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Monday 19th April 2010

[redacted]
Level 1A City Tower
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BY E-MAIL

Re: Single Technology Appraisal – Tocilizumab for the treatment of rheumatoid arthritis

Dear [redacted],

Following our response to the 3rd ACD for tocilizumab we are providing NICE with a more 'user-friendly' version of the economic model accompanying our response. The aim of providing an updated model was to address 2 limitations with the previous version. Firstly to enable tocilizumab to be utilised later in the treatment sequence and secondly to enable the degradation of ACR rates specific to the chosen position within the treatment sequence (see assumptions in section B below).

To confirm, the updated model does was not necessary to provide updated ICER estimates for those scenarios illustrated within our latest ACD response. Roche had already provided an economic model to enable the validation and review of the ACD response ICERs. Instead the model simply aims to reduce the number of complex manual adjustments required by the user in order to account for those latest scenarios and assumptions of interest to the committee.

Apologies for the minor delay on providing this model version, however the complexity of the modelling refinements proved difficult to estimate.

A) Changes to the model functionality

1. We have included a functionality within the model with which the user can now change the order of tocilizumab in both the 'study drug arm' and 'comparator arm' of the model.

2. We increased the number of treatment options within the model to account for possible ACR degradation. In this version of the model a user can set-up

additional treatments and their respective inputs. In this context we have added 4 additional treatments and their respective clinical inputs:

- **Etanercept Bio-IR** – This input is used when etanercept is used after tocilizumab in the 3-biologic treatment sequence. The ACR rates utilised are as reported within our response to the 3rd ACD (Table 6)
- **Rituximab (2xBio-IR)** – This input is used when rituximab is used after tocilizumab and etanercept in the 3-biologic treatment sequence. The ACR rates utilised are as reported within our response to the 3rd ACD (Table 6)
- **Tocilizumab TNF-IR** – This input is used when tocilizumab is used after etanercept in the 3-biologic treatment sequence. The ACR response rates are identical with the rates used in the TNF-IR version of the model (provided in the original Roche submission)
- **Tocilizumab (2xBio-IR)** – This input is used when tocilizumab is used after etanercept and rituximab in the 3-biologic treatment sequence. The ACR rates used have been given as part of the response to the 3rd ACD (Table 6)

3. This updated version enables the user to have an alternative treatment (other than tocilizumab) as the first treatment in the sequence of the intervention arm. This enables the user to run a scenario in which etanercept is used as the first biologic, and tocilizumab in either the 2nd (post TNF) or 3rd biologic (post rituximab). This was not previously possible.

B) Clarification of Model Assumptions

In order to be able to run any scenarios in which a 2-biologic regimen is compared to a 3-biologic regimen the following assumptions were made:

1. Etanercept Bio-IR, tocilizumab (2xBio-IR) and rituximab (2xBio-IR) withdrawal rates

These were assumed to be 1-exp(1-0.10) as per the Appraisal Committee's recommendations around decreased efficacy when biologics are used in sub-optimal position.

2. Tocilizumab HAQ score change while patients are on treatment

The model utilises the data from the phase III extension trials.

(i) Tocilizumab used in 1st-Bio position – Slope parameter has 2 inputs: -0.0198 for first 3 years, 0 afterwards.
(ii) Tocilizumab used in 2nd-Bio position – Slope parameter has 1 input: Patients stay on tocilizumab treatment in the model for 3.5 years. According to the TNF-IR trial extension data patients exhibit a reduction in HAQ of -0.0126 (per 6-month cycle) for the

first 2.5 years followed by a 0 slope. We have calculated the average HAQ slope to be -0.0084 per cycle

(iii) Tocilizumab used in 3rd-Bio position – Slope parameter has 1 input: slope is equal to 0. This is an assumption as no trial data exist on the HAQ change while patients are on tocilizumab treatment having already had an inadequate response to 2 biologics.

c) Rounding error notification

We would also like to take this opportunity to highlight a rounding error that affected the 3-biologic scenario in which tocilizumab is used after etanercept and before rituximab. The updated total lifetime costs and QALYs and ICER versus the 2-biologic regimen are found in the table below.

		Model ACD 3 (ACD 3 response tables 1 and 3)	Correction
Tocilizumab used post TNF (3-biologic regime)	Total costs	£102,935	£102,469
	Total QALYs	8.851	8.836
	ICER vs 2-biologic regimen	**£23,409 per QALY**	**£23,285 per QALY**

3-biologic regimen: etanercept→tocilizumab→rituximab
2-biologic regimen: etanercept→rituximab

We hope this information further assists in the validation of the latest estimates of the cost effectiveness of tocilizumab by both the committee and NICE technical team.

Please do not hesitate to contact us if you require more information or explanation on the updated version of the model.

Yours sincerely,

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