The Clinical and cost-effectiveness of epoprostenol, iloprost, bosentan, sitaxentan and sildenafil for the treatment of pulmonary arterial hypertension in adults

Initial submission to the National Institute of Health and Clinical Excellence from
The West Midlands Specialised Commissioning Team (WMSCG)
South Staffordshire Primary Care Trust
North West London Specialised Commissioning Team (London SCG)

It is recognised that the cluster of conditions of interest are serious and that targeted therapy provide benefits for some patients. Most commissioners are sympathetic to some treatment but not without limit and regardless of cost and cost-effectiveness.

1. Comments in response to material presented to consultees

1.1. Inclusions and exclusions

We recognise that this is a difficult area to scope because of the way in which practice has spread ahead of the evidence base and licensing.

Clarification is sought on the grounds on which unlicensed treatments and regimens can be considered. Reference is made to considering the 'licensed dose only where appropriate'. This is particularly pertinent given the approach to other technology assessments in which anything other than the licensed regimen appeared to be allowed to be considered. While we have some sympathy with the view that a broader approach should be allowed – any approach has to be applied to either all appraisals or none.

There is also some concern over the use of functional class as the basis for determining access to treatment. This is a highly subjective measure which introduces the potential for considerable variation in interpretation. We would not wish to adopt such a loose criterion on which to determine access to potentially £125,000+ funding for an individual patient. We would therefore ask NICE to consider this in their policy formulation and aim to adopt a more objective measure. Currently the West Midlands SC Team use physiological measure from the cardiac catheterisation which is available in virtually all patients.

1.2 Subgroup analysis

It is important to undertake subgroup analysis. The basis of this is that it is clear that individual diseases have very different natural histories. Congenital disease generally has a better prognosis, while systemic sclerosis appears to have a considerably worse prognosis.

Although the information is sparse some attempt should be made to assess the potential differences in response of the different disease subgroups. This becomes essential when considering incremental gain of adding in other drugs.

We would like to express our concern that the drug companies have failed to produce information which enables distinct subgroup analysis not only by disease but also by class.

1.3 Outcome measures

Although quality of life measures are important – the financial commitment to patients involved can only really be justified on grounds of improved survival. We therefore feel that this should be the prime outcome of interest.

This the raises concerns over the proxy measures used for survival such as the 6 minute walking test. While this test clearly aids clinicians in assessing prognosis – what is not clear is whether an improvement in the distance walked is accompanied by an equivalent improvement in survival. This would suggest reversibility of the disease process. A particular distance walked at baseline assessment, therefore, is unlikely to be equivalent to when it is walked at post treatment assessment. Treating the pre- and post-assessments as equal may introduce a positive bias in the interpretation of the results. This point needs clarifying.

Commissioners remain concerned about the duration of the trials on which license is given and policy makers are require to assess treatments. We would support any move to direct drug companies or the NHS to undertake more rigorous and long term trials.

1.4 Assessment of industry submissions on economic evaluations

Commissioners are concerned generally that decision making is based on industry submissions which have a bias towards more positive benefits than is the reality. We would hope that the assumptions made are scrutinised and that the final assumptions adopted will be made available to consultees. This is a crucial piece of information on which to judge the basis of the recommendations.

2. Comments on important principles

The major issue of concern in relation to the assessment of these drugs relate to much more fundamental principles.

The lack of a written framework for decision making above the indicative threshold.

It is agreed in principle there needs to be a threshold over which treatments would not generally be funded – regardless of what level the threshold is set. Without this the whole task of assessing cost effectiveness would be unnecessary.

It is expected that at least some of the treatments will fall above the line.

The question then is on what basis would an exceptional situation be considered (and then possibly agreed). The lack of a written coherent, ethical and sustainable framework for considering exceptions is deeply problematic.

Any agreed exceptions must be, by definition, highly unusual. Commissioners are therefore of the view that severity of illness and lack of alternative treatment alone cannot be grounds. Nor can rarity as none of these are in themselves exceptional. If NICE does consider funding above the threshold – then what is the limit? How are the factors which are taken into account translated into the degree to which the cost-

effectiveness is above the threshold? Are the factors different at £50,000 and £100,000/ QALY?

These are vital questions in relation to this group of treatments.

In the absence of this framework it is difficult to see how funding for treatments above the line can be supported. If such a decision was to be taken it is expected that the basis of the decision is made public.

Health gain

It is also of concern that nationally there is not clarity over the health gain which is considered worth the public investing in. Unfortunately, the current health economic model adopted for assessing treatments do not enable the decision maker to discriminate between one individual gaining one year good quality of life – or twelve people gaining one month each. However the two health gains are very different.

This issue is particularly relevant here because of the clinicians' wish to use dual and triple therapy. The incremental health gain of adding in another therapy therefore becomes important. The health gain associated with drug 1 and then the additional health gain achieved by adding in drug 2 at a later stage does not mean the same as the total health gain for the two combined. Commissioners are therefore interested in what is the additional value of adding the second drug – in the same way one would consider any different type of treatment. What we wish to avoid is spending ever greater sums on ever smaller marginal benefits.

The approach is even more crucial if NICE takes the view it wishes to see treatments which are above the threshold available. In this instance it is difficult to envisage any barrier to dual therapy unless incremental benefits are looked at.

NICE are asked to be mindful that clinicians envisage dual therapy and indeed triple therapy as routine in the future.