**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Highly Specialised Technologies Evaluation**

# Human alpha 1-proteinase inhibitor for treating emphysema

**Final scope**

## Remit/evaluation objective

To evaluate the benefits and costs of human alpha 1-proteinase inhibitor within its marketing authorisation for treating emphysema for national commissioning by NHS England.

## Background

Emphysema is a chronic lung disease in which the walls of the air sacs are damaged and break down causing them to enlarge. This makes the lungs baggy and less able to move the air in and out. The symptoms include coughing, wheezing, breathlessness, and frequent chest infections. Exacerbations often occur, where there is a rapid and sustained worsening of symptoms.

Alpha 1-antitrypsin is a protein made in the liver that circulates in blood plasma. It protects the lungs from damage by enzymes such as neutrophil elastase. Some people have a genetic mutation that causes them to have low levels of alpha 1-antitrypsin. This deficiency can mean that neutrophil elastase damages cells in the lungs, causing emphysema. Severe alpha 1-antitrypsin deficiency is defined as serum alpha 1-antitrypsin concentration below 11 micromolar.[1] Alpha1-antitrypsin associated emphysema is often rapidly progressive and more severe than other forms of chronic obstructive pulmonary disease (COPD). People with alpha1-antitrypsin deficiency who smoke can have COPD symptoms in their 20s, whereas people with alpha1-antitrypsin deficiency who have never smoked are more likely to have symptoms over the age of 40. Severe alpha 1-antitrypsin deficiency can also cause disease in other organs such as the liver.

Between 1 in 1600 and 1 in 5000 newborn babies have alpha 1-antitrypsin deficiency, but not all will develop emphysema.[2] Based on a disease registry in the West Midlands, it is estimated that 670 people in England have emphysema caused by alpha 1-antitrypsin deficiency.[1] About 540 of these people (80%) will have clinically significant emphysema that requires treatment.[2] Some people with COPD have undiagnosed alpha 1-antitrypsin deficiency.[3]

Currently, the treatment for emphysema is the same regardless of whether people have alpha 1-antitrypsin deficiency or they do not. NICE clinical guideline 101 recommends that people with COPD should be provided with help to stop smoking and should be offered pneumococcal vaccination and an annual influenza vaccination. NICE clinical guideline 101 recommends initial

treatment with short-acting bronchodilators. For people who remain breathless or have exacerbations despite using short-acting bronchodilators as required, NICE clinical guideline 101 recommends a sequence of inhaled treatments. These treatments may include a long-acting beta2 agonist (LABA), a long-acting muscarinic antagonist (LAMA) or inhaled corticosteroids, alone or in combination. Some people may have oral therapy with slow-release theophylline or a mucolytic. Additional treatment options include pulmonary rehabilitation (a multidisciplinary programme of supervised exercise training and education), oxygen therapy and, for those with severe disease, lung transplantation and lung volume reduction. With the exception of smoking cessation and the avoidance of other environmental risk factors, current treatments for emphysema caused by alpha 1-antitrypsin deficiency aim to alleviate symptoms and do not slow down the progression of the disease.

Replacement therapy (also known as augmentation therapy) aims to boost the levels of alpha 1-antitrypsin in the blood. It involves an intravenous infusion of alpha 1-proteinase inhibitor derived from the blood plasma of healthy donors. NICE clinical guideline 101 does not recommend replacement therapy for people with alpha1-antitrypsin deficiency and COPD. NICE clinical guideline 101 notes that people with alpha 1-antitrypsin deficiency should be the opportunity to be referred to a specialist centre to discuss the clinical management of this condition.

## The technology

Human alpha 1-proteinase inhibitor (Respreeza, CSL Behring UK Limited) inhibits neutrophil elastase and other proteases in the lower respiratory tract to slow the underlying destruction of lung tissue. It is administered by intravenous (IV) infusion at 60mg/kg, once weekly.

Human alpha 1-proteinase inhibitor has a marketing authorisation in the UK ‘for maintenance treatment, to slow the progression of emphysema in adults with documented severe alpha1-proteinase inhibitor deficiency (e.g. genotypes PiZZ, PiZ(null), Pi(null,null), PiSZ). Patients are to be under optimal pharmacologic and non-pharmacologic treatment and show evidence of progressive lung disease (e.g. lower forced expiratory volume per second (FEV1) predicted, impaired walking capacity or increased number of exacerbations) as evaluated by a healthcare professional experienced in the treatment of alpha 1-proteinase inhibitor deficiency.’

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| **Intervention(s)** | Human alpha 1-proteinase inhibitor in addition to established clinical management |
| **Population(s)** | Adults with severe alpha 1-proteinase inhibitor deficiency who have progressive lung disease |

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| **Comparators** | Established clinical management without alpha 1-proteinase inhibitor, which may include but is not restricted to:<br>• short-acting bronchodilators<br>• long-acting beta2 agonists (LABA)<br>• long-acting muscarinic antagonists (LAMA)<br>• inhaled corticosteroids<br>• oral therapy with slow-release theophylline or a mucolytic<br>• pulmonary rehabilitation<br>• oxygen therapy<br>• lung transplantation<br>• lung volume reduction. |
| **Outcomes** | The outcome measures to be considered include:<br>• incidence, duration and severity of acute exacerbations, including hospitalisation<br>• change in lung density<br>• lung function<br>• symptom control (e.g shortness of breath)<br>• exercise capacity<br>• mortality<br>• adverse effects of treatment<br>• health-related quality of life (for patients and carers). |
| **Nature of the condition** | • disease morbidity and patient clinical disability with current standard of care<br>• impact of the disease on carer's quality of life<br>• extent and nature of current treatment options |

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| **Clinical Effectiveness** | • overall magnitude of health benefits to patients and, when relevant, carers<br>• heterogeneity of health benefits within the population<br>• robustness of the current evidence and the contribution the guidance might make to strengthen it<br>• treatment continuation rules (if relevant) |
| **Value for Money** | • Cost effectiveness using incremental cost per quality-adjusted life year<br>• Patient access schemes and other commercial agreements<br>• The nature and extent of the resources needed to enable the new technology to be used |
| **Impact of the technology beyond direct health benefits** | • whether there are significant benefits other than health<br>• whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services<br>• the potential for long-term benefits to the NHS of research and innovation<br>• the impact of the technology on the overall delivery of the specialised service<br>• staffing and infrastructure requirements, including training and planning for expertise. |
| **Other considerations** | • Guidance will only be issued in accordance with the marketing authorisation.<br>• Guidance will take into account any Managed Access Arrangements<br>• If evidence allows, consideration may be given to subgroups based on the characteristics and progression of the disease (including for example, speed of decline, distribution of disease and frequency of exacerbations) |

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| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br>'Roflumilast for treating chronic obstructive pulmonary disease' (2017). NICE Technology Appraisal 461. Review date July 2020. *Note: this guidance covers COPD associated with chronic bronchitis only*.<br>Appraisals in development:<br>'Mepolizumab for treating chronic obstructive pulmonary disease' NICE technology appraisal guidance [ID1237]. Publication date to be confirmed.<br>Related Guidelines:<br>'Chronic obstructive pulmonary disease in over 16s: diagnosis and management' (2010). NICE guideline 101. Anticipated update publication date November 2018<br>Related Interventional Procedures:<br>'Endobronchial valve insertion to reduce lung volume in emphysema' (2017). NICE interventional procedures guidance 600.<br>'Insertion of endobronchial nitinol coils to improve lung function in emphysema' (2015). NICE interventional procedures guidance 517.<br>Lung volume reduction surgery for advanced emphysema (2005). NICE interventional procedures guidance 114.<br>Related Quality Standards:<br>'Chronic obstructive pulmonary disease in adults' (2011, updated 2016). NICE quality standard 10. Review date: August 2018<br>Related NICE Pathways:<br>Chronic obstructive pulmonary disease NICE pathway |
| **Related National Policy** | NHS England: Manual for prescribed specialised services 2017/18. Pages 22-23. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf<br>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf |

## References


1. Miravitlles M, Herr C, Ferrarotti I et al. (2010) Laboratory testing of individuals with severe alpha1-antitrypsin deficiency in three European centres. European Respiratory Journal 35(5):960-8
2. NIHR Horizon Scanning Centre, 2014. Briefing note: Alpha-1 antitrypsin (Respreeza) for emphysema associated with alpha-1 antitrypsin deficiency – maintenance therapy. Accessed: February 2018
3. Alpha-1 UK Support Group, 2015. A healthcare professional's guide to alpha-1 antitrypsin deficiency. Accessed: February 2018