Adalimumab	£80,209	30.32	6.04	£33,503	1.67	£20,106	£20,106
Ustekinumab	**£86,304**	**30.32**	**5.89**	**£6,095**	**-0.15**	**Dominated**	**£26,129**
Golimumab	£87,522	30.32	6.48	£7,313	0.43	£16,843	£19,431
Etanercept	£87,938	30.32	6.54	£416	0.06	£6,457	£19,045
Infliximab	£147,951	30.32	6.72	£60,013	0.18	£330,342	£43,144
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 32: Scenario analysis 5: PASI score related costs include phototherapy – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£46,706	30.32	4.38				
Ustekinumab	**£79,427**	**30.32**	**5.89**	**£32,721**	**1.52**	**£21,592**	**£21,592**
Adalimumab	£80,209	30.32	6.04	£781	0.15	£5,178	£20,106
Golimumab	£87,522	30.32	6.48	£7,313	0.43	£16,843	£19,431
Etanercept	£87,938	30.32	6.54	£416	0.06	£6,457	£19,045
Infliximab	£147,951	30.32	6.72	£60,013	0.18	£330,342	£43,144
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 33: Scenario analysis 6: Annual risk of withdrawal from treatment is 11.4% – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Adalimumab	£69,038	30.32	6.50	£42,930	2.12	£20,221	£20,221
Ustekinumab	**£74,652**	**30.32**	**6.24**	**£5,614**	**-0.26**	**Dominated**	**£26,058**
Etanercept	£78,387	30.32	7.15	£9,349	0.65	£14,446	£18,872
Golimumab	£79,168	30.32	7.05	£782	-0.10	Dominated	£19,859
Infliximab	£145,140	30.32	7.39	£66,753	0.24	£277,978	£39,541
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 34: Scenario analysis 6: Annual risk of withdrawal from treatment is 11.4% – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Ustekinumab	**£65,995**	**30.32**	**6.24**	**£39,887**	**1.86**	**£21,411**	**£21,411**
Adalimumab	£69,038	30.32	6.50	£3,043	0.26	£11,699	£20,221
Etanercept	£78,387	30.32	7.15	£9,349	0.65	£14,446	£18,872
Golimumab	£79,168	30.32	7.05	£782	-0.10	Dominated	£19,859
Infliximab	£145,140	30.32	7.39	£66,753	0.24	£277,978	£39,541
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 35: Scenario analysis 7: HAQ rebounds to a lower HAQ score than baseline (score =1) on withdrawal from active treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,040	30.32	4.55				
Adalimumab	£60,128	30.32	6.20	£34,088	1.65	£20,666	£20,666
Ustekinumab	**£65,800**	**30.32**	**6.06**	**£5,672**	**-0.15**	**Dominated**	**£26,475**
Etanercept	£67,121	30.32	6.70	£6,993	0.49	£14,133	£19,158
Golimumab	£67,701	30.32	6.63	£580	-0.07	Dominated	£20,041
Infliximab	£129,038	30.32	6.88	£61,917	0.18	£342,706	£44,301
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 36: Scenario analysis 7: HAQ rebounds to a lower HAQ score than baseline (score =1) on withdrawal from active treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,040	30.32	4.55				
Ustekinumab	**£58,923**	**30.32**	**6.06**	**£32,884**	**1.50**	**£21,896**	**£21,896**
Adalimumab	£60,128	30.32	6.20	£1,204	0.15	£8,154	£20,666
Etanercept	£67,121	30.32	6.70	£6,993	0.49	£14,133	£19,158
Golimumab	£67,701	30.32	6.63	£580	-0.07	Dominated	£20,041
Infliximab	£129,038	30.32	6.88	£61,917	0.18	£342,706	£44,301
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 37: Scenario analysis 8: Baseline weight is 77.4kg based on the general population – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Adalimumab	£60,185	30.32	6.04	£34,077	1.67	£20,450	£20,450
Ustekinumab	**£62,174**	**30.32**	**5.89**	**£1,989**	**-0.15**	**Dominated**	**£23,786**
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,855	30.32	6.48	£680	-0.06	Dominated	£19,862
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 38: Scenario analysis 8: Baseline weight is 77.4kg based on the general population – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	4.38				
Ustekinumab	**£58,791**	**30.32**	**5.89**	**£32,684**	**1.52**	**£21,555**	**£21,555**
Adalimumab	£60,185	30.32	6.04	£1,394	0.15	£9,290	£20,450
Etanercept	£67,175	30.32	6.54	£6,990	0.50	£14,018	£18,969
Golimumab	£67,855	30.32	6.48	£680	-0.06	Dominated	£19,862
Infliximab	£129,092	30.32	6.72	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 39: Scenario analysis 9: No excess mortality is associated with PsA; mortality based on general population all-cause mortality – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£27,566	34.62	4.41				
Adalimumab	£62,993	34.62	6.14	£35,426	1.73	£20,453	£20,453
Ustekinumab	**£68,677**	**34.62**	**5.98**	**£5,684**	**-0.16**	**Dominated**	**£26,099**
Etanercept	£70,050	34.62	6.66	£7,057	0.52	£13,700	£18,905
Golimumab	£70,634	34.62	6.59	£585	-0.06	Dominated	£19,712
Infliximab	£129,342	34.62	6.84	£59,293	0.19	£317,888	£41,820
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 40: Scenario analysis 9: No excess mortality is associated with PsA; mortality based on general population all-cause mortality – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£27,566	34.62	4.41				
Ustekinumab	**£61,744**	**34.62**	**5.98**	**£34,178**	**1.58**	**£21,698**	**£21,698**
Adalimumab	£62,993	34.62	6.14	£1,248	0.16	£7,954	£20,453
Etanercept	£70,050	34.62	6.66	£7,057	0.52	£13,700	£18,905
Golimumab	£70,634	34.62	6.59	£585	-0.06	Dominated	£19,712
Infliximab	£129,342	34.62	6.84	£59,293	0.19	£317,888	£41,820
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 41: Scenario analysis 10: EQ-5D utilities from Bojke et al. used (with age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	2.95				
Adalimumab	£60,185	30.32	4.62	£34,077	1.67	£20,450	£20,450
Ustekinumab	**£65,857**	**30.32**	**4.47**	**£5,673**	**-0.15**	**Dominated**	**£26,230**
Etanercept	£67,175	30.32	5.12	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	5.05	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	5.30	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 42: Scenario analysis 10: EQ-5D utilities from Bojke et al. used (with age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	2.95				
Ustekinumab	**£58,981**	**30.32**	**4.47**	**£32,874**	**1.52**	**£21,692**	**£21,692**
Adalimumab	£60,185	30.32	4.62	£1,204	0.15	£7,979	£20,450
Etanercept	£67,175	30.32	5.12	£6,990	0.50	£14,018	£18,969
Golimumab	£67,755	30.32	5.05	£579	-0.06	Dominated	£19,827
Infliximab	£129,092	30.32	5.30	£61,917	0.18	£340,821	£43,885
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 43: Scenario analysis 11: EQ-5D utilities from PSUMMIT used (with age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	6.20				
Adalimumab	£60,185	30.32	7.42	£34,077	1.22	£27,907	£27,907
Ustekinumab	**£65,857**	**30.32**	**7.32**	**£5,673**	**-0.11**	**Dominated**	**£35,768**
Etanercept	£67,175	30.32	7.80	£6,990	0.37	£18,856	£25,799
Golimumab	£67,755	30.32	7.74	£579	-0.05	Dominated	£27,047
Infliximab	£129,092	30.32	7.92	£61,917	0.13	£494,605	£59,979
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 44: Scenario analysis 11: EQ-5D utilities from PSUMMIT used (with age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	6.20				
Ustekinumab	**£58,981**	**30.32**	**7.32**	**£32,874**	**1.11**	**£29,580**	**£29,580**
Adalimumab	£60,185	30.32	7.42	£1,204	0.11	£10,967	£27,907
Etanercept	£67,175	30.32	7.80	£6,990	0.37	£18,856	£25,799
Golimumab	£67,755	30.32	7.74	£579	-0.05	Dominated	£27,047
Infliximab	£129,092	30.32	7.92	£61,917	0.13	£494,605	£59,979
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 45: Scenario analysis 12: EQ-5D utilities from PSUMMIT used (no age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	6.15				
Adalimumab	£60,185	30.32	7.37	£34,077	1.22	£27,907	£27,907
Ustekinumab	**£65,857**	**30.32**	**7.26**	**£5,673**	**-0.11**	**Dominated**	**£35,768**
Etanercept	£67,175	30.32	7.74	£6,990	0.37	£18,856	£25,799
Golimumab	£67,755	30.32	7.69	£579	-0.05	Dominated	£27,047
Infliximab	£129,092	30.32	7.87	£61,917	0.13	£494,605	£59,979
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 46: Scenario analysis 12: EQ-5D utilities from PSUMMIT used (no age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,107	30.32	6.15				
Ustekinumab	**£58,981**	**30.32**	**7.26**	**£32,874**	**1.11**	**£29,580**	**£29,580**
Adalimumab	£60,185	30.32	7.37	£1,204	0.11	£10,967	£27,907
Etanercept	£67,175	30.32	7.74	£6,990	0.37	£18,856	£25,799
Golimumab	£67,755	30.32	7.69	£579	-0.05	Dominated	£27,047
Infliximab	£129,092	30.32	7.87	£61,917	0.13	£494,605	£59,979
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 47: Scenario analysis 13: Efficacy for ustekinumab 45mg and 90mg based on full analysis set – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,127	30.32	4.38				
Adalimumab	£60,633	30.32	6.07	£34,506	1.70	£20,336	£20,336
Ustekinumab	**£66,088**	**30.32**	**5.90**	**£5,455**	**-0.18**	**Dominated**	**£26,273**
Etanercept	£66,631	30.32	6.50	£5,998	0.43	£13,937	£19,041
Golimumab	£67,963	30.32	6.49	£1,332	-0.01	Dominated	£19,788
Infliximab	£128,634	30.32	6.73	£62,003	0.22	£276,003	£43,586
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 48: Scenario analysis 13: Efficacy for ustekinumab 45mg and 90mg based on full analysis set – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£26,127	30.32	4.38				
Ustekinumab	**£59,170**	**30.32**	**5.90**	**£33,043**	**1.52**	**£21,725**	**£21,725**
Adalimumab	£60,633	30.32	6.07	£1,463	0.18	£8,320	£20,336
Etanercept	£66,631	30.32	6.50	£5,998	0.43	£13,937	£19,041
Golimumab	£67,963	30.32	6.49	£1,332	-0.01	Dominated	£19,788
Infliximab	£128,634	30.32	6.73	£62,003	0.22	£276,003	£43,586
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

TNF alpha inhibitor-exposed population: sequencing analysis

Table 49: Scenario analysis 1: All treatments assessed for initial response at week 12 – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	3.08	£83	-0.02	Dominated	£31,509
Ustekinumab	**£56,906**	**30.83**	**3.28**	**£12,247**	**0.18**	**£68,001**	**£39,829**
Infliximab	£105,250	30.83	3.15	£48,344	-0.14	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 50: Scenario analysis 1: All treatments assessed for initial response at week 12 – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	3.08	£83	-0.02	Dominated	£31,509
Ustekinumab	**£50,832**	**30.83**	**3.28**	**£6,173**	**0.18**	**£34,275**	**£31,177**
Infliximab	£105,250	30.83	3.15	£54,418	-0.14	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 51: Scenario analysis 2: All treatments assessed for initial response at week 24 – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,319	30.83	2.91				
Adalimumab	£45,183	30.83	3.32	£16,865	0.41	£41,128	£41,128
Golimumab	£45,881	30.83	3.34	£697	0.02	£31,063	£40,606
Etanercept	£46,399	30.83	3.40	£518	0.05	£9,716	£37,215
Ustekinumab	**£61,643**	**30.83**	**3.60**	**£15,244**	**0.20**	**£75,395**	**£48,435**
Infliximab	£111,540	30.83	3.37	£49,897	-0.23	Dominated	£182,703
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 52: Scenario analysis 2: All treatments assessed for initial response at week 24 – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,319	30.83	2.91				
Adalimumab	£45,183	30.83	3.32	£16,865	0.41	£41,128	£41,128
Golimumab	£45,881	30.83	3.34	£697	0.02	£31,063	£40,606
Etanercept	£46,399	30.83	3.40	£518	0.05	£9,716	£37,215
Ustekinumab	**£54,182**	**30.83**	**3.60**	**£7,784**	**0.20**	**£38,496**	**£37,591**
Infliximab	£111,540	30.83	3.37	£57,358	-0.23	Dominated	£182,703
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 53: Scenario analysis 3: PsARC or PASI 75 responders continue treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Etanercept	£49,662	30.83	3.39	£20,715	0.80	£25,790	£25,790
Adalimumab	£52,863	30.83	3.54	£3,201	0.15	£21,246	£25,072
Golimumab	£55,906	30.83	3.67	£3,043	0.14	£22,490	£24,751
Ustekinumab	**£70,642**	**30.83**	**3.84**	**£14,737**	**0.17**	**£89,061**	**£33,233**
Infliximab	£122,706	30.83	3.93	£52,064	0.09	£549,998	£69,486
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 54: Scenario analysis 3: PsARC or PASI 75 responders continue treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Etanercept	£49,662	30.83	3.39	£20,715	0.80	£25,790	£25,790
Adalimumab	£52,863	30.83	3.54	£3,201	0.15	£21,246	£25,072
Golimumab	£55,906	30.83	3.67	£3,043	0.14	£22,490	£24,751
Ustekinumab	**£60,788**	**30.83**	**3.84**	**£4,883**	**0.17**	**£29,509**	**£25,379**
Infliximab	£122,706	30.83	3.93	£61,917	0.09	£654,095	£69,486
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 55: Scenario analysis 4: PsARC and PASI 75 responders continue treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Etanercept	£38,551	30.83	2.73	£9,604	0.15	£65,571	£65,571
Adalimumab	£39,507	30.83	2.78	£956	0.05	£18,894	£53,587
Golimumab	£41,183	30.83	2.88	£1,677	0.10	£16,895	£41,298
Ustekinumab	**£51,133**	**30.83**	**3.20**	**£9,950**	**0.32**	**£30,640**	**£35,725**
Infliximab	£102,124	30.83	2.99	£50,991	-0.21	Dominated	£178,928
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 56: Scenario analysis 4: PsARC and PASI 75 responders continue treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Etanercept	£38,551	30.83	2.73	£9,604	0.15	£65,571	£65,571
Adalimumab	£39,507	30.83	2.78	£956	0.05	£18,894	£53,587
Golimumab	£41,183	30.83	2.88	£1,677	0.10	£16,895	£41,298
Ustekinumab	**£46,593**	**30.83**	**3.20**	**£5,410**	**0.32**	**£16,659**	**£28,414**
Infliximab	£102,124	30.83	2.99	£55,531	-0.21	Dominated	£178,928
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 57: Scenario analysis 5: PASI score related costs include phototherapy – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£52,990	30.83	2.58				
Adalimumab	£67,662	30.83	2.98	£14,673	0.40	£36,502	£36,502
Golimumab	£69,379	30.83	3.08	£1,717	0.10	£17,288	£32,696
Etanercept	£69,598	30.83	3.10	£218	0.02	£10,603	£31,824
Ustekinumab	**£86,477**	**30.83**	**3.57**	**£16,879**	**0.47**	**£36,154**	**£33,869**
Infliximab	£129,653	30.83	3.15	£43,176	-0.42	Dominated	£135,315
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 58: Scenario analysis 5: PASI score related costs include phototherapy – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£52,990	30.83	2.58				
Adalimumab	£67,662	30.83	2.98	£14,673	0.40	£36,502	£36,502
Golimumab	£69,379	30.83	3.08	£1,717	0.10	£17,288	£32,696
Etanercept	£69,598	30.83	3.10	£218	0.02	£10,603	£31,824
Ustekinumab	**£79,016**	**30.83**	**3.57**	**£9,418**	**0.47**	**£20,174**	**£26,323**
Infliximab	£129,653	30.83	3.15	£50,637	-0.42	Dominated	£135,315
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 59: Scenario analysis 6: Annual risk of withdrawal from treatment is 16.5% (same as TNF inhibitor naïve-population) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£46,286	30.83	3.15	£17,339	0.57	£30,575	£30,575
Etanercept	£48,917	30.83	3.32	£2,631	0.17	£15,172	£26,968
Golimumab	£49,055	30.83	3.29	£138	-0.03	Dominated	£28,421
Ustekinumab	**£72,057**	**30.83**	**3.88**	**£23,140**	**0.56**	**£41,278**	**£33,133**
Infliximab	£111,338	30.83	3.39	£39,281	-0.49	Dominated	£101,987
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 60: Scenario analysis 6: Annual risk of withdrawal from treatment is 16.5% (same as TNF inhibitor naïve-population) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£46,286	30.83	3.15	£17,339	0.57	£30,575	£30,575
Etanercept	£48,917	30.83	3.32	£2,631	0.17	£15,172	£26,968
Golimumab	£49,055	30.83	3.29	£138	-0.03	Dominated	£28,421
Ustekinumab	**£61,879**	**30.83**	**3.88**	**£12,962**	**0.56**	**£23,122**	**£25,311**
Infliximab	£111,338	30.83	3.39	£49,459	-0.49	Dominated	£101,987
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 61: Scenario analysis 7: HAQ rebounds to a lower HAQ score than baseline (score =1) on withdrawal from active treatment – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,251	30.83	4.40				
Adalimumab	£42,263	30.83	4.78	£14,012	0.38	£37,068	£37,068
Etanercept	£43,997	30.83	4.89	£1,734	0.11	£15,154	£31,977
Golimumab	£44,081	30.83	4.87	£84	-0.02	Dominated	£33,651
Ustekinumab	**£61,418**	**30.83**	**5.34**	**£17,421**	**0.45**	**£38,748**	**£35,209**
Infliximab	£104,589	30.83	4.93	£43,172	-0.41	Dominated	£142,508
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 62: Scenario analysis 7: HAQ rebounds to a lower HAQ score than baseline (score =1) on withdrawal from active treatment – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,251	30.83	4.40				
Adalimumab	£42,263	30.83	4.78	£14,012	0.38	£37,068	£37,068
Etanercept	£43,997	30.83	4.89	£1,734	0.11	£15,154	£31,977
Golimumab	£44,081	30.83	4.87	£84	-0.02	Dominated	£33,651
Ustekinumab	**£53,957**	**30.83**	**5.34**	**£9,960**	**0.45**	**£22,153**	**£27,288**
Infliximab	£104,589	30.83	4.93	£50,633	-0.41	Dominated	£142,508
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 63: Scenario analysis 8: Baseline weight is 77.4kg based on the general population – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,792	30.83	3.08	£132	-0.02	Dominated	£31,575
Ustekinumab	**£57,914**	**30.83**	**3.61**	**£13,255**	**0.50**	**£26,350**	**£28,263**
Infliximab	£105,250	30.83	3.15	£47,336	-0.46	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 64: Scenario analysis 8: Baseline weight is 77.4kg based on the general population – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	2.58				
Adalimumab	£42,932	30.83	2.98	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	3.10	£1,727	0.12	£14,408	£30,107
Golimumab	£44,792	30.83	3.08	£132	-0.02	Dominated	£31,575
Ustekinumab	**£55,304**	**30.83**	**3.61**	**£10,645**	**0.50**	**£21,162**	**£25,717**
Infliximab	£105,250	30.83	3.15	£49,946	-0.46	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 65: Scenario analysis 9: No excess mortality is associated with PsA; mortality based on general population all-cause mortality – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£30,534	35.07	2.56				
Adalimumab	£45,583	35.07	2.97	£15,049	0.41	£36,629	£36,629
Etanercept	£47,318	35.07	3.09	£1,735	0.12	£14,207	£31,491
Golimumab	£47,401	35.07	3.07	£83	-0.02	Dominated	£32,896
Ustekinumab	**£64,752**	**35.07**	**3.57**	**£17,434**	**0.48**	**£36,366**	**£33,799**
Infliximab	£106,132	35.07	3.14	£41,380	-0.43	Dominated	£130,716
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 66: Scenario analysis 9: No excess mortality is associated with PsA; mortality based on general population all-cause mortality – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£30,534	35.07	2.56				
Adalimumab	£45,583	35.07	2.97	£15,049	0.41	£36,629	£36,629
Etanercept	£47,318	35.07	3.09	£1,735	0.12	£14,207	£31,491
Golimumab	£47,401	35.07	3.07	£83	-0.02	Dominated	£32,896
Ustekinumab	**£57,264**	**35.07**	**3.57**	**£9,946**	**0.48**	**£20,747**	**£26,403**
Infliximab	£106,132	35.07	3.14	£48,868	-0.43	Dominated	£130,716
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 67: Scenario analysis 10: EQ-5D utilities from Bojke et al. used (with age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	1.08				
Adalimumab	£42,932	30.83	1.48	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	1.60	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	1.58	£83	-0.02	Dominated	£31,509
Ustekinumab	**£62,037**	**30.83**	**2.07**	**£17,378**	**0.47**	**£37,222**	**£33,467**
Infliximab	£105,250	30.83	1.65	£43,213	-0.42	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 68: Scenario analysis 10: EQ-5D utilities from Bojke et al. used (with age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	1.08				
Adalimumab	£42,932	30.83	1.48	£13,985	0.40	£34,790	£34,790
Etanercept	£44,659	30.83	1.60	£1,727	0.12	£14,408	£30,107
Golimumab	£44,742	30.83	1.58	£83	-0.02	Dominated	£31,509
Ustekinumab	**£54,576**	**30.83**	**2.07**	**£9,917**	**0.47**	**£21,241**	**£25,921**
Infliximab	£105,250	30.83	1.65	£50,674	-0.42	Dominated	£134,679
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 69: Scenario analysis 11: EQ-5D utilities from PSUMMIT used (with age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	4.87				
Adalimumab	£42,932	30.83	5.16	£13,985	0.29	£47,425	£47,425
Etanercept	£44,659	30.83	5.25	£1,727	0.09	£19,362	£40,907
Golimumab	£44,742	30.83	5.23	£83	-0.02	Dominated	£42,962
Ustekinumab	**£62,037**	**30.83**	**5.59**	**£17,378**	**0.34**	**£50,914**	**£45,615**
Infliximab	£105,250	30.83	5.28	£43,213	-0.31	Dominated	£183,985
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 70: Scenario analysis 11: EQ-5D utilities from PSUMMIT used (with age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	4.87				
Adalimumab	£42,932	30.83	5.16	£13,985	0.29	£47,425	£47,425
Etanercept	£44,659	30.83	5.25	£1,727	0.09	£19,362	£40,907
Golimumab	£44,742	30.83	5.23	£83	-0.02	Dominated	£42,962
Ustekinumab	**£54,576**	**30.83**	**5.59**	**£9,917**	**0.34**	**£29,055**	**£35,330**
Infliximab	£105,250	30.83	5.28	£50,674	-0.31	Dominated	£183,985
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 71: Scenario analysis 12: EQ-5D utilities from PSUMMIT used (no age-adjustment) – *without* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	4.88				
Adalimumab	£42,932	30.83	5.17	£13,985	0.29	£47,425	£47,425
Etanercept	£44,659	30.83	5.26	£1,727	0.09	£19,362	£40,907
Golimumab	£44,742	30.83	5.25	£83	-0.02	Dominated	£42,962
Ustekinumab	**£62,037**	**30.83**	**5.60**	**£17,378**	**0.34**	**£50,914**	**£45,615**
Infliximab	£105,250	30.83	5.29	£43,213	-0.31	Dominated	£183,985
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

Table 72: Scenario analysis 12: EQ-5D utilities from PSUMMIT used (no age-adjustment) – *with* the PAS for ustekinumab

Technologies	Total			Incremental		ICER (cost per QALY)	ICER vs. conv. mgmt.
	Costs	LY	QALYs	Costs	QALYs		
Conv. mgmt.	£28,947	30.83	4.88				
Adalimumab	£42,932	30.83	5.17	£13,985	0.29	£47,425	£47,425
Etanercept	£44,659	30.83	5.26	£1,727	0.09	£19,362	£40,907
Golimumab	£44,742	30.83	5.25	£83	-0.02	Dominated	£42,962
Ustekinumab	**£54,576**	**30.83**	**5.60**	**£9,917**	**0.34**	**£29,055**	**£35,330**
Infliximab	£105,250	30.83	5.29	£50,674	-0.31	Dominated	£183,985
ICER, incremental cost-effectiveness ratio; LY, life-years; QALYs, quality-adjusted life-years							

TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

Table 73: Scenario analyses: TNF alpha inhibitor-exposed population, ustekinumab vs. conventional management

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£) incremental (QALYs)
Scenario analysis 1: All treatments assessed for initial response at Week 12						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£66,265	30.83	3.54	£36,268	1.01	£36,007
***with* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£57,812	30.83	3.54	£27,814	1.01	£27,614
Scenario analysis 2: All treatments assessed for initial response at Week 24						
***without* the PAS**						
Conv. mgmt	£29,565	30.83	2.85			
Ustekinumab	£72,613	30.83	3.86	£43,049	1.01	£42,705
***with* the PAS**						
Conv. mgmt	£29,565	30.83	2.85			
Ustekinumab	£62,435	30.83	3.86	£32,871	1.01	£32,608
Scenario analysis 3: PsARC or PASI 75 responders continue treatment						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£85,729	30.83	4.24	£55,732	1.71	£32,683
***with* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£71,901	30.83	4.24	£41,903	1.71	£24,574
Scenario analysis 4: PsARC and PASI 75 responders continue treatment						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£56,003	30.83	3.32	£26,005	0.78	£33,211
***with* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£50,280	30.83	3.32	£20,282	0.78	£25,903
Scenario analysis 5: PASI score related costs include phototherapy						
***without* the PAS**						
Conv. mgmt	£56,969	30.83	2.54			
Ustekinumab	£97,878	30.83	3.86	£40,909	1.32	£30,922
***with* the PAS**						
Conv. mgmt	£56,969	30.83	2.54			
Ustekinumab	£87,700	30.83	3.86	£30,731	1.32	£23,229
Scenario analysis 6: Annual risk of withdrawal from treatment is 11.4%						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£82,374	30.83	4.16	£52,376	1.62	£32,257
***with* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£69,544	30.83	4.16	£39,546	1.62	£24,355
Scenario analysis 7: HAQ rebounds to a lower HAQ score than baseline (score = 1) on withdrawal from active treatment						
***without* the PAS**						
Conv. mgmt	£29,308	30.83	4.34			
Ustekinumab	£72,027	30.83	5.55	£42,719	1.21	£35,341
***with* the PAS**						
Conv. mgmt	£29,308	30.83	4.34			
Ustekinumab	£61,849	30.83	5.55	£32,541	1.21	£26,921

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£) incremental (QALYs)
Scenario analysis 8: Baseline weight is 77.4 kg based on the general population (HSE, 2012)						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£67,124	30.83	3.91	£37,127	1.37	£27,035
***with* the PAS**						
Conv. mgmt	£29,998	30.83	2.54			
Ustekinumab	£63,550	30.83	3.91	£33,552	1.37	£24,432
Scenario analysis 9: No excess mortality is associated with PsA; mortality based on general population all-cause mortality						
***without* the PAS**						
Conv. mgmt	£31,633	35.07	2.51			
Ustekinumab	£75,568	35.07	3.87	£43,936	1.36	£32,281
***with* the PAS**						
Conv. mgmt	£31,633	35.07	2.51			
Ustekinumab	£65,313	35.07	3.87	£33,680	1.36	£24,746
Scenario analysis 10: EQ-5D utilities from Bojke et al. used - with age-adjustment						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	1.03			
Ustekinumab	£72,618	30.83	2.36	£42,620	1.32	£32,215
***with* the PAS**						
Conv. mgmt	£29,998	30.83	1.03			
Ustekinumab	£62,440	30.83	2.36	£32,442	1.32	£24,522
Scenario analysis 11: EQ-5D utilities from PSUMMIT used - with age-adjustment						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	4.84			
Ustekinumab	£72,618	30.83	5.81	£42,620	0.97	£44,113
***with* the PAS**						
Conv. mgmt	£29,998	30.83	4.84			
Ustekinumab	£62,440	30.83	5.81	£32,442	0.97	£33,578
Scenario analysis 12: EQ-5D utilities from PSUMMIT used - no age-adjustment						
***without* the PAS**						
Conv. mgmt	£29,998	30.83	4.86			
Ustekinumab	£72,618	30.83	5.82	£42,620	0.97	£44,113
***with* the PAS**						
Conv. mgmt	£29,998	30.83	4.86			
Ustekinumab	£62,440	30.83	5.82	£32,442	0.97	£33,578
Conv. mgmt = conventional management strategies; ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years						

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 because the PAS does not depend on any clinical variable (see Section 3.5).

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.

The results of the scenario analyses detailed in Section 4.11 above are summarised in Table 74, Table 75 and Table 76 below.

TNF alpha inhibitor-naïve population

Without the PAS, ustekinumab is dominated by adalimumab in the vast majority of scenarios. However, with the PAS, ustekinumab becomes the least expensive among all the biologic treatment options. Moreover, ustekinumab's ICER vs. conventional management is below £30k/QALY in all scenarios when the PAS is applied.

The extensive scenario analyses demonstrate that, with the PAS, ustekinumab is a cost-effective treatment option for the TNF alpha inhibitor-naïve population.

Table 74: Impact of the PAS on ICERs – TNF alpha inhibitor-naïve population

	ICER for intervention versus:			
	conv. mgmt		adalimumab	
	Without PAS	With PAS	Without PAS	With PAS
Base-case	£26,230	£21,692	Dominated	UST cheaper
Scenario 1	£29,962	£24,826	Dominated	UST cheaper
Scenario 2	£33,806	£27,914	Dominated	UST cheaper
Scenario 3	£26,202	£21,512	Dominated	UST cheaper
Scenario 4	£29,290	£24,929	Dominated	UST cheaper
Scenario 5	£26,129	£21,592	Dominated	UST cheaper
Scenario 6	£26,058	£21,411	Dominated	UST cheaper
Scenario 7	£26,475	£21,896	Dominated	UST cheaper
Scenario 8	£23,786	£21,555	Dominated	UST cheaper
Scenario 9	£26,099	£21,698	Dominated	UST cheaper
Scenario 10	£26,230	£21,692	Dominated	UST cheaper
Scenario 11	£35,768	£29,580	Dominated	UST cheaper
Scenario 12	£35,768	£29,580	Dominated	UST cheaper
Scenario 13	£26,273	£21,725	Dominated	UST cheaper
PAS: patient access scheme, UST: ustekinumab				

TNF alpha inhibitor-exposed population: sequencing analysis

When the PAS is applied, ustekinumab's ICER vs. TNF alpha inhibitors is below £30k/QALY in all cases, except under scenario 1 (All treatments assessed for initial response at week 12) and scenario 2 (All treatments assessed for initial response at week 24) (Table 75). It must be noted, however, that neither of these scenarios is in fact realistic; whilst response to TNF alpha inhibitors should be assessed at week 12 as recommended in NICE TA199 and TA220(5, 6), the SmPC for ustekinumab states "Consideration should be given to discontinuing treatment in patients who have shown no response up to 28 weeks of treatment"(2).

The extensive scenario analyses using the sequencing model demonstrate that ustekinumab is a cost-effective treatment option compared against TNF alpha inhibitors for the TNF alpha inhibitor-exposed population.

Table 75: Impact of the PAS on ICERs – sequencing analysis

	ICER for intervention versus:			
	etanercept		golimumab	
	Without PAS	With PAS	Without PAS	With PAS
Base-case	£37,222	£21,241	GOL dominated	GOL dominated
Scenario 1	£68,001	£34,275	GOL dominated	GOL dominated
Scenario 2	£75,395	£38,496	GOL cheaper than ETA	GOL cheaper than ETA
Scenario 3	ETA cheaper than GOL	ETA cheaper than GOL	£89,061	£29,509
Scenario 4	ETA cheaper than GOL	ETA cheaper than GOL	£30,640	£16,659
Scenario 5	£36,154	£20,174	GOL cheaper than ETA	GOL cheaper than ETA
Scenario 6	£41,278	£23,122	GOL dominated	GOL dominated
Scenario 7	£38,748	£22,153	GOL dominated	GOL dominated
Scenario 8	£26,350	£21,162	GOL dominated	GOL dominated
Scenario 9	£36,366	£20,747	GOL dominated	GOL dominated
Scenario 10	£37,222	£21,241	GOL dominated	GOL dominated
Scenario 11	£50,914	£29,055	GOL dominated	GOL dominated
Scenario 12	£50,914	£29,055	GOL dominated	GOL dominated
ETA: etanercept; GOL: golimumab, PAS: patient access scheme, UST: ustekinumab				

TNF alpha inhibitor-exposed population: ustekinumab vs. conventional management

The results of the scenario analyses indicate that, if the PAS is applied, ustekinumab's ICER is well below £30k/QALY in most scenarios.

Table 76: Impact of the PAS on ICERs – vs. conventional management

	ICER for intervention versus conv. mgmt	
	Without PAS	**With PAS**
Base-case	£32,215	£24,522
Scenario 1	£36,007	£27,614
Scenario 2	£42,705	£32,608
Scenario 3	£32,683	£24,574
Scenario 4	£33,211	£25,903
Scenario 5	£30,922	£23,229
Scenario 6	£32,257	£24,355
Scenario 7	£35,341	£26,921
Scenario 8	£27,035	£24,432
Scenario 9	£32,281	£24,746
Scenario 10	£32,215	£24,522
Scenario 11	£44,113	£33,578
Scenario 12	£44,113	£33,578
PAS: patient access scheme		

One of the exceptions is scenario 2 (All treatments assessed for initial response at week 24) for which the ICER is £32.6k/QALY. However, this result should be treated with caution for a number of reasons.

First, as we commented in our response to the ACD, the British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) guideline stated that: "…in most cases patients should have had adequate therapeutic trials of two standard DMARDs (either sequentially or in combination) prior to the prescription of biologic therapies. An adequate therapeutic trial is defined either as failure to tolerate a DMARD or active disease despite treatment of at least 12 weeks at target therapeutic dose of a conventional DMARD"(7). Regarding this guideline, TA Guidance 313 stated that "[the Committee] noted that this did not preclude assessment of response at 24 weeks". However, it is also true that assessment of response at week 12 is not precluded. Moreover, there is no intrinsic reason why the timing of assessment for ustekinumab and conventional management has to be exactly the same in the economic model.

Second, as we also commented in our response to the ACD, the Committee's preference for assessing treatment response for conventional management at week 24 would create a discrepancy among the modelling methodologies across NICE appraisals in the same condition. In the York model for the NICE TA199 and in the

de novo model for TA 220, treatment response to conventional management was assumed to be assessed at week 12-16.(5, 6)

Therefore, the result of scenario 2 should be deemed as the worst case for ustekinumab's cost-effectiveness and treated with caution.

The scenarios 11 and 12 are based on the utility equations derived from the PSUMMIT study results. These scenarios are in fact now redundant since "the Committee concluded that using the previously published equation [i.e. Bojke et al. equation as in the base case] would be more appropriate and would support a consistent approach between appraisals" (TA Guidance 313, para.4.14).(3)

The extensive scenario analyses demonstrate that, with the PAS, ustekinumab is a cost-effective treatment option compared against conventional management for the TNF alpha inhibitor-exposed population.

Conclusion

There is currently a lack of NICE-recommended treatment alternatives to TNF alpha inhibitors for treating active PsA, particularly for patients who are TNF alpha inhibitor-exposed and for whom TNF alpha inhibitors are not suitable. Indeed, the "potential value of additional treatment options for people with psoriatic arthritis" was recognised by the Committee (TA Guidance 313 para. 4.5)(3).

As stated in the Guidance, ustekinumab can be considered an "innovative technology, because it is in a different class to TNF alpha inhibitors and targets a different inflammatory pathway" (para. 4.22)(3). It has a unique mode of action, and therefore represents a new option that may prove effective in those patients who have failed currently available options. The TA Guidance stated; "Clinical specialists considered that ustekinumab has the potential to offer an innovative treatment option to fulfil this need. The Committee acknowledged that [a group of people with psoriatic arthritis for whom TNF alpha inhibitors are not suitable] represents a distinct group with an important unmet need that warrants additional consideration" (para. 4.5)(3). Furthermore, regarding the TNF alpha inhibitor-naïve population for whom TNF alpha inhibitors are inappropriate, the Committee "emphasised that ustekinumab is innovative for this population, as it potentially fulfils an important unmet need" (para. 4.19)(3).

The extension of the PAS to the new PsA indication considerably improves the cost effectiveness of ustekinumab. Janssen has conducted extensive scenario and sensitivity analyses using the three economic models presented above. The models used are "similar to the models used in previous NICE appraisals of treatments for psoriatic arthritis" (para. 3.8)(3), thereby reducing decision uncertainty. The results of the analyses presented above clearly demonstrate that, with the PAS, ustekinumab is a cost effective treatment option for both TNF alpha inhibitor-naïve and -exposed populations, whether it is compared with conventional management or with TNF alpha inhibitors.

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.

Patient registration form (to be used when Bupa Home Healthcare is chosen by a NHS trust as a homecare provider)

STELARA® PATIENT SUPPORT PROGRAMME: PATIENT REGISTRATION

janssen

Bupa Home Healthcare

Please complete, print, sign and then either fax or scan and email to Bupa Home Healthcare.
This registration form will not be processed unless it is completed as directed and accompanied by a valid prescription.
Bupa Home Healthcare **Harlow** - Scimitar Park, Roydon Road, Harlow, Essex CM19 5GU Fax: 0845 8888 366 Email: BUPA.Biologics@nhs.net
Scotland – Units 3 & 5 Weardale Lane, Queenslie Industrial Estate, Glasgow G33 4JJ Tel: 0845 8888 238 Fax: 0845 8888 371

For Home Care Service enrolment, please complete all sections of this form except section 3
For Hospital Delivery enrolment, please complete sections 3, 4 & 6 only

1. PATIENT DETAILS

Title (tick as appropriate) Mr ☐ Mrs ☐ Ms ☐ Miss ☐ Master ☐
First name Initials
Surname
Date of birth Male ☐ Female ☐
Address
Postcode
Telephone Mobile
Email address
NHS number

Patient Status *(please tick as appropriate)*
Biologic naïve Yes ☐ No ☐
If No what is the biologic switch therapy?

2. HOMECARE SERVICE ONLY

I wish to enrol the above named patient for the homecare service ☐
Primary diagnosis Psoriasis ☐ Psoriatic Arthritis ☐
Other (please specify)
Patient requires: *(please tick one only)*
- Injection training only by Bupa Home Healthcare Nurse ☐
- Regular & continuous home nursing support service ☐

Patient Weight less than or equal to 100kg ☐ >100kg ☐
Date of first delivery
Patient information pack supplied by:
Referring Centre ☐ Homecare provider ☐

3. HOSPITAL DELIVERY ONLY

I wish to order for Hospital Delivery only ☐
Encrypted Patient Identifier
Patient Weight less than or equal to 100kg ☐ >100kg ☐
Date of first delivery
Primary diagnosis Psoriasis ☐ Psoriatic Arthritis ☐
Other (please specify)

4. REFERRING HOSPITAL

Hospital
Address
Postcode
Telephone
Consultant
Telephone Ext/bleep
Pharmacist
Telephone Ext/bleep
Nurse
Telephone Ext/bleep

5. GP DETAILS

GP name
Address
Postcode
Telephone

6. INVOICING DETAILS – IF APPLICABLE

(please tick as appropriate) TRUST ☐ CCG ☐ OTHER ☐
Contact
Address
Postcode
Email address
Purchase Order required? YES ☐ NO ☐
Purchase Order number

Patient consent – to be signed by the patient/parent/guardian
Bupa Home Healthcare need your consent to keep and use information about you and your health on their computer systems. Please read the following statements and confirm your agreement. I confirm my agreement for Bupa Home Healthcare to hold, update and use my information for the purpose of providing, monitoring and improving a home care service. I understand that the information they hold may include personal identification data (name, address, telephone number etc), details of my medical condition and medication prescribed to me. I understand that from time to time this information may be provided to other organisations involved in my homecare but this will always occur in accordance with the provisions of the Data Protection Act. I understand that I have the right to gain access to and to correct this information.

Name
Signed
Date

To be completed by the referring clinician/Trust representative
(if the patient is unable to sign)

The homecare service has been fully explained and discussed with the patient and he/she has given their explicit informed consent to receive this service from Bupa Home Healthcare.

The patient understands and consents to his/her personal and health information being passed to and processed by Bupa Home Healthcare, under the provisions of the Data Protection Act 1998, in order for the homecare service to be provided to them.

Health professional signature/Trust representative (on behalf of the patient)
Name
Signed
Date

BHH033 09/13
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bupa.com
Version 1.0

Patient registration form (to be used when another homecare provider is chosen by a NHS trust)

STELARA® PATIENT ACCESS SCHEME

janssen

This forms outlines the information needed to register a patient for the Stelara Patient Access Scheme.

This form should accompany all Hospital, Private and Homecare orders for Stelara or alternatively the information contained within this form should be included within standard Hospital order or Homecare registration forms which are designed for ordering Stelara.

Encrypted Patient Identifier

Stelara dose: 45mg 90mg (please tick as appropriate)

Patient Weight: less than or equal to 100kg ☐ >100kg ☐ (please tick as appropriate)

Primary diagnosis Psoriasis ☐ Psoriatic Arthritis ☐

Other (please specify)

Patient referral guide

Patient Referral Guide.pdf

Patient information guide

Patient Info Guide - Generic.pdf

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.

N/A

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.

N/A

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.

N/A

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).

N/A

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.

N/A

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.

N/A

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.

N/A

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.

N/A

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.

N/A

6 References

1. National Institute for Health and Care Excellence. TA180: Ustekinumab for the treatment of adults with moderate to severe psoriasis: NICE; 2010 [cited 2013 August 2013]. Available from: http://www.nice.org.uk/nicemedia/live/12235/45461/45461.pdf.
2. Janssen-Cilag Limited. Ustekinumab (Stelara®). Summary of Product Characteristics (SPC)2014.
3. National Institute for Health and Care Excellence. TA313: Ustekinumab for treating active psoriatic arthritis 2014 [Aug 2014]. Available from: http://www.nice.org.uk/guidance/TA313.
4. Craig D, O'Connor J, Rodgers M, Smith A, Woolacott N. Ustekinumab for treating active and progressive psoriatic arthritis: A Single Technology Appraisal. Centre for Reviews and Dissemination. 2013.
5. National Institute for Health and Care Excellence. TA199: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis 2010 [July 2013]. Available from: http://www.nice.org.uk/TA199.
6. National Institute for Health and Care Excellence. TA220: Golimumab for the treatment of psoriatic arthritis 2011 [July 2013]. Available from: http://www.nice.org.uk/TA220.
7. British Society for Rheumatology. Guidelines for the treatment of psoriatic arthritis with biologics: British Society for Rheumatology; 2012 [July 2013]. Available from: http://www.rheumatology.org.uk/includes/documents/cm_docs/2012/b/bsr_guidelines_2012_treatment_of_psoriatic_arthritis_with_biologics.pdf.