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2nd February 2015

Bijal Joshi
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Dear Bijal,

Celltrion Healthcare (CTHC) / Napp Pharmaceuticals Limited response to Assessment Report:

TNF-alpha inhibitors for ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis (including a review of technology appraisal 143 and technology appraisal 233).

We have read the Assessment report with great interest and are grateful for the opportunity to comment on the content.

We are delighted to note that the Assessment Group have made reference to the inclusion of biosimilars for this MTA in the summary (1.3, page 23) and are listed in the range of interventions on page36. However due to the timing of the start of this MTA Napp / CTHC were not able to make a submission for Remsima® (infliximab).

We note from the Appendices, section 11.1 (that Remsima was included in the search criteria along with Remicade®, Inflectra® and infliximab. This allowed the AG the opportunity to evaluate the PlanetAS trial for the infliximab biosimilar known as CT-P13 (in its development). The trial has been published by Park et al; ref. 105 and 106 on page 360 of the report. We would like to point out that in the PlanetAS publication (ref 105) the biosimilar CT-P13 is not referred to as Inflectra. NICE normally refers to medicines by the generic term and not by brand. We are surprised therefore at the wide use of Inflectra throughout this Assessment Report.

Remsima (marketed in the UK by Napp) and Inflectra (marketed in the UK by Hospira) are the brand names for exactly the same biosimilar correctly identified as CT-P13 in the PlanetAS trial.

Whilst the search criteria used highlighted the PlanetAS trial, the AG have in fact assigned the data only to Inflectra which is factually incorrect. We feel that this has inadvertently placed some bias on that particular brand by not mentioning that Remsima and Inflectra are

the same biosimilar and that the PlanetAS study for CT-P13 applies to both. This data was used as part of the regulatory process for each of the brands.

We would suggest that the AG clarifies that CT-P13 is both Remsima and Inflectra or refers to the biosimilar infliximab CT- P13 or alternatively Remsima should be added to any reference made to Inflectra throughout the Assessment Report as the data is identical for both brands.

We note the following use of Inflectra in:

- Section4.2 Clinical Effectiveness Results: **Study characteristics** page 42 line 5*"....one compared infliximab with an infliximab biosimilar (Inflectra)."* The statement is in fact incorrect as the study used CT-P13.
- Table 2, Trial characteristics, page 45 uses Inflectra but not Remsima
- Table 4, Risk of bias assessment results, page 53, specifically mentions Inflectra but refers to the PlanetAS trial which uses CT-P13.
- Section 4.2.2 page54, Exclusions from the meta-analyses refers *"to one trial*[105] ....This is the Park et al PlanetAS study again and Inflectra should be referred to as CT-P13 or change *"Inflectra"* to Inflectra / Remsima.
- Section 4.2.2.3, Page 62 In the last paragraph the sentence starting *"Another trial...* also refers directly to Inflectra and quotes Park et al – reference 105 which is for CT-P13. This paragraph which extends onto page 63 mentions Inflectra a further 6 times.
- Table 15 in the notes below the table, superscript e refers to *"Inflectra and infliximab combined"* from the Park et al trial.
- Section 4.2.5, in paragraph 2 of the Randomised trials – sentence starting with *"of the eight trials"....* Again this refers to Inflectra and references the Park et al publication.
- Section 7.8, Page 217 the last sentence – *"A final limitation...* refers to a generic version of infliximab (Inflectra). The term used here should be biosimilar not generic and should include Remsima.
- Section 9.2, Page 223, bullet point 4 mentions that the patents of anti-TNFs are due to expire shortly. The statement goes on to suggest that Inflectra will be available early in 2015. This again biases against Remsima and we strongly suggest that this is corrected to say that both of the biosimilars, Remsima and Inflectra will be available after the expiry of the patent for the originator infliximab.
- Section 11.4, Appendix 4, Trial results, Table 111, page 252 refers yet again to the Park et al publication and mentions Inflectra. We refer you to our note earlier as Inflectra is not mentioned in this publication. Biosimilar infliximab is named as CT-P13 throughout the publication.
- Section 11.4, Appendix 4, Table 112, Page 255we draw your attention to the comment above as yet again CT-P13 is referred to as Inflectra. Please revise.
- Section 11.4, Appendix4, Table of Binary response to outcomes results, page 258. In the reference to Park 2013 Inflectra is specifically mentioned again, please revise.

- Section 11.7 Appendix 7, Long Term efficacy data. References to Park 105 and 213. Inflectra is specifically mentioned as the comparator. In the Park reference 105 we would like to reiterate, the study uses the term CT-P13 for the biosimilar not Inflectra.
- Section 11.8 Adverse Events pages 287/288 Park, Reference 105 is used again we recommend that Inflectra should be deleted from this table and the term CT-P13 used instead.

We are concerned that it has not been possible for the AG to consider the lower acquisition price of the biosimilars. As a manufacturer we have not been contacted for price information relating to Remsima. We are pleased to be able to share our price which we negotiated with the DH in 2014. We have made the price available to key stakeholders in the NHS for budgetary planning purposes and to both SMC and AWMSG. We would encourage the AG to consider our lower NHS price compared to Remicade (see below) and furthermore the AG needs to understand that there will be greater savings opportunities for the NHS as biosimilar infliximab is subject to the tendering processes. Whilst NICE is able to accept a PAS price it is therefore somewhat disappointing that at a time when the NHS needs to realise savings that the tender price which is the true acquisition price cannot be considered in some form within a NICE appraisal. AGs should be encouraged to think about the wider impact on the NHS and carry out some form of sensitivity around the acquisition price of biosimilars to ensure that the true value is accounted for within the ICERs.

NHS List price Remsima 1 x 100mg vial £377.66.

Our own estimates of the ICER would suggest that at the true acquisition price, Remsima is in the same range of cost effectiveness as the other anti-TNFs.

We hope that you will find our comments useful and should you need any further information please contact us either by email or telephone.

Yours sincerely