From: [redacted]
Sent: 21 September 2007 19:34
To: Shaun Minehan
Cc: Reetan Patel; Natalie Bemrose; [redacted]
Subject: Health Technology Appraisal : Drugs for the treatment of pulmonary arterial hypertension

Dear Shaun

Thank you for sending us the assessment report for the PAH appraisal to review.

In general we found the report to be very accurate. Our one comment refers to the choice of comparator which is outlined in more detail below.

In the assessment report the oral agents and inhaled iloprost are each considered in the same place in the treatment pathway with each compared to "usual care" in FCIII, and being followed by usual care in FCIV. Usual care once patients have progressed to FCIV is assumed to include epoprostenol.

This seems counter-intuitive to us since it is not what happens in clinical practice and the assessment group themselves consider that the data generated for iloprost describes a different group of patients from the evidence generated for oral agents. For example:

> In section 3.3.1.2 it states that 'inhaled iloprost is often seen as an additional treatment to the oral drugs in this assessment, bridging the gap for those patients in whom oral interventions do not adequately reduce progression of disease but who are either not so severely affected that epoprostenol treatment is indicated or epoprostenol treatment is not suitable for them.'
>
> In Table 42 the assessment group calculated that the probability of transition from FCIII to FCIV in the absence of treatment was 0.25 per cycle for the patients eligible for iloprost and only 0.09 per cycle for patients eligible for oral treatment.
>
> In the economic evaluation in section six the expected number of quality adjusted life years (QALYs) in the absence of treatment was 1.958 for iloprost eligible patients (table 56) and 2.201 for patients eligible for oral treatments (tables 58, 60 and 62).

In our submission we proposed that inhaled iloprost be considered for patients who are at FCIII, have failed or who are unable to tolerate oral therapy and who would otherwise require intravenous epoprostenol.1 The use of inhaled iloprost in this patient group is consistent with the licensed indications for the products and current clinical guidelines.2,3 The assessment group model assumes however that when patients fail on oral agents they will simultaneously enter FCIV and receive iv epoprostenol.
This does not consider that many patients who fail oral treatments will still be in FCIII and may require prostanoid treatment (iloprost or epoprostenol) whilst in that disease stage.

We contend that the assessment group model has not considered the use of iloprost in the patient group most consistent with current guidelines and clinical practice, and that the evidence available is consistent with the use of inhaled iloprost in these patients. We contend that it would be appropriate to consider iloprost in patents in FCIII who have failed or who are unable to tolerate oral therapy and who would otherwise require intravenous epoprostenol.

Inhaled iloprost is less expensive than epoprostenol and also avoids the possibility of complications relating to the insertion and/or presence of an indwelling venous catheter. Failing to evaluate the use of inhaled iloprost in patients who have failed oral agents, are still in FCIII, and otherwise require epoprostenol will deny patients access to a non-invasive and cost-effective therapy and force them to move directly to higher cost therapy that carries measurable risks relating to the route of administration.

In the presence of multiple treatment options, given the ease of use and favourable tolerability profile, inhaled iloprost is likely to be considered in patients who fail or no longer tolerate oral treatment, in stage III disease, as an alternative to continuous prostanoid therapy for some patients with PAH.

Kind Regards
[redacted]

1 Please note Schering Health Care are now known as Bayer Schering Pharma, following an acquisition by Bayer Plc.

2 Galie N et al. Guidelines on diagnosis and treatment of pulmonary arterial hypertension: task force on diagnosis and management of pulmonary arterial hypertension of the European Society of Cardiology. European Heart Journal 2004; 25:2243-2278.

3 Humbert MH, Sitbon O et al. Treatment of pulmonary arterial hypertension. New Engl J Med 2004; 351:1425-36

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