East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Evidence review for Surrey Prescribing Clinical Network

Medicine and proposed indication	Secukinumab (Cosentyx®, Novartis) for treating moderate to severe plaque psoriasis. Adults
Requested by	NICE Technology Appraisal Guidance 350. Issued July 2015. Full guidance available at: https://www.nice.org.uk/guidance/ta350

SUMMARY

Clinical Effectiveness

Secukinumab is recommended, within its marketing authorisation, as an option for treating adults with plaque psoriasis only when:

- the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10
- the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them
- the company provides secukinumab with the discount agreed in the patient access scheme.

Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these people. An adequate response is defined as either:

- a 75% reduction in the PASI score from when treatment started (PASI 75) or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

Overview of the clinical trials

The company did a systematic review of the literature to identify studies evaluating the clinical effectiveness and safety of secukinumab for treating people with moderate to severe chronic plaque psoriasis. It identified 5 relevant international, multicentre, phase 3, double-blind, randomised, controlled trials: 3 superiority trials compared secukinumab with placebo (ERASURE; JUNCTURE; FEATURE) and 1 compared secukinumab with both placebo and etanercept (FIXTURE). Another trial (SCULPTURE) was a non-inferiority trial comparing 2 different dosing regimens of secukinumab: a regular dose regimen of secukinumab compared with re-treatment with secukinumab only at relapse.

The company did not find any other head-to-head studies, and therefore did a network meta-analysis to compare secukinumab with all 5 comparators identified in the scope (best supportive care, etanercept, ustekinumab, adalimumab and infliximab). The company did not find any relevant non-randomised controlled or observational studies.

The co-primary outcome measures in all 4 placebo-controlled trials were measured at week 12: PASI 75 (that is, a 75% reduction from baseline in PASI score), and an IGA score of 0 or 1 (indicating clear or almost clear of disease). The PASI response was used in the model and the network meta-analysis. Therefore, this final appraisal determination presents results only for PASI outcomes. The company analysed the data using intention-to-treat methods. The company reported odds ratios for FIXTURE and ERASURE, and 'risk differences' (the difference in proportions of patients in whom the outcome was reached) for JUNCTURE and FEATURE.

In all 4 placebo-controlled trials, there were statistically significant improvements with secukinumab in the

co-primary outcomes compared with placebo. For example, across trials, at week 12, 75.9% to 86.7% of patients randomised to secukinumab had a PASI 75 response, compared with a 0% to 4.9% ($p<0.0001$ all trials) of patients randomised to placebo. There were also statistically significant improvements with secukinumab compared with etanercept. PASI 75 response was 77.1% with secukinumab compared with 44% with etanercept ($p<0.0001$). The company also noted that response to secukinumab for these outcomes continued to increase between week 12 and week 16 in the FIXTURE and ERASURE trials.

Secondary outcomes in the placebo-controlled trials included assessing PASI 75 at different time points (weeks 16 and 52), different PASI responses, for example, at week 12, PASI 50/90/100 responses, and maintenance of PASI 75 and health-related quality of life. The effectiveness of secukinumab for these secondary outcomes was consistent with the results for 12-week PASI 75 in that there were improvements with secukinumab compared with placebo across the 4 placebo-controlled trials (statistical significance was achieved for some outcomes, but the company did not perform or present statistical analyses for all outcomes). For example, week-12 PASI 100 (that is, complete clearance of the disease) ranged from 24% to 43% for secukinumab (across all trials), was 4.3% for etanercept (FIXTURE trial) and ranged from 0% to 0.8% for placebo. In the FIXTURE trial at week 52, 36.2% of patients had a PASI 100, which was higher than with etanercept (9.9%). The company had not predefined this as an outcome, so did not do statistical analyses.

In section 4.7, the committee noted that a PASI 100 response (that is, complete clearance of disease), occurred more often with secukinumab than with either placebo or etanercept, and that complete clearance of disease was the most important outcome for patients'.

Reproduced from the Summary of Appraisal Committee's Key Conclusions (section 4 page 36 of the full guidance) with reference to the section within the full guidance.

Full guidance available at: https://www.nice.org.uk/guidance/ta350

Key conclusion
Section 1.1, 4.7.

The Committee concluded that the clinical evidence had shown that secukinumab was clinically superior to both placebo and etanercept for all primary and secondary outcomes.

Availability, nature and quality of evidence
Section 3.1, 4.4, 4.8

The company included 5 relevant international, multicentre, phase 3, double-blind, randomised, controlled trials. The Committee agreed that the company had included relevant, high-quality trials.

The Committee considered that the network meta-analysis excluded outcomes other than effectiveness, such as utility values, and did not address possible heterogeneity of the patients involved in the trials (for example, prior treatments received). However, it noted that the secukinumab trial populations were likely to be similar with respect to heterogeneity to the trials to which they were being compared, and which formed the basis for previous NICE guidance. The network meta-analysis also generated a low value of people who achieved PASI 75 (3.6%).

Overall, the Committee agreed that, despite the limitations of the network meta-analysis, it was sufficient for the purposes of decision-making.

Safety

Adverse reactions
Section 4.9

The Committee concluded that secukinumab did not appear to be associated with adverse events not already known for biological treatments in general.

Patient factors

Clinical need of patients, including the availability of alternative treatments
Section 4.1, 4.2

The Committee heard from the patient and clinical experts that psoriasis can be physically and psychologically debilitating, particularly if located on the hands, feet and genitals.

The Committee heard that, because psoriasis is visible, it can make people feel isolated and lonely, which could lead to them losing self-confidence and avoiding social situations, and could affect career opportunities and influence intimate relationships.

The clinical experts informed the Committee that, if the disease no longer responds to treatment with 1 biological, they offer patients another biological. This pattern is likely to be repeated over a patient's lifetime; clinical experts noted that it is therefore valuable to have a range of biological treatment options with different mechanisms of action available.

The technology
Section 4.18

The Committee noted that secukinumab offers a different mechanism of action to the other NICE-recommended biological treatments, and some patients experience complete clearance of disease.

The Committee also heard from clinical and patient experts that severe psoriasis can be associated with a stigma, apart from its effect on health-related quality of life, and that NICE methods acknowledge giving extra weight to such conditions.

The Committee agreed that these benefits had not been captured when calculating the quality-adjusted life years (QALYs), that secukinumab reflected a step change in treatment and that the drug could be considered innovative.

Equalities considerations and social value judgements
Section 4.9, 4.22

A patient organisation expressed the view that people with psoriatic arthritis affecting their fingers could find using the pre-filled syringe difficult, as could those with a needle phobia.

The Committee concluded that the monthly administration of secukinumab would be easier to manage for these patients than of other biological agents that need to be injected more frequently. Bearing in mind that the Committee had recommended secukinumab, it concluded that there was no need to alter or add to its recommendations.

Cost implications

The recommended dosage is 300 mg at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4. The undiscounted price for 2 × 150 mg prefilled pen or syringe is **£1218.78** (excluding VAT, 'Monthly Index of Medical Specialities' [MIMS] May 2015).[2]

The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of secukinumab, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.[2]

18,600 people in England may be eligible for treatment with secukinumab for psoriasis each year. This equates to 35 people per 100,000 population.[4]

Expert clinical opinion estimated that it may be up to 20% of the eligible population.[4]

Relevant guidance / reviews

Secukinumab for treating moderate to severe plaque psoriasis

NICE technology appraisal guidance 350
Issued July 2015
SMC Secukinumab 150mg pre-filled syringe, 150mg pre-filled pen (Cosentyx®) SMC No. (1054/15).
08 May 2015

Likely place in therapy relative to current treatments

What is the position of the treatment in the pathway of care for the condition?
Section 4.2

The Committee heard from the clinical experts that, if psoriasis is not adequately controlled by first-line treatments including topical treatments, systemic non-biological therapies (such as methotrexate) and phototherapy, people may receive second-line biological treatments, which they continue to receive as long as the drugs continue to work. If the disease no longer responds to treatment with 1 biological, clinicians offer patients another biological.

The Committee agreed that biological treatments were the most appropriate comparators for secukinumab.

Secukinumab will be incorporated into the local treatment with biologics for plaque psoriasis pathway.

Recommendation to PCN

RED – Payment by Results excluded (PbRe).

Secukinumab is recommended, within its marketing authorisation, as an option for treating adults with plaque psoriasis only when:

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- the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them
- the company provides secukinumab with the discount agreed in the patient access scheme.

Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these people. An adequate response is defined as either:

- a 75% reduction in the PASI score from when treatment started (PASI 75) or
- a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.

Notification of treatment initiation will be made through Blueteq tick box forms as per usual for funding PbRe drugs.

Medicine details	
Name and brand name	Secukinumab (Cosentyx®) 150mg – Novartis Pharmaceuticals UK Ltd
Licensed indication, formulation and usual dosage	Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Secukinumab (Cosentyx®)150 mg solution for injection in pre-filled syringe Secukinumab (Cosentyx®)150 mg solution for injection in pre-filled pen Each pre-filled syringe contains 150 mg secukinumab in 1 ml. Each pre-filled pen contains 150 mg secukinumab in 1 ml. The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at Weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg. Consideration should be given to discontinuing treatment in patients who have shown no response up to 16 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 16 weeks. *Elderly patients (aged 65 years and over)* No dose adjustment is required *Renal impairment / hepatic impairment* Cosentyx has not been studied in these patient populations. No dose recommendations can be made. *Paediatric population* The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.[1] SPC available at: http://www.medicines.org.uk/emc/medicine/29848
Summary of mechanism of action, and relevant pharmacokinetics	Secukinumab (Cosentyx, Novartis) is a high-affinity, fully human monoclonal antibody that binds to and neutralises interleukin-17A, which is thought to be involved in the body's autoimmune response in diseases such as psoriasis.[2] Secukinumab is of the IgG1/κ-class produced in Chinese Hamster Ovary (CHO) cells.[1] Secukinumab is to be administered by subcutaneous injection.[1] Store in a refrigerator (2°C - 8°C). Do not freeze.[1] Contraindications - clinically important, active infection (e.g. active tuberculosis; see SPC section 4.4).[1]
Important drug interactions	Live vaccines should not be given concurrently with secukinumab (see SPC section 4.4). No interaction studies have been performed in humans. There is no direct evidence for the role of IL-17A in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A inhibitor secukinumab, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised co-medications. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, where the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of secukinumab therapy in patients being

	treated with these types of medicinal products, therapeutic monitoring should be considered.[1]
Monitoring requirements	The summary of product characteristics includes the following adverse reactions for secukinumab: upper respiratory tract infections (most frequently nasopharyngitis, rhinitis), oral herpes simplex, rhinorrhoea, diarrhoea and urticaria. For full details of adverse reactions and contraindications, see the summary of product characteristics.
Prescribing considerations	PbRe - RED
Other considerations	

Potential patient group (if appropriate to include)	
Brief description of disease	Plaque psoriasis is a lifelong condition. The physical effects of inflamed, itchy or painful scaling and flaking skin and scalp, with cracked fingers, toes, palms and soles can cause difficulty with washing and dressing, standing and anything that involves working with hands. Owing to the highly visible nature of psoriasis, patients often avoid social situations and it can affect employability. The psychological effects combined with the physical discomfort impact on all aspects of their lives. Amongst long-term conditions moderate to severe plaque psoriasis produces some of the greatest reductions in quality of life indices.[3]
Potential patient numbers per 100,000	18,600 people in England may be eligible for treatment with secukinumab for psoriasis each year. This equates to 35 people per 100,000 population.[4] Expert clinical opinion estimated that it may be up to 20% of the eligible population.[4]
Outcomes required	

Summary of current treatment pathway
Pathway for the use of biologics in plaque psoriasis waiting to be ratified by clinicians.

Evidence review
Secukinumab for treating moderate to severe plaque psoriasis NICE technology appraisal guidance 350 Issued July 2015 Full guidance available at: https://www.nice.org.uk/guidance/ta350

Equity / Stakeholder views (if relevant)	
Decisions of local Trusts DTCs and neighbouring APCs	
Recommendations from national / regional decision making groups	SMC Secukinumab 150mg pre-filled syringe, 150mg pre-filled pen (Cosentyx®) SMC No. (1054/15)[3] 08 May 2015 **ADVICE**: following a full submission **secukinumab (Cosentyx®)** is accepted for restricted use within NHS Scotland. **Indication under review:** treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. **SMC restriction:** for 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. Secukinumab was superior to placebo and to a tumour necrosis factor (TNF) antagonist for improving symptoms of patients with moderate to severe plaque psoriasis. This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost effectiveness of secukinumab. It is contingent upon the continuing availability of the Patient Access Scheme in NHS Scotland or a list price that is equivalent or lower.
Stakeholder views	
CCG priorities	

Health economic considerations

Cost per year per patient

Secukinumab is given subcutaneously. The recommended dosage is 300 mg at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4. The undiscounted price for 2 × 150 mg prefilled pen or syringe is £1218.78 (excluding VAT).[2]

Annual costs = £1218.78 x 13 = £19,500 per patient
Subsequent annual costs = £14,625.36 per patient

Additionally, tariff costs for one-off training as it is assumed that secukinumab will be delivered by homecare and patients will administer their own treatment, OPD at trust for monitoring and various monitoring tests based on NHS reference costs.

Alternative treatments cost per patient per year

Cost of relevant comparators:[3]

Drug	Dose Regimen	Cost per year (£)
Secukinumab	300mg SC at weeks 0, 1, 2, 3, and 4 and then monthly	First year: 19,500 Subsequent years: 14,625
Infliximab#	5 mg/kg IV at weeks 0, 2 and 6 weeks, then every 8 weeks	First year: 12,088 – 13,424 Subsequent years: 9,066 – 10,071
Etanercept	25mg SC twice weekly; or 50mg SC weekly*	9,295
Ustekinumab	45mg (or 90mg**) SC at weeks 0 and 4 then every 12 weeks	First year: 12,882 Subsequent years: 8,588
Adalimumab	80mg SC, then 40 mg alternate weeks***	First year: 9,860 Subsequent years: 9,156

Doses are for general comparison and do not imply therapeutic equivalence.
Costs for adalimumab and etanercept are from eVadis on 3 March 2015 and costs for ustekinumab and infliximab from MIMs March 2015. Costs for secukinumab from MIMs June 2015. Costs based on a bodyweight of 70kg.
* If necessary, etanercept 50mg SC twice weekly may be given for 12 weeks then 25mg twice weekly or 50mg weekly.
** ustekinumab 90mg given if bodyweight >100kg.
*** costs are based on one year of treatment but this will be shorter if there is no response.
# Costs for infliximab reflect the range of list prices for the reference product and biosimilar products.
SC = subcutaneous. IV = intravenous

Other financial considerations (if relevant)

The following assumptions have been made in the local costing template:

- The prevalence of psoriasis is 1.75% of the adult population of England (around 731,000 people).
- Of these people, 2.55% would be eligible for biological treatments (around 18,600 people).
- Organisations should estimate the uptake of secukinumab locally; expert clinical opinion estimated that it may be up to 20% of the eligible population.
- People move between biological treatments when the treatment that they are on is no longer clinically effective.
- The cost impact is measured using the maintenance dose for treatments that

	have an initial and a maintenance dose. • Costs of monitoring have not been included because they will be the same for all treatments. There may be savings from using secukinumab, depending on the mix of treatments replaced. Secukinumab is administered subcutaneously, so if there is a movement from treatments that are infused there may be savings in the cost of administration. The Committee noted that secukinumab has a different mechanism of action from the other biological treatments recommended by NICE for psoriasis. It also noted that some patients have complete clearance of their disease with secukinumab. Where people have complete clearance of their disease future treatment costs may be avoided. It is not possible to estimate the number of people who will have complete clearance based on currently available data.[4]
Health economic data (if available)	

References

1 emc. SPC Cosentyx 150mg solution for injection. Last updated on eMC on 11 May 2015. Available at: https://www.medicines.org.uk/emc/medicine/29848 <accessed 7.9.15>

2 National Institute for Health and Care Excellence. Secukinumab for treating moderate to severe plaque psoriasis. NICE TA 350. July 2015. Available at: https://www.nice.org.uk/guidance/ta350 <accessed 7.9.15>

3 Secukinumab 150mg pre-filled syringe, 150mg pre-filled pen (Cosentyx®) SMC No. (1054/15). Scottish Medicines Committee. May 2015. Available at: http://www.scottishmedicines.org/SMC_Advice/Advice/1054_15_secukinumab_Cosentyx/secukinumab_Cosentyx <accessed 7.9.15>

4 National Instiitute for Health and Care Excellence. Costing statement: Secukinumab for treating moderate to severe plaque psoriasis(TA350). July 2015. Available at: https://www.nice.org.uk/guidance/ta350/resources/costing-statement2 <accessed 7.9.15>

Date:7.9.15

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Declaration of interest: None

Reviewed by:

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1	7.9.15	T. Bahra	Draft	Available for comment

East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Comments on Evidence review for Surrey Prescribing Clinical Network

Please include any comments you have answers to any questions asked as well as any additional references you feel may need to be included in the review. If there are any other of your colleagues that you feel we need to engage with please also let us know their names and where/how they can be contacted.

Medicine and proposed indication	
Prepared by	Name, designation and organisation
Comments on evidence review	
Additional evidence and references for consideration	Include any additional evidence and references you would like to submit for inclusion in the evidence review
Specific clinical questions	Specific questions arising from review
Other colleagues who should be contacted	Include name, designation and contact details of any other colleagues who should be consulted about this evidence
Declaration of interests	For example – any teaching, training, grants, consultancy, research funding, stock holding, nurse funding, equipment

Signature …….. Date ……