NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Sotatercept for treating pulmonary arterial hypertension

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of sotatercept within its marketing authorisation for treating pulmonary arterial hypertension.

Background

Pulmonary hypertension is characterised by high blood pressure in the pulmonary arteries, the blood vessels that supply the lungs. Pulmonary arterial hypertension (PAH) is a rare, severe and progressive form of pulmonary hypertension caused by changes in the smaller branches of the pulmonary arteries, restricting blood flow through the lungs. The condition causes the walls of the pulmonary arteries to become thick and stiff, narrowing the space for blood to pass through and increasing blood pressure. As the pulmonary arteries are less able to stretch, the heart has to work harder to pump blood to the lungs, which causes damage to the heart, and makes it less efficient at pumping blood around the body and getting oxygen to the muscles. People with PAH experience increasingly debilitating symptoms which severely impact day to day living and quality of life, including breathlessness during exercise and sometimes during rest, extreme tiredness, weakness and chest pain. PAH is a progressive illness, meaning that if not detected and treated early, people with PAH are at increased risk of other illnesses, such as pneumonia, frequent hospitalisations, and ultimately, right heart failure leading to premature death.

The estimated annual incidence of PAH in the UK general population ranges from 0.9 to 7.6 cases per 1,000,000 people and the estimated prevalence of PAH in the UK general population is between 6.6 and 26 per 1,000,000 people. These figures are thought to be underestimates due to misdiagnosis or underdiagnoses of PAH patients.[1] Data from a 2015 National Audit of Pulmonary Hypertension estimated that there were 2,657 people being treated for PAH within an active specialist centre in England.[2]

There are a range of treatments that can help to improve symptoms and manage PAH. These can be broadly split into 3 categories:

- conventional treatments, including oxygen therapy, anticoagulant medication (such as warfarin) and diuretic medication (such as furosemide, bumetanide, and metolazone);

- targeted treatments intended to slow disease progression and potentially reverse damage to the heart and lungs. These include calcium channel blockers (such as nifedipine, diltiazem, nicardipine, and amlodipine), endothelin receptor antagonists (such as ambrisentan, bosentan, and macitentan), phosphodiesterase 5 inhibitors (such as sildenafil and tadalafil), prostaglandins (such as epoprostenol and selexipag), and soluble guanylate cyclase stimulators (such as riociguat);

- surgical interventions, including pulmonary endarterectomy (removal of blood clots in the pulmonary artery), arterial septostomy (hole made between the left and right atria of the heart to reduce pressure in the right side of the heart, improving blood flow to the lungs), transplant surgery (of heart and lungs or lungs alone), and balloon pulmonary angioplasty.

The technology

Sotatercept (brand name unknown, MSD) does not currently have a marketing authorisation in the UK for treating PAH. Sotatercept in combination with background therapy has been studied in clinical trials where it has been compared with placebo in combination with background therapy in people with PAH.

Intervention(s)	Sotatercept
Population(s)	Adults with pulmonary arterial hypertension
Comparators	Established clinical management without sotatercept, (including but not limited to); • anticoagulant medication: warfarin • diuretic medication: furosemide, bumetanide, and metolazone • calcium channel blockers: nifedipine, diltiazem, nicardipine, and amlodipine • endothelin receptor antagonists: ambrisentan, bosentan, and macitentan • phosphodiesterase 5 inhibitors: sildenafil and tadalafil • prostaglandins: epoprostenol and selexipag • soluble guanylate cyclase stimulators: riociguat
Outcomes	The outcome measures to be considered include: • time to first confirmed morbidity or mortality event • overall survival • transplant-free survival • exercise capacity • haemodynamic assessment (e.g. cardiac index, cardiac output, right atrial pressure, pulmonary arterial pressure and pulmonary vascular resistance) • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related NICE guidelines:** Hypertension in adults: diagnosis and management (2019) NICE guideline NG136. Updated March 2022 **Related interventional procedures:** Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension (2016) NICE interventional procedures guidance 554 **Related quality standards:** Hypertension in adults (2013) NICE quality standard QS28. Updated September 2015
Related National Policy	NHS England (2015) Commissioning Policy: Targeted Therapies for use in Pulmonary Hypertension in Adults NHS England (2018) Clinical Commissioning Policy: Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension (all ages) NHS England (2018) Clinical Commissioning Policy Selexipag for treating pulmonary arterial hypertension (adults) NHS England (2017) Clinical Commissioning Policy: iociguat for pulmonary arterial hypertension The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 2 and 3.

Questions for consultation

Where do you consider sotatercept will fit into the existing care pathway for PAH?

Have all the relevant comparators been included in the scope?

What is standard of care for PAH?

What is the accepted definition of background therapy in the context of PAH?

Is the World Health Organization (WHO) Functional Class measure used to determine which treatments people with PAH would be offered?

In clinical trials of sotatercept, participants were classified according to functional class, whether or not symptomatic, time since diagnosis and risk score. In which populations would sotatercept be used?

Would sotatercept be a candidate for managed access?

Do you consider that the use of sotatercept can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sotatercept will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-tehnology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS England. Clinical Commissioning Policy: National policy for targeted therapies for the treatment of pulmonary hypertension in adults. 2014. Available from: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2014/06/a11-ps-b.pdf (Accessed June 2023)

2. NHS England/NICE (2018) Clinical Commissioning Policy Proposition: Selexipag for treating pulmonary arterial hypertension (adults) (Accessed June 2023)