

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

**Gefapixant for treating refractory or unexplained chronic cough**

**Draft scope**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of gefapixant within its marketing authorisation for treating refractory or unexplained chronic cough.

**Background**

Cough is a reflex response to airway irritation. It is triggered by stimulation of airway cough receptors, either by irritants or by conditions that distort the airway. Chronic cough is a cough lasting more than 8 weeks<sup>1</sup>. Chronic cough can be associated with increased sensitivity of nerve cells involved in a person's cough reflex making a person more likely to cough in response to stimuli that trigger this reflex<sup>2</sup>. Chronic cough is most commonly caused by smoking, use of angiotensin-converting enzyme (ACE) inhibitors, upper airway cough syndrome (post-nasal drip), asthma, gastro-oesophageal reflux disease (GORD) or eosinophilic bronchitis<sup>1</sup>. Refractory coughs do not respond to treatments for the underlying cause of the cough. In some people the cause of the cough cannot be diagnosed.

Refractory or unexplained chronic cough can cause physical, social and psychological stress. Complications may include, but are not limited to, stress urinary incontinence, impairment of speech, depression and anxiety, chest pain, rib fracture, sleep disturbance and exhaustion, which can impact a person's quality of life<sup>2</sup>.

The prevalence of chronic cough varies but it is estimated to be around 10% of the population. Two-thirds of people with chronic cough are women and it is most common in people between 50 and 70 years of age<sup>1</sup>. The proportion of people with refractory or unexplained cough is unknown.

There is no NICE guidance on, or licensed treatments for, treating chronic refractory or unexplained cough.

- The NICE clinical knowledge summary on cough states that for people presenting with chronic cough, potential causes are identified and treated accordingly. If after these initial investigations the diagnosis of the cause of the cough is unclear, sequential trials of treatments for upper airway cough syndrome, asthma and GORD may be tried<sup>1</sup>. Following this, a trial of low dose morphine (5 mg to 10 mg twice daily), gabapentin or a speech and language intervention are options for people with chronic refractory cough<sup>1</sup>.
- European Respiratory Society guidelines on the treatment of chronic cough in adults and children also suggest that off-label treatments which affect the sensitivity of nerve cells such as low-dose opioids, gabapentin or pregabalin may be tried. These guidelines also suggest non-pharmacological approaches like cough control therapy as treatment options<sup>2</sup>.

For people who have idiopathic pulmonary fibrosis or lung cancer with chronic cough, NICE clinical guidelines CG163 and NG122 also recommend opioids as a treatment option.

### The technology

Gefapixant (MK-7264, MSD) is a selective P2X3 receptor antagonist. Inhibiting P2X3 stops sensory neurons that are involved in coughs triggered by injury or infection from becoming hyper-sensitised. This prevents an exaggerated, persistent and frequent urge to cough. It is administered orally.

Gefapixant does not have a marketing authorisation in the UK for treating refractory or unexplained chronic cough. It has been studied in randomised placebo-controlled trials in people aged 18 and over who have had chronic cough for at least 1 year with a diagnosis of refractory chronic cough or unexplained chronic cough. The trials included people without any abnormality identified by radiograph or CT scan of the thorax or clinically significant lung disease which would be contributing to the cough. The trials excluded current smokers and people who had given up within the last 12 months, and some former smokers. They also excluded people with a history of respiratory tract infection or recent clinically significant change in pulmonary status, people with a history or chronic bronchitis or people currently taking an angiotensin converting enzyme inhibitor.

<b>Intervention(s)</b>	Gefapixant
<b>Population(s)</b>	People with refractory or unexplained chronic cough.
<b>Comparators</b>	Established care without gefapixant
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• cough frequency</li> <li>• cough severity</li> <li>• complications of cough</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>

<b>Other considerations</b>	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.
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals: None</p> <p>Related Guidelines: <a href="#">Idiopathic pulmonary fibrosis in adults: diagnosis and management (2013, updated 2017). NICE guideline CG163</a> <a href="#">Chronic obstructive pulmonary disease in over 16s: diagnosis and management (2019) NICE guideline NG115</a> <a href="#">Lung cancer: diagnosis and management (2019) NICE guideline NG122</a></p> <p>Related Interventional Procedures: None</p> <p>Related Public Health Guidance/Guidelines: None</p> <p>Related Quality Standards: None</p> <p>Related NICE Pathways: <a href="#">Respiratory conditions.</a></p>
<b>Related National Policy</b>	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2,4, 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a>

### Questions for consultation

How are people with refractory or unexplained chronic cough identified in clinical practice?

- Which treatments would people have had before being considered refractory to treatment?

What is current established care for people with refractory or unexplained chronic cough that would be displaced by gefapixant?

- Are neuromodulatory drugs such as low-dose opioids (morphine), gabapentin and pregabalin used off-label for this indication in NHS clinical practice?

- Are there any non-pharmacological cough control therapies used in NHS clinical practice that would be displaced by gefapixant?
- Are any other treatments used for this indication that would be displaced by gefapixant?
- Does the choice of current treatments depend on the severity of the person's cough?

Are the outcomes listed appropriate?

- What are the main complications of chronic cough that should be included as outcomes?
- Would the impact of complications of chronic cough be captured by health-related quality of life assessments?
- Would mortality be a relevant outcome (does chronic cough or any potential complications of chronic cough reduce life expectancy)?

Are there any subgroups of people in whom gefapixant is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider gefapixant will fit into the existing NICE pathway, [respiratory conditions](#)?

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 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.

Do you consider gefapixant to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of gefapixant can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>).

### References

1. NICE Clinical Knowledge Summary: Cough available from [Cough | Topics A to Z | CKS | NICE](#) (accessed January 2021)
2. Morice A, Millqvist E, Bieksiene K et al. (2019) ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *European Respiratory Journal* 2020 55: 1901136