Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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NHS SCOTLAND

# secukinumab 150mg solution for injection in pre-filled pen and pre-filled syringe (Cosentyx®) SMC No. (1167/16)

## Novartis Pharmaceuticals UK Limited

08 July 2016

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

**ADVICE**: following a full submission

**secukinumab (Cosentyx®)** is accepted for restricted use within NHS Scotland.

**Indication under review:** alone or in combination with methotrexate, for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.

**SMC restriction:** Use in patients whose disease has not responded to adequate trials of at least two standard DMARDs either individually or in combination.

In phase III, randomised, placebo-controlled studies in patients with active psoriatic arthritis, a significantly greater proportion of patients who received secukinumab achieved at least 20% improvement in the American College of Rheumatology response criteria (ACR20) at 24 weeks compared with those who received placebo.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of secukinumab. 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**

## Indication

Secukinumab, alone or in combination with methotrexate, is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.

## Dosing Information

For patients with concomitant moderate to severe plaque psoriasis or who are anti-tumour necrosis factor alpha (TNFα) inadequate responders, the recommended dose is 300mg by subcutaneous injection with initial dosing at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4. Each 300mg dose is given as two subcutaneous injections of 150mg.

For other patients, the recommended dose is 150mg by subcutaneous injection with initial dosing at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4.

If possible, areas of the skin that show psoriasis should be avoided as injection sites. After proper training in subcutaneous injection technique, patients may self-inject secukinumab if a physician determines that this is appropriate.

Secukinumab is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriatic arthritis.

## Product availability date

19 November 2015

## Summary of evidence on comparative efficacy

Secukinumab is an IgG1 monoclonal antibody that binds to and neutralises interleukin-17A (IL-17A), a pro-inflammatory cytokine. Inhibiting the effects of IL-17A on various cells reduces the release of pro-inflammatory cytokines, chemokines and mediators of tissue damage and limits IL-17A-mediated contributions to autoimmune and inflammatory diseases such as psoriatic arthritis (PsA).[1, 2]

The key evidence for secukinumab in PsA comprises the phase III, multi-centre, randomised, double-blind, placebo-controlled study, FUTURE 2.[3] This is supported with results from the FUTURE 1 study.[4]

FUTURE 2 randomised 397 adults meeting the classification criteria for PsA (CASPAR). Patients had symptoms for at least six months and active disease, defined as a minimum of 3/78 tender joints and 3/76 swollen joints, and had active or a history of plaque psoriasis. Patients were required to have been taking non-steroidal anti-inflammatory drugs (NSAIDs) for PsA for at least four weeks with inadequate control of symptoms, or to be intolerant of NSAIDs. Patients' current and treatment history factored into their eligibility for the study; concomitant oral corticosteroids (≤10mg/day prednisone or equivalent) and methotrexate (≤25mg/week) and NSAIDs were permitted if the doses were stable. Other biologic agents, disease modifying anti-rheumatic drugs (DMARDs) and specific psoriasis treatments were not permitted; these were

stopped (followed by a washout period). Patients with a history of treatment with up to three anti-tumour necrosis factor alpha (TNFα) agents were eligible if they had had an inadequate response after at least three months of treatment, or if the agent(s) had not been tolerated or stopped because of safety concerns. Patients with a history of treatment with other biologic agents were excluded.[1,3]

Following screening and washout, patients were randomised equally, stratified by previous anti-TNFα use, to receive subcutaneous (SC) injections of either placebo or secukinumab 75mg, 150mg or 300mg. Loading consisted of five once-weekly injections, followed by doses at four-weekly intervals. Efficacy was assessed at week 16 and non-responders (those not achieving ≥20% improvements in tender and swollen joint counts) who were allocated to placebo were re-randomised to secukinumab escape treatment (150mg or 300mg in a 1:1 ratio). Placebo responders were re-randomised to either 150mg or 300mg secukinumab at week 24.[3]

The primary outcome was the proportion of patients achieving an improvement of at least 20% in the American College of Rheumatology response criteria, ACR20, at week 24. ACR20 response is defined as at least a 20% improvement in tender and swollen joint counts coupled with at least three of five criteria: patient's global assessment, physician's global assessment, pain, disability, and an acute-phase reactant. Patients not meeting response criteria at week 16 were imputed as non-responders at week 24.[3] Results for the licensed doses of secukinumab and placebo are presented in Table 1 below.

**Table 1: Primary outcome results for the licensed doses of secukinumab in FUTURE 2.[3]**

| Treatment | ACR20 response rate (week 24) | Odds ratio (95% CI) versus placebo, p-value |
|---|---|---|
| secukinumab 150mg (n=100) | 51% | 6.52 (3.25 to 13.08) p<0.0001 |
| secukinumab 300mg (n=100) | 54% | 6.81 (3.42 to 13.56) p<0.0001 |
| placebo (n=98) | 15% | - |

ACR20: ≥20% improvement in the American College of Rheumatology response criteria.
CI = confidence interval.

To manage multiple testing and control type I error, secondary outcomes were tested in a hierarchical order.

Of the secondary outcomes assessing joint symptoms, placebo-adjusted mean differences in Disease Activity Score-28 (DAS28-CRP) from baseline to week 24 were -0.62 for secukinumab 150mg, and -0.65 for 300mg ($p<0.01$ for both doses versus placebo). The proportions achieving a 50% improvement in ACR response criteria (ACR50) were 35% for both doses of secukinumab and 7.1% in the placebo group. This was significant for the comparison between secukinumab 300mg and placebo; however, no formal comparison between 150mg and placebo was conducted due to the hierarchical testing sequence. There was no formal testing of the resolution of dactylitis and enthesitis in patients with these signs of disease at baseline due to the hierarchical sequencing. Resolution of dactylitis was achieved in 50%, 56% and 15% of secukinumab 150mg, 300mg and placebo patients respectively. Enthesitis resolved in 42%, 48% and 22% of patients respectively.[3, 5]

Secukinumab was associated with significantly greater proportions of patients achieving substantial improvements in the coverage and severity of their psoriasis compared with

placebo-treated patients. The proportions of patients achieving at least a 75% improvement in Psoriasis Area and Severity Index (PASI75) score were 48%, 63% and 16% in the secukinumab 150mg, 300mg and placebo groups respectively (p-values versus placebo were <0.01). PASI90 (90% improvement from baseline) was achieved by 33%, 49% and 9.3% of secukinumab 150mg, 300mg and placebo, respectively (p-values versus placebo <0.01).[3]

Multiple tools were used to measure patient-reported outcomes. The Short-Form 36 (physical component summary), SF36-PCS, and Health Assessment Questionnaire Disability Index (HAQ-DI) were specified secondary outcomes. Statistically significant improvements from baseline to week 24 were observed for both doses of secukinumab versus placebo for SF36-PCS. No significant improvement in HAQ-DI score was observed for secukinumab 150mg versus placebo (-0.48 versus -0.31, p=0.056). While there was a statistically significant improvement for patients treated with secukinumab 300mg (-0.56 versus -0.31, p<0.01), this treatment difference was smaller than the minimal clinically important difference of 0.35 in PsA. Exploratory patient-reported outcomes (the SF36 mental component summary, Functional Assessment of Chronic Illness Therapy – Fatigue, Psoriatic Arthritis Quality of Life, and Dermatology Life Quality Index) tended to favour secukinumab treatment over placebo.[3,6,7]

Sub-group analyses according to anti-TNFα treatment history were pre-specified and exploratory in nature. No significant interaction for prior anti-TNFα use on the treatment effect of secukinumab was reported (p=0.24). Response rates (ACR and PASI) for both secukinumab doses were similar in anti-TNFα naive patients although secukinumab 300mg dose resulted in numerically higher response rates when compared with secukinumab 150mg in anti-TNFα inadequate responders.[3]

The study is ongoing with follow-up planned to continue for up to five years of treatment.[3]

The FUTURE-1 study is a two-year, ongoing, multicentre, randomised, placebo-controlled phase III study which has reported data for the primary outcome at 24 weeks and interim follow-up analysis at 52 weeks. Patient eligibility criteria were similar to the FUTURE-2 study. Patients were randomly assigned equally to four-weekly SC injections of secukinumab 150mg, 75mg or placebo, commencing from week 8 following an intravenous (IV) loading regimen of 10mg/kg secukinumab at baseline and weeks 2 and 4 in each of the secukinumab groups, or placebo in the control group. Outcomes assessed were similar to the FUTURE-2 study with ACR20 response rate as the primary outcome. Radiographic progression (in the hands, wrists and feet) was also assessed with the use of the van der Hejde-modified total Sharp score (mTSS). The mTSS ranges from 0 to 528 with higher scores associated with greater erosion and narrowing of joint spaces. ACR20 response was achieved by 50% of patients assigned to secukinumab 150mg and by 17% of placebo patients at week 24, p<0.001. Secukinumab was significantly better than placebo for all secondary outcomes: PASI75, PASI90 responses, change from baseline in DAS28-CRP, SF-36 PCS, HAQ-DI, ACR50 response and resolution of dactylitis or enthesitis. Changes from baseline in mTSS score were statistically significantly lower in the secukinumab group compared with placebo, but the clinical significance of a treatment difference of 0.44 is not clear.[4]

## Summary of evidence on comparative safety

In FUTURE-2, similar proportions of patients reported adverse events (AEs) up to week 16; 57% (57/100) of secukinumab 150mg patients, 56% (56/100) of secukinumab 300mg patients and 58% (57/98) of placebo patients. During the entire treatment period (up to week 52), AEs were reported in 117/143 (82%) patients who received secukinumab 150mg, 113/145 (78%) patients who received secukinumab 300mg and 61/98 (62%) of placebo patients.

The incidences of serious AEs per 100-patient years of exposure were 5.1, 6.4 and 8.6 in secukinumab 150mg, 300mg and placebo-treated patients respectively.[3]

AE with a greater incidence (per 100-patient years) in any of the secukinumab-treated groups compared with placebo were sinusitis (3.8, 6.5 and 2.9 in the 150mg, 300mg and placebo groups respectively), and psoriatic arthropathy (6.5, 3.1 and 5.8 respectively).

Patients treated with secukinumab had a lower incidence of infection or infestation compared with placebo patients: 87, 79 and 108 incidences per 100-patient years in the 150mg, 300mg and placebo-treated groups respectively.[3]

Three patients in the secukinumab groups developed squamous cell carcinoma (two in the 75mg group and one in the 150mg group); this led to discontinuation in two patients.[3]

Treatment-emergent antibodies to secukinumab were detected in one patient who had switched to 150mg from placebo at week 24; no immune-related AEs or loss of efficacy were reported in this patient.[3]

## Summary of clinical effectiveness issues

PsA is a chronic, progressive, inflammatory arthropathy affecting peripheral synovial, entheseal connective tissue and axial structures which can occur in up to 40% of patients with skin or nail psoriasis.[1,8] It most commonly occurs in adults aged between 30 and 50 years with spinal manifestations being more prevalent in males and polyarticular arthritis more common in females. The severity of skin and joint symptoms do not correlate, and common manifestations include nail lesions, back pain, enthesitis (inflammation at sites of tendon insertion, eg Achilles' tendon) and dactylitis ("sausage digit").[9]

Secukinumab is the first in therapeutic class (IL-17A inhibitor) licensed for the management of PsA. Other biologic agents licensed for PsA act either as inhibitors of TNFα or of IL-12/23. UK clinical guidelines recommend that biologic therapy be considered in patients who have had adequate trials of at least two DMARDs.[8]

ACR20 is a validated measure of treatment response in many rheumatological conditions.[10] In both FUTURE studies, secukinumab was associated with significantly greater ACR20 response rates when compared with placebo. Based on the results of the studies, approximately half of patients treated with secukinumab will achieve an ACR20 response at six months.[3,4] However, patients achieving an ACR20 may still have significant disease, given the threshold of improvement is 20% from baseline.

Secondary outcomes related to the joint manifestations of the disease favoured secukinumab over placebo; however, due to the hierarchical testing procedure used to control for type I error, comparisons between secukinumab 150mg and placebo for the ACR50 response, or for the analysis of enthesitis and dactylitis could not be formally tested. As expected, given that secukinumab is also licensed for the management of plaque psoriasis, both doses of secukinumab improved psoriasis symptoms in a significantly greater proportion of patients than placebo. A number of patient-reported outcomes were measured in FUTURE 2. In general, they supported the use of secukinumab in this patient group. FUTURE 2 demonstrated the efficacy of secukinumab in patients naive and experienced with anti-TNFα therapy.[3]

Limitations of the evidence relate to the dosing of secukinumab in the studies. FUTURE 1 utilised an IV loading dose regimen. While patients in FUTURE 2 were given SC doses of secukinumab, they were not assigned a dose of secukinumab based on the severity of their plaque psoriasis or on their treatment history with regard to anti-TNFα therapy; efficacy of the 300mg dose in patients with previous inadequate response to anti-TNFα therapy is based on exploratory subgroup analysis.

UK clinical guidelines recommend that biologic therapy be considered in patients who have had adequate trials of up to two DMARDs. Not all patients recruited to the FUTURE studies fulfilled the eligibility criteria for biologic therapy in UK practice;[8] recruitment was based on poor response to NSAIDs[12]. Approximately one third of patients in the FUTURE 2 study had previous experience with anti-TNFα therapy. Methotrexate was used by 44% to 51% of patients at baseline.[3]

There are no direct active comparative data in patients with PsA. To support the economic case, the company presented Bayesian network meta-analyses (NMA) of both doses of secukinumab and approved biologic and targeted synthetic treatments (adalimumab, certolizumab pegol, etanercept, infliximab, golimumab, ustekinumab and apremilast). Efficacy outcomes compared response rates for ACR (20, 50 and 70) and PASI (50, 75 and 90) at weeks 12 to 16 (analysed together). In addition, a matched-adjusted indirect comparison of secukinumab and adalimumab looked at ACR and PASI responses after 48 or 52 weeks of treatment. An indirect comparison of secukinumab with ustekinumab at 24 weeks was also provided upon SMC request.

The NMA included data from 19 studies. Subgroup analyses compared outcomes in patients naive to anti-TNFα therapy and those with inadequate responses to anti-TNFα therapy. No important differences in efficacy between secukinumab and the comparators were observed.

The company conducted meta-regression of baseline characteristics identified as sources of heterogeneity between studies but this could only be performed on the comparison of ACR outcomes and it was not feasible to correct for all identified covariates.

On balance, the cost-minimisation approach taken for the economic analysis was justified based on the analyses presented.

Clinical experts consulted by SMC considered that secukinumab is a therapeutic advancement due to its novel mode of action. They considered that the place in therapy of secukinumab would be in patients who have had inadequate responses to or side effects from current therapies, specifically anti-TNFα agents.

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

## Summary of comparative health economic evidence

The company submitted a cost minimisation analysis comparing secukinumab, alone or in combination with methotrexate, to a range of comparators including apremilast, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab (including biosimilars) and ustekinumab, for the treatment of adult patients with psoriatic arthritis whose response to previous DMARD therapy has been inadequate. Results were provided over a five year time horizon.

The assumption of comparable efficacy between secukinumab and comparators was derived from an NMA, which used placebo as a common comparator. Based on the analysis, no significant differences between secukinumab 150mg or 300mg were demonstrated versus the comparators for the primary outcome ACR 20, ACR 50 and ACR 70 at weeks 12 to 16 (with credible intervals overlapping 1).

Drug acquisition costs were included in the analysis. Within the base case analysis, secukinumab drug costs were based on a weighted average of the 150mg and 300mg doses (using company data, 46% of patients were assumed to receive 300mg while 54% were assumed to receive 150mg dose). Drug administration costs were also included in the analysis. This involved a one-off training cost of £41, which was assumed to apply to all subcutaneous treatments. It should be noted that infliximab was associated with higher administration costs than other treatments, due to the intravenous nature of the treatment. Monitoring costs and adverse events costs were not considered.

**Secukinumab weighted average dose (without PAS)**

| Medicine | Cumulative cost year 5 | Incremental results versus comparator |
|---|---|---|
| Secukinumab | £53,492 | |
| Apremilast | £33,494 | £19,998 |
| Ustekinumab 45mg (90mg) | £44,949 | £8,543 |
| Adalimumab | £42,826 | £10,666 |
| Certolizumab pegol | £44,550 | £8,942 |
| Etanercept | £43,477 | £10,015 |
| Golimumab | £42,826 | £10,666 |
| Infliximab | £75,778 | -£22,286 |
| Infliximab Biosimilar | £69,301 | -£15,806 |

A Patient Access Scheme (PAS) was submitted by the company and has been accepted by the Patient Access Scheme Assessment Group (PASAG) for implementation in NHS Scotland. Under the PAS, a discount was given on the price of the medicine. It should be noted that a PAS is in place for certolizumab pegol and the with-PAS analysis also included an estimate of the PAS price for this medicine.

SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, as the PAS is commercial in confidence, only the without-PAS figures can be presented. However, with the PAS, secukinumab became a cost-effective treatment option.

In terms of uncertainties with the analysis:

- There is some uncertainty surrounding the proportion of patients on the different doses of secukinumab used within the base case analysis as this was derived from company data ie 54% assumed to receive 150mg while 46% assumed to receive 300mg. Based on the assumption that 100% of patients are TNF inadequate responders or have moderate to severe plaque psoriasis and thus would use a dose of 300mg, secukinumab was cost-minimising against all but one comparators at year 5 (apremilast). However, based on discussion at the New Drugs Committee, apremilast was not considered to be the primary comparator.
- There is also some uncertainty around the number of doses of secukumab used from year 2 onwards. As a conservative scenario, additional sensitivity analysis was provided whereby the dose for secukinumab was increased to 13 from year two onwards (as opposed to 12) and all patients were assumed to receive the 300mg dose of secukinumab. Based on this analysis (with PAS), secukinumab was more costly than some comparators and less costly than others.

Despite the weakness outlined above, 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 Psoriasis & Psoriatic Arthritis Alliance (PAPAA) and the Psoriasis Association, which are both registered charities.

- PAPAA has not received any pharmaceutical company funding in the last two years and the Psoriasis Association has received <15% pharmaceutical company funding in the past two years, but none from the submitting company.

- Psoriatic arthritis causes inflammation in the joints and areas where tendon joins to bone, which creates symptoms such as pain, stiffness, swelling and fatigue. It varies widely in its severity and impact. For those with severe disease, it can be life changing and affect every aspect of daily life, including getting dressed, work, study, and relationships.

- Non-steroidal anti-inflammatory drugs and steroid injections are used to improve symptoms but a reliance on these will not prevent long term irreversible damage ro improvement in long term outlook. A number of biologic and non-biologic 'disease-modifying' treatments are available, which can prevent progression and irreversible damage. However, not all treatments work equally well for each patient.

- Secukinumab (Cosentyx©) is a novel treatment, which works differently to currently available treatments to slow down or stop the progression of the psoriatic arthritis. It provides an option both for patients who are 'biologic-naive', or have not had adequate results from other available treatments.

## Additional information: guidelines and protocols

The European League Against Rheumatism (EULAR) updated guidelines for the management of PsA in 2015.[13] Recommendations included:

- commence therapy with a biologic DMARD (bDMARD), usually an anti-TNFα, in patients with peripheral arthritis and an inadequate response to at least one conventional synthetic DMARD (csDMARD)
- bDMARDs targeting IL-12/23 or IL-17 pathways may be considered in patients with peripheral arthritis and an inadequate response to at least one csDMARD, if an anti-TNFα is not appropriate, for example, patients with comorbidities or those with a history of infections or patients who prefer not to be treated with an anti-TNFα therapy. The guideline acknowledges the efficacy demonstrated by secukinumab in clinical trials.
- consider switching to another bDMARD, including switching between anti-TNFα agents, in patients who fail to respond adequately to a bDMARD.

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) also published guidelines in 2015.[14] These guidelines also recommend the use of IL-17 inhibitors alongside other biologics in patients who have previously received treatment with conventional therapy (standard therapeutic route). The use of IL-17 inhibitors is recommended for use across all PsA domains, including peripheral arthritis, axial disease and skin involvement. At the time of publication, these recommendations were conditional due to the availability of trial data from abstracts only and/or the absence of regulatory approval.

The British Society for Rheumatology and The British Health Professionals in Rheumatology guideline for the treatment of psoriatic arthritis with biologics (2012) provides a treatment algorithm for the management of the condition.[8] If there is an inadequate response to the use of NSAIDs and/or local intra-articular steroids, use of up to two DMARDs (alone or in combination) should be trialled before the use of biologic therapies. In the absence of a response to the DMARDs (i.e. intolerance or active disease despite at least 12 weeks treatment at a therapeutic dose), a trial of up to two anti-TNFα therapies is indicated in those patients with more than three tender or swollen joints or in those with persistent severe oligoarthritis. In those patients with active disease, the presence of five or more swollen joints and a raised c-reactive protein for at least 3 months, or structural joint damage, use of a biologic can be considered after inadequate response to just one DMARD. Choice of anti-TNFα therapy is at the discretion of the physician, taking into account patient co-morbidities, preference and cost. Treatment with an anti-TNFα therapy should continue if there is an adequate response within three months of treatment. In those patients with only a partial response to treatment (i.e. some improvement in the swollen/tender joint score and no decline in the PsARC global scores), a further 12 weeks of treatment can be considered, continuing if a full response is achieved.

The Scottish Intercollegiate Guidelines Network (SIGN) guideline 121 on the diagnosis and management of psoriasis and psoriatic arthritis in adults (October 2010) advises that treatment of psoriatic arthritis, depending on the type and severity of the condition, may include the use of NSAIDs, DMARDs and intra-articular steroid injections. Recommendations in the guideline include:

- NSAIDs for short-term symptom relief in patients with psoriatic arthritis
- Leflunomide for the treatment of active peripheral psoriatic arthritis (or sulfasalazine as an alternative)
- Methotrexate in the treatment of psoriatic arthritis
- Adalimumab, etanercept or infliximab for the treatment of active psoriatic arthritis in patients who have failed to respond to, are intolerant of, or have had contraindications to, at least two DMARDs.[11]

The National Institute for Health and Care Excellence technology appraisal guidance 199 on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (August 2010) advises that etanercept, infliximab and adalimumab are recommended for the treatment of adults with active and progressive psoriatic arthritis when:

- The person has peripheral arthritis with three or more tender joints and three or more swollen joints, and
- The psoriatic arthritis has not responded to adequate trials of at least two standard DMARDs, administered either individually or in combination.

Treatment should be discontinued in those patients whose psoriatic arthritis has not shown an adequate response in the PsARC at 12 weeks.[15]

## Additional information: comparators

Biologic DMARDs licensed for PsA include: adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and ustekinumab. Apremilast is a targeted synthetic DMARD also licensed for this stage in treatment.

## Cost of relevant comparators

| Drug | Dose Regimen | Cost per year (£) |
|---|---|---|
| **secukinumab** | **150mg or 300mg by subcutaneous injection once weekly for four weeks (5 doses at day 0, week 1,2,3 and 4), then once every month** | **First year: 9,750 to 19,500 Subsequent years: 7,313 to 14,625** |
| golimumab* | 50mg by subcutaneous injection once every month, or if bodyweight >100kg, 50mg once every month for first three or four doses then 100mg every month | First year: 9,156 to 16,022 Subsequent years: 9156 to 18,311 |
| ustekinumab | 45mg by subcutaneous injection at weeks 0 and 4, then 45mg or 90mg (if bodyweight >100kg) once every 12 weeks | First year: 12,882 Subsequent years: 8,588 to 10,735 |

| | | |
|---|---|---|
| infliximab** | 5mg/kg by intravenous infusion at weeks 0, 2 and 6, then once every 8 weeks | First year: 12,085<br>Subsequent years: 9,064 to 10,574 |
| certolizumab pegol | 400mg by subcutaneous injection at weeks 0, 2 and 4, then 200mg every two weeks or 400mg every 4 weeks | First year: 10,725<br>Subsequent years: 9,295 |
| adalimumab | 40mg by subcutaneous injection every two weeks | 9,156 |
| etanercept** | 25mg by subcutaneous injection twice weekly or 50mg once weekly | 8,528 |
| apremilast | Dose titration over six days to maintenance dose of 30mg orally twice daily | First year: 7,140<br>Subsequent years: 7,150 |

Doses are for general comparison and do not imply therapeutic equivalence. Costs from MIMS online on 25 April 2016. Costs do not take any patient access schemes into consideration. *SMC restricted the use of golimumab to the 50mg dose. **Costs for infliximab and etanercept reflect the lowest of the list prices for the reference and biosimilar products. Infliximab cost based on 70kg body weight.

## Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 679 patients in year 1 and 688 patients in year 5 to which confidential estimates of treatment 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.**

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.


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This assessment is based on data submitted by the applicant company up to and including 17 June 2016.

**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*.

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.*