Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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ixekizumab 80mg solution for injection (Taltz®) SMC No. (1223/17)

Eli Lilly and Company Ltd.

10 March 2017

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug Therapeutic Committees (ADTCs) on its use in Scotland. The advice is summarised as follows:

ADVICE: following a full submission

ixekizumab (Taltz®) is accepted for restricted use within NHS Scotland.

Indication under review: moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

SMC restriction: patients who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contra-indication to these treatments.

Ixekizumab was superior to placebo and to a tumour necrosis factor (TNF) antagonist for improving symptoms of adults with moderate to severe plaque psoriasis.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of ixekizumab. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Published 10 April 2017

Indication

For the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.[1]

Dosing Information

The recommended dose of ixekizumab is 160mg by subcutaneous (SC) injection (two 80mg injections) at Week 0, followed by 80mg (one injection) at Weeks 2, 4, 6, 8, 10, and 12, then maintenance dosing of 80mg (one injection) every four weeks.

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 to 20 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 20 weeks.

Ixekizumab is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.[1]

Product availability date

July 2016

Summary of evidence on comparative efficacy

Ixekizumab is a biologic medicine for the systemic treatment of psoriasis. It is a humanised monoclonal antibody designed to selectively bind to and inhibit interleukin 17A (IL-17A), a pro-inflammatory cytokine.[1]

The submitting company has requested that SMC considers ixekizumab when positioned for use in patients who have failed to respond to standard systemic therapies, or in patients who are intolerant to, or have a contraindication to these treatments. This includes patients who have failed, are contraindicated to, or are intolerant to one or more tumour necrosis factor (TNF) antagonists.

The key evidence to support the marketing authorisation included three phase III, multi-centre, double-blind, randomised controlled studies in patients with moderate to severe plaque psoriasis, UNCOVER-1, -2 and -3. All studies had a placebo-controlled induction dosing period (weeks 0 to 12), with an active control, etanercept, included in UNCOVER-2 and -3. In UNCOVER -1 and -2, induction was followed by a double-blind randomised comparison of ixekizumab maintenance with placebo-controlled withdrawal of treatment (weeks 12 to 60). All studies have an ongoing open-label single-arm long-term extension period (up to week 264).[2] The studies included adults with a confirmed diagnosis of chronic plaque psoriasis for at least six months, who were candidates for phototherapy and/or systemic therapy, and who had ≥10% body surface area (BSA) involvement, a static Physician Global Assessment (sPGA) score of ≥3, and Psoriasis Area and Severity Index (PASI) score ≥12 at screening and at baseline. Limited concurrent topical therapies were permitted. Patients with prior etanercept use were excluded from UNCOVER-2 and -3.[2]

In the induction period, patients were randomised to receive ixekizumab 160mg by subcutaneous (SC) injection at Week 0, followed by 80mg every two weeks (licensed dosing schedule), ixekizumab 160mg by SC injection at Week 0, followed by 80mg every four weeks, etanercept 50mg by SC injection twice weekly (UNCOVER -2 and -3 only) or placebo. Randomisation was in a 1:1:1 ratio in UNCOVER-1 and a 2:2:2:1 ratio in UNCOVER-2 and -3. In UNCOVER-1, patients were stratified by geographic regions, previous non-biologic systemic therapy (inadequate response, intolerance, or contraindication to <3 or ≥3 conventional systemic therapies), and weight (<100kg or ≥100kg). In UNCOVER-2 and -3, patients were stratified by centre.[2,3]

In UNCOVER-1 and -2, ixekizumab-treated patients who entered the maintenance dosing period were classified as responders or non-responders based on sPGA score (0 or 1 [plus at least a two-point improvement from baseline] classified as response). Ixekizumab responders were re-randomised equally to ixekizumab 80mg by SC injection every four weeks (licensed dosing schedule), 80mg by SC injection every 12 weeks, or placebo. Patients were stratified by weight (<100kg or ≥100kg) and by ixekizumab induction dosing regimen (80mg every two weeks or 80mg every four weeks). Placebo (and etanercept for UNCOVER-2) responders received placebo until relapse (sPGA score of ≥3) occurred. Non-responders who received any treatment during the induction dosing period were assigned to receive ixekizumab 80mg by SC injection every four weeks. In all active and placebo groups during the maintenance period, patients who relapsed (sPGA ≥3) were subsequently treated with ixekizumab 80mg by SC injection every four weeks for the remainder of this phase. All treatment assignments or changes during this phase were blinded.[2,3]

In UNCOVER-3, after the induction dosing period, all patients were to enter the open-label long-term extension period and received ixekizumab 80mg by SC injection every four weeks from week 12 up to week 264.[2]

The co-primary outcomes, measured in the intention-to-treat population, which comprised all randomised patients, at week 12 were the proportion of patients with a sPGA of 0 or 1 and PASI 75 response (at least a 75% improvement from baseline PASI score) at week 12. The primary analysis compared the ixekizumab groups with placebo and in subsequent analyses, in UNCOVER-2 and -3, non-inferiority to etanercept and superiority over etanercept were then also assessed.[2,3] The co-primary objectives were met for all studies; ixekizumab was superior to placebo and etanercept at 12 weeks as measured by the proportion of patients achieving sPGA of 0 or 1 with at least a two point improvement from baseline, and PASI 75 ($p<0.001$).[2] See table 1 for the co-primary outcomes results, table 2 for the secondary outcomes ($p<0.001$ for all comparisons) and table 3 for the patient reported outcomes ($p<0.001$ for all comparisons). Only the ixekizumab licensed dosing regimen results are presented.

Table 1. Co-primary outcomes for UNCOVER-1, -2 and -3 reported at week 12.[2-4]

	PASI 75	sPGA (0,1)
UNCOVER-1		
Ixekizumab SC 80mg every two weeks	89%(386/433)	82% (354/433)
Placebo	3.9% (17/431)	3.2% (14/431)
UNCOVER-2		
Ixekizumab SC 80mg every two weeks	90% (315/351)	83% (292/351)
Etanercept SC 50mg twice weekly	42% (149/358)	36% (129/358)
Placebo	2.4% (4/168)	2.4% (4/168)
UNCOVER-3		
Ixekizumab SC 80mg every two weeks	87% (336/385)	81% (310/385)
Etanercept SC 50mg twice weekly	53% (204/382)	42% (159/382)
Placebo	7.3% (14/193)	6.7% (13/193)

PASI 75: at least a 75% improvement in Psoriasis Area and Severity Index score from baseline, sPGA (0,1): static physicians global assessment score of zero or one with at least a two point improvement from baseline, SC: subcutaneous.

Table 2. Key secondary outcomes for UNCOVER-1, -2 and -3 reported at week 12[2-4]

	sPGA (0)	PASI 90	PASI 100
UNCOVER-1			
Ixekizumab SC 80mg every two weeks	37% (160/433)	71% (307/433)	35% (153/433)
Placebo	0	0.5% (2/431)	0
UNCOVER-2			
Ixekizumab SC 80mg every two weeks	42% (147/351)	71% (248/351)	40% (142/351)
Etanercept SC 50mg twice weekly	5.9% (21/358)	19% (67/358)	5.3% (19/358)
Placebo	0.6% (1/168)	0.6% (1/168)	0.6% (1/168)
UNCOVER-3			
Ixekizumab SC 80mg every two weeks	40% (155/385)	68% (262/385)	38% (145/385)
Etanercept SC 50mg twice weekly	8.6% (33/382)	26% (98/382)	7.3% (28/382)
Placebo	0	3.1% (6/193)	0

sPGA (0): static physicians global assessment score of zero, PASI 90: at least a 90% improvement in Psoriasis Area and Severity Index score from baseline, PASI 100; 100% improvement in Psoriasis Area and Severity Index score from baseline, SC: subcutaneous.

Table 3. Patient reported outcomes for UNCOVER-1, -2 and -3 reported at week 12[2, 4, 5]

	DLQI LS mean change from baseline	Itch NRS responder rate	Itch NRS LS mean change from baseline
UNCOVER-1			
Ixekizumab SC 80mg every two weeks	-11.1	86% (336/391)	-
Placebo	-1.0	16% (58/374)	-
UNCOVER-2			
Ixekizumab SC 80mg every two weeks	-10.4	-	-5.2
Etanercept SC 50mg twice weekly	-7.7	-	-3.6
Placebo	-2.0	-	-0.4
UNCOVER-3			
Ixekizumab SC 80mg every two weeks	-10.2	82% (264/320)	-
Etanercept SC 50mg twice weekly	-8.0	64%	-
Placebo	-1.7	21% (33/158)	-

DLQI: Dermatology Life Quality Index, LS: least square, NRS: Numeric Rating Scale, Itch NRS responder defined as achieving at least a four-point reduction on the Itch NRS (range 0 to 10), SC: subcutaneous.

Maintenance of response was measured by sPGA (0,1) at week 60; significantly more patients who received ixekizumab 80mg by SC injection every two weeks during the induction period and every four weeks in the maintenance period achieved sPGA (0,1) compared with patients who received ixekizumab 80mg by SC injection every two weeks in the induction period and placebo during the maintenance period in UNCOVER-1 and -2, (75% versus 7.7%, p<0.001 in UNCOVER-1).[2,3,6,7]

The 12-week efficacy results from IXORA-S have recently been presented. This ongoing 52-week phase III, randomised, multi-centre, double-blind study compares ixekizumab with ustekinumab, both dosed as per their respective marketing authorisations, in 302 patients with moderate to severe plaque psoriasis (PASI score ≥10) who had previously received at least one systemic therapy (including ciclosporin, methotrexate or phototherapy). The primary outcome, PASI 90, was achieved by 75% (n=99) of patients allocated to ixekizumab and 42% (n=70) of patients allocated to ustekinumab, treatment difference 32% (97.5% CI: 20 to 44), p<0.001. The secondary outcome PASI 75 was achieved by 91% of patients in the ixekizumab group and 69% of patients in the ustekinumab group, p<0.05. The proportion of patients achieving a DLQI score of 0 or 1 was 63% and 45%, respectively.[8,9]

*Other data were also assessed but remain commercially confidential.**

Summary of evidence on comparative safety

The three pivotal studies in plaque psoriasis (UNCOVER-1, -2, and -3) were pooled to evaluate the safety of ixekizumab 80mg by SC injection every two weeks and ixekizumab 80mg by SC injection every four weeks in comparison with placebo and with etanercept 50mg by SC injection twice weekly for the 12-week induction period and the 48-week maintenance period.

In the Psoriasis Placebo- and Active-Controlled Integrated Analysis Set (which included the ixekizumab, placebo and etanercept arms from the induction periods of UNCOVER-2 and -3) there was a similar incidence of treatment emergent adverse events (AEs) in the ixekizumab 80mg every two weeks (58% [424/734]) and the etanercept treatment group (54% [399/739]).

Serious adverse events (SAEs) were experienced by 1.9% (14/734), and 1.9% (14/739) of patients in the respective groups, and 2.0% (15/734) and 1.2% (9/739) of patients discontinued the study due to an AE, in the respective groups. A higher proportion of patients experienced AEs considered possibly related to study treatment in the ixekizumab 80mg every two weeks group compared with the etanercept treatment group (30% [220/734] versus 24% [176/739]).[2,3,10]

Common adverse events reported during the induction phase are listed in table 5.

Table 5: Common adverse events reported during Weeks 0 to 12 in the Psoriasis Placebo- and Active-Controlled Integrated Analysis Set.[4]

Adverse Events	Ixekizumab n=734	Etanercept n=739	Placebo n=360
Nasopharyngitis	8.3% (61)	7.4% (55)	7.8% (28)
URTI	3.7% (27)	4.6% (34)	3.3% (12)
Injection site reaction	10% (76)	11% (80)	1.1% (4)
Headache	4.5% (33)	4.2% (31)	2.2% (8)
Arthralgia	2.7% (20)	2.3% (17)	2.2% (8)

URTI: upper respiratory tract infection.

Ixekizumab was well tolerated in the maintenance period, and the long-term safety assessed over the 48 weeks following the induction period showed a similar profile to the induction period.[2]

Selected adverse events of special interest included injection site reactions, infections, hypersensitivity reactions, Candida, staphylococcal infections, confirmed Major Cardiovascular and Cerebrovascular Events (MACE), and Crohn's disease. There was an increased incidence of Candida infections and neutropaenia in patients receiving ixekizumab compared with placebo. There was no difference between ixekizumab and placebo in the proportion of patients experiencing serious anaphylaxis, but the frequency of non-anaphylactic reactions such as urticaria and dermatitis was greater with ixekizumab compared with placebo. [2]

*Other data were also assessed but remain commercially confidential.**

Summary of clinical effectiveness issues

Psoriasis is a chronic, relapsing-remitting disease of the skin, which is characterised by red, scaly patches, plaques and pustules that usually itch. Plaque psoriasis – which affects the elbows, knees, scalp and back – is the most common type of psoriasis. There are three main types of treatment for psoriasis: topical therapy; phototherapy; and systemic therapy with either conventional agents (e.g. methotrexate, ciclosporin), or biologic agents.

Ixekizumab is the second monoclonal antibody licensed for treatment of psoriasis which targets IL-17A; secukinumab was the first and this was accepted for restricted use by SMC (advice number 1054/15) in May 2015. Other available biologic agents are the TNF antagonists (adalimumab, etanercept, infliximab) and the anti-IL-12/IL-23, ustekinumab.[2] Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area, namely that psoriasis is difficult to manage and ixekizumab would provide another therapeutic option.

Ixekizumab, at the licensed dosing schedule, was associated with superior efficacy in three phase III double-blind randomised controlled studies, compared with placebo (UNCOVER-1, -2 and -3) and etanercept (UNCOVER -2 and -3), measured by PASI 75 and sPGA (0,1) at week 12. Efficacy of ixekizumab was maintained up to week 60.[2] The recently presented IXORA-S study suggests superior efficacy for ixekizumab over ustekinumab. The Committee for Medicinal Products for Human Use (CHMP) guidelines on clinical investigation of medicinal products for treatment of psoriasis recommends PASI and a physician global assessment scale (e.g. sPGA) to assess response to treatment.[11] The results were statistically significant and clinically relevant.

Ixekizumab was associated with statistically significant and clinically relevant improvements from baseline in quality of life measured by DLQI, a standard measure of quality of life in patients with psoriasis (response to treatment defined as ≥5 reduction).[2,12] There were also significant quality of life benefits measured by Itch NRS which was developed and rated by the sponsor company so has not been independently assessed.[2]

The UNCOVER study population is broader than the proposed positioning; around two thirds of patients in the UNCOVER studies had received previous standard systemic treatment so would be eligible for a biologic treatment in Scottish practice. A quarter of patients had received prior biologic treatment. The results from UNCOVER-2 suggest that non-response to etanercept does not prevent patients from achieving a clinically meaningful response with ixekizumab.[2]

No major differences in sPGA (0,1) and PASI 75 response rates were observed between patients who had previously received systemic therapy compared with those who had not; however, responses rates tended to be lower in patients who had received several different biologics previously. Response rates were lower in those with greater body weight, although treatment effect remained significant versus placebo in all subgroups. In practice the likelihood of achieving a response may be influenced by a patient's bodyweight.[2]

There is limited direct evidence comparing ixekizumab to the biologic medicines accepted for use in NHS Scotland. The company presented a Bayesian network meta-analysis (NMA) of 36 studies using random effects, comparing ixekizumab with adalimumab, etanercept, infliximab, secukinumab and ustekinumab for patients with moderate, severe or very severe psoriasis. PASI response rates were used as these were consistently reported across the studies:

- PASI 50 defined as a minimum of 50% improvement of PASI score from baseline
- PASI 75 defined as a minimum of 75% improvement of PASI score from baseline
- PASI 90 defined as a minimum of 90% improvement of PASI score from baseline
- PASI 100 defined as complete resolution of disease.

Ixekizumab 80mg every two weeks had the highest probability of being ranked best for all outcomes. The credible intervals around the absolute probability of achieving PASI 75 response for ixekizumab, secukinumab, infliximab and ustekinumab 90mg (not the licensed dosing schedule) overlapped.

Limitations of the NMA include: no comparison of safety or health-related quality of life data, the fact that it was not possible to provide a scenario analyses that matched the proposed positioning and there was heterogeneity in time points for assessment of PASI response and in the baseline characteristics of the studies, including duration of psoriasis, PASI score and prior use of biologic medicines.

Clinical experts consulted by SMC considered that ixekizumab is a therapeutic advancement due to its mechanism of action. They considered that ixekizumab may provide another treatment option for patients with moderate to severe plaque psoriasis that potentially works faster than other available biologic treatments. Its adverse event profile is characteristic of medicines within the class of immunomodulators and appears acceptable. Once maintenance dosing is established, ixekizumab is administered every four weeks by SC injection, which maybe be more convenient for patients than other biologic therapies, which are given at shorter intervals, such as etanercept[13] (once or twice weekly by SC injection) and adalimumab[14] (every two weeks by SC injection) or by the intravenous route, such as infliximab[15] (every eight weeks IV infusion). It has a similar administration interval to secukinumab and a shorter administration interval than ustekinumab[16] (every 12 weeks by SC injection).

*Other data were also assessed but remain commercially confidential.**

Summary of comparative health economic evidence

The submitting company provided a cost utility analysis comparing a sequence of ixekizumab, ustekinumab 90mg, infliximab and best supportive care (BSC) to seven other sequences involving the following medicines: adalimumab, apremilast, etanercept, infliximab, ustekinumab and secukinumab. All patients were assumed to have moderate to severe plaque psoriasis, had failed on prior systemic treatments and be eligible for a biologic medicine.

A Markov state-transition model, with monthly cycles was used. The model had five PASI response health states, four treatment-related health states and adopted a lifetime horizon. Patients entered the model in the induction stage at the end of which they were assigned to a PASI state, based on PASI response. Patients achieving a response of PASI 75 or better continued that treatment in the maintenance state; otherwise they received the next treatment line. It was assumed that response rates observed in the maintenance phase continued while the patient remained on treatment. An annual discontinuation rate of 20% was applied whilst in the maintenance state. After three active treatments, patients received BSC. Patients could die in any state.

In the absence of head-to-head studies of ixekizumab to comparators other than etanercept and placebo, the company conducted an NMA as noted above. BSC was modelled using the results of a retrospective observational study of 76 patients managed at a London teaching hospital for 12 months prior to commencing biologics. Utility values were derived from responses to an EQ-5D-5L questionnaire from the 3 pivotal studies and valued using an England-specific value set. These varied by PASI response. No costs or utility decrements were included for adverse events.

A patient access scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS a discount was offered on the list price of the medicine.

Incremental cost effectiveness ratios (ICERs) were presented for a fully incremental analysis and pairwise analyses for each comparator sequence versus the ixekizumab sequence. In the fully incremental analysis, the ixekizumab sequence, using the PAS price, had an ICER of £41,921 per quality adjusted life year (QALY) compared to the cheapest regimen (apremilast, ustekinumab, infliximab, BSC). The key cost driver was the cost of ixekizumab.

Results from sensitivity analyses that removed two comparators judged not relevant by SMC clinical experts (those with infliximab and apremilast as first line) under the fully incremental analysis reduced the ICER for ixekizumab to £33,825 with PAS. The cheapest treatment in this option started with etanercept as first line.

Deterministic sensitivity analyses showed the pairwise ICER comparisons were sensitive to the cost of ixekizumab, the annual discontinuation rate with biologic treatments and the PASI 75 rate of the first treatment in the comparator sequence. A scenario analysis was provided where ixekizumab was used as a second line biologic (adalimumab first line and infliximab third line) using the response rates derived in the base case NMA. The ixekizumab sequence, using the PAS price, had an ICER of £38,937 compared to the cheapest regimen (adalimumab, apremilast, infliximab, BSC).

While there were some weaknesses with the NMA underpinning the cost-utility analysis and some concerns in relation to the underlying clinical data generalising to the Scottish population who have failed on prior systemic treatments, the main issue related to the representativeness of the treatment sequences which were modelled. Clinical experts advised that all available biologic treatments are used in practice and choices are guided by patient characteristics so the sequences presented may not accurately reflect current Scottish practice. Expert views suggested that ixekizumab may be used as an alternative to secukinumab which also targets IL-17A, and, therefore, a cost-minimisation analysis was a relevant approach to consider. On request, the submitting company provided a cost-minimisation analysis against secukinumab and the other comparator medicines. Using a 5-year time horizon, the results without the PAS indicated that ixekizumab was not cost-minimising against secukinumab or other medicines. However, with the PAS, ixekizumab became a cost-effective treatment option.

As such, the economic case has been demonstrated.

*Other data were also assessed but remain commercially confidential.**

Summary of patient and public involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from The Psoriasis Association and the Psoriasis and Psoriatic Arthritis Alliance (PAPAA), both are registered charities.

- The Psoriasis Association has received less than 15% pharmaceutical company funding in the past two years, with none from the submitting company. PAPAA has not received any pharmaceutical company funding in the past two years.

- Psoriasis is a lifelong, visible condition which can occur at any age and any point in the lifespan. It can be a debilitating disease that impacts all aspects of life, physically and psychologically. Many Psoriasis Association members and supporters describe a difficult and lonely life living with the condition. Psoriasis can have a significant impact on the wider family, as well as a person's ability to take part in various activities and certain employment.

- Many of the treatments that are currently available for psoriasis contribute to the burden of the condition due to their messy, time consuming nature, or worries about side effects and irreversible toxicity. Ixekizumab, as with other biologics, may offer an advantage from this perspective.

- In the hope of leading a life unhindered by disease or treatment, patients want access to a range of treatments in the pathway and a wide choice if initial treatments fail. Ixekizumab would provide another biologic treatment option.

Additional information: guidelines and protocols

Several European and British guidelines exist regarding systemic treatment of psoriasis; these predate the availability of secukinumab and ixekizumab.

The Scottish Intercollegiate Guidelines Network (SIGN) guideline on Diagnosis and management of psoriasis and psoriatic arthritis in adults was published in 2010. This recommends that patients with severe psoriasis who have failed to respond to, or have a contraindication to, or are intolerant of phototherapy and systemic therapies including ciclosporin and methotrexate, should be offered biologic therapy unless they have contraindications or are at increased risk of hazards from these therapies. Adalimumub, etanercept, ustekinumab and infliximab are recommended as treatment options for patients with severe psoriasis.

Good practice points note that the use of biologic treatments should conform to the British Association of Dermatologists (BAD) guidelines. The comparative long-term safety of systemic and biologic treatments for severe psoriasis is currently being investigated in a five-year treatment register, the British Association of Dermatologists Biologic Interventions Register (BADBIR) (www.badbir.org). Patients on biologic therapies should be offered the opportunity to join the long term safety register BADBIR.[17]

The National Institute for Health and Care Excellence (NICE) published a clinical guideline on the assessment and management of psoriasis in 2012.[18] The guideline makes broadly similar recommendations as the SIGN guideline regarding the use of biologics.

The British Association of Dermatologists (BAD) guidelines for biologic interventions for psoriasis published in 2009, and referred to in the SIGN guideline, are currently being updated.[12]

Additional information: comparators

Etanercept, adalimumab, ustekinumab, secukinumab and infliximab.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
Ixekizumab	**160mg SC at week 0, followed by 80mg SC at weeks 2, 4, 6, 8, 10, and 12, then maintenance dosing of 80mg every 4 weeks**	**First year: 20,250 Subsequent years: 14,625**
Secukinumab	300mg SC at weeks 0, 1, 2, 3, and 4 and then monthly	First year: 19,500 Subsequent years: 14,625
Infliximab	5mg/kg IV at weeks 0, 2 and 6 weeks, then every 8 weeks	First year: 12,064 Subsequent years: 9,802
Ustekinumab	45mg (or 90mg*) SC at weeks 0 and 4 then every 12 weeks	First year: 12,882 Subsequent years: 9,304
Adalimumab	80mg SC, then 40mg SC every two weeks	First year: 9,860 Subsequent years: 9,156
Etanercept	25mg SC twice weekly; or 50mg SC weekly**	8,528

Doses are for general comparison and do not imply therapeutic equivalence. Costs for adalimumab and etanercept are from eVadis and for ixekizumab, secukinumab, infliximab and ustekinumab from eMC Dictionary of Medicines and Devices browser on 7 December 2016. Costs calculated using a bodyweight of 70kg and the full cost of the vial assuming wastage. * ustekinumab 90mg given if bodyweight >100kg. ** If necessary, etanercept 50mg SC twice weekly may be given for 12 weeks then 25mg twice weekly or 50mg weekly. SC: subcutaneous, IV: intravenous. Costs do not take any patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 2,306 patients eligible for treatment with ixekizumab in all years to which confidential estimates of uptake were applied.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain commercially confidential.**

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This assessment is based on data submitted by the applicant company up to and including 17 February 2017.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*
http://www.scottishmedicines.org.uk/About_SMC/Policy_statements/Policy_Statements

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a drug and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG, established under the auspices of NHS National Services Scotland reviews and advises NHS Scotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.