Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2308

secukinumab 150mg solution for injection in pre-filled syringe and 150mg solution for injection in pre-filled pen (Cosentyx®)

Novartis Pharmaceuticals UK Limited

04 December 2020

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

secukinumab (Cosentyx ®) is accepted for use within NHSScotland.

Indication under review: treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein and/or magnetic resonance imaging evidence in adults who have responded inadequately to non steroidal anti inflammatory drugs.

In a randomised phase III study, secukinumab, compared with placebo, significantly improved symptoms in adults with active non-radiographic axial spondyloarthritis.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chairman
Scottish Medicines Consortium

Indication

Treatment of active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence in adults who have responded inadequately to non steroidal anti inflammatory drugs (NSAIDs).[1]

Dosing Information

The recommended dose is 150mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

Available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Secukinumab is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of conditions for which secukinumab is indicated.

Product availability date

29 April 2020

Summary of evidence on comparative efficacy

Secukinumab is an immunoglobulin G1 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 non-radiographic axial spondyloarthritis (nr-axSpA).[1]

The key evidence supporting the efficacy and safety of secukinumab in the indication under review comes from PREVENT, an international, randomised, double-blind, phase III study that evaluated the efficacy and safety of secukinumab compared with placebo. The study recruited adults with a diagnosis of axial spondyloarthritis (axSpA), according to Assessment of Spondyloarthritis International Society (ASAS) axSpA criteria, with inflammatory back pain for at least 6 months, onset before 45 years of age and sacroiliitis on MRI with ≥1 spondyloarthritis (SpA) feature or human leukocyte antigen (HLA)-B27 positive with ≥2 SpA features. Patients could participate if they had objective signs of inflammation, spinal pain as measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) question 2 ≥4cm (0 to 10cm), and total back pain as measured by visual analogue scale at baseline ≥4cm (0 to 10cm). Patients with active axSpA as assessed by total BASDAI ≥4cm (0 to 10cm) at baseline could participate. Patients must have been treated with at least two different NSAIDs at the highest recommended dose for at least 4 weeks in total prior to randomisation with an inadequate response or failure to respond, or less if therapy had to be withdrawn due to intolerance, toxicity or contraindications. Patients who were regularly taking

NSAIDs as part of their axSpA therapy were required to be on a stable dose for at least 2 weeks before randomisation. Patients who had been on a tumour necrosis factor (TNF)-alpha inhibitor (not more than one) had to have experienced an inadequate response to treatment given at an approved dose for at least 3 months prior to randomisation or had been intolerant to at least one administration.[2]

Patients were randomised in a 1:1:1 ratio to receive: secukinumab 150mg subcutaneously (SC) at baseline, weeks 1, 2 and 3, followed by administration every 4 weeks starting at week 4 (secukinumab 150mg with loading, n=185); secukinumab 150mg SC at baseline, placebo at weeks 1, 2 and 3, followed by secukinumab administration every 4 weeks starting at week 4 (secukinumab 150mg without loading, n=184); or placebo (n=186). Treatment continued until week 52, following which all patients received open label secukinumab 150mg SC, except for patients who discontinued study treatment. From week 20, inadequate responders could receive open-label secukinumab 150mg SC or other biologic therapy such as a TNF-alpha inhibitor. Patients could continue to receive methotrexate (≤25mg/week) or sulfasalazine (≤3g/day) if they had taken it for at least 3 months and had been on a stable dose for at least 4 weeks prior to randomisation. Patients could also continue systemic corticosteroids if they were on a stable dose (≤10mg/day prednisone or equivalent) for at least 2 weeks before randomisation.[2]

The primary outcome was response to treatment assessed in TNF-alpha naïve patients only, according to the ASAS 40 response criteria (ASAS40) at week 16. ASAS40 response was defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four main, patient-assessed domains (patient global assessment, back pain, function, and morning stiffness) and an absence of deterioration in the potential remaining domain). Efficacy analyses were performed in the full analysis set (FAS) population, which included all patients who underwent randomisation and met all eligibility criteria.

Secukinumab was associated with a statistically significant improvement in ASAS40 compared with placebo in TNF-alpha inhibitor naive patients at week 16. Results are provided in Table 1 only for the groups of patients receiving either placebo or secukinumab 150mg with loading, which is the licensed dosing regimen.[2]

Table 1: Primary outcome of PREVENT:ASAS40 response at week 16 among TNF-alpha inhibitor naive patients (FAS population)[2]

	Secukinumab 150mg with loading (n=164)	**Placebo (n=171)**
ASAS40 response (TNF-alpha inhibitor naïve patients) (%)	41%	29%
Odds ratio (95% CI)	1.72 (1.09 to 2.70)	
p-value	0.0197	

ASAS, Assessment of Spondyloarthritis International Society; CI, confidence interval; FAS, full analysis set

A hierarchical statistical testing strategy was applied in the study to primary and secondary outcomes with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Results of hierarchically tested secondary outcomes are presented in Table 2 in the testing order used.[2]

Table 2: Secondary outcome results at week 16 of PREVENT (FAS population)[2]

	Secukinumab 150mg with loading (n=185)	Placebo (n=186)	Odds ratio (95% CI)
Overall ASAS40 response, %	40%	28%	1.77 (1.14 to 2.74)
ASAS 5/6 response, %	40%	24%	2.26 (1.43 to 3.58)
Change from baseline in total BASDAI score (0 to 10 scale), LS Mean	-2.35	-1.46	-0.89 (-1.39 to -0.38) [a]
BASDAI50 response, % (n)	37%	21%	2.53 (1.58 to 4.07)
Change from baseline in hsCRP, geometric mean ratio week 16/baseline	0.64	0.91	0.70 (0.58 to 0.84) [b]
Change from baseline in total BASFI score (0 to 10 scale), LS Mean	-1.75	-1.01	-0.75 (-1.26 to -0.24) [a]
Change from screening in MRI SI joint oedema score (0 to 24 scale)	-1.68	-0.39	-1.24[c]
ASAS20 response, %	57%	46%	1.60 (1.06 to 2.43)
Change from baseline in SF-36 PCS score, LS Mean	5.71	2.93	2.77 (1.20 to 4.34) [a]
Change from baseline in ASQoL score (0 to 18 scale), LS Mean	-3.45	-1.84	-1.61 (-2.54 to -0.67) [a]
ASAS partial remission response, %	22%	7.0%	3.80 (1.95 to 7.39)

All p-values were statistically significant.

ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CI, confidence interval; hsCRP, high sensitivity c-reactive protein; LS, least square; MRI SI, magnetic resonance imaging sacroiliac; OR, odds ratio. a) Treatment contrast in LS Mean (95% CI). b) Relative treatment effect (95% CI). c) Estimate of treatment difference.

Health Related Quality of Life (HRQoL) was assessed using five questionnaires: Ankylosing Spondylitis Quality of Life (ASQoL), Euro-QoL 5-Dimension Health Status Questionnaire (EQ-5D), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue assessment, Short Form-36 Physical Component Summary Score (SF-36 PCS) and Work Productivity and Activity Impairment - General Health (WPAI-GH). At week 16, the QoL improvements, from baseline, were observed in the hierarchically tested ASQoL (decrease score) and SF-36 PCS (increase score) and were statistically significantly greater for secukinumab 150mg (with loading) than for placebo (least square [LS] mean changes of -3.45 versus -1.84 in ASQoL, and of 5.71 versus 2.93 in SF-36 PCS). At week 16, the improvements (increases) from baseline in FACIT-Fatigue and EQ-5D (exploratory endpoints) were also greater for secukinumab 150mg (with loading) group compared with the placebo group (LS mean changes in FACIT-Fatigue: 7.19 versus 3.43; in EQ-5D: 14.10 versus 7.14). No data were reported for the WPAI-GH.[2]

Efficacy outcomes were also assessed at week 52. Overall, the EMA considered that maintenance of effect until week 52 was demonstrated based on the primary endpoint (ASAS40 response rate

of 35% [58/164] versus 20% [34/171] in TNF-alpha inhibitor naive patients at week 52) as well as most secondary endpoints. [2]

The submitting company presented several Bayesian network meta-analyses (NMAs) that compared secukinumab, adalimumab, certolizumab pegol, etanercept, and golimumab in adult patients with nr-axSpA, after inadequate response or intolerance to NSAIDs. Seven studies were included in the NMAs, comparing the outcomes of ASAS40 and BASDAI50 response criteria, as well as changes from baseline in BASDAI and BASFI scores.

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

Summary of evidence on comparative safety

In the PREVENT study at data cut-off 1 July 2019, the median duration of treatment in all patients that received secukinumab 150mg SC, with or without loading during the entire treatment period, was 540 days and in the placebo group was 145.5 days.[2]

Up to week 20 (the time at which patients could switch to secukinumab open label or another treatment), any treatment-emergent adverse event (AE) was reported by 61% (225/369) of patients receiving secukinumab and 54% (100/186) in the placebo group and these were considered treatment-related in 24% and 14% of patients respectively. Over the entire treatment period, in the secukinumab (with or without loading) and placebo groups respectively, patients with any AE were 79% (431/543) versus 65% (121/186); patients with a reported serious AE were 7.2% (39/543) versus 4.3% (8/186), the proportion of AEs that led to temporary dose interruptions were 14% versus 8.1% and patients discontinuing therapy due to an AE was 4.4% versus 1.6%.[2]

Over the entire treatment period, the most frequently reported treatment-emergent AEs of any grade with an incidence >5% in the secukinumab group were: nasopharyngitis (22% [122/543] versus 17% [32/186] in the placebo group), upper respiratory tract infection (11% versus 6.9%), diarrhoea (9.2% versus 5.4%), headache (8.5% versus 4.8%), back pain (6.4% versus 2.2%), arthralgia (6.3% versus 5.9%) and urinary tract infection (5.9% versus 2.2%).[2]

Overall, the EMA noted that secukinumab safety profile was well established and that no new safety concerns were identified. The Agency also noted that there was a lack of long-term follow-up safety data in this indication but that there was extensive data on long-term safety follow-up in the other licensed indications.[2]

Summary of clinical effectiveness issues

AxSpA is a chronic inflammatory condition, which predominantly involves the spine and sacroiliac joints, with or without extra-spinal manifestations (such as psoriasis, and inflammatory bowel disease). AxSpA is classified into radiographic (ankylosing spondylitis; AS), and nr-axSpA based primarily on the presence of defined structural changes in the sacroiliac joints as detected on plain radiography. Patients with axSpA experience significant pain, stiffness and impaired physical function that may increase mortality. For patients with nr-axSpA, NSAIDs should be used as a first-

line treatment. TNF-alpha inhibitors such as adalimumab, certolizumab pegol, etanercept and golimumab are licensed and recommended for use in patients with severe nr-axSpA whose disease has responded inadequately to, or who cannot tolerate, NSAIDs. Treatment with another TNF-alpha inhibitor is recommended for people who cannot tolerate, or whose disease has not responded to, treatment with a first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response.[3-5] Secukinumab is the first IL-17A inhibitor to be licensed for the management of nr-axSpA. Clinical experts consulted by SMC considered that secukinumab fills an unmet need for adults who have responded inadequately to TNF-alpha inhibitors or where these are not suitable.

The primary outcome of ASAS40 at week 16 was achieved in 41% (68/164) of TNF-alpha inhibitor naïve patients receiving secukinumab and 29% (50/171) of TNF-alpha inhibitor naïve patients receiving placebo. This outcome is the most appropriate according to the EMA clinical guideline[6]. Results were statistically significant and considered clinically meaningful by the EMA..[2] Secondary outcomes at week 16, including HRQoL outcomes (SF-36 and ASQoL) supported the primary outcome. However, some important outcomes were not included in the hierarchical testing; for example, the spinal mobility assessment (Bath Ankylosing Spondylitis Metrology Index [BASMI]) considered important by the EMA, and the Ankylosing Spondylitis Disease Activity Score (ASDAS) response considered clinically relevant for prescribers were not included. Maintenance of effect until week 52 was also demonstrated. However, by week 52, 51% (94/185) patients in the secukinumab 150mg (with loading) group and 64% (119/186) of patients in the placebo group had switched to either open-label secukinumab 150mg (n=297) or standard of care (n=3). Due to permitted treatment switching at week 20 and allowed changes to concomitant therapies after week 16, the ability to interpret the relative safety and efficacy of secukinumab versus placebo beyond week 16 is limited. Assessments of efficacy and safety of beyond week 52 in the PREVENT study are not yet available, and it is unknown if treatment with secukinumab should be continued indefinitely.

A number of exploratory subgroup analyses were conducted and these were generally consistent with the primary analysis, including the subgroup of patients who previously received a TNF-alpha inhibitor. Only 10% (54/555) of patients had previously been treated with a TNF-alpha inhibitor so the effectiveness in this group is uncertain.

Some concomitant therapies were allowed, for example methotrexate [≤25mg/week] was permitted for patients who received it for at least 3 months and were on a stable dose for at least 4 weeks before randomisation; however, the study did not assess the role of any combination therapy and the effect of combination is uncertain.

There are no direct comparative data versus all the relevant comparators in patients with nr-axSpA. The submitting company conducted NMAs to compare secukinumab with relevant comparators (adalimumab, certolizumab pegol, etanercept, and golimumab). SMC is unable to present the results of the NMAs. The NMAs were limited by the small size of the network, the absence of any direct evidence and considerable heterogeneity across studies regarding patients' characteristics, population, imputation methods employed, and reported placebo response rates. Therefore, the conclusions are highly uncertain.

Clinical experts consulted by SMC generally considered that secukinumab is a therapeutic advancement as it is a new treatment option with a new mechanism of action. They considered that its place in therapy would be after TNF-alpha inhibitor therapy or after NSAID in patients unsuitable for TNF-alpha inhibitors. Secukinumab may have an advantage over currently used TNF-alpha inhibitors (except golimumab administered monthly) in that it administered monthly after loading.

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

Summary of comparative health economic evidence

The company submitted cost-utility analyses for the comparison of secukinumab versus licensed TNF-alpha inhibitors including adalimumab, adalimumab (biosimilar), etanercept, etanercept (biosimilar), golimumab, certolizumab pegol, and conventional care in biologic-naïve adult patients (primary analysis) and biologic-experienced patients (secondary analysis) versus conventional care only in the licensed indication. A cost-minimisation analysis was also presented.

A short-term decision-tree followed by a long-term cohort Markov model were used, with three health states: treatment maintenance for responders, conventional care for non-responders and dead. The time horizon for the cost-utility analysis was 60 years due to the chronic nature of the disease and early age of onset and the cycle length was 3 months.

All patients received either secukinumab for 16 weeks or a TNF-alpha inhibitor for 12 weeks, at the respective licensed doses, and only responders continued treatment thereafter. Clinical effectiveness data on BASDAI50 response rates, BASDAI change from baseline and BASFI change from baseline came from a Bayesian network meta-analysis in biologic-naïve patients consistent with the clinical case. Clinical effectiveness data in the biologic-experienced papulation came from the PREVENT trial. Following assessment of response, responders continued treatment until discontinuation due to loss of response or toxicity at a constant per- cycle rate of 0.015 or mortality modelled using general population all-cause mortality adjusted for sex and disease-specific mortality. Long term disease progression was modelled using BASFI score at time of response assessment as a function of Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) which measures radiographic progression. A relative treatment effect (versus conventional care) of 0.42 was assumed for all biologic therapy responders on entering the Markov model until treatment discontinuation. BASDAI score was assumed to remain constant for responders and initial gain was assumed to revert upon treatment discontinuation after which BASDAI remained constant.

HRQoL data were collected in the PREVENT study and analysed using a linear regression model with BASFI and BASDAI scores and an interaction term as dependent variables (best statistical fit). Utilities in the economic analysis were modelled as a function of changes in BASFI and BASDAI scores over time.

Aside from medicine acquisition and administration, other costs in the model included costs of disease monitoring and management associated with disease progression. Monitoring costs

included cost of specialist visits, full blood count, erythrocyte sedimentation rate, liver function test, urea and electrolytes, chest radiograph, tuberculosis Heaf test, antinuclear antibiotics, DNA test, MRI and CRP in the first three months. Following that, patients were assumed to only receive specialist visits, full blood count, erythrocyte sedimentation rate, liver function test, urea and electrolytes and chest radiograph per cycle. Disease progression costs were modelled as a function of BASFI score. Costs of management of adverse events were also accounted for in the analysis.

The cost-minimisation analysis compared the acquisition costs across medicines in the first year of treatment. Due to the loading dose in year 1, second-year costs were also presented for secukinumab only.

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 NHSScotland. Under the PAS, a simple discount was offered on the list price for secukinumab. A PAS discounts are also in place for golimumab and certolizumab pegol and were included in the results used for decision-making by using estimates of the comparator PAS prices.

Table 3: Base case results: secukinumab versus comparators (with PAS for secukinumab; list price for comparators)

Comparator	ICER
Conventional care	£7,613
Adalimumab	SW quadrant
Adalimumab (biosimilar)	SW quadrant
Etanercept	SW quadrant
Etanercept (biosimilar)	SW quadrant
Abbreviations: SW, south-west quadrant of the ICER plane- cheaper but less effective; ICER, incremental cost-effectiveness ratio	

Table 4: Base case results: secukinumab versus comparators (list price for all medicines)

Comparator	ICER
Golimumab	SW quadrant
Certolizumab pegol	SW quadrant
Abbreviations: SW, south-west quadrant of the ICER plane- cheaper but less effective; ICER, incremental cost-effectiveness ratio	

The results presented do not take account of the PAS for golimumab and certolizumab pegol but these were considered in the results used for decision-making. SMC is unable to present the results provided by the company which used an estimate of the PAS prices for golimumab and certolizumab pegol due to commercial confidentiality and competition law issues.

Table 5: Base case: cost-minimisation (list price for all medicines)

Comparator		Cost/dose	Doses/year	Total cost
Secukinumab	Year 1†	£609.39	16	£9,750
	Year 2+		12	£7,313
Certolizumab pegol		£357.50	26	£9,295
Etanercept		£178.75	52	£9,295
Etanercept biosimilar		£164.00	52	£8,528

Adalimumab	£352.14	26	£9,156
Adalimumab biosimilar	£308.13	26	£8,011
Golimumab	£762.97	12	£9,156

Table 6: Secondary analysis results: biologics-experienced population (with PAS for secukinumab)

	ICER
Conventional care	
Secukinumab	Dominant
Abbreviations: ICER, incremental cost-effectiveness ratio	

Selected scenario analyses presented in tables 7 and 8 are consistent with base case results.

Table 7: Selected scenario analyses: secukinumab versus comparators (with PAS for secukinumab; list price for all comparators)

Scenario	**Adalimumab**	**Adalimumab (biosimilar)**	**Etanercept**	**Etanercept (biosimilar)**
Time horizon: 5 years	SW quadrant	SW quadrant	SW quadrant	SW quadrant
Time horizon: 10 years	SW quadrant	SW quadrant	SW quadrant	SW quadrant
Using ASAS40 response criteria	SW quadrant	SW quadrant	SW quadrant	SW quadrant
Including treatment sequencing	SW quadrant	SW quadrant	SW quadrant	SW quadrant
BASDAI and BASFI reverting to natural history	SW quadrant	SW quadrant	SW quadrant	SW quadrant
Abbreviations: ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; SW, south-west quadrant of the ICER plane- cheaper but less effective; ICER, incremental cost-effectiveness ratio				

Table 8: Selected scenario analyses: secukinumab versus comparators (list price for all medicines)

Scenario	**Golimumab**	**Certolizumab**
Time horizon: 5 years	SW quadrant	SW quadrant
Time horizon: 10 years	SW quadrant	SW quadrant
Using ASAS40 response criteria	SW quadrant	SW quadrant
Including treatment sequencing	SW quadrant	SW quadrant
BASDAI and BASFI reverting to natural history	SW quadrant	SW quadrant
Abbreviations: ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; SW, south-west quadrant of the ICER plane- cheaper but less effective; ICER, incremental cost-effectiveness ratio		

The main limitations associated with the analyses were:

- Lack of direct comparative clinical-effectiveness data for secukinumab and TNF-alpha inhibitors leading to reliance on a NMA associated with uncertainties, as described in the clinical effectiveness section above.
- Lack of clinical effectiveness evidence for TNF-alpha inhibitors in biologic-experienced population leading to the assumption of non-responding patients only receiving conventional care in the economic model. In clinical practice, patients who lose response

are likely to start treatment with a different TNF-alpha inhibitor. The scenario analysis which included treatment-sequencing produced consistent results but was primarily based on assumptions. Experts suggested that secukinumab might be used as a second line of therapy for TNF-alpha inhibitors non-responders.

- There are uncertainties around the long-term disease progression in terms of BASFI and treatment discontinuation associated with secukinumab due to lack of clinical data. The economic model assumed secukinumab-treated patients to progress and discontinue treatment at the same rate as patients treated with TNF-alpha inhibitors. Additionally, important outcomes such as assessment of spinal mobility were not considered in the model.
- The cost-minimisation analysis compared annual medicine acquisition costs without accounting for discontinuation. Therefore, the results are only applicable to living responders. Results from the cost-utility analysis were considered by the committee as most relevant for decision-making.

Despite these limitations, the economic case has been demonstrated.

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

Summary of patient and carer involvement

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

- We received a patient group submission from the National Axial Spondyloarthritis Society (NASS), which is a registered charity.
- NASS has received 20.79% pharmaceutical company funding in the past two years, including from the submitting company.
- Axial spondyloarthritis (axSpA) including ankylosing spondylitis, is a form of inflammatory arthritis that mainly affects the spine. It is a painful and progressive long-term condition for which there is no cure. In addition to the spinal pain most often associated with axSpA, people with the condition can also have a range of complications and co-morbidities. Some of the less visible complications of axSpA can be the most debilitating – many people will suffer from severe fatigue and most will have a flare at some point which can make socialising, work and exercising problematic. The invisibility of this condition means it is often difficult to communicate its impact to loved ones, leading to a profound effect on relationships. The burden of disease for those with non-radiographic axSpA is not less than those with radiographic progression.
- Where NSAIDs are not effective or cannot be tolerated patients may need to move to anti TNF therapy. Anti TNF can be life changing for patients with axSpA. There are currently no

alternative treatments for non radiographic axial spondyloarthritis after anti TNF, unlike ankylosing spondylitis, and thus it is likely that this group of patients will have had to go back to anti-inflammatory medication and / or codeine based medications if they fail on anti TNF. Patients on anti TNF therapy and doing well worry about the future and have concerns about what would happen if efficacy started to decline or they developed side effects.

- Patients value the reassurance that another medicine such as secukinumab is available if needed. Having an alternative medicine could potentially help people with non radiographic axSpA stay economically active and live independent lives.

Additional information: guidelines and protocols

The British Society of Rheumatology and the British Health Professionals in Rheumatology published the "BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics" in 2017.[4] The guidance predates the availability of secukinumab and therefore no specific recommendations are made, however the guidance makes the following relevant recommendations:

- Patients with active disease who do not meet modified New York criteria for AS (radiographic axSpA) should also have had a positive MRI and/or raised CRP before starting treatment in a patient with nr-axSpA.
- Extra-articular manifestations and patient choice should be considered when selecting an anti-TNF agent. There are insufficient data to comment on relative efficacy in nr-axSpA. However, not all biologics are licensed for or effective in the treatment of extra-articular disease, so treatment choice should take into account comorbidities and the preferred route and frequency of administration.
- Initial efficacy response should be assessed following 3 to 6 months of therapy and responders should then be reassessed every 6 months.
- Response is defined as a reduction in the BASDAI and spinal pain VAS of ≥2 U from baseline.
- In the absence of an initial clinical response by 6 months, or failure to maintain response at two consecutive assessments, withdrawal of that anti-TNF agent should be considered.
- In the event of anti-TNF failure due to inefficacy or adverse events, an alternative anti-TNF agent should be offered if clinically appropriate.[4]

The National Institute for Health and Care Excellence (NICE) "Spondyloarthritis in over 16s: diagnosis and management (NG65)" was updated in 2017. The guidance recommends the use of adalimumab, certolizumab pegol and etanercept, within their marketing authorisations, as options for treating severe non-radiographic axial spondyloarthritis in adults whose disease has responded inadequately to, or who cannot tolerate, NSAIDs. The guideline also advises that the choice of

treatment should be made after discussion between the clinician and the patient and recommends that if more than one treatment is suitable, the least expensive (taking into account administration costs and patient access schemes) should be chosen. The guidance recommends that people who cannot tolerate, or whose disease has not responded to, treatment with a first TNF-alpha inhibitor, or whose disease has stopped responding after an initial response, be treated with another TNF-alpha inhibitor.[5]

The Assessment of SpondyloArthritis international Society (ASAS) in collaboration with the European League Against Rheumatism (EULAR) published a guidance in 2006 (ASAS-EULAR) which was last updated in 2016. This guidance states that axial spondyloarthritis (axSpA) "*comprises the whole spectrum of patients with radiographic sacroiliitis (AS or radiographic axSpA) and without radiographic sacroiliitis (non-radiographic axSpA)*", however the guideline predates the availability of secukinumab and therefore no specific recommendations are made. The guidance does however make the following relevant recommendations:[3]

- Patients suffering from pain and stiffness should use an NSAID as first-line treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs continuous use is preferred if symptomatic otherwise
- Patients with purely axial disease should normally not be treated with conventional synthetic DMARDs (csDMARDs); sulfasalazine may be considered in patients with peripheral arthritis
- bDMARDs should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start with TNF-alpha inhibitor therapy
- If TNF-alpha inhibitor therapy fails, switching to another TNF-alpha inhibitor or an anti-IL-17 therapy should be considered.

Additional information: comparators

Adalimumab (and its biosimilar), certolizumab pegol, etanercept (and its biosimilar), and golimumab.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
Secukinumab	**150mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.**	**First year: 9,750** **Subsequent years: 7,313**

Costs from BNF online on 02 October 2020. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 33 patients estimated to receive treatment in year 1 rising to 119 patients in year 5.

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. This template does not incorporate any PAS discounts associated with comparator medicines.

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

References

1. Novartis Pharmaceuticals UK Ltd. Secukinumab 150 mg solution for injection in pre-filled pen (Cosentyx®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated [19 Aug 2020].

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3. Van Der Heijde D, Ramiro S, Landewe R, Baraliakos X, Van Den Bosch F, Sepriano A*, et al.* 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Annals of the Rheumatic Diseases. 2017;76(6):978-91.

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6. Agency EM. Guideline on the Clinical Investigation of Medicinal Products for the Treatment of Axial Spondyloarthritis. 2017 [cited 14/09/2020]; Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-medicinal-products-treatment-axial-spondyloarthritis-revision-1_en.pdf.

This assessment is based on data submitted by the applicant company up to and including 12 October 2020.

**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*

Medicine 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 medicine 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 NHSScotland 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 NHSScotland 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.