

News release for medical media and national newspapers

National Institute for Health and Clinical Excellence (NICE) releases appraisal consultation document on treatment of pulmonary arterial hypertension in adults

Newbury, Berkshire – 3 March, 2008 – The National Institute for Health and Clinical Excellence (NICE) has today published on its website the preliminary recommendations of its Appraisal Committee on the use of epoprostenol, iloprost, bosentan, sitaxentan and sildenafil for the treatment of pulmonary hypertension in adults.

This document is for consultation only and does not constitute the Institute's final guidance to the National Health Service (NHS). However, if implemented without any revisions, these proposals will significantly limit the prescribing options for pulmonary hypertension. This will be of particular concern to those patients in the more advanced stages of primary pulmonary hypertension (PPH), which is a very rare, incurable and relentlessly progressive disease. In the event that their disease progresses to the point where oral therapy can no longer control symptoms or cannot be tolerated, patients with PPH would have no alternative disease-specific drug treatment available to them on the NHS.

Primary pulmonary hypertension is defined by NICE as an ultra-orphan disease (i.e. very rare, occurring in less than 1,000 people in the UK)¹ and before the advent of targeted therapies for PPH, when only symptomatic treatments were available, the median survival after diagnosis was only 2.8 years.

In UK clinical practice, patients with PPH normally begin with symptomatic treatment alone. As the disease progresses, the patient will require disease-specific oral therapies and will eventually need a prostanoid in order to control the advancement of the disease and maintain quality of life. Prostanoids can be inhaled or given by intravenous infusion. The appraisal consultation document from NICE proposes that patients are to be denied access to prostanoid therapy and that other therapeutic choices are limited to one first line oral therapy (sildenafil) and two alternative oral therapies (bosentan and sitaxentan), for patients in whom sildenafil is contraindicated or poorly tolerated.

Ventavis[®] (inhaled iloprost) has a vital role in bridging the gap between oral therapy alone and the need for continuous IV prostanoids (e.g. epoprostenol). It is not intended as a replacement for oral therapies. Ventavis[®] offers advantages over IV therapy in respect to convenience and tolerability and avoids both tachyphylaxis (large increases in dose, therefore cost, over time) and the risks associated with the IV route of administration.

The appraisal of Ventavis[®] by NICE omits two important considerations:

1. It does not evaluate the subgroup in which Ventavis[®] is actually used in current UK clinical practice (i.e. in patients who have failed oral agents and otherwise require IV epoprostenol).

2. It does not take into account either the ultra-orphan status of PPH or the ultra-orphan drug status of Ventavis® (by EMEA criteria²), even though a draft discussion paper produced by NICE in 2006¹ suggests there is a case for not applying the normal cost-effectiveness thresholds in the appraisal of ultra-orphan diseases and specifically references iloprost in PPH as an example.

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About Pulmonary Hypertension

Pulmonary hypertension is a rare, long-term disease that affects people of all ages and races. The cause of it is unknown and there is no cure. However, there are several treatments which may help and information is provided on these later.

“Pulmonary” means the disease is in the lungs. “Hypertension” is another word for high blood pressure. In pulmonary hypertension it is harder for blood to flow to the lungs and pressure builds up in the pulmonary artery.

Pressure is measured in millimetres of mercury or mm Hg. In healthy people who are resting, the pressure in the pulmonary artery is about 14 mm Hg. In pulmonary hypertension, pressure in the pulmonary artery rises above 25 mm Hg. This means the heart has to work harder and pump faster than normal to get blood to the lungs and the rest of the body.

The heart muscle and right ventricle may get bigger than normal, to cope with the extra work. With time the right ventricle may become weak and unable to pump enough blood. Eventually the heart may fail completely.

Pulmonary hypertension can make the patient feel tired. Although, many patients ignore the tiredness at first because they think it is a result of not being particularly fit. They are likely to have difficulty in breathing or feel like they are not getting enough air. This is called dyspnoea or shortness of breath. The patient may experience dizzy spells and fainting, which is called syncope. The lips and skin may appear bluer than normal (cyanosis) and sometimes the patient will experience pain in their chest (angina).

These are all common symptoms of pulmonary hypertension that happen because there is not enough blood going to the lungs collecting oxygen for the rest of the body. Also, ankles or legs may swell (oedema) because blood is not being pumped around the body properly, so fluid collects in the legs and ankles, especially if the patient stays on their feet for a long time.

NYHA Class

The doctor will decide how severe the disease is by using one of four classes to describe it. These classes are from the New York Heart Association (NYHA) and this is the NYHA classification.

What is Ventavis® (iloprost trometamol)?

Iloprost trometamol is a liquid containing a drug called iloprost. Iloprost acts in the same way as a natural chemical in the body called prostacyclin. Prostacyclin relaxes blood vessels, which helps to stop them becoming narrow or blocked. Prostacyclin also makes blood less sticky so clots are a little less likely to develop. Iloprost trometamol is used to treat some, but not all cases of moderate pulmonary hypertension.

How iloprost trometamol works

By acting like prostacyclin, iloprost trometamol helps more blood get to the lungs and collect oxygen. This tends to lower blood pressure in the pulmonary artery and will hopefully mean less strain on the heart.

Iloprost is needed in the lungs but not in the rest of the body. For this reason iloprost trometamol is inhaled or breathed in. This means the iloprost trometamol liquid has to be changed into a fine spray or mist by a device called a nebuliser. The nebuliser is then used to breathe iloprost trometamol into the lungs.

About the NICE appraisal

NICE is appraising epoprostenol, iloprost, bosentan, sitaxentan and sildenafil for the treatment of pulmonary arterial hypertension in adults.

The process the Institute will follow after the consultation period is summarised below. For further details, see the 'Guide to the technology appraisal process' (this document is available on the Institute's website; www.nice.org.uk).

- The Appraisal Committee will meet again to consider the original evidence and this appraisal consultation document in the light of the views of the formal consultees.
- At that meeting, the Committee will also consider comments made on the document by people who are not formal consultees in the appraisal process.
- After considering feedback from the consultation process, the Committee will prepare the final appraisal determination (FAD) and submit it to the Institute.
- Subject to any appeal by consultees, the FAD may be used as the basis for the Institute's guidance on the use of the appraised technology in the NHS in England and Wales.

Closing date for comments: 25 March 2008

Second Appraisal Committee meeting: 3 April 2008

About Bayer Schering Pharma

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For more information, please visit www.bayerscheringpharma.co.uk

References:

1. Appraising Orphan Drugs, National Institute for Health and Clinical Excellence, 16 March 2006.
http://www.nice.org.uk/aboutnice/whoweare/seniormanagementteam/seniormanagementteammeetings/2005/12july2005/appraising_orphan_drugs.jsp
2. COMP Report to the Commission in relation to Article 10 of Regulation 141/2000 on orphan medicinal products, European Medicines Agency (EMA), <http://www.emea.europa.eu/pdfs/human/comp/3521805en.pdf>