Reviewer's report

Title: Cost Utility Analysis of Reduced Intensity Hematopoietic Stem Cell Transplantation in Adolescence and Young Adult with Severe Thalassemia Compared to Hypertransfusion and Iron Chelation Program

Version: 2 Date: 7 November 2012

Reviewer: Jon Karnon

Reviewer's report:

The submitted manuscript addresses an important health condition – thalassaemia, and a novel intervention with huge potential for health gain – reduced intensity hematopoietic stem cell transplantation (RI-HSCT). Cost utility analysis is appropriate, as is the model-based framework.

The key effectiveness parameters are based on a limited evidence based of 18 patients who received RI-HSCT, who are compared to a literature-base comparator of patients receiving lifelong iron chelation therapy. Whilst not ideal, I think such an evidence base is reasonable for such a condition area, where a randomised clinical trial is unlikely to be feasible.

In terms of the analysis of the 18 patients, it is stated that survival models were fitted for time to death or failure, but Table 1 describes a constant probability of graft failure during the first 6months, and then an assumption of a zero probability of failure in all subsequent time periods. How was time to failure estimated?

For the time to death, why was the estimated probability of death added to the age-specific general population mortality rate?

With respect to the mortality effect for patients receiving ICT, the model applies a RR of 3.9 to the general population mortality rate. This, however, severely underestimates mortality in ICT patients. In the referenced Delea model (and in our own model – Karnon et al, Clinical Drug Investigation 2012), a RR of 3.9 is applied to the non-cardiac general population mortality rate. The effect of thalassaemia on cardiac mortality is much higher. This may require some significant adjustment to the model.

For the cost data, especially for the ICT group, what costs did the direct medical costs study cover, e.g. costs associated with complications?

The analysis of the model should be more clearly described, e.g. the characteristics of the assumed patient population – were they the 18 patients who received RI-HSCT? Or a cohort of similarly aged patients?

The reported sensitivity analysis makes particular reference to the utility and discounting parameters. It is not clear how uncertainty in the survival and time to failure parameters were represented – this should be more clearly explicated.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have received research funding from Novartis to undertake cost-effectiveness analyses of their iron chelation therapy Exjade