
in collaboration with:

ERASMUS UNIVERSITEIT ROTTERDAM
INSTITUTE OF HEALTH POLICY & MANAGEMENT

Maastricht University

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# Ixekizumab for treating active psoriatic arthritis following inadequate response to disease-modifying anti-rheumatic drugs

# ERRATUM

This document contains errata in respect to the ERG report. The ERG noted an error in the company's implementation of the PSA. The ERG has now fixed this error and provides the corrected probabilistic results in tables as well as in the text of the report. The ERG also added critique points to the report to reflect this error. Furthermore, the ERG noted that the CiC marking was missing from one set of results and has updated the CiC marking of all ERG results.

The table below lists the page to be replaced in the original document and the nature of the change:

| **Page nr:** | **Change:** |
|---|---|
| 18 | Added more detail to description of ERG ICERs |
| 118 | Added critique point on PSA to ERG comment |
| 123 | Added a bullet point about the PSA to Fixing errors |
| 124 | Corrected probabilistic ICERs |
| 128-132 | Replaced Table 6.1 with corrected probabilistic analyses and CiC marking |
| 133-146 | Replaced Table 6.2 with corrected CiC marking |
| 149 | Added more detail to description of ERG ICERs |

typographical errors, incorrect truncation and syntax mistakes in several of the cost effectiveness PubMed searches. Searches of the health technology assessment database (HTA) and the Health Economic Evaluations Database (HEED) contained unnecessary costs or HRQoL/Utilities search filters which were overly restrictive. Searching the NHS Economic Evaluation database would have been beneficial. Due to these issues, it is possible that potentially relevant studies may have been missed, however the impact of this is difficult to assess without undertaking these reviews independently.

Health states in the cost effectiveness model are based on a relative measure of response (reductions in symptoms), which may lead to health states being composed of heterogeneous patient populations, for which it is arguably difficult to assign costs and HRQoL estimates. Further limitations are the exclusion of comparators identified in the scope and the omission of adverse events from the economic model. For the b/tsDMARD-experienced patient population, only a limited network was used, which omitted PASI 50 as an outcome. Moreover, the ERG considers the assumption of equal treatment discontinuation rates for all b/tsDMARD treatments as a weakness. The representativeness of the patient population in the SPIRIT trial programme, excess mortality in this population, resource use and cost estimates associated with HAQ-DI and PASI pose areas of uncertainty.

### *1.7 Summary of exploratory and sensitivity analyses undertaken by the ERG*

The company's deterministic base-case ICERs of ixekizumab (with PAS) compared with other comparators showed that ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population. In the b/tsDMARD-experienced population, ixekizumab (with PAS) had ICERs [redacted] per QALY gained when compared with BSC. It [redacted] when compared with ustekinumab in no and mild-to moderate psoriasis and [redacted] in moderate-to severe psoriasis. The ERG incorporated various adjustments to the company base-case (probabilistic results for the b/tsDMARD-naïve population and deterministic results for the b/tsDMARD-experienced population). In the ERG base-case, ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population and had ICERs [redacted] per QALY gained versus BSC (no and mild-to-moderate psoriasis subgroups) and certolizumab pegol (moderate-to-severe psoriasis subgroup) in the b/tsDMARD-experienced population. In all psoriasis severity levels of the b/tsDMARD-experienced population, ixekizumab led to [redacted] compared to ustekinumab (the only other comparator for which an ICER was calculated in the fully incremental analyses for the no and mild-to-moderate psoriasis subgroups). Additionally, the ERG explored different scenarios based on the ERG base-case analysis. In those analyses, ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population except in the scenario in which both PASI 75 and PsARC were used to determine treatment response. In that scenario, ixekizumab had an ICER of [redacted] per QALY gained versus BSC in the moderate-to-severe psoriasis subgroup. In the b/tsDMARD-experienced population, ixekizumab had ICERs [redacted] per QALY gained versus BSC in all psoriasis severity levels in all scenarios, except when both PASI 75 and PsARC were used to determine treatment response. In this scenario, ixekizumab [redacted]. In conclusion, despite the ERG criticism and amendments to the company cost effectiveness analysis, ixekizumab remained [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population. Ixekizumab provided ICERs [redacted] per QALY gained versus BSC or certolizumab pegol in the b/tsDMARD-experienced population. In this population, when compared to ustekinumab, ixekizumab [redacted] in all psoriasis severity levels. Using both PASI 75 and PsARC responses simultaneously to determine treatment response was the most influential scenario analysis performed by the ERG.

These scenarios do have an impact on absolute costs and QALYs but do not change the cost effectiveness conclusions based on list prices, as the ixekizumab sequence was either extendedly dominated or dominated in all scenario analyses which were based on the list price of ixekizumab. Assumptions that had the greatest impact on the ICER for the ixekizumab sequences versus BSC relative to the base-case were HAQ-DI rebound to natural history in the BSC treatment state, the York utility model coefficients, the Poole et al. 2010 algorithm for costs associated with HAQ-DI,[72] and combining PsARC and PASI rates as the treatment continuation rule. Furthermore, the inclusion of certolizumab pegol and secukinumab in the b/tsDMARD-experienced population led to certolizumab pegol being cost effective (at list prices for ixekizumab and secukinumab but with PAS schemes for certolizumab pegol and ustekinumab being accounted for).

**ERG comment:** The ERG considers the deterministic sensitivity analyses to be sufficient. The PSA implementation was flawed and corrected by the ERG, and the PSA does not include all relevant parameters for all scenarios, e.g. the Convergence Diagnostic and Output Analysis (CODA) for the extended network for the b/tsDMARD experienced population is not available in the model file. PSA results reported were incorrect, and were not provided for the analyses with ixekizumab PAS price.

### 5.2.12 Model validation and face validity check

**Face validity**
Face validity of the conceptual model was assessed in an advisory board with clinical and health economic experts.

**Internal validity**
The model was developed by an external consultancy company and internal validation was undertaken by another external consultancy company. The programming of the model was checked to identify errors or omissions. A cell-by-cell technical validation was carried out and the VBA code was checked.

**Cross validity**
The company stated that cross validation by replicating comparisons from previous submissions was difficult because PAS prices for secukinumab and apremilast are confidential.

**External validity**
The company stated that external validity was difficult to assess, because long term observational studies have not been carried out for ixekizumab.

**Predictive validity**
A head-to-head study comparing ixekizumab and adalimumab is currently underway and could later be used to assess the predictive validity of the cost effectiveness model.

**ERG comment:** The ERG has concerns related to the lack of detailed cross validity. The company did provide a cross validation exercise in response to clarification question B21.[25] TA445[13] and TA433[15] were the most relevant studies for cross-validity, as these were also based on the York model and were the most recent TAs. Compared with TA445 (the revised York model):

- Total costs of comparators were generally lower in the current model for b/tsDMARD-naive- and higher for b/tsDMARD-experienced patients.
- Total QALYs of comparators were generally higher in the current model for b/tsDMARD-naive and lower for b/tsDMARD-experienced patients.

Based on all considerations in section 5.2 (summarised in Table 5.20), the ERG defined a new base-case. This base-case included multiple adjustments to the original base-case presented in the previous sections. These adjustments made by the ERG form the ERG base-case and were subdivided into three categories (derived from Kaltenthaler 2016[103])

- Fixing errors (correcting the model where the company's submitted model was unequivocally wrong)
- Fixing violations (correcting the model where the ERG considered that the NICE reference case, scope or best practice had not been adhered to)
- Matters of judgement (amending the model where the ERG considers that reasonable alternative assumptions are preferred)

Additionally, exploratory sensitivity analyses were performed by the ERG to examine the potential impact of alternative assumptions on the cost effectiveness estimates.

**The ERG's base-case:**

*Fixing errors*

1. Flawed implementation of the PSA, resulting in deterministic results being reported.

   The ERG corrected the code used for the PSA.
2. NMA results for the reduction in HAQ-DI scores for ixekizumab q4w that are inconsistent with trial data.

   The ERG used the trial data instead of the NMA results.

*Fixing violations*

3. Use of the limited NMA results for the b/tsDMARD-experienced population, which does not consider PASI50.

   The ERG used the extended NMA for the b/tsDMARD experienced population, which considers PASI50.
4. Exclusion of secukinumab and certolizumab pegol as comparators in b/tsDMARD-experienced patients.

   The ERG included these by using the extended NMA, as per scope.
5. Utilities were not adjusted to general population utility values.
   The ERG adjusted utilities.

*Matters of judgment*

6. The use of a potentially dated and high SMR.
   The ERG used a SMR derived from more recent data.
7. The use of calculations for PASI change in the model that are inconsistent with the CS report.
   The ERG used the calculations detailed in the CS report (Table 42).

### 5.3.1 ERG base-case results

The ERG base-case was performed probabilistically for b/tsDMARD-naïve patients and deterministically for b/tsDMARD-experienced patients because there were no probabilistic estimates provided for secukinumab and certolizumab pegol when using the extended NMA (due to CODA not provided for this network). All ERG base-case analyses are conditional on the PAS price of ixekizumab. Additionally, the ERG used secukinumab 300 mg for all psoriasis severity levels in the b/tsDMARD-experienced population because no results were provided for secukinumab 150 mg in the extended NMA. For all analyses including biosimilar etanercept as a comparator, a correlation coefficient of 0.26, instead of 0.4, was used to derive the distribution of PASI 75 responders amongst patients who achieve a PsARC response.

Ixekizumab was [redacted] in all b/tsDMARD-naïve subgroups while, in the b/tsDMARD-experienced population, it resulted in ICERs of [redacted] and [redacted] per QALY gained versus BSC in the no psoriasis and mild-to-moderate psoriasis subgroups respectively, and [redacted] per QALY gained versus certolizumab pegol in the moderate-to-severe psoriasis subgroup. In all psoriasis severity levels of the b/tsDMARD-experienced population, ixekizumab led to [redacted] compared to ustekinumab (the only other comparator for which an ICER was calculated in the fully incremental analyses for the no psoriasis and mild-to-moderate psoriasis subgroups).

### 5.3.2 Additional exploratory analyses performed based on the ERG base-case

Additional sensitivity analyses were performed to examine the potential impact of the following alternative assumptions on the cost effectiveness estimates. These were all performed using the ERG base-case. Results are presented in Table 6.2 in section 6. The ERG used secukinumab 300 mg for all psoriasis severity levels in the b/tsDMARD-experienced population because no results were provided for secukinumab 150 mg in the extended NMA.

Exploratory analyses using the ERG base-case:

1. The use of the company's preferred network for the b/tsDMARD-experienced population, excluding secukinumab and certolizumab pegol from the analysis.
2. Use of Poole et al for HAQ-DI related costs instead of Kobelt et al.
3. Use of the York model baseline PASI scores.
4. Alternative second line treatment in b/tsDMARD-naive patients.
5. Use of PASI 75 and PsARC instead of only PsARC.

### 5.3.3 Subgroup analyses performed based on the ERG base-case

No subgroup analyses were performed.

## *5.4 Conclusions of the cost effectiveness section*

The ERG considers that the company's approach to use the revised York model as a basis for developing their model was appropriate.

The economic model described in the CS is considered by the ERG to meet the NICE reference case, with the notable exceptions of a) the exclusion of comparators identified in the scope, and b) a network meta-analysis that did not consider all the relevant outcomes as identified in the scope.

a) The absence of secukinumab and certolizumab pegol from the b/tsDMARD-experienced patient population analysis was justified by the unavailability of data in that population, however, it should be noted that studies on these two treatments were conducted in mixed (b/tsDMARD-naive and -experienced) populations.
b) The omission of adverse events from the economic model was considered a major limitation by the ERG. The ERG considers that treatment-specific adverse events could have an impact on treatment discontinuation, HRQoL and cost and resource use, and that not reflecting this in the model could lead to biased outcomes. The direction of this bias is difficult to determine.

The company's deterministic base-case ICERs of ixekizumab (with PAS) compared with other comparators showed that ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population and had ICERs [redacted] per QALY gained in the b/tsDMARD-experienced population when compared with BSC but was [redacted] when compared with ustekinumab in that population. The cost effectiveness results were fairly robust to scenario and one-

**Table 6.1: Probabilistic ERG base-case; PAS price**

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | ICER versus baseline (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| **Company base-case (probabilistic, performed by the ERG)** | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £54,514 | 8.09 | - | - | - | [redacted] |
| APR - UST - BSC | £94,340 | 9.50 | [redacted] | 1.41 | [redacted] | [redacted] |
| IXE Q4W - UST - BSC | [redacted] | 9.72 | [redacted] | 1.62 | [redacted] | Referent |
| CZP - UST - BSC | £101,135 | 9.44 | [redacted] | 1.34 | [redacted] | [redacted] |
| SEC 150 - UST - BSC | £101,314 | 9.80 | [redacted] | 1.70 | [redacted] | [redacted] |
| ADA - UST - BSC | £102,621 | 9.73 | [redacted] | 1.64 | [redacted] | [redacted] |
| ETA - UST - BSC | £104,074 | 10.00 | [redacted] | 1.91 | [redacted] | [redacted] |
| GOL - UST - BSC | £109,091 | 9.91 | [redacted] | -0.10 | [redacted] | [redacted] |
| INF - UST - BSC | £129,033 | 10.15 | [redacted] | 0.14 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £70,174 | 7.75 | - | - | - | [redacted] |
| APR - UST - BSC | £106,250 | 9.18 | [redacted] | 1.43 | [redacted] | [redacted] |
| IXE Q4W - UST - BSC | [redacted] | 9.41 | [redacted] | 1.66 | [redacted] | Referent |
| SEC 150 - UST - BSC | £112,555 | 9.49 | [redacted] | 1.74 | [redacted] | [redacted] |
| CZP - UST - BSC | £113,045 | 9.13 | [redacted] | 1.38 | [redacted] | [redacted] |
| ADA - UST - BSC | £113,950 | 9.42 | [redacted] | 1.66 | [redacted] | [redacted] |
| ETN - UST - BSC | £115,270 | 9.71 | [redacted] | 1.95 | [redacted] | [redacted] |
| GOL - UST - BSC | £119,971 | 9.62 | [redacted] | -0.09 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | ICER versus baseline (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| INF - UST - BSC | £139,567 | 9.86 | [redacted] | 0.15 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £99,797 | 6.20 | - | - | - | [redacted] |
| APR - UST - BSC | £128,058 | 7.71 | [redacted] | 1.51 | [redacted] | [redacted] |
| CZP - UST - BSC | £133,696 | 7.68 | [redacted] | 1.48 | [redacted] | [redacted] |
| ADA - UST - BSC | £134,631 | 7.99 | [redacted] | 1.79 | [redacted] | [redacted] |
| IXE Q2W - UST - BSC | [redacted] | 8.14 | [redacted] | 1.94 | [redacted] | Referent |
| ETA - UST - BSC | £134,951 | 8.27 | [redacted] | 2.07 | [redacted] | [redacted] |
| GOL - UST - BSC | £139,232 | 8.25 | [redacted] | -0.03 | [redacted] | [redacted] |
| SEC 300 - UST - BSC | £156,842 | 8.00 | [redacted] | -0.27 | [redacted] | [redacted] |
| INF - UST - BSC | £158,762 | 8.54 | [redacted] | 0.27 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis | | | | | | |
| BSC | £55,815 | 7.38 | - | - | - | [redacted] |
| IXE Q4W - BSC | [redacted] | 8.24 | [redacted] | 0.86 | [redacted] | Referent |
| UST - BSC | £83,137 | 8.27 | [redacted] | 0.03 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £70,137 | 7.07 | - | - | - | [redacted] |
| IXE Q4W - BSC | [redacted] | 7.97 | [redacted] | 0.90 | [redacted] | Referent |
| UST - BSC | £95,039 | 8.00 | [redacted] | 0.03 | [redacted] | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £99,959 | 2.31 | - | - | - | [redacted] |
| IXE Q2W - BSC | [redacted] | 3.31 | [redacted] | 1.00 | [redacted] | Referent |
| UST - BSC | £119,976 | 3.27 | [redacted] | -0.03 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | ICER versus baseline (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| **ERG base-case** | | | | | | |
| bDMARD-naïve; no psoriasis (probabilistic) | | | | | | |
| BSC | £ 57,674 | 8.37 | - | - | - | [redacted] |
| APR - UST - BSC | £ 98,358 | 9.81 | [redacted] | 1.44 | [redacted] | [redacted] |
| IXE Q4W - UST - BSC | [redacted] | 9.98 | [redacted] | 1.61 | [redacted] | Referent |
| SEC 150 - UST - BSC | £ 105,259 | 10.07 | [redacted] | 1.70 | [redacted] | [redacted] |
| CZP - UST - BSC | £ 105,272 | 9.75 | [redacted] | 1.37 | [redacted] | [redacted] |
| ADA - UST - BSC | £ 106,764 | 10.03 | [redacted] | 1.66 | [redacted] | [redacted] |
| ETA - UST - BSC | £ 108,248 | 10.25 | [redacted] | 1.88 | [redacted] | [redacted] |
| GOL - UST - BSC | £ 113,357 | 10.23 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF - UST - BSC | £ 133,602 | 10.39 | [redacted] | 0.14 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis (probabilistic) | | | | | | |
| BSC | £ 74,457 | 8.01 | - | - | - | [redacted] |
| APR - UST - BSC | £ 110,847 | 9.51 | [redacted] | 1.50 | [redacted] | [redacted] |
| IXE Q4W - UST - BSC | [redacted] | 9.70 | [redacted] | 1.69 | [redacted] | Referent |
| SEC 150 - UST - BSC | £ 117,141 | 9.79 | [redacted] | 1.78 | [redacted] | [redacted] |
| CZP - UST - BSC | £ 117,606 | 9.47 | [redacted] | 1.46 | [redacted] | [redacted] |
| ADA - UST - BSC | £ 118,552 | 9.75 | [redacted] | 1.74 | [redacted] | [redacted] |
| ETA - UST - BSC | £ 119,897 | 9.99 | [redacted] | 1.98 | [redacted] | [redacted] |
| GOL - UST - BSC | £ 124,677 | 9.96 | [redacted] | -0.03 | [redacted] | [redacted] |
| INF - UST - BSC | £ 144,619 | 10.11 | [redacted] | 0.12 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | ICER versus baseline (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| bDMARD-naïve; moderate-to-severe psoriasis (probabilistic) | | | | | | |
| BSC | £ 105,156 | 6.42 | - | - | - | [redacted] |
| APR - UST - BSC | £ 133,529 | 8.21 | [redacted] | 1.79 | [redacted] | [redacted] |
| CZP - UST - BSC | £ 139,134 | 8.21 | [redacted] | 1.78 | [redacted] | [redacted] |
| ADA - UST - BSC | £ 140,118 | 8.49 | [redacted] | 2.07 | [redacted] | [redacted] |
| IXE q2w - UST - BSC | [redacted] | 8.56 | [redacted] | 2.14 | [redacted] | Referent |
| ETA - UST - BSC | £ 140,454 | 8.82 | [redacted] | 2.39 | [redacted] | [redacted] |
| GOL-UST-BSC | £ 144,780 | 8.76 | [redacted] | -0.06 | [redacted] | [redacted] |
| SEC300-UST-BSC | £ 162,661 | 8.44 | [redacted] | -0.38 | [redacted] | [redacted] |
| INF - UST - BSC | £ 164,601 | 8.95 | [redacted] | 0.13 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis (deterministic) | | | | | | |
| BSC | £58,838 | 7.61 | - | - | - | [redacted] |
| IXE q4w -BSC | [redacted] | 8.54 | [redacted] | 0.93 | [redacted] | Referent |
| CZP -BSC | £83,355 | 8.53 | [redacted] | -0.02 | [redacted] | [redacted] |
| UST-BSC | £88,828 | 8.64 | [redacted] | 0.09 | [redacted] | [redacted] |
| SEC300-BSC | £106,747 | 8.54 | [redacted] | -0.10 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis (deterministic) | | | | | | |
| BSC | £73,880 | 7.26 | - | - | - | [redacted] |
| IXE q4w-BSC | [redacted] | 8.36 | [redacted] | 1.09 | [redacted] | Referent |
| CZP-BSC | £95,702 | 8.35 | [redacted] | -0.01 | [redacted] | [redacted] |
| UST-BSC | £101,087 | 8.46 | [redacted] | 0.11 | [redacted] | [redacted] |
| SEC300-BSC | £119,384 | 8.31 | [redacted] | -0.15 | [redacted] | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis (deterministic) | | | | | | |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | ICER versus baseline (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| BSC | £104,602 | 2.23 | - | - | - | [redacted] |
| CZP-BSC | £121,172 | 3.98 | [redacted] | 1.75 | [redacted] | [redacted] |
| IXE q2w-BSC | [redacted] | 4.11 | [redacted] | 0.13 | [redacted] | Referent |
| UST-BSC | £126,390 | 4.13 | [redacted] | 0.02 | [redacted] | [redacted] |
| SEC300-BSC | £145,424 | 3.91 | [redacted] | -0.22 | [redacted] | [redacted] |

ADA = adalimumab; APR = apremilast; bDMARD = biologic disease-modifying anti-rheumatic drug; BSC = best supportive care; CZP = certolizumab pegol; ERG = Evidence Review Group; ETA = etanercept; GOL = golimumab; ICER = Incremental cost effectiveness ratio; INF = infliximab; IXE = ixekizumab; PAS = patient access scheme; q2w = once every two weeks; q4w = once every four weeks; QALY = quality-adjusted life year; SEC = secukinumab; UST = ustekinumab

**Table 6.2: Deterministic scenario analyses conditional on ERG base-case, PAS price**

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| **ERG base-case (deterministic)** | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £56,906 | 8.35 | - | - | - | [redacted] |
| APR-UST-BSC | £99,754 | 9.89 | [redacted] | 1.54 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 10.04 | [redacted] | 1.69 | [redacted] | Referent |
| CZP-UST-BSC | £106,247 | 10.08 | [redacted] | 1.73 | [redacted] | [redacted] |
| SEC150-UST-BSC | £106,591 | 10.15 | [redacted] | 1.80 | [redacted] | [redacted] |
| ADA-UST-BSC | £107,703 | 10.12 | [redacted] | 1.77 | [redacted] | [redacted] |
| ETA-UST-BSC | £109,998 | 10.34 | [redacted] | 1.99 | [redacted] | [redacted] |
| GOL-UST-BSC | £114,501 | 10.31 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF-UST-BSC | £133,706 | 10.41 | [redacted] | 0.07 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.99 | - | - | - | [redacted] |
| APR-UST-BSC | £112,192 | 9.61 | [redacted] | 1.62 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.76 | [redacted] | 1.78 | [redacted] | Referent |
| CZP-UST-BSC | £118,101 | 9.80 | [redacted] | 1.82 | [redacted] | [redacted] |
| SEC150-UST-BSC | £118,438 | 9.89 | [redacted] | 1.91 | [redacted] | [redacted] |
| ADA-UST-BSC | £119,574 | 9.84 | [redacted] | 1.85 | [redacted] | [redacted] |
| ETA-UST-BSC | £121,313 | 10.09 | [redacted] | 2.10 | [redacted] | [redacted] |
| GOL-UST-BSC | £125,644 | 10.05 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-UST-BSC | £144,833 | 10.17 | [redacted] | 0.08 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 6.38 | - | - | - | [redacted] |
| APR-UST-BSC | £134,903 | 8.33 | [redacted] | 1.95 | [redacted] | [redacted] |
| CZP-UST-BSC | £139,690 | 8.56 | [redacted] | 2.18 | [redacted] | [redacted] |
| ADA-UST-BSC | £141,198 | 8.59 | [redacted] | 2.22 | [redacted] | [redacted] |
| IXEq2w-UST-BSC | [redacted] | 8.68 | [redacted] | 2.30 | [redacted] | Referent |
| ETA -UST-BSC | £141,826 | 8.96 | [redacted] | 2.58 | [redacted] | [redacted] |
| GOL-UST-BSC | £145,815 | 8.85 | [redacted] | -0.11 | [redacted] | [redacted] |
| SEC300-UST-BSC | £162,971 | 8.55 | [redacted] | -0.41 | [redacted] | [redacted] |
| INF-UST-BSC | £164,972 | 9.07 | [redacted] | 0.11 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis | | | | | | |
| BSC | £58,838 | 7.61 | - | - | - | [redacted] |
| IXEq4w -BSC | [redacted] | 8.54 | [redacted] | 0.93 | [redacted] | Referent |
| CZP-BSC | £83,355 | 8.53 | [redacted] | -0.02 | [redacted] | [redacted] |
| UST-BSC | £88,828 | 8.64 | [redacted] | 0.09 | [redacted] | [redacted] |
| SEC300-BSC | £106,747 | 8.54 | [redacted] | -0.10 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,880 | 7.26 | - | - | - | [redacted] |
| IXEq4w-BSC | [redacted] | 8.36 | [redacted] | 1.09 | [redacted] | Referent |
| CZP-BSC | £95,702 | 8.35 | [redacted] | -0.01 | [redacted] | [redacted] |
| UST-BSC | £101,087 | 8.46 | [redacted] | 0.11 | [redacted] | [redacted] |
| SEC300-BSC | £119,384 | 8.31 | [redacted] | -0.15 | [redacted] | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,602 | 2.23 | - | - | - | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP-BSC | £121,172 | 3.98 | [redacted] | 1.75 | [redacted] | [redacted] |
| IXEq2w-BSC | [redacted] | 4.11 | [redacted] | 0.13 | [redacted] | Referent |
| UST-BSC | £126,390 | 4.13 | [redacted] | 0.02 | [redacted] | [redacted] |
| SEC300-BSC | £145,424 | 3.91 | [redacted] | -0.22 | [redacted] | [redacted] |
| **Scenario 1: The use of the company's preferred network for the bDMARD-experienced population, excluding secukinumab and certolizumab pegol from the analysis.** | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £56,906 | 8.35 | - | - | - | [redacted] |
| APR-UST-BSC | £96,450 | 9.77 | [redacted] | 1.42 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.92 | [redacted] | 1.57 | [redacted] | Referent |
| CZP-UST-BSC | £103,043 | 9.96 | [redacted] | 1.61 | [redacted] | [redacted] |
| SEC 150-UST-BSC | £103,393 | 10.03 | [redacted] | 1.68 | [redacted] | [redacted] |
| ADA-UST-BSC | £104,495 | 10.00 | [redacted] | 1.65 | [redacted] | [redacted] |
| ETA 150-UST-BSC | £106,901 | 10.22 | [redacted] | 1.87 | [redacted] | [redacted] |
| GOL-UST-BSC | £111,437 | 10.20 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF-UST-BSC | £130,648 | 10.30 | [redacted] | 0.07 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.99 | - | - | - | [redacted] |
| APR-UST-BSC | £109,258 | 9.48 | [redacted] | 1.49 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.63 | [redacted] | 1.65 | [redacted] | Referent |
| CZP-UST-BSC | £115,255 | 9.67 | [redacted] | 1.69 | [redacted] | [redacted] |
| SEC150-UST-BSC | £115,598 | 9.76 | [redacted] | 1.78 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| ADA-UST-BSC | £116,725 | 9.71 | [redacted] | 1.73 | [redacted] | [redacted] |
| ETA-UST-BSC | £118,563 | 9.96 | [redacted] | 1.98 | [redacted] | [redacted] |
| GOL-UST-BSC | £122,924 | 9.93 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-UST-BSC | £142,118 | 10.04 | [redacted] | 0.08 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 6.38 | - | - | - | [redacted] |
| APR-UST-BSC | £132,710 | 8.14 | [redacted] | 1.76 | [redacted] | [redacted] |
| CZP-UST-BSC | £137,563 | 8.38 | [redacted] | 2.00 | [redacted] | [redacted] |
| ADA-UST-BSC | £139,069 | 8.42 | [redacted] | 2.04 | [redacted] | [redacted] |
| IXEq2w-UST-BSC | [redacted] | 8.50 | [redacted] | 2.12 | [redacted] | Referent |
| ETA-UST-BSC | £139,770 | 8.79 | [redacted] | 2.41 | [redacted] | [redacted] |
| GOL-UST-BSC | £143,781 | 8.68 | [redacted] | -0.10 | [redacted] | [redacted] |
| SEC300-UST-BSC | £160,813 | 8.36 | [redacted] | -0.42 | [redacted] | [redacted] |
| INF-UST-BSC | £162,942 | 8.90 | [redacted] | 0.11 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis | | | | | | |
| BSC | £58,838 | 7.61 | - | - | - | [redacted] |
| IXEq4w-BSC | [redacted] | 8.40 | [redacted] | 0.79 | [redacted] | Referent |
| UST-BSC | £85,151 | 8.49 | [redacted] | 0.10 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,880 | 7.26 | - | - | - | [redacted] |
| IXEq4w -BSC | [redacted] | 8.18 | [redacted] | 0.92 | [redacted] | Referent |
| UST-BSC | £97,830 | 8.28 | [redacted] | 0.10 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,602 | 2.23 | - | - | - | [redacted] |
| IXEq2w -BSC | [redacted] | 3.80 | [redacted] | 1.57 | [redacted] | Referent |
| UST-BSC | £123,956 | 3.77 | [redacted] | -0.03 | [redacted] | [redacted] |
| **Scenario 2: Use of Poole et al.[72] for HAQ-DI related costs instead of Kobelt et al.[100]** | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £36,728 | 8.35 | - | - | - | [redacted] |
| APR-UST-BSC | £72,980 | 9.89 | [redacted] | 1.54 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 10.04 | [redacted] | 1.69 | [redacted] | Referent |
| CZP-UST-BSC | £79,793 | 10.08 | [redacted] | 1.73 | [redacted] | [redacted] |
| SEC150-UST-BSC | £80,172 | 10.15 | [redacted] | 1.80 | [redacted] | [redacted] |
| ADA-UST-BSC | £81,297 | 10.12 | [redacted] | 1.77 | [redacted] | [redacted] |
| ETA-UST-BSC | £83,130 | 10.34 | [redacted] | 1.99 | [redacted] | [redacted] |
| GOL-UST-BSC | £87,305 | 10.31 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF-UST-BSC | £106,666 | 10.41 | [redacted] | 0.07 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £36,728 | 7.99 | - | - | - | [redacted] |
| APR-UST-BSC | £72,980 | 9.61 | [redacted] | 1.62 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.76 | [redacted] | 1.78 | [redacted] | Referent |
| CZP-UST-BSC | £79,793 | 9.80 | [redacted] | 1.82 | [redacted] | [redacted] |
| SEC150-UST-BSC | £80,172 | 9.89 | [redacted] | 1.91 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| ADA-UST-BSC | £81,297 | 9.84 | [redacted] | 1.85 | [redacted] | [redacted] |
| ETA-UST-BSC | £83,130 | 10.09 | [redacted] | 2.10 | [redacted] | [redacted] |
| GOL-UST-BSC | £87,305 | 10.05 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-UST-BSC | £106,666 | 10.17 | [redacted] | 0.08 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £37,361 | 6.38 | - | - | - | [redacted] |
| APR-UST-BSC | £73,474 | 8.33 | [redacted] | 1.95 | [redacted] | [redacted] |
| CZP-UST-BSC | £80,270 | 8.56 | [redacted] | 2.18 | [redacted] | [redacted] |
| ADA-UST-BSC | £81,772 | 8.59 | [redacted] | 2.22 | [redacted] | [redacted] |
| IXEq2w-UST-BSC | [redacted] | 8.68 | [redacted] | 2.30 | [redacted] | Referent |
| ETA-UST-BSC | £83,580 | 8.96 | [redacted] | 2.58 | [redacted] | [redacted] |
| GOL-UST-BSC | £87,757 | 8.85 | [redacted] | -0.11 | [redacted] | [redacted] |
| SEC300-UST-BSC | £103,068 | 8.55 | [redacted] | -0.41 | [redacted] | [redacted] |
| INF-UST-BSC | £107,108 | 9.07 | [redacted] | 0.11 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis | | | | | | |
| BSC | £44,052 | 7.61 | - | - | - | [redacted] |
| IXEq4w -BSC | [redacted] | 8.54 | [redacted] | 0.93 | [redacted] | Referent |
| CZP-BSC | £63,939 | 8.53 | [redacted] | -0.02 | [redacted] | [redacted] |
| UST-BSC | £69,163 | 8.64 | [redacted] | 0.09 | [redacted] | [redacted] |
| SEC300-BSC | £87,760 | 8.54 | [redacted] | -0.10 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £37,680 | 7.26 | - | - | - | [redacted] |
| IXEq4w -BSC | [redacted] | 8.36 | [redacted] | 1.09 | [redacted] | Referent |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP -BSC | £58,297 | 8.35 | [redacted] | -0.01 | [redacted] | [redacted] |
| UST-BSC | £63,602 | 8.46 | [redacted] | 0.11 | [redacted] | [redacted] |
| SEC300-BSC | £82,091 | 8.31 | [redacted] | -0.15 | [redacted] | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £36,414 | 2.23 | - | - | - | [redacted] |
| CZP -BSC | £57,191 | 3.98 | [redacted] | 1.75 | [redacted] | [redacted] |
| IXEq2w -BSC | [redacted] | 4.11 | [redacted] | 1.88 | [redacted] | Referent |
| UST-BSC | £62,512 | 4.13 | [redacted] | 0.02 | [redacted] | [redacted] |
| SEC300 -BSC | £80,978 | 3.91 | [redacted] | -0.22 | [redacted] | [redacted] |
| **Scenario 3: Use of the York model baseline PASI scores.** | | | | | | |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.67 | - | - | - | [redacted] |
| APR-UST-BSC | £112,192 | 9.36 | [redacted] | 1.69 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.52 | [redacted] | 1.85 | [redacted] | Referent |
| CZP-UST-BSC | £118,101 | 9.56 | [redacted] | 1.89 | [redacted] | [redacted] |
| SEC150-UST-BSC | £118,438 | 9.66 | [redacted] | 1.99 | [redacted] | [redacted] |
| ADA-UST-BSC | £119,574 | 9.60 | [redacted] | 1.93 | [redacted] | [redacted] |
| ETA-UST-BSC | £121,313 | 9.87 | [redacted] | 2.20 | [redacted] | [redacted] |
| GOL-UST-BSC | £125,644 | 9.82 | [redacted] | -0.05 | [redacted] | [redacted] |
| INF-UST-BSC | £144,833 | 9.95 | [redacted] | 0.08 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 7.12 | - | - | - | [redacted] |
| APR-UST-BSC | £134,903 | 8.91 | [redacted] | 1.79 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP-UST-BSC | £139,690 | 9.12 | [redacted] | 2.00 | [redacted] | [redacted] |
| ADA-UST-BSC | £141,198 | 9.16 | [redacted] | 2.04 | [redacted] | [redacted] |
| IXEq2w-UST-BSC | [redacted] | 9.23 | [redacted] | 2.11 | [redacted] | Referent |
| ETA-UST-BSC | £141,826 | 9.48 | [redacted] | 2.36 | [redacted] | [redacted] |
| GOL-UST-BSC | £145,815 | 9.39 | [redacted] | -0.09 | [redacted] | [redacted] |
| SEC300-UST-BSC | £162,971 | 9.12 | [redacted] | -0.36 | [redacted] | [redacted] |
| INF-UST-BSC | £164,972 | 9.57 | [redacted] | 0.09 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,880 | 6.32 | - | - | - | [redacted] |
| IXEq4w -BSC | [redacted] | 7.53 | [redacted] | 1.21 | [redacted] | Referent |
| CZP-BSC | £95,702 | 7.52 | [redacted] | 0.00 | [redacted] | [redacted] |
| UST-BSC | £101,087 | 7.65 | [redacted] | 0.12 | [redacted] | [redacted] |
| SEC300-BSC | £119,384 | 7.51 | [redacted] | -0.14 | [redacted] | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,602 | 5.09 | - | - | - | [redacted] |
| CZP-BSC | £121,172 | 6.48 | [redacted] | 1.39 | [redacted] | [redacted] |
| IXEq2w-BSC | [redacted] | 6.60 | [redacted] | 1.51 | [redacted] | Referent |
| UST-BSC | £126,390 | 6.61 | [redacted] | 0.01 | [redacted] | [redacted] |
| SEC300-BSC | £145,424 | 6.44 | [redacted] | -0.17 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| **Scenario 4: Alternative second line treatment in bDMARD-naive patients.** | | | | | | |
| Second-line certolizumab pegol | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £56,906 | 8.35 | - | - | - | [redacted] |
| APR-CZP-BSC | £94,747 | 9.80 | [redacted] | 1.45 | [redacted] | [redacted] |
| IXEq4w-CZP-BSC | [redacted] | 9.95 | [redacted] | 1.60 | [redacted] | Referent |
| SEC150-CZP-BSC | £101,737 | 10.07 | [redacted] | 1.71 | [redacted] | [redacted] |
| ADA-CZP-BSC | £102,840 | 10.03 | [redacted] | 1.68 | [redacted] | [redacted] |
| ETA-CZP-BSC | £105,293 | 10.25 | [redacted] | 1.90 | [redacted] | [redacted] |
| GOL-CZP-BSC | £109,844 | 10.23 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF-CZP-BSC | £129,054 | 10.33 | [redacted] | 0.07 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.99 | - | - | - | [redacted] |
| APR-CZP-BSC | £107,261 | 9.51 | [redacted] | 1.53 | [redacted] | [redacted] |
| IXEq4w-CZP-BSC | [redacted] | 9.67 | [redacted] | 1.68 | [redacted] | Referent |
| SEC150-CZP-BSC | £113,658 | 9.80 | [redacted] | 1.81 | [redacted] | [redacted] |
| ADA-CZP-BSC | £114,785 | 9.75 | [redacted] | 1.76 | [redacted] | [redacted] |
| ETA-CZP-BSC | £116,679 | 10.00 | [redacted] | 2.02 | [redacted] | [redacted] |
| GOL-CZP-BSC | £121,058 | 9.96 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-CZP-BSC | £140,252 | 10.08 | [redacted] | 0.08 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 6.38 | - | - | - | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| APR-CZP-BSC | £130,123 | 8.22 | [redacted] | 1.84 | [redacted] | [redacted] |
| ADA-CZP-BSC | £136,556 | 8.49 | [redacted] | 2.12 | [redacted] | [redacted] |
| IXEq2w-CZP-BSC | [redacted] | 8.58 | [redacted] | 2.20 | [redacted] | Referent |
| ETA-CZP-BSC | £137,333 | 8.86 | [redacted] | 2.49 | [redacted] | [redacted] |
| GOL-CZP-BSC | £141,368 | 8.76 | [redacted] | -0.10 | [redacted] | [redacted] |
| SEC300-CZP-BSC | £158,263 | 8.44 | [redacted] | -0.42 | [redacted] | [redacted] |
| INF-CZP-BSC | £160,531 | 8.97 | [redacted] | 0.11 | [redacted] | [redacted] |
| Second-line secukinumab | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £56,906 | 8.35 | - | - | - | [redacted] |
| APR-SEC-BSC | £115,979 | 9.77 | [redacted] | 1.42 | [redacted] | [redacted] |
| IXEq4w-SEC-BSC | [redacted] | 9.93 | [redacted] | 1.58 | [redacted] | Referent |
| CZP-SEC-BSC | £121,980 | 9.96 | [redacted] | 1.61 | [redacted] | [redacted] |
| ADA-SEC-BSC | £123,452 | 10.00 | [redacted] | 1.65 | [redacted] | [redacted] |
| ETA-SEC-BSC | £125,210 | 10.23 | [redacted] | 1.88 | [redacted] | [redacted] |
| GOL-SEC-BSC | £129,547 | 10.21 | [redacted] | -0.02 | [redacted] | [redacted] |
| INF-SEC-BSC | £148,725 | 10.30 | [redacted] | 0.07 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.99 | - | - | - | [redacted] |
| APR-SEC-BSC | £128,749 | 9.49 | [redacted] | 1.51 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| IXEq4w-SEC-BSC | [redacted] | 9.65 | [redacted] | 1.66 | [redacted] | Referent |
| CZP-SEC-BSC | £134,155 | 9.69 | [redacted] | 1.71 | [redacted] | [redacted] |
| ADA-SEC-BSC | £135,646 | 9.73 | [redacted] | 1.74 | [redacted] | [redacted] |
| ETA-SEC-BSC | £136,836 | 9.98 | [redacted] | 2.00 | [redacted] | [redacted] |
| GOL-SEC-BSC | £140,998 | 9.95 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-SEC-BSC | £160,160 | 10.06 | [redacted] | 0.08 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 6.38 | - | - | - | [redacted] |
| APR-SEC-BSC | £152,123 | 8.20 | [redacted] | 1.83 | [redacted] | [redacted] |
| CZP-SEC-BSC | £156,388 | 8.44 | [redacted] | 2.06 | [redacted] | [redacted] |
| ADA-SEC-BSC | £157,914 | 8.48 | [redacted] | 2.10 | [redacted] | [redacted] |
| ETA-SEC-BSC | £157,970 | 8.85 | [redacted] | 2.47 | [redacted] | [redacted] |
| IXEq2w-SEC-BSC | [redacted] | 8.56 | [redacted] | -0.29 | [redacted] | Referent |
| GOL-SEC-BSC | £161,783 | 8.74 | [redacted] | -0.10 | [redacted] | [redacted] |
| INF-SEC-BSC | £180,913 | 8.96 | [redacted] | 0.11 | [redacted] | [redacted] |
| **Scenario 5: Use of PASI 75 & PsARC instead of only PsARC** | | | | | | |
| bDMARD-naïve; no psoriasis | | | | | | |
| BSC | £56,906 | 8.35 | - | - | - | [redacted] |
| APR-UST-BSC | £88,297 | 9.41 | [redacted] | 1.06 | [redacted] | [redacted] |
| ETA-UST-BSC | £89,270 | 9.45 | [redacted] | 1.10 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP-UST-BSC | £89,445 | 9.47 | [redacted] | 1.12 | [redacted] | [redacted] |
| ADA-UST-BSC | £93,971 | 9.59 | [redacted] | 1.24 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.79 | [redacted] | 1.44 | [redacted] | Referent |
| SEC-UST-BSC | £98,711 | 9.82 | [redacted] | 1.46 | [redacted] | [redacted] |
| GOL-UST-BSC | £100,301 | 9.79 | [redacted] | -0.03 | [redacted] | [redacted] |
| INF-UST-BSC | £124,354 | 10.13 | [redacted] | 0.32 | [redacted] | [redacted] |
| bDMARD-naïve; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,609 | 7.99 | - | - | - | [redacted] |
| APR-UST-BSC | £102,249 | 9.10 | [redacted] | 1.12 | [redacted] | [redacted] |
| ETA-UST-BSC | £103,121 | 9.14 | [redacted] | 1.16 | [redacted] | [redacted] |
| CZP-UST-BSC | £103,147 | 9.16 | [redacted] | 1.18 | [redacted] | [redacted] |
| ADA-UST-BSC | £107,381 | 9.29 | [redacted] | 1.30 | [redacted] | [redacted] |
| IXEq4w-UST-BSC | [redacted] | 9.50 | [redacted] | 1.51 | [redacted] | Referent |
| SEC-UST-BSC | £111,545 | 9.53 | [redacted] | 1.55 | [redacted] | [redacted] |
| GOL-UST-BSC | £113,031 | 9.50 | [redacted] | -0.04 | [redacted] | [redacted] |
| INF-UST-BSC | £136,306 | 9.87 | [redacted] | 0.34 | [redacted] | [redacted] |
| bDMARD-naïve; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,874 | 6.38 | - | - | - | [redacted] |
| APR-UST-BSC | £128,012 | 7.71 | [redacted] | 1.33 | [redacted] | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP-UST-BSC | £128,430 | 7.79 | [redacted] | 1.41 | [redacted] | [redacted] |
| ETA-UST-BSC | £128,704 | 7.77 | [redacted] | 1.40 | [redacted] | [redacted] |
| ADA-UST-BSC | £132,082 | 7.93 | [redacted] | 1.55 | [redacted] | [redacted] |
| GOL-UST-BSC | £136,374 | 8.19 | [redacted] | 1.81 | [redacted] | [redacted] |
| IXEq2w-UST-BSC | [redacted] | 8.34 | [redacted] | 1.96 | [redacted] | Referent |
| SEC300-UST-BSC | £155,462 | 8.19 | [redacted] | -0.15 | [redacted] | [redacted] |
| INF-UST-BSC | £158,093 | 8.70 | [redacted] | 0.36 | [redacted] | [redacted] |
| bDMARD-experienced; no psoriasis | | | | | | |
| BSC | £58,838 | 7.61 | - | - | - | [redacted] |
| SEC300-BSC | £63,744 | 7.70 | [redacted] | 0.08 | [redacted] | [redacted] |
| IXEq4w-BSC | [redacted] | 8.13 | [redacted] | 0.52 | [redacted] | Referent |
| CZP-BSC | £73,787 | 8.18 | [redacted] | 0.57 | [redacted] | [redacted] |
| UST-BSC | £84,054 | 8.45 | [redacted] | 0.27 | [redacted] | [redacted] |
| bDMARD-experienced; mild-to-moderate psoriasis | | | | | | |
| BSC | £73,880 | 7.26 | - | - | - | [redacted] |
| SEC300-BSC | £78,735 | 7.35 | [redacted] | 0.09 | [redacted] | [redacted] |
| IXEq4w-BSC | [redacted] | 7.87 | [redacted] | 0.61 | [redacted] | Referent |
| CZP-BSC | £87,175 | 7.94 | [redacted] | 0.68 | [redacted] | [redacted] |
| UST-BSC | £96,859 | 8.24 | [redacted] | 0.30 | | [redacted] |
| bDMARD-experienced; moderate-to-severe psoriasis | | | | | | |
| BSC | £104,602 | 2.23 | - | - | - | [redacted] |

| Treatment sequence | Total costs (£) | Total QALYs | Incremental Costs | Incremental QALY | Full incremental ICER (£/QALY) | ICER IXE versus comparator |
|---|---|---|---|---|---|---|
| CZP-BSC | £114,685 | 3.32 | [redacted] | 1.09 | [redacted] | [redacted] |
| IXEq2w-BSC | [redacted] | 3.34 | [redacted] | 0.02 | [redacted] | Referent |
| UST-BSC | £123,230 | 3.78 | [redacted] | 0.46 | [redacted] | [redacted] |
| SEC300-BSC | £139,794 | 3.63 | [redacted] | -0.15 | [redacted] | [redacted] |

Note: Small discrepancies between full incremental and pairwise ICERs are caused by rounding. Full incremental ICERs are correct.

ADA = adalimumab; APR = apremilast; bDMARD = biologic disease-modifying anti-rheumatic drug; BSC = best supportive care; CZP = certolizumab pegol; ERG = Evidence Review Group; ETA = etanercept; GOL = golimumab; ICER = Incremental cost effectiveness ratio; INF = infliximab; IXE = ixekizumab; PAS = patient access scheme; q2w = once every two weeks; q4w = once every four weeks; QALY = quality-adjusted life year; SEC = secukinumab; UST = ustekinumab

Additional NMA results for ACR 20/50/70 response and adverse events (AEs) were provided in the response to request for clarification. These showed that for bDMARD-naïve patients [redacted] was the most effective treatment across all categories of ACR response but it was [redacted]. For bDMARD-experienced patients, both ixekizumab regimens had [redacted] compared to ustekinumab but the differences were [redacted]. Estimated conditional probabilities of treatment-emergent AEs were [redacted] for ixekizumab q2w and [redacted] for ixekizumab q4w; serious AEs were [redacted] for ixekizumab q2w and [redacted] for ixekizumab q4w; and discontinuations due to AEs were [redacted] for ixekizumab q2w and [redacted] for ixekizumab q4w.

**Economic evaluation**

The company's deterministic base-case ICERs of ixekizumab (with PAS) compared with other comparators showed that ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population. In the b/tsDMARD-experienced population, ixekizumab (with PAS) had ICERs [redacted] per QALY gained when compared with BSC. It was [redacted] when compared with ustekinumab in no and mild-to moderate psoriasis and [redacted]ustekinumab in moderate-to severe psoriasis. The ERG incorporated various adjustments to the company base-case (probabilistic results for the b/tsDMARD-naïve population and deterministic results for the b/tsDMARD-experienced population). In the ERG base-case, ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population and had ICERs [redacted] per QALY gained versus BSC (no and mild-to-moderate psoriasis subgroups) and certolizumab pegol (moderate-to-severe psoriasis subgroup) in the b/tsDMARD-experienced population. In all psoriasis severity levels of the b/tsDMARD-experienced population, ixekizumab led to [redacted] compared to ustekinumab (the only other comparator for which an ICER was calculated in the fully incremental analyses for the no and mild-to-moderate psoriasis subgroups). Additionally, the ERG explored different scenarios based on the ERG base-case analysis. In those analyses, ixekizumab [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population except in the scenario in which both PASI 75 and PsARC were used to determine treatment response. In that scenario, ixekizumab had an ICER of [redacted]per QALY gained versus BSC in the moderate-to-severe psoriasis subgroup. In the b/tsDMARD-experienced population, ixekizumab had ICERs below [redacted]per QALY gained versus BSC in all psoriasis severity levels in all scenarios, except when both PASI 75 and PsARC were used to determine treatment response. In this scenario, ixekizumab [redacted].

In conclusion, despite the ERG criticism and amendments to the company cost effectiveness analysis, ixekizumab remained [redacted] in all psoriasis severity levels in the b/tsDMARD-naive population. Ixekizumab provided ICERs [redacted] per QALY gained versus BSC or certolizumab pegol in the b/tsDMARD-experienced population. In this population, when compared to ustekinumab, ixekizumab [redacted] in all psoriasis severity levels. Using both PASI 75 and PsARC responses simultaneously to determine treatment response was the most influential scenario analysis performed by the ERG.

### *8.2 Strengths and limitations of the assessment*

Following clarification, the company submission searches were well presented and reproducible. Searches were carried out on a range of databases and supplementary resources. However, the ERG was concerned about the overall quality of the searches conducted, as there were numerous inconsistencies, inaccuracies, errors and redundancy throughout. The extensive use of restrict to focus, date limit (2000-2017), omission of the NHS EED database and application of language limits were all considered overly restrictive. It is possible that relevant evidence may have been missed as a consequence.