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

3rd Appraisal Committee meeting, 28 February 2017

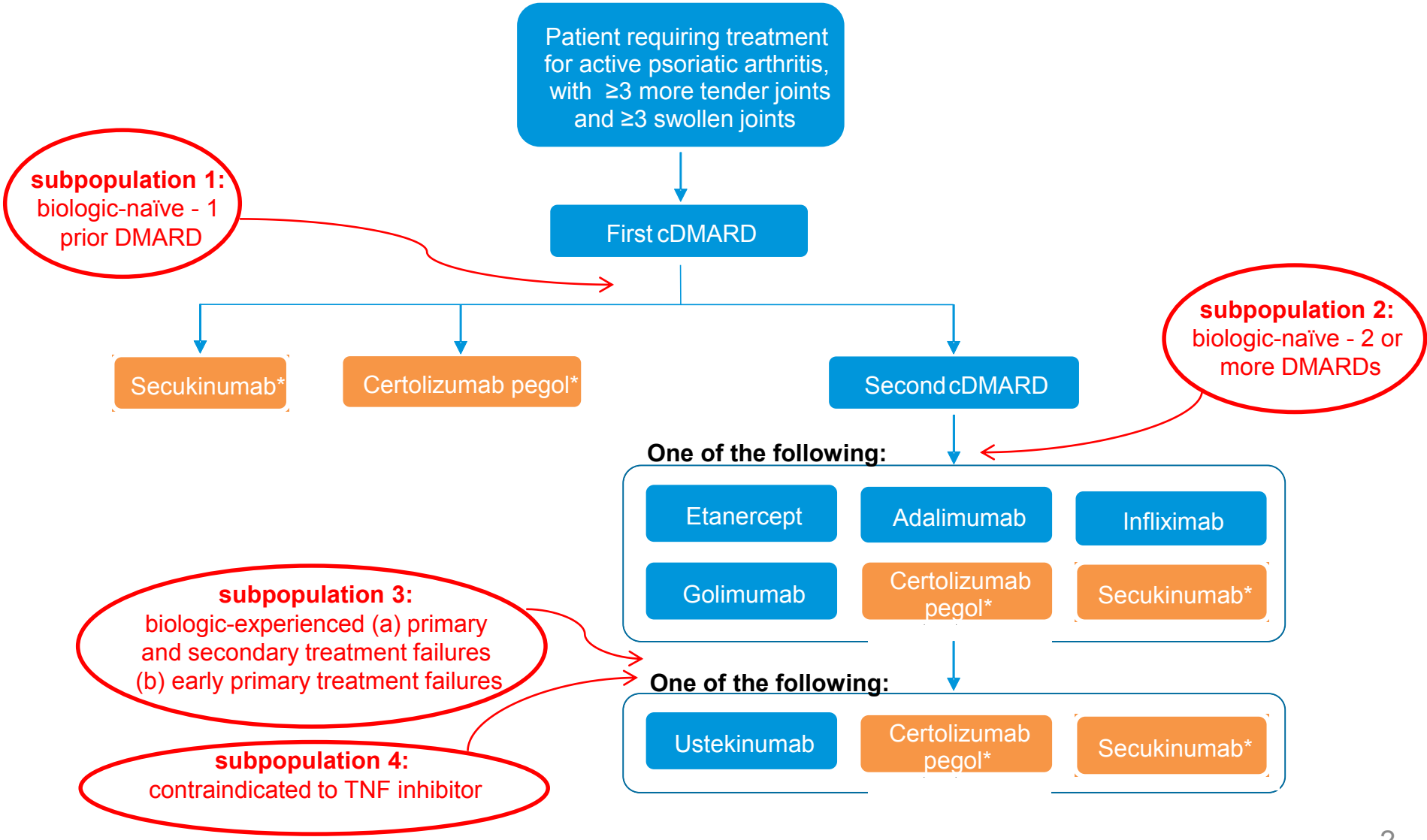
Committee D

Assessment Group: CRD and CHE Technology Assessment Group, University of York

Lead team: Malcolm Oswald, Andrew Black

Companies: UCB (certolizumab pegol) and Novartis (secukinumab)

Position of certolizumab pegol (CZP) and secukinumab (SEC) in the treatment pathway



Abbreviations: cDMARD, conventional disease modifying anti-rheumatic drugs. *Technologies under consideration in this appraisal

ACD: preliminary recommendations

Certolizumab pegol alone, or in combination with methotrexate	Secukinumab alone, or in combination with methotrexate
is recommended as an option for treating active psoriatic arthritis in adults only if	
• it is used as described for the tumour necrosis factor (TNF) inhibitor treatments in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis *, that is: – The person has peripheral arthritis with three or more tender joints and three or more swollen joints, and – their disease has not responded to adequate trials of at least 2 disease-modifying antirheumatic drugs (DMARDs) administered individually or in combination **[subpopulation 2]**	
• **or**, the person has had a TNF-alpha inhibitor but their disease has stopped responding after the first 12 weeks **[subpopulation 3a]**	• **or,** the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks **[subpopulation 3b and 3a]**
	• **or,** TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)* **[subpopulation 4]**

* *see TA199 for additional conditions in 1.2 - 1.4 of the guidance*

ACD2: key conclusions

1st meeting *Aug 2016*

- ACD issued with positive recommendations for subpopulations 2, 3a/b and 4; negative recommendation for subpopulation 1

2nd meeting *Nov 2016*

- Novartis submitted additional evidence for subpopulation 1
- ACD2 issued with same recommendations as ACD1
- Key issues:

4.2	**Uncertainty around established clinical practice**	Uncertainty around whether TNF-alpha inhibitor after 1 DMARD is established clinical practice in the NHS
4.16	**More certainty required due to the potential shift in use of biological therapy**	Subpopulation 1

Comments on ACD2

Consultees	• Novartis (secukinumab) • UCB (certolizumab pegol) • Psoriasis Association (PA)
Commentators	• Celgene (apremilast) • AbbVie (adalimumab)
Clinical experts	• No comments
Web	• No comments

Consultation comments – subpopulation 1

- **[NOVARTIS & UCB] Uncertainty of the committee's conclusion to not recommend SEC in subpopulation 1**
  - SEC is a clinically and cost-effective treatment option for subpopulation 1
  - NICE guidance should be in line with BSR, GRAPPA and EULAR guidelines and recognise the value of anti-TNF and/or biologic therapy after only 1 prior DMARD, and particularly where there is evidence of adverse prognostic factors
  - Evidence on anti-TNF usage after only 1 cDMARD within the NHS is limited creating a cycle whereby formal audited data on their use is not available
- **[CELGENE] Review of existing guidance needed for recommendation in subpopulation 1**
  - Should the Committee wish to evaluate SEC and CZP in sub population 1, this should take place alongside a review of existing NICE Guidance for recommended technologies for PsA to ensure a consistent approach
  - Agree that the full range of comparators may not have been included for sub population 1, but do not agree that the important omission relates primarily to TNF-alpha inhibitors. Based on expert opinion, TNF-alpha inhibitors are not routinely used after 1 DMARD in NHS practice as existing NICE Guidance (TA199 and TA220) restricts reimbursement to after 2 or more DMARDs

Consultation comments – placebo creep and class effect; timing of response assessment

- **[UCB] Suggestion to revise the statement related to 'placebo creep' and "class effect"**
  - ACD states "*The committee concluded that because these issues had either not been accounted for (secukinumab) or because* ***it was unclear how they had been accounted for (certolizumab pegol)*** *in the company submissions, it was not possible to make reliable conclusions about the difference in the efficacy of certolizumab pegol and secukinumab using the companies' analyses*"
  - Statement does not accurately reflect the evidence submitted, the adjusted NMA accounting for the placebo creep and class effect were used as inputs in the UCB cost-effectiveness model and this was similar to the AG approach. NICE should revise the statement to reflect the UCB submission
- **[ABBVIE] Timing of response assessment**
  - ACD states *"Assess the response to certolizumab pegol and secukinumab after 12 weeks and 16 weeks"*
  - Concern that this statement introduces an unwarranted level of complexity in clinical practice, with the risk that some patients may unnecessarily be delayed in their subsequent disease assessment if 2 thresholds (of 12 and 16 weeks) are recommended

Consultation comments – lack of effectiveness in bowel disease for SEC

- **[ABBVIE]**
  - Psoriatic arthritis is a multi-faceted disease composed of arthritis, psoriasis and extra-articular manifestations/comorbidities such as inflammatory bowel disease
  - ACD states: *"The clinical experts stated that they could not distinguish between the TNF-alpha inhibitors in improving joint symptoms in clinical practice and would therefore choose 1 of the therapies based on availability and the patient's comorbidities"* NICE should take into consideration the Hueber et al (2012) study, and should add ***"Secukinumab has failed to demonstrate clinical effectiveness in the extra-articular component of psoriatic arthritis, as demonstrated in patients with Crohn's disease"***
  - ACD states: *"The committee heard from the clinical experts that psoriatic arthritis not only affects joints and tendons but can also be associated with other debilitating conditions of the skin, bowel and eye and with metabolic syndrome."*

    Should be followed by: "***The Committee recognizes that secukinumab has not demonstrated clinical effectiveness in inflammatory bowel disease***"

Consultation comments – Impact of PsA on patients

- **[PSORIASIS ASSOCIATION]**
  - Psoriatic arthritis can affect people of any age, and often it affects people in young or ‘mid’ adulthood who should, otherwise, be ‘in their prime’, pursuing careers, relationships and families. Without timely and effective treatment, the damage caused by psoriatic arthritis can be permanent
  - Both treatments work to modify the disease itself, and also work in a different manner to the currently-available anti-TNFs, meaning they are both useful options for people who may not have experienced adequate results with anti-TNFs, or cannot take them

Key issues for discussion

- Do any of the responses to consultation change the committee's preliminary recommendations?

BACK-UP SLIDES

Summary of clinical evidence: CZP and SEC (1)

- **Companies**' clinical evidence mainly from RAPID-PsA (CZP) and FUTURE 2 (SEC) for short and long term efficacy: Phase III RCT of good quality and low overall risk of bias but all subgroups based on previous biologic use did not match NICE scope

Subgroup	Novartis submission (SEC)	UCB submission (CZP)
1	As per NICE scope	As per NICE scope
2	As per NICE scope	Defined as "all-biologic naïve" people
3	Include only biologic experienced patients and therefore do not include people who are contraindicated to biologic therapies	

- **RAPID-PsA trial** (CZP) was more selective than other trials in recruiting its biologic-experienced patients; it excluded patients whose disease did not respond to a TNF-alpha inhibitor in the first 12 weeks of treatment (primary treatment failure)
- The populations recruited **across clinical trials** have changed over time, with earlier trials excluding biologic-experienced patients and later trials including such patients
- **'Placebo creep'** or increase of placebo response rates over time across in all trials

Summary of evidence CZP and SEC (2)

- **Assessment Group** presented a network meta-analysis (NMA) for the biologic naive and experienced subgroups to assess short term efficacy:
  - ***Biologic naive population network:*** insufficient data to subdivide biologic naïve patients into those who have failed one conventional DMARD and those who have failed two conventional DMARDs, as per NICE scope
  - ***Biologic experienced network:*** exclusion of CZP treatment data in the NMA as the definition of treatment experienced patients in RAPID PsA was different from other trials
- Use of the same disease management costs as previous York model (TA199) which only addresses the arthritis component of PsA whereas Poole's *et al.* costs are derived from comparable patients with PsA