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Worldwide Biopharmaceutical Businesses

Dr. Rosie Bennyworth
Appeals Committee Vice Chair
National Institute for Health & Care Excellence
10 Spring Gardens
LONDON
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26 September 2017

Dear Dr. Bennyworth,

Appeal against the final appraisal determination for inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia

Thank you for your letter dated 12 September 2017 in which you provided your initial view of Pfizer's appeal dated 4 September 2017 in relation to the FAD for inotuzumab ozogamicin ("inotuzumab") for treating relapsed or refractory B-cell acute lymphoblastic leukaemia.

In your letter you agreed that four of the points raised by Pfizer were valid points of appeal and should be passed to an appeal panel for consideration. You requested further submissions from Pfizer in relation to two points of appeal. Our response to your letter of 12 September 2017 is provided below, using the same numbering as that in our letter of appeal.

Appeal point 1.1: The Appraisal Committee has seemingly failed to consider the cost-effectiveness of inotuzumab, applicable to UK clinical practice, when used in accordance with its marketing authorisation

Noted

Appeal point 1.2: The fact that the clinical experts were not invited to the second meeting of the Appraisal Committee meant that important clinical advice was not available to guide the preparation of the FAD

Noted

Appeal point 1.3: The Committee has provided no explanation for its decision to reject the utilities proposed in the revised Pfizer base case for the post HSCT period and submitted in response to consultation

Pfizer's point of appeal related to the Committee's rejection of the utilities we proposed for the period following the "cure-point" post hematopoietic stem cell transplantation (HSCT), in response to consultation on the ACD. The assumptions in the period post-cure point are classed as disease-specific and we believe unrelated to the original treatment pre-HSCT. Significantly, the rationale is lacking for the inconsistency in utility choice with that accepted by the Appraisal Committee which considered the same period in the context of the appraisal of blinatumomab which, as explained in our appeal, is indicated for the treatment of substantially the same patient population as that eligible for inotuzumab; the Committee provided no explanation for the difference in its approach when considering inotuzumab.

In your letter of 12 September you referred to brief comments provided in the FAD at paragraph 3.20, which noted the opinion of the ERG that the utility originally proposed by Pfizer was based on a published paper (Kurosawa et al. 2016) and was therefore preferable to the assumption proposed in response to the ACD, "which is not supported by evidence", and the Committee's statement that the utilities from Kurosawa were "its preferred assumptions". Based on these statements you expressed the preliminary view that "the reason therefore seems to be that the Kurosawa values are based on a published study and the values proposed post-consultation are not".

The comments quoted in your letter of 12 September do not however address the matters set out in our appeal letter and do not provide any adequate explanation for the Committee's decision. Pfizer's point of appeal arose from the fact that the Committee which considered the appraisal of blinatumomab, which proceeded in parallel but slightly in advance of that for inotuzumab, accepted that utility post-cure point should reflect those in the general population. After the cure point, the effects of the specific treatments administered pre-HSCT are no longer relevant and it is difficult to see any basis for a different approach to be applied in different appraisals within the same disease area. This was the issue raised by Pfizer, after the decision in relation to blinatumomab, in our response to consultation on the ACD. However the Committee in the current appraisal of inotuzumab has seemingly disregarded Pfizer's submission, stating simply that it "agreed with the ERG", while providing no explanation for an approach to utilities post cure point, which is wholly inconsistent with that of the committee which considered blinatumomab.

Our point of appeal was advanced under Ground 1, for the reasons set out above, on the basis that reasoning to explain the difference in approach from that adopted in relation to blinatumomab was lacking. If, however, the reason for the Committee's decision was simply as suggested in your letter (without any consideration of the data themselves or the fact that the approach proposed by Pfizer in response to the ACD had already been accepted by another appraisal committee in the same disease area), such a decision would be arbitrary and therefore unreasonable and our point of appeal should be admitted under Ground 2.

Appeal point 2.1: The Appraisal Committee's reasons for disregarding key assumptions used for the purposes of NICE's appraisal of blinatumomab do not explain the choices that were made in relation to inotuzumab

Noted

Appeal point 2.2: The Committee has seemingly misunderstood the utilities submitted by Pfizer in response to consultation on the ACD

Noted

Appeal point 2.3: The Committee has misinterpreted Pfizer's revised submission on administration costs

Following your request for further elaboration on this point, we would like to clarify the interpretation this ground is based on.

Administration is just one reason a patient may be admitted to hospital, with others including underlying disease, comorbid conditions, and adverse events. These other causes of admission are not part of the estimates that are being considered in 3.22 of the FAD which concern administration related stay ***only***. For example, the model already accounts separately for costs related to hospital admission in the treatment of adverse events. The estimates the committee discuss in 3.22 (one day for inotuzumab and fourteen days for standard of care) are estimates ***solely*** related to in/outpatient days directly attributable to administration.

Despite these (one and fourteen) being administration only estimates, the Committee have misinterpreted these as estimates related to ***all*** inpatient stay (i.e. including beyond administration). This is illustrated in 3.22 as the FAD cites only a decision being made for "inpatient days", with the whole section excluding the word "administration"; this shows the Committee were not aware the decision at hand was administration-related. Additionally, multiple clinical expert comments that were received during the ACD consultation around administration (quoted in Pfizer's 4 September letter) fail to be acknowledged in 3.22, further suggesting the Committee did not understand the assumption in question was related specifically to administration.

As the Committee have misinterpreted the estimates of one and fourteen days presented to them as being reflective of ***all*** inpatient stay whereas in fact they were estimates for administration stay only, the Committee's conclusion that "the ICER is underestimated" is an unreasonable consequence of this misinterpretation.

Should you require any further information or clarification, please let us know and we will provide this. Alternatively, we look forward to receiving your final determination on the admissibility of our appeal.

Yours sincerely

[redacted], Pfizer UK