EXECUTIVE SUMMARY

Clinical Effectiveness

- Pulmonary Arterial Hypertension (PAH) is a devastating, life-threatening condition, despite major advances in therapy.
- Modern therapies (prostanoids, phosphodiesterase 5 inhibitors and endothelin receptor antagonists (ETRAs) have approximately doubled life expectancy in patients with idiopathic PAH relative to the era when only supportive care was available.
- Oral therapies for PAH have been shown to improve patient outcomes and can offer an effective treatment option that allows patients to live a more indepent life compared to more invasive therapy with intravenous or nebulised substances. Current oral therapies include two ETRAs, Thelin and bosentan and the phosphodiesterase Type 5 inhibitor sildenafil.
- These therapies should be the first option in the treatment of PAH.
- Within the scope of this assessment, there is insufficient published evidence to compare the clinical and cost-effectiveness of the three oral therapies. In particular, current long-term data on outcomes of supportive care are not available, rendering indirect comparisons unfeasible.
- Thelin® (sitaxentan sodium) is a new oral drug for PAH and only became available in the UK in November 2006. It is taken as one tablet once a day. Thelin belongs to the group of endothelin receptor antagonists (ETRA). It is highly selective, with specific selectivity (6500:1) for the ET_A receptor than for the ET_B receptor subtype. This gives Thelin a theoretical advantage over a non-selective ETRA, as it leaves the ET_B receptor intact allowing clearance of ET-1, together with stimulation of nitric oxide and prostacyclin, which act as powerful vasodilators.
- Two double-blind placebo controlled RCTs have shown efficacy of Thelin in patients with IPAH and PAH associated with connective tissue disease (CTD). Thelin has a favourable safety profile and has no clinically relevant interactions with sildenafil.
- The results of the only head-to-head trial in oral PAH treatments indicated that Thelin compared favourably to bosentan over a 12-month treatment period with respect to time on monotherapy, discontinuations associated with adverse events, time to occurrence of, and discontinuation due to, elevated liver enzyme levels, time to occurrence of first clinical worsening event and survival. The trial was open label, but several of the results (elevated liver enzyme levels, clinical worsening, and survival) are unlikely to be influenced by the open-label nature of the study.
- For patients, this means that they can be maintained longer on oral therapy which may delay the need for more invasive treatments due to disease progression, which is often associated with higher drug costs, hospitalisations and ultimately death.

Cost Effectiveness

- The economic impact of PAH is unknown. Taking the perspective of the NHS and Personal Social Services in England and Wales, hospitalisations and the need for continuous intravenous therapies represent the biggest cost driver in patients with PAH. Unfortunately no quality of life data or utilities that could assess the overall impact of therapies, in particular in relation to hospitalisations, have been published. It was hence

not feasible to express the cost-effectiveness for Thelin as cost per quality adjusted life year and an economic analysis using cost per life years gained was developed instead, based on the population for which Thelin is licensed in the UK

- The results of the presented Markov model would suggest that Thelin is at least as cost effective as bosentan; should longer term data for bosentan provide a better estimate of its cost effectiveness then one can assume that the differential benefits of Thelin persist and may achieve similar results.
- The acquisition cost of Thelin is almost identical to bosentan, thus Thelin offers added choice without increasing NHS drug costs. However the potential added benefits of Thelin therapy may, over time, save the NHS funds as compared to the overall cost of therapy for patients treated with bosentan Any increases in prescribing by specialists in PAH can be assumed to be due to currently unmet need and increased patient numbers due to better diagnosis.

Conclusions

In a complex orphan disease like PAH, clinical data is often not available to fully assess the impact on different patient subpopulations or on patients' quality of life. More research is needed to assess more accurately the impact of various treatments on resource use, health-related quality of life and utilities.

Thelin, alongside other effective drugs for the treatment of PAH should be made availabe to specialists in PAH, so they can offer their patients the best possible therapy during the progression of this rare but fatal disease.