# National Institute for Health and Care Excellence
# Centre for Health Technology Evaluation

## Pro-forma Response

## ERG report

## Secukinumab for treating moderate to severe plaque psoriasis in people for whom other systemic therapies have been inadequately effective, not tolerated or contraindicated [ID718]

You are asked to check the ERG report from Aberdeen HTA to ensure there are no factual inaccuracies contained within it.

If you do identify any factual inaccuracies you must inform NICE by **5pm** on **23 February** using the below proforma comments table. All factual errors will be highlighted in a report and presented to the Appraisal Committee and will subsequently be published on the NICE website with the Evaluation report.

The proforma document should act as a method of detailing any inaccuracies found and how and why they should be corrected.

## Issue 1 Description of secukinumab approved indication

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 1(paragraph 1): Incorrect text describing the licensed indication: "for whom other systemic therapies have been inadequately effective, not tolerated or contraindicated." | Text should be amended to "for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy." | Correct wording of licensed indication should be used. | Not a factual error. This definition is consistent with that of the decision problem reported on page 32 of the company's submission. |

## Issue 2 Comparison of NICE final scope with decision problem addressed by company

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 22 (final bullet point): no comment in right hand side column regarding PAS in place for secukinumab in this submission | Page 22: add that a patient access scheme is in place for secukinumab | Ensures decision problem addressed in the submission is clear. | The proposed revision is accepted.<br><br>Add another bullet "The analyses submitted by the company include the effect of the CIC PAS" |

## Issue 3 Removal of commercial in confidence 'exclusion criteria' data

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 28-29 (Table 3): the | Un mark the CIC status for the exclusion | ERG report reflects information in | In the version of the company' |

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| main exclusion criteria are marked CIC but in a later manufacturer submission version (Jan 16 2015) submitted at NICE request this information had the CIC status removed. | criteria | manufacturer's submission. | submission sent to the ERG the main exclusion criteria are marked CIC. |

## Issue 4 Description of SCULPTURE trial

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 26: SCULPTURE trial does not contain a placebo arm as stated in sections 4.1.3 (line 4) and 4.1.4 (line 2). | Text should be amended to "All trials involved the comparison of secukinumab (150mg and 300mg doses) versus placebo, with the exception of SCULPTURE which did not have a placebo arm and FIXTURE, which also included a comparison with etanercept." | Correct representation of secukinumab clinical trial program. | Not a factual error. The proposed revision is not accepted. |
| Page 34 (section 4.2) : "Another randomised trial, SCULPTURE, compared patients receiving secukinumab 300mg with those receiving secukinumab 150mg." | Text should give more detail on trial design: "SCULPTURE compared patients receiving a fixed treatment interval regimen of either secukinumab 300mg or 150mg versus a treatment at start of relapse regimen of either secukinumab 300mg or 150mg in patients who had achieved a PASI 75 response following the induction phase at week 12." | Correct representation of secukinumab clinical trial program. | Not a factual error. The proposed revision is not accepted. |
| Page 36 (paragraph 3): "However, non-inferiority of a secukinumab 'treatment on relapse' regimen compared with a fixed treatment regimen | Text should read: "However, non-inferiority of a secukinumab 'treatment on relapse' regimen compared with a fixed treatment regimen for maintaining week 12 PASI **75** response up to week 52 could | Correct representation of secukinumab clinical trial program. | Not a factual error. The proposed revision is not accepted. |

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| for maintaining week 12 PASI response up to week 52 could not be achieved.” | not be achieved.” | | |

### Issue 5 Reporting of NMA results

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 59 (section 5.2.6): “For the base case the time point for the assessment of response is assumed to be 12 weeks for all the comparators with the exception of adalimumab for which it is 16 weeks.” | Page 59: Amend text to “For the base case the time point for the assessment of response is assumed to be 12 weeks for etanercept, ustekinumab and secukinumab, 10 weeks for infliximab and 16 weeks for adalimumab.” | Accurate description of NMA methodology | The proposed revision is correct and is accepted.<br>The ERG error arose from the electronic model describing the infliximab induction treatment period as 12 weeks. |
| Page 60 (paragraph 1): “Infliximab has a slightly lower PASI <50 response than secukinumab” should read slightly higher (8% vs 7%) | Page 60: amend text to “slightly higher” | True representation of NMA results | The proposed revision is correct and is accepted. |
| Page 62 (paragraph 1): “infliximab PASI<50 being slightly less” | Page 62: amend text to “slightly more” | True representation of NMA results | The proposed revision is correct and is accepted. |

## Issue 6 Inaccurate reporting of results

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 64 (last line of page): ustekinumab used instead of secukinumab | Page 64: change ustekinumab to secukinumab | Ensures paragraph refers to the intervention under review. | The proposed revision is correct and is accepted. |
| Page 65 (second paragraph, line 10): ustekinumab used instead of secukinumab | Page 65: change ustekinumab to secukinumab | Ensures paragraph refers to the intervention under review. | The proposed revision is correct and is accepted. |

## Issue 7 Sensitivity analysis of annual discontinuation rate

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 91 (last sentence of page): "This argues for sensitivity analyses around the discontinuation rate, and around the discontinuation rate specific to secukinumab" | Page 91: remove this sentence | One way sensitivity analyses were conducted around discontinuation rate varying from 5% to 43% page 221(Table 129) of manufacturer's submission. | Not a factual error. The proposed revision is not accepted.<br>The text does not suggest that the company has not undertaken these sensitivity analyses, only that the ERG in its analyses should do so. |

## Issue 8 Description of complete case analysis in EQ-5D regression

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 98 (paragraph 3). | Correction to ERG assessment of | The "complete case" analysis refers | The proposed revision is correct and |

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| Misinterpretation of handling of missing data in EQ-5D regression analysis.<br><br>Page 98: "The company argue that a complete case analysis is justified as this only excluded 125 patients out of a total of 3,366 (i.e. less than 5% of the total). However, the ERG struggle to understand the rationale for adopting a complete case analysis. The more natural approach would seem to be that even if a patient had some missing data at, say, week 24 to still include that patient's week 36 data if the week 36 data were complete." | handling of missing data. | to the fact that missing observations for individual patients were not imputed and therefore observations for which measurements were expected but not collected were excluded. If patients had missing observations at a given time point but data were available at previous or subsequent time points then these observations were included in the analysis in line with the approach suggested by the ERG. The statement that 125 patients (5%) were excluded refers to the fact that observations pertaining to 125 patients were excluded from the analysis, not that these patients were excluded entirely. | is accepted (deletion of 3rd para of page 98).<br><br>Please note that it is only with the current justification for the proposed amendment that the way the "complete case analysis" was applied has finally become clear. |

## Issue 9 Method of inclusion of SAE costs for those on biologics in the first year

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 102 (3rd bullet point and footnote r): Inaccurate inclusion of SAE costs for those on biologics in the first year.<br><br>Page 102 (footnote r): In order to include the SAE costs for those on biologics in the first year the ERG implemented | The ERG's approach does not take into consideration the length of time in the first year that a patient may be on a biologic. Therefore, the following amendments should be implemented in the Markov sheets (except for SoC, adalimumab and infliximab): | The method used by ERG did not take into consideration the fact that patients in the PASI<50 and PASI 50-75 categories were on biologics for the induction period only and instead applied a lump sum of the full SAE costs for patients in the first year. | The proposed revision is not accepted.<br><br>The company is correct to state that the ERG revision assumes that those on a biologic experience the annual SAE rate in year 1 regardless of whether they stop after induction or continue. The ERG views this assumption as more accurate than |

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| this ‘within the Markov_Trace_ worksheets, with the exception of the Markov_Trace_SoC worksheet, by revising cell F56=SUM($AJ$72,$AJ$96:$AK$96)+F23’ | AK76=F76*$F$23*(IF(Clin_Data_Source=5,16,IF(Clin_Data_Source=1,12,12))/52)<br>AK79=F79*$F$23*(IF(Clin_Data_Source=5,16,IF(Clin_Data_Source=1,12,12))/52)<br>AK82=F82*$F$23<br>AK85=F85*$F$23<br>F56=SUM($AJ$72,$AJ$96:$AK$96)+SUM(AK76:AK85)<br><br>For adalimumab the first 2 lines would change to:<br>AK76=F76*$F$23*(IF(Clin_Data_Source=5,16,IF(Clin_Data_Source=1,12,16))/52)<br>AK79=F79*$F$23*(IF(Clin_Data_Source=5,16,IF(Clin_Data_Source=1,12,16))/52)<br><br>For infliximab the first 2 lines would change to:<br><br>AK76=F76*$F$23*(IF(Clin_Data_Source=1,12,10))/52)<br>AK79=F79*$F$23*(IF(Clin_Data_Source=1,12,10))/52) | | that of the company base case, which assumed that no biologic SAEs were experienced in the first year. There is an open question about what SAE risk any exposure to the biologics results in and when the SAEs are incident from this risk.<br>Please note that the impact of the company proposed revision upon results will be extremely slight. |

## Issue 10 Incorrect induction period for infliximab used

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 101 (section 5.4, footnote o), page 102 (footnote o): Incorrect use of 16 weeks induction period for infliximab when 'Revise the QALY calculations for those with a PASI 50-74 response during the first year to apply the PASI <50 quality of life value for the post induction period'.<br><br>Page 101,102 (footnote o): Implemented within the Markov_ worksheets by setting cell L79= IF(Clin_Data_Source=5,16,IF(Clin_Data_Source=1,12,12)) with the exception of adalimumab where L79= IF(Clin_Data_Source=5,16, IF(Clin_Data_Source=1,12,16)) and infliximab where L79= IF(Clin_Data_Source=5,16, IF(Clin_Data_Source=1,12,10)), and M79=52-L79 | For infliximab the correct formula should be:<br><br>L79=IF(Clin_Data_Source=1,12,10) | Although this does not affect results in the basecase it would be more accurate to change as the length of the induction periods for infliximab are 12 weeks for clinical data source 1 and then 10 weeks in every other case. | The proposed revision is correct and is accepted.<br><br>Amend footnote 'o' to:<br><br>… and infliximab where L79= IF(Clin_Data_Source=1,12,10), and M79=52-L79, |

## Issue 11 Incorrect application of flattening SoC costs in SAs

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Page 105 (6th bullet point, footnote ee) Incorrect application of sensitivity analyses when flattening the SoC costs so that the costs in years one and two of the model are the same as in subsequent years.<br><br>The ERG report states that it was 'Implemented within the Monitoring_costs_calculations worksheet by setting cells Q22=12/52*P50 and<br><br>P31=(52-12)/52*P50, and within the Tx_cost_calculation worksheet by setting cells E238=12/52*H238,<br><br>F238=(52-12)/52*h238 and G238=H238' | P31 on Monitoring_costs_calculations does not refer to SoC and therefore the underlined section would need to be corrected to P37=(52-12)/52*P50 | Cell P31 relates to secukinumab and should not be used when flattening costs of SoC. | The proposed revision is correct and is accepted.<br><br>Amend footnote 'ee' to:<br><br>… P37=(52-12)/52*P50<br><br>Note that within the ERG modelling it was cell P37 that was revised and the results of the sensitivity analyses are correct. |

## Issue 12 Typographical errors

| Description of problem | Description of proposed amendment | Justification for amendment | ERG Comments |
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| Incorrect spelling of the following words: Page 1 – "prsoriasis" | correct spelling : psoriasis<br><br>correct spelling: "etanercept" | | Spelling mistakes not factual errors. |

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| Page 8 - “etanercept”<br>Page 32- “SCULPURE”<br>Page 36 - “eternercept”<br>Page 53 - “company”<br>Page 74-“udalimumab” | correct spelling : “SCULPTURE”<br>Correct spelling “company”<br>Correct spelling “adalimumab” | | |