Technology Assessment Report commissioned by the NIHR HTA Programme on behalf of NICE – Final protocol

1. Title of the project

Certolizumab pegol and secukinumab for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs

2. Name of TAR team and 'lead'

Team: CRD/CHE Technology Assessment Group (Centre for Reviews and Dissemination/Centre for Health Economics), University of York

Lead: Dr Nerys Woolacott, Senior Research Fellow, Centre for Reviews and Dissemination, University of York, York, YO10 5DD.
Tel: 01904 321074, Fax: 01904 321041, nerys.woolacott@york.ac.uk

3. Plain English Summary

Psoriatic arthritis is an inflammatory disease where body joints become painful, inflamed and sore. It is often preceded by psoriasis, which is a skin and nail condition that causes a red, scaly rash, which can affect any part of the body. It has been estimated that psoriatic arthritis occurs in around 6% of patients with psoriasis. There is no specific test for psoriatic arthritis, with diagnosis being based on patient symptoms and physical examination. As psoriatic arthritis involves both skin and joints it can greatly reduce a person's quality of life impairment and reduce life expectancy.

Conventional treatment for severe active psoriatic arthritis usually begins with non-steroidal anti-inflammatory drugs, followed by disease-modifying anti-rheumatic drugs. Where necessary these may then be followed by one of several available biologic therapies (these are derived from biological rather than chemical sources).

The purpose of this project is to assess the benefits and adverse effects of two of the newer biologic therapies - certolizumab pegol and secukinumab - for treating active and progressive psoriatic arthritis in patients who have an inadequate response to conventional treatment. This will be done by identifying and analysing data from relevant clinical trials. This study will also evaluate whether these two biologic therapies are a cost-effective use of NHS resources when compared with the other therapies currently recommended by NICE for treating psoriatic arthritis.

4. Decision problem

- **Objectives**

The aims of the study are to determine the clinical effectiveness and cost effectiveness of certolizumab pegol and secukinumab within their marketing authorisations for treating active psoriatic arthritis in adults for whom disease-modifying anti-rheumatic drugs have been inadequately effective.

- **Background**

Psoriatic arthritis is an inflammatory arthritis closely associated with psoriasis of the skin and nails but distinct from rheumatoid arthritis. Although any joint may be affected, psoriatic arthritis typically affects joints in the hands, feet and spine. It is a long-term condition that progresses in the joints

although its course may be erratic, with flare-ups and remissions. Arthritis symptoms include inflamed (swollen), stiff and painful joints; psoriasis symptoms include patchy, raised, red areas of inflamed skin with scaling.[1] Overall, because psoriatic arthritis involves both skin and joints it can result in significant quality of life impairment, joint deformity and psychosocial disability.[2, 3]

It is difficult to define psoriatic arthritis because there are no precise classification criteria or diagnostic markers.[4] Psoriatic arthritis can be difficult to diagnose because it has similar symptoms to people with other forms of arthritis. The difference between psoriatic arthritis and rheumatoid arthritis is that the pattern of joint involvement is commonly asymmetric, and involves the distal interphalangeal joints (in the hands and feet) and nail lesions. Most patients with psoriatic arthritis will have developed psoriasis first, although joint involvement appears first in 19% of patients and concurrently with psoriasis in 16% of cases.[3] The prevalence of psoriatic arthritis in England in 2013 was estimated to be around 53,900 to 161,600 people. Unlike rheumatoid arthritis which is more common in women, psoriatic arthritis affects men and women equally and its incidence peaks between the ages of 30 and 55 years.[5]

The clinical management of psoriatic arthritis aims to suppress joint, tendon and ligament inflammation, and to manage the skin symptoms of the disease. Current practice involves early diagnosis and early use of non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular corticosteroid injections. For patients who do not respond to these treatments disease-modifying anti-rheumatic drugs (DMARDs) are then used (i.e. methotrexate, sulfasalazine, leflunomide, azathioprine or ciclosporin). When DMARDs are ineffective, or not tolerated, biologic therapies may be used.[6] As patents for the early biologics expire, biosimilar therapies are likely to become available; infliximab biosimilars are already licensed for treating psoriatic arthritis.

- **Interventions**

Certolizumab pegol (Cimzia, UCB Pharma) is a biologic therapy (a monoclonal antibody which targets tumour necrosis factor (TNF)) which is administered subcutaneously. Certolizumab pegol in combination with methotrexate has a marketing authorisation in the UK for treating active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. Certolizumab pegol can be given as monotherapy if methotrexate cannot be tolerated or when continued treatment with methotrexate is inappropriate. Normally, treatment starts with two (200mg) injections. This is followed by a further two injections at the same dose, two and four weeks later. After this, a maintenance dose of 200 mg given as one injection, every fortnight.

Secukinumab (Cosentyx, Novartis), which is also administered subcutaneously, is a different type of biologic therapy to certolizumab pegol, being a monoclonal antibody which targets the interleukin 17A (IL-17A) receptor (rather than targeting TNF). Secukinumab alone or in combination with methotrexate has a marketing authorisation in the UK for treating active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. The recommended dose is 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4. For patients with concomitant moderate-to-severe plaque psoriasis, or who are anti-TNF inadequate responders, the recommended dose is 300 mg.

- **Place of the interventions in the treatment pathway**

It is anticipated that trials may have recruited a range of patients with respect to their position in the treatment pathway. Therefore, where data permit, sub-group analyses will be performed to determine

the efficacy and cost-effectiveness of certolizumab pegol and secukinumab at the following positions in the treatment pathway:

- Patients who have only received one prior non-biological disease modifying anti-rheumatic drug (DMARD)
- Patients whose disease has inadequately responded to at least 2 DMARDs
- Patients whose disease has inadequately responded to both DMARDs and biological therapies

- **Previous NICE appraisals**

There have been no previous NICE Technology Appraisals (TA) of certolizumab pegol or secukinumab for psoriatic arthritis, though there have been several appraisals of other biologics for psoriatic arthritis: TA199 (etanercept, infliximab and adalimumab), TA 220 (golimumab), and TA340 (ustekinumab).[9-11] Apremilast, which is not a biologic, is currently undergoing a NICE appraisal for treating adults with active psoriatic arthritis that has not responded to prior DMARD therapy, or where such therapy is not tolerated.[12]

NICE recommends the use of etanercept, infliximab, adalimumab and golimumab when a person has peripheral arthritis (in large joints i.e. elbows, wrists, knees, and ankles) with three or more tender joints and three or more swollen joints, and the psoriatic arthritis has not responded to at least two other DMARDs, given on their own or together.[10, 11] Ustekinumab (a monoclonal antibody that targets interleukin-12 (IL-12) and IL-23) is another biologic recommended as a possible treatment, specifically when DMARDs have not worked well enough, providing that treatment with TNF alpha inhibitors is not suitable, or the person has had a TNF alpha inhibitor before.[9]

A number of key areas of uncertainty and potential limitations of the evidence base were identified from the previous appraisals.
These include:

1. The lack of direct head-to-head trial evidence evaluating the relative efficacy and safety of the biologics
2. Some limitations in the external validity of the trial populations (i.e. the trial populations had some differences from populations seen in routine clinical practice)
3. Lack of patient registry data for psoriatic arthritis
4. The long-term effectiveness of biologics in controlling disease activity
5. The prescription cost of biologics and also the cost of treating psoriasis in different levels of severity
6. The progression of Health Assessment Questionnaire (HAQ) score on and off treatment, and the length of time biologics are assumed to be effective
7. Long term progression of psoriatic arthritis with and without biologics
8. The lack of an optimal outcome measure for psoriatic arthritis
9. The rate of treatment withdrawal and the adverse effects associated with the long-term use of biologics
10. A lack of evidence on the efficacy and safety of the sequential use of biologics

The assessment group will consider and attempt to address these limitations and areas of uncertainty using relevant evidence where available.

5. Report methods for synthesis of evidence of clinical effectiveness

The protocol details will be submitted for registration on PROSPERO, an international database of prospectively registered systematic reviews in health and social care. A systematic review of the clinical effectiveness will be performed following the general principles recommended in CRD's guidance and the PRISMA statement.

A pragmatic approach will be applied to the additional assessment questions: systematic methods will be used to identify studies, although full systematic review methodology will not be undertaken for every question.

- **Search strategy**

Searches of electronic databases will be carried out to identify relevant randomised controlled trials (RCTs), open-label or patient registry studies of certolizumab pegol, secukinumab, etanercept, adalimumab, infliximab, golimumab, apremilast and ustekinumab for psoriatic arthritis. The searches will cover biosimilars which have been licensed for psoriatic arthritis (see Appendix).

The searches for certolizumab pegol and secukinumab for psoriatic arthritis will not be restricted by date. However, as etanercept, adalimumab, infliximab, golimumab, apremilast and ustekinumab for psoriatic arthritis have already been subject to previous technology appraisals, the relevant studies identified in these appraisals will be included with update searches performed based on the search dates of the previous appraisals.

A draft search strategy developed in MEDLINE (Ovid) is provided in the Appendix. This will be adapted as necessary to run on the other databases to be searched. A sensitivity-maximising RCT search filter will be used; this should ensure that both all relevant RCTs and many potentially useful non-RCT studies will be retrieved. The database searches will not be restricted by language. The following databases will be searched: MEDLINE, MEDLINE In-Process, PubMed, EMBASE, Science Citation Index, Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) database, and the Cochrane Central Register of Controlled Trials (CENTRAL).

Information on studies in progress, unpublished research or research reported in the grey literature will also be sought by searching a range of relevant resources including: Conference Proceedings Citation Index - Science, PROSPERO, ClinicalTrials.gov, WHO International Clinical Trials Registry portal and the EU Clinical Trials Register. The U.S. Food and Drug Administration website and the European Medicines Agency website will be searched to identify any relevant additional trial data or analyses.

In addition to the data in RCTs, open-label and registry studies, information on adverse events will be sought from systematic reviews of biologics across indications. Citation searches will be carried out as necessary to identify any open-label extension studies, patient registry studies, systematic reviews or clinical guidelines which have not been identified by the main searches.

Update searches will be performed at the time of receipt of the company submissions.

- **Eligibility criteria**

Two reviewers will independently screen all titles and abstracts. Full manuscripts of any titles/abstracts that may be relevant will be obtained where possible, and the relevance of each study assessed by two

reviewers according to the criteria below. Any discrepancies will be resolved by consensus and, if necessary, a third reviewer will be consulted. Eligible studies which are available only as conference abstracts will be included (and attempts will be made to contact authors for further data).

The following eligibility criteria will be used to identify relevant studies:

Study designs

Randomised or quasi-randomised controlled trials will be eligible for the review of clinical efficacy and safety. For the eligible interventions (see below), all open-label extension studies of RCTs will also be included. For the comparators (below), open-label extensions will be identified and listed with the main focus being on those studies which report data relating to the longest duration of follow up available for each individual comparator.

To evaluate the adverse effect profiles of the different biologics the eligible study designs will be systematic reviews which cover a range of diseases, and large observational studies in patients with psoriatic arthritis.

Prospective registry studies which include psoriatic arthritis patients receiving biologics will be eligible to identify data on treatment adherence, treatment withdrawal, and the rates and efficacy of switching to new biologics (i.e. sequential use). Potentially relevant registry studies will be sought and identified with a focus on those deemed to be most clinically relevant and appropriate to the UK setting. This will be decided based on examination of study characteristics and discussion with our clinical adviser.

Studies will also be sought on the longer-term natural history of psoriatic arthritis in populations which have not taken a biologic therapy.

Interventions

Certolizumab pegol and secukinumab will be eligible at their licensed doses. Studies comparing these two treatments with each other will also be eligible.

Comparators

The following comparators will be eligible for inclusion:

- Placebo
- DMARDs: methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, azathioprine and ciclosporin
- Biologic therapies: adalimumab, etanercept, golimumab, infliximab and ustekinumab, including any licensed biosimilars
- Apremilast
- Best supportive care.

Biologics and apremilast may be used with or without concomitant DMARDs. Only studies which include treatments used at their licensed dose will be eligible.

Head-to-head trials of the five biologic comparators (and biosimilars) and apremilast are eligible, but are anticipated to be rare. Therefore, to allow comparisons of active treatments via network

meta-analysis, the biologic comparators and apremilast may also be compared with either placebo or with a DMARD.

Participants

Eligible studies will be of adults with active psoriatic arthritis for whom disease-modifying anti-rheumatic drugs have been inadequately effective.

Outcomes

For RCTs and their associated open-label studies the eligible outcomes will be:

- Disease activity, using the following multi-domain measures: PsARC, ACR 20/50/70
- Functional capacity (assessed using HAQ)
- Radiographic assessment of disease progression
- Response of psoriatic skin lesions (assessed using PASI)
- Measures of dactylitis, enthesitis, and tendonitis
- Mortality
- Health-related quality of life (assessed using EQ-5D or SF-36)
- Adverse effects of treatment, focusing on the key adverse events identified from previous studies of biologics: malignancies, serious infections, reactivation of latent tuberculosis, injection site reactions, and withdrawals due to adverse events

For patient registry and natural history studies, outcomes will be restricted to those detailed in the *Study designs* section, and to outcomes identified as being useful to inform parameters in the economic model.

- **Data extraction strategy**

Data relating to both study design and quality will be extracted by one reviewer using a standardised data extraction form and independently checked for accuracy by a second reviewer. Disagreements will be resolved through consensus, and if necessary, a third reviewer will be consulted. If time constraints allow, attempts will be made where possible to contact authors for missing data. Data from relevant studies with multiple publications will be extracted and reported as a single study.

To avoid unnecessary duplication of work, where possible, relevant data presented in previous NICE technology appraisal reports may be extracted (and then checked for any transcription errors); additional data may also be extracted where appropriate.[9-11]

Subgroup data relating to patient position in the treatment pathway (see section 4) and reasons for previous treatment failure may be requested from manufacturers depending on the availability of the data submitted originally.

- **Quality assessment strategy**

The quality of RCTs will be assessed using the Cochrane risk of bias tool, with additional assessments made for baseline imbalance of important prognostic factors. The relevant prognostic and treatment response indicators will be identified from both published research and clinical advice. The risk of bias assessments will be performed by one reviewer, and independently checked by a second. Disagreements will be resolved through consensus, and if necessary, a third reviewer will be consulted.

- **Methods of analysis/synthesis**

The analysis and synthesis of clinical data will be performed in distinct sections. Study characteristics and risk of bias assessments will be presented in a series of structured tables and summarised narratively.

Where sufficient clinically and statistically homogenous data are available, studies will be pooled for the review outcomes using meta-analytic techniques. It is anticipated there will be very few head-to-head trials comparing the different interventions and comparators (most trials are expected to be placebo-controlled). Therefore, if feasible and appropriate, network meta-analyses using Bayesian statistical methods will be performed for the outcomes required to populate the economic model. This will provide information on the benefits of the active treatments relative to each other. The approaches used in previous appraisals will be explored for their relevance to this assessment.

Clinical and methodological heterogeneity will be evaluated, with sensitivity or subgroup analyses performed where appropriate, and where available data permit. Studies judged to be at high risk of bias will be removed in sensitivity analyses.

If the available evidence allows, subgroup analyses will explore the impact of :

- different patient positions in the care pathway (as described in section 4) and
- different reasons for previous treatment failure (e.g. due to lack of efficacy, contraindication, or adverse events)

6. Report methods for synthesising evidence of cost-effectiveness

- **Review of existing cost-effectiveness evidence**

A systematic search will be used to identify studies of the cost-effectiveness of certolizumab pegol and secukinumab within their marketing authorisations for treating active psoriatic arthritis in adults for whom disease-modifying anti-rheumatic drugs have been inadequately effective. The following databases will be searched: NHS Economic Evaluations Database, EconLIT, MEDLINE, MEDLINE in process, PubMed, EMBASE, CENTRAL, Science Citation Index, and Conference Proceedings Citation Index – Science. The search strategy will consist of a set of terms for each drug combined with terms for psoriatic arthritis. A search strategy filter to limit retrieval to economic studies will also be applied.

A broad range of studies will be considered in the assessment of cost-effectiveness including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Only economic evaluations that compare two or more options and consider both costs and consequences (including cost-effectiveness, cost-utility and cost-benefit analyses) will be included in the review of economic literature for certolizumab pegol and secukinumab.

The quality of the cost-effectiveness studies will be assessed according to a checklist updated from that developed by Drummond *et* al.[13] This checklist will reflect the criteria for economic evaluation detailed in the methodological guidance developed by the National Institute for Health and Care Excellence (NICE). This information will be tabulated and summarised within the text of the report. In particular, information will be extracted on the comparators, study population, main analytic approaches (e.g. patient-level analysis/decision-analytic modelling), primary outcome specified for the economic analysis, details of adjustment for quality-of life, direct costs and indirect costs, estimates of

incremental cost-effectiveness and approaches to quantifying decision uncertainty (e.g. deterministic/probabilistic sensitivity analysis).

To further inform the conceptualisation of a de-novo model, a separate and broader search will also be undertaken to identify relevant cost-effectiveness studies for the comparators specified in the final scope, including etanercept, adalimumab, infliximab, golimumab, apremilast, and ustekinumab. These may include DMARDS as comparators; however we will not specifically search for cost-effectiveness studies of DMARDS. The following databases will be searched: NHS Economic Evaluations Database, EconLIT, MEDLINE, MEDLINE in process, EMBASE, CENTRAL, Science Citation Index, and Conference Proceedings Citation Index – Science. The search strategy will consist of a set of terms for each drug combined with terms for psoriatic arthritis. A search strategy to limit retrieval to economic studies will also be applied. This separate search will be date restricted to identify studies published since the previous MTA (TA199). Additional hand-searching of related Technology Appraisals (TA 199, 220, 340 and ID682) will also be undertaken.

A more restricted set of studies will be included in this broader review; specifically only modelling studies. The review of these studies will further inform the conceptualisation of the de-novo model, focusing on the main structural assumptions, key areas of uncertainty and potential sources for specific parameter inputs (UK studies only). This review will be used to identify the central issues associated with adapting existing decision models to inform the development of a new decision model. We will also consult with clinical advisors at this conceptualisation stage.

A separate search will also be undertaken to identify published studies reporting utility estimates associated with disease progression in psoriatic arthritis. It is expected that measures of disease progression will be expressed in terms of multiple domain response criteria (e.g. ACR, PSARC, PASI) and other instruments of disease activity and functional capacity (e.g. PASI, HAQ-DI). Therefore a systematic search of utility studies will be carried out to identify relevant studies which i) directly estimate EQ-5D utility values; and ii) establish the relationship between generic measures of utility (in particular, the EQ-5D) and measures of disease progression (including mapping studies). This review will further inform the model conceptualisation stage as well as providing a potential source for the parameter inputs of the final model.

Several other key areas of uncertainty have been identified in previous appraisals. These include:

1. The assumption regarding the long-term extrapolation of the rate of disease progression in responders and non-responders to treatment (e.g. the rate of decline/improvement and whether this rate is linear or non-linear over time)
2. The rate of treatment withdrawal and the degree to which a patient's condition might be expected to rebound if therapy is withdrawn.
3. The proportion of patients who experience an initial improvement in their condition without biological therapy.
4. The use of radiographic evidence of progression and particularly the link to instruments measuring disease activity/functional capacity and quality of life.
5. Uncertainties regarding the effectiveness of treatments in TNF-alpha inhibitor naïve and exposed populations and possible variation in clinical effectiveness depending on the reason for withdrawal of the first TNF-alpha inhibitor (e.g. initial lack of efficacy, gradual loss of efficacy over time or adverse reactions.
6. The time horizon appropriate for evaluating cost-effectiveness.

7. Any association between the psoriasis measure of response, e.g. PASI and the arthritis response, e.g. PSARC.

The areas will be further considered within the cost-effectiveness reviews to further inform the findings from clinical effectiveness reviews. The presence of any additional data gaps that may need to be filled during the development of the model will be identified and additional searches may be required. We will also work with our clinical advisors at the start of the project to identify relevant UK data sources and will make contact with the relevant investigators with a view to securing access to this data should this be required.

- **Development of a new decision-analytic model**

A new decision-analytic model will be developed to estimate the cost-effectiveness of certolizumab pegol and secukinumab within their marketing authorisations for treating active psoriatic arthritis in adults. Where data permits, the comparators included will be consistent with the final NICE scope. This includes:
For people who have only received one prior non-biological DMARD

- Disease modifying anti-rheumatic drugs
- For people whose disease has inadequately responded to at least 2 DMARDs:
- Biological therapies (with or without methotrexate including etanercept, adalimumab, infliximab, golimumab, apremilast [subject to ongoing NICE appraisal],
- For people whose disease has not adequately responded to both DMARDs and biological therapies (including etanercept, adalimumab, infliximab and golimumab):
- Ustekinumab
- Apremilast [subject to ongoing NICE appraisal]
- Best supportive care

The model will be developed in accordance with the NICE reference case. The model will have 40-year horizon and will consider costs from the perspective of the National Health Services and Personal Social Services. Both costs and quality-adjusted life years (QALYs) will be discounted at 3.5% per annum.

Where sufficient data permits, the cost-effectiveness assessment will also explore the sequential use of certolizumab pegol and secukinumab as this has been identified as an important area of uncertainty in several previous appraisals (e.g. TA 340 and ID682). It is envisaged that, due to limitations in existing data, such analyses are likely to exploratory in nature. Furthermore, we do not envisage these analyses will specifically address the optimal sequence for certolizumab pegol and secukinumab and all potential comparators but will be more focused on how the cost-effectiveness of certolizumab pegol and secukinumab might be affected in different scenarios, e.g. in patients who have not had an adequate response, or who are intolerant to, one of the therapies or who have received multiple prior biological therapies.

The specific objectives of the cost-effectiveness analysis are:

- To structure an appropriate decision model to characterise patients' care and subsequent disease progression and the impacts of alternative therapies on the condition, in a way that is clinically acceptable.
- To populate this model using the most appropriate data. This is likely to be identified systematically from published literature, routine data sources and potentially using data elicited from relevant clinical experts.
- To relate initial and intermediate outcomes (such as response to treatment and HAQ-DI) to final health outcomes, expressed in terms of QALYs and resource use/costs. This is necessary in order to provide decision makers with an indication of the health gain achieved by each intervention, relative to its additional cost, in units which permit comparison with other uses of health service resources.
- To estimate the mean cost-effectiveness of each of the therapies based on an assessment of long-term NHS and Personal Social Service costs and quality-adjusted survival. A 40-year horizon will be assumed in the base-case to ensure consistency with previous appraisals.
- To characterise the uncertainty in the data used to populate the model and to present the uncertainty in these results to decision makers. A probabilistic model will be developed which requires that each input in the model is entered as an uncertain, rather than a fixed, parameter. Using Monte-Carlo simulation, this *parameter uncertainty,* is translated into uncertainty in the overall results. This helps decision makers understand the probability that, in choosing to fund an intervention, they are making the wrong decision – that is, *decision uncertainty.* This is presented using cost-effectiveness acceptability curves which show the probability that each intervention is cost-effective conditional on a range of possible threshold values which NHS decision makers attach to an additional QALY.
- To use scenario analysis to explore the sensitivity of the cost-effectiveness results to changes in the structural assumptions of the model and the time horizon.

The specific details of the data to be used to populate the model will have to await the development of the structure, the systematic searches of the literature and the manufacturers' submissions. In terms of the structure, we anticipate developing a similar 2-part model commonly used in previous appraisals: comprising a decision-tree to capture the initial response period (i.e. 12 and/or 24-weeks) and a longer-term Markov model to inform longer term progression assumptions. Estimates of short-term response are likely to be derived from the clinical effectiveness review and associated syntheses. Estimates of the natural history progression of psoriatic arthritis and patients' prognosis if they continue or withdraw from treatment may use observational evidence relevant to UK clinical practice, identified by the reviews of clinical and cost-effectiveness. The model will be developed in either Excel or R.

7. Handling the company submissions

All data submitted by the drug manufacturers will be considered if received by the review team no later than 18th April 2016. Data arriving after this date will only be considered if time constraints allow.

If efficacy and/or adverse effects data meet the inclusion criteria for the review then they will be extracted and quality assessed in accordance with the procedures outlined in this protocol.

Any economic evaluations included in the company submission will be assessed. This will include a detailed analysis of the appropriateness of the parametric and structural assumptions involved in any models in the submission and an assessment of how robust the models are to changes in key assumptions. Clarification on specific aspects of the model may be sought from the relevant manufacturer. An assessment of any differences between the published economic evaluations, those submitted by the manufacturers and any economic evaluation developed by us will be reported.

Any 'commercial in confidence' and 'academic in confidence' data taken from a company submission will be clearly marked in the NICE report (*highlighted*, *underlined and followed by an indication of the relevant company name e.g. in brackets)* and removed from the subsequent submission to the HTA.

8. Competing interests of authors

None.

9. References

1. Shiel WC. *Psoriatic arthritis*. MedicineNet.com; 2015. [cited 25th November 2015]. Available from: http://www.medicinenet.com/psoriatic_arthritis/article.htm.
2. Ruderman EM. Evaluation and management of psoriatic arthritis: The role of biologic therapy. *J Am Acad Dermatol* 2003;**49**:S125-32.
3. Galadari H, Fuchs B, Lebwohl M. Newly available treatments for psoriatic arthritis and their impact on skin psoriasis *Int J Dermatol* 2003;**42**:231-7.
4. Helliwell P, Taylor W. Classification and diagnostic criteria for psoriatic arthritis. *Ann Rheum Dis* 2005;**64**:ii3-ii8.
5. Gladman D, Antoni C, Mease P, Clegg D, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;**64**:ii14-ii7.
6. Coates LC, Tillett W, Chandler D, Helliwell PS, Korendowych E, Kyle S, et al. The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. *Rheumatology (Oxford)* 2013;**52**:1754-7.
7. European Medicines Agency. *Summary of opinion (post authorisation): Cosentyx*. London: European Medicines Agency; 2015.
8. *Novartis receives positive CHMP opinion for the first IL-17A inhibitor Cosentyx(TM) to treat ankylosing spondylitis and psoriatic arthritis*. Novartis; 2015. [cited 11th December 2015]. Available from: https://www.novartis.com/news/media-releases/novartis-receives-positive-chmp-opinion-first-il-17a-inhibitor-cosentyxtm-treat.
9. National Institute for Health and Care Excellence. *Ustekinumab for treating active psoriatic arthritis (TA340)*. London: National Institute for Health and Care Excellence; 2015.
10. National Institute for Health and Care Excellence. *Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (TA199)*. London: National Institute for Health and Care Excellence; 2010.
11. National Institute for Health and Clinical Excellence. *Golimumab for the treatment of psoriatic arthritis (TA220)*. London: National Institute for Health and Clinical Excellence; 2011.
12. National Institute for Health and Care Excellence. *Apremilast for treating active psoriatic arthritis (TA372)*. London: National Institute for Health and Care Excellence; 2015.
13. Drummond M, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the economic evaluation of health care programmes. 3rd edition*: Oxford; 2005.

Appendix: Literature searching – draft search strategy for MEDLINE

1946-present (24/11/15)

1 Arthritis, Psoriatic/ (4137)
2 (psoria$ adj2 (arthrit$ or arthropath$)).ti,ab. (6682)
3 1 or 2 (7525)
4 (Certolizumab or Cimzia or CZP or CDP870 or CDP-870 or 428863-50-7).af. (885)
5 3 and 4 (67)
6 (secukinumab or Cosentyx or AIN457 or AIN-457 or 1229022-83-6).af. (130)
7 3 and 6 (27)
8 (golimumab or simponi or CNTO148 or CNTO-148 or 476181-74-5).af. (525)
9 (2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$).ed. (6001360)
10 3 and 8 and 9 (95)
11 (apremilast or otezla or otezia or CC10004 or CC-10004 or 608141-41-9).af. (134)
12 (2014$ or 2015$).ed. (1997500)
13 3 and 11 and 12 (25)
14 (ustekinumab or stelara or CNTO1275 or CNTO-1275 or 815610-63-0).af. (681)
15 (2012$ or 2013$ or 2014$ or 2015$).ed. (3980101)
16 3 and 14 and 15 (90)
17 (inflectra or remsima or CT-P13).af. (35)
18 3 and 17 (1)
19 (etanercept or enbrel or 185243-69-0).af. (6359)
20 (infliximab or remicade or 170277-31-3).af. (10643)
21 (adalimumab or humira or D2E7 or (D2 adj E7) or 331731-18-1).af. (4816)
22 19 or 20 or 21 (15973)
23 (2009$ or 2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$).ed. (6779075)
24 3 and 22 and 23 (689)
25 randomized controlled trial.pt. (416942)
26 controlled clinical trial.pt. (92231)
27 randomized.ab. (338877)
28 placebo.ab. (169974)
29 drug therapy.fs. (1859408)
30 randomly.ab. (244545)
31 trial.ab. (352929)
32 groups.ab. (1522429)
33 or/25-32 (3706497)
34 exp animals/ not humans/ (4150916)
35 33 not 34 (3188749)
36 5 or 7 or 10 or 13 or 16 or 18 or 24 (838)
37 35 and 36 (736)