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Dear Reetan,

Response to Assessment Report Addenda 3'' and 4': Coronary Artery Stents for the Treatment of Ischaemic Heart Disease (Update to Guidance No. 71)

Thank you for the opportunity to comment on these two further Addenda to the Assessment Report. There has been some progress in addressing the flaws in the original Assessment Report, although important issues raised by the Appraisal Committee after the February 2006 meeting have still not been addressed by the Assessment Group and this remains a matter of serious concern.

1. **Risk Factors for Repeat Revascularisation**

1.1. We are pleased to see that the Appraisal Committee's request to include long lesions, small vessels and diabetes in the economic model has been implemented. This reflects the wealth of literature showing these factors to be the most commonly occurring predictors of repeat revascularisation in both randomised trials and clinical databases.

1.2. We are disappointed to see that the relative risks of these independent risk factors **taken from the trials** has not been included in the model, when this was specifically requested by the Appraisal Committee in the specification of additional work leading to Addendum (3'). Instead, the Assessment Group have used relative risks from the CTC audit dataset, which the Appraisal Committee has already concluded is not representative of repeat revascularisation rates (and by implication to the relative risks that are derived from that dataset).

1.3. An example of the perversity of using the CTC dataset lies in the relative risk associated with diabetes shown in Table 4. According to the Assessment Group's analysis, diabetes confers a relative risk of 1.38 in elective patients and 0.90 in non-elective patients. Given that the literature shows diabetes to be predictive of increased repeat

revascularisation rates, why have the Assessment Group employed a relative risk that reduces the rate associated with diabetes in non-elective patients? This factor is clearly an example of the unreliability of the CTC dataset, yet the Assessment Group continues to rely on it.

2. **Absolute Risk of Repeat Revascularisation with Bare Metal Stents**

2.1. Contrary to the Appraisal Committee's request in the specification of additional work that led to Addendum 3', the Assessment Group have not used the absolute risk of repeat revascularisation from the Scottish registry as the base-case scenario. Instead, they have continued to use the absolute risks from the CTC registry.

2.2. As per our previous responses, the 12-month repeat revascularisation rate from the Scottish registry is approximately 13%, thus this number should form the base-case in the economic model so that it reflects realistic repeat revascularisation rates.

3. **Risk Reduction Associated with Drug-eluting Stents**

3.1. The Assessment Group continues to rely on total revascularisation rates, The added complication of manipulating data to total revascularisation is unnecessary clinically (as TLR or TVR capture all of the additional impact of DES), introduces additional statistical uncertainty and relies on further unclear estimations of the risk reduction DES confer on total revascularisations.

3.2. The cost-effectiveness results presented in Addenda 3'' and 4' are still biased against drug-eluting stents because the Assessment Group have continued to use a 41% relative risk reduction due to DES from the BASKET trial 6-month results (Addendum 3', page 38). This underestimates the DES treatment effect at 12 months and consequently biases against the cost-effectiveness of DES.

3.3. We are aware that the Appraisal Committee is concerned that protocol-mandated angiographic follow up in the randomised trials may cause the treatment effect of DES to be overstated. However, we would point out 3 important pieces of information that do not feature in the Assessment Report or Addenda:

3.4. In the small vessel sub-group of BASKET, the risk reduction associated with DES at 12 months was approximately **61%** (Kaiser et al 2006).

3.5. In the real-world RESEARCH registry, the risk reduction associated with sirolimus-eluting stents at 12 months was **67%** (Lemos et al 2004).

3.6. In the TAXUS IV cohort of patients who did not receive angiographic follow up, the risk reduction associated with the use of paclitaxel-eluting stents at 12 months was **65%** (Pinto et al 2006).

4. **Impact of Additional Clopidogrel**

4.1. Addendum 4' applied the cost of 9-months additional Clopidogrel to all patients when in reality, patients presenting with acute coronary syndromes (ACS) already receive at least 12 months of Clopidogrel, even if they are treated with a bare metal stent. This cost should only be applied to the proportion not already receiving 12-months Clopidogrel therapy (approximately 56%, according to the BCIS audit data referenced in our previous submissions).

5. **Summary**

5.1. We propose that the economic model be re-run using:

5.1.1. A base-case repeat revascularisation rate of 13% from the Scottish registry.

5.1.2. Relative risks for the independent risk factors of small vessel, long lesions and diabetes representative of the trials and wider clinical databases.

5.1.3. 12-month DES risk reductions derived from the trials and wider clinical databases, particularly the risk reductions pertaining to higher-risk sub-groups.

5.1.4. Additional 9-months Clopidogrel costs applied to only 56% of patients.

Yours sincerely,

Beverley Charters
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References

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