01 June 2010

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Dear [redacted],

Re: Single Technology Appraisal – Aripiprazole for the treatment of schizophrenia in people aged 15-17

The Evidence Review Group (ERG), Southampton Health Technology Assessment Centre (SHTAC) and the technical team at NICE have now had an opportunity to take a look at the submission received by Bristol Myers Squibb, Otsuka Pharmaceuticals on 10th May 2010. In general terms they felt that it is well presented and clear. However, the ERG and the NICE technical team would like further clarification relating to the clinical and cost effectiveness data.

Both the ERG and the technical team at NICE will be addressing these issues in their reports. As there will not be any consultation on the evidence report prior to the Appraisal Committee meeting you may want to address the points raised and provide further discussion from your perspective at this stage.

We request you to provide a written response to this letter to NICE by 15th June 2010. Two versions of this written response should be submitted; one with academic/commercial in confidence information clearly marked and one from which this information is removed.

Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise, and all information submitted under 'academic in confidence' in yellow.

If you present data that is not already referenced in the main body of your submission and that data is seen to be academic/commercial in confidence information, please complete the attached checklist for in confidence information.

If you have any further queries on the technical issues raised in this letter then please contact Fay McCracken (fay.mccracken@nice.org.uk) – Technical

Lead). Any procedural questions should be addressed to Lori Farrar – Project Manager (lori.farrar@nice.org.uk) in the first instance.

Yours sincerely

Frances Sutcliffe
Associate Director Technology Appraisals
Centre for Health Technology Evaluation

Encl. checklist for in confidence information

Section A: Clarification of effectiveness data

Evidence

A1. In order to verify that the clinical data reported in your submission has been correctly presented, could you please provide copies of the Clinical Study Reports cited in your submission?

Literature searches

A2. Please could you confirm which clinical trials registries (e.g. controlled-trials.com, UKCRN clinicaltrials.gov) and conference abstracts were searched?

A3. Please could you provide clarification of the approach used, and the content of, the hand-searching?

A4. The ERG has identified an additional publication of an analysis from the Findling et al RCT (Robb, et al, 2010, Journal of Child and Adolescent Psychopharmacology; 20(1): 33-38). Could you please comment on the relevance of this study to your submission?

Comparators

A5. Could you please provide details of the methodology adopted for assessing studies for inclusion in the indirect comparison and the non-RCT evidence base supporting your submission?

A6. Please provide details of the methodologies for the studies included in the indirect comparison.

A7. Please provide all of the results from the RCT (Study No. 31-03-239) that was included in the indirect comparison. It is noted that only a table on the quality assessment for this study has been provided in the submission.

A8. The submission includes clozapine as a third line treatment in the economic model, despite not being listed as a comparator in the submission. Please could you clarify why a systematic search to identify studies which include data for this treatment was not undertaken and why the results, methodology and quality assessment of any identified studies were not presented in the submission.

A9. Section 2.6: Please provide further details and justification of whether the conference abstract identified for risperidone had sufficient data for the clinical review, and explain why the data was deemed insufficient for model parameters.

Population

A10. Section 3.1.1: Your submission states that 'other areas of mental health disorders such as learning disabilities are not appropriate for this review'. Please could you clarify what is meant by this, and provide your inclusion and exclusion criteria used to identify people with learning difficulties?

Clinical evidence

A11. Please could you provide information as to why 'head to head studies with less than two arms including the intervention of interest were excluded' from the clinical evidence, and provide a list of these 78 excluded studies, Please also provide a list of all other excluded studies and the reasons for their exclusion from stages e2 and e3 of the screening process.

A12. Please provide justification for the LOCF approach to data analysis, and provide for each study arm, information on how many observations in each week were carried forward.

A13. There is inconsistency in the reporting of analyses from the included trial (Study No. 31-03-239), with some outcome data reported for baseline and endpoint only, whereas others are provided for 0,1,2,3,4,5 and 6 weeks. Please could you clarify the reason for this?

A14. Please provide clarification why P-QLES-Q was classed as an 'other' (not primary or secondary) outcome measure in your submission, the definition of 'other' in this context, and what the implications are for interpreting the P-QLES-Q data as presented.

A15. For each of the PANSS, GCI, CGAS, and P-QLES-Q, please provide details of what would be a clinically meaningful change or difference in these measures, and whether the sample size used was considered adequate to provide reasonable power to detect this meaningful change or difference.

Section B: Clarification of health economic model

B1. Please could you provide more detail of the methods, quality and results of the study that was used to estimate the relative risk of relapse in the economic model. It is noted that the study from which the relative risk was sourced was not reviewed in your submission.

B2. Please provide more detail of the methods, quality and results of the study used to obtain HRQoL data for your submission.

B3. Could you provide more detail on the methods of the prescription cost analysis study described in your submission?

B4. It is noted that your submission refers to MIMS online 2010 (no access date given) as the source used for drug acquisition costs, while your electronic model lists the source for drug acquisition costs as BNF No 59, March 2010. lease state which source is correct and provide the date this information was accessed, if using electronic sources. Please not that the technology appraisal process prefers the use of the price quoted in the BNF, where available.

B5. The submission states that the acute hospital cost per day used in the model was based on the national average unit cost for HRG code PA52 (page 99 and 102). The 2008/09 NHS Reference Costs lists the national average unit cost for PA52C (Behavioural Disorders with length of stay 8 days or more) as £23,595. In table 42 you have listed this cost as £24,581 (which is the national average unit cost for PA53B (Eating Disorders with length of stay 8

days or more)). Please clarify which HRG code and cost is correct and the reference you have used.