The cost-effectiveness of secukinumab versus tumour necrosis factor alpha inhibitor biosimilars for ankylosing spondylitis in the UK

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BACKGROUND

- Ankylosing spondylitis (AS) is a chronic and burdensome inflammatory arthritis.[1]
- Secukinumab is the first selective, fully human interleukin-17A inhibitor to hold a licence for the treatment of active AS in adults who have responded inadequately to conventional therapy (non-steroidal anti-inflammatory drugs [NSAIDs]) in the UK. In 2016, it received positive recommendations from the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium.[3, 4]
- Other biologic therapies currently licensed in the UK for active AS comprise a number of tumour necrosis factor alpha inhibitors (TNFis). For two such TNFis, etanercept and infliximab, biosimilar versions are now available that offer equivalent efficacy at a reduced cost compared with their branded originator products.
- Biosimilars have the potential to provide cost savings to the UK National Health Service (NHS). However, due to existing differences in effectiveness profiles versus current therapies used in clinical practice, biosimilars should still be subject to thorough cost-effectiveness analyses.

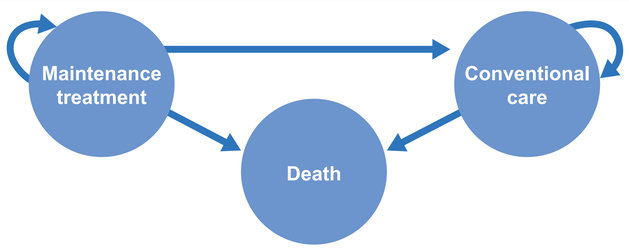
OBJECTIVE

- To evaluate the cost-effectiveness of secukinumab versus currently available biosimilar products in the UK for the treatment of biologic-naïve patients with active AS.

METHODS

- The cost-effectiveness analysis was based on a similar health economic model to that reviewed by NICE in reaching a positive recommendation for secukinumab in AS in the UK.[3]
- This model initially considered response rates for secukinumab and the relevant comparators at Week 12, based on achievement of a ≥50% reduction from baseline in Bath Ankylosing Spondylitis Disease Activity Index score (BASDAI 50).
- Response rates were taken from a network meta-analysis (NMA) of the MEASURE 2 randomised controlled trial (RCT) of secukinumab and relevant comparator TNFi RCTs in biologic-naïve patients with active AS.[5]
- Following assessment of treatment response, a Markov model was used to model patient movement between health states over a time horizon of 40 years **(Figure 1)**.

Figure 1. Markov model following response assessment at Week 12



- Week 12 BASDAI 50 responders continued maintenance treatment with their initial biologic until discontinuation of therapy, based on biologic-specific withdrawal rates sourced from the literature, at which point they moved to receive conventional care (i.e. NSAIDs and physiotherapy). Week 12 BASDAI 50 non-responders discontinued biologic therapy immediately and moved to receive conventional care.
- Clinical outcomes were modelled as:
  - Short-term (up to Week 12) changes in BASDAI and Bath Ankylosing Spondylitis Functional Index (BASFI) scores, conditional on BASDAI 50 response status and based on post-hoc analyses of MEASURE 1 and MEASURE 2 and available conditional response data for the relevant comparators;[6] and
  - Long-term changes in BASFI score, modelled as a function of Modified Stoke Ankylosing Spondylitis Spinal Score.
- In cases where clinical outcomes data were unavailable for a given TNFi, an average of all other TNFis was assumed.
- Mortality was incorporated by applying gender-specific relative risks (RR) of AS-related mortality to general population mortality rates (RR: 1.63 for males, 1.38 for females).[7]
- Adverse events (AEs) were included in the model for serious infections, with rates sourced from the literature.
- Health-related quality of life was estimated based on patient BASDAI and BASFI score, gender and age. Observed data (i.e. no imputation for missing data) from MEASURE 1 (up to 2 years) and MEASURE 2 (up to Week 52) were used to estimate utility in a linear mixed regression model with the following algorithm:

$$\text{Utility} = 0.9610 - 0.0330 \times \textit{BASFI} - 0.0442 \times \textit{BASDAI} - 0.0111 \times \textit{Gender}\ (1\text{=male; } 0\text{=female}) - 0.0005 \times \textit{Age}$$

- The interventions included in the cost-effectiveness analysis and their associated costs are presented in **Table 1**. Further cost sources for the model included monitoring costs (medical visits and laboratory tests), disease management costs dependent on BASFI score, and the costs of AEs.

Table 1. Drug acquisition and administration costs of the interventions evaluated in the model

	Posology	Cost per dose	Administration cost
Secukinumab	150 mg at Weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at Week 4	£609.39	£43.00[a]
Etanercept originator	50 mg once weekly	£178.75	£43.00[a]
Etanercept biosimilar	50 mg once weekly	£164.00 (8.3% discount on originator list price)	£43.00[a]
Infliximab originator	5 mg/kg repeated 2 weeks and 6 weeks after initial infusion, then every 8 weeks	£1,850.59[b]	£326.46[c]
Infliximab biosimilar	5 mg/kg repeated 2 weeks and 6 weeks after initial infusion, then every 8 weeks	£1,665.54[b] (10.0% discount on originator list price)	£326.46[c]

All therapies are presented at list price from the British National Formulary 2017. [a]Subcutaneous administration cost incurred only once for the first use of subcutaneous therapy. [b]The average number of vials required by each patient for infliximab was calculated based on a mean weight of 78.20 kg (SD 16.88 kg) – the mean weight of patients pooled across the MEASURE 1 and MEASURE 2 trials of secukinumab – and assumed to be normally distributed.[5] [c]Intravenous administration cost incurred per dose.

RESULTS

- The incremental cost-effectiveness ratios (ICERs) for secukinumab versus etanercept originator and etanercept biosimilar at list price were £10,173 per quality-adjusted life year (QALY) gained and £11,417 per QALY gained, respectively **(Table 2)**. Both of these ICERs are well below the conventional cost-effectiveness threshold of NICE (£20,000–£30,000 per QALY gained).
- Further analysis found that even if etanercept biosimilar were to be associated with a 100% discount to the etanercept originator list price (current discount 8.3%), secukinumab would still be cost-effective at the £30,000 per QALY gained threshold **(Table 3)**.
- In the comparisons with infliximab originator and infliximab biosimilar, secukinumab dominated both comparators (i.e. secukinumab provided positive health gains at a lower overall cost) **(Table 2)**.
- Similar further analysis found that up to a 46% discount to the infliximab originator list price, secukinumab would still be cost-saving versus infliximab biosimilar **(Table 3)**. Furthermore, up to a discount of 51% to the list price of infliximab originator, secukinumab would remain cost-effective versus infliximab biosimilar at the £30,000 per QALY gained threshold.

Table 3. Cost-effectiveness results for secukinumab versus etanercept and infliximab biosimilars at varying discounts to the list price of their originator products

Discount to etanercept/infliximab originator list price	ICER for secukinumab versus etanercept biosimilar	ICER for secukinumab versus infliximab biosimilar
0%	£10,173	Secukinumab dominates
10%	£11,680	Secukinumab dominates
20%	£13,188	Secukinumab dominates
30%	£14,695	Secukinumab dominates
40%	£16,202	Secukinumab dominates
50%	£17,710	£21,820
60%	£19,217	£79,471
70%	£20,725	£137,123
80%	£22,232	£194,774
90%	£23,740	£252,425
100%	£25,247	£310,076

Green shading represents the discounts to the etanercept/infliximab originator list prices at which secukinumab is cost-effective versus etanercept/infliximab biosimilar at the £30,000 per QALY gained threshold.

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

DISCUSSION

- This analysis found secukinumab to be associated with more QALYs than each of the biosimilar comparator therapies. As a result, even when large discounts were applied to the list price of etanercept and infliximab originators, secukinumab still represented a cost-effective use of NHS resources versus etanercept and infliximab biosimilars at the £30,000 per QALY gained threshold. These results reflect the value placed on the positive incremental health benefits achieved with secukinumab.
- Although biosimilars provide lower cost alternatives to their originator products, there remains a need to conduct cost-effectiveness analyses of biosimilars versus current therapies used in clinical practice to ensure that existing differences in effectiveness profiles remain accounted for and treatment recommendations still maximise population health within the context of a fixed NHS budget. Indeed, as emphasised in the recently updated ASAS-EULAR guidelines, cost-effectiveness analyses should be a cornerstone in the treatment decision for patients with active AS.[8]
- Finally, a confidential patient access scheme is available to the UK NHS for secukinumab, which would further increase the cost-effectiveness of secukinumab versus these biologic therapies relative to the results presented here.

CONCLUSION

- Secukinumab represents a highly cost-effective first-line biologic treatment compared to etanercept, infliximab and their lower cost licensed biosimilars for patients in the UK with active AS and an inadequate response to conventional therapy.

Table 2. Summary of cost-effectiveness results for secukinumab versus the relevant comparators

	Total QALYs	Total costs (£)	Incremental QALYs	Incremental costs (£)	ICER (£ per QALY gained)
Secukinumab	8.919	£125,473	-	-	-
Etanercept biosimilar	8.049	£115,546	0.870	£9,928	£11,417
Etanercept originator	8.049	£116,627	0.870	£8,846	£10,173
Infliximab biosimilar	8.853	£139,164	0.066	-£13,691	Secukinumab dominates
Infliximab originator	8.853	£142,944	0.066	-£17,471	Secukinumab dominates

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

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