**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

# Vanzacaftor–tezacaftor–deutivacaftor for treating cystic fibrosis with 1 or more F508del mutations in the CFTR gene in people 6 years and over [ID6372]

**Final scope**

## Remit/evaluation objective

To appraise the clinical and cost effectiveness of vanzacaftor–tezacaftor–deutivacaftor within its marketing authorisation for treating cystic fibrosis with 1 or more *F508del* mutations in the *CFTR* gene in people 6 years and over.

## Background

Cystic fibrosis is an inherited disease caused by genetic mutations. The cystic fibrosis transmembrane conductance regulator (*CFTR*) gene normally creates a protein that regulates levels of sodium and chloride in cells. If the *CFTR* gene is faulty, cells are unable to make functioning versions of this protein, leading to a build-up of thick, sticky mucus in the body's tubes and passageways. These blockages damage the lungs, digestive system and other organs, resulting in persistent cough, recurring chest and lung infections and poor weight gain. Cystic fibrosis is a progressive condition that limits life expectancy.

Cystic fibrosis affects about 11,000 people in the UK.[1] About 1 in 25 people are carriers of a faulty gene (or 'mutation') that can cause cystic fibrosis.[2] There are over 2,000 known mutations that can cause cystic fibrosis.[3] For someone to be born with cystic fibrosis, they must inherit a faulty gene from both parents. These mutations can either be homozygous, the same, or heterozygous, different mutations. The most common mutation is the *F508del* mutation and around 89% of people with cystic fibrosis carry at least 1 copy of the *F508del* mutation.[1]

NICE technology appraisal guidance 988 recommends ivacaftor–tezacaftor–elexacaftor as an option for treating cystic fibrosis in people 2 years and over who have at least 1 *F508del* mutation in the *CFTR* gene, lumacaftor–ivacaftor for treating cystic fibrosis in people 1 year and over who have 2 copies of the *CFTR* gene with *F508del* mutations, and tezacaftor–ivacaftor for treating cystic fibrosis in people 6 years and over who have 2 copies of the *CFTR* gene with *F508del* mutations, or a copy of the *CFTR* gene with an *F508del* mutation and a copy of the *CFTR* gene with 1 of the following mutations: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, or 3849+10kbC→T.

## The technology

Vanzacaftor-tezacaftor-deutivacaftor (brand name unknown, Vertex Pharmaceuticals) does not currently have a marketing authorisation in the UK for treating cystic fibrosis with 1 or more *F508del* mutations in the *CFTR* gene in people 6 years and over. It has been studied in clinical trials compared with elexacaftor-tezacaftor-ivacaftor and placebo in people 1 year and older.

| | |
|---|---|
| **Intervention(s)** | Vanzacaftor-tezacaftor-deutivacaftor |
| **Population(s)** | People 6 years and over with cystic fibrosis with at least 1 *F508del* mutation |
| **Subgroups** | People who have<br>• 2 copies of the *CFTR* gene with *F508del* mutations<br>• 1 copy of the *CFTR* gene with a *F508del* mutation and 1 copy with another mutation |
| **Comparators** | • Ivacaftor–tezacaftor–elexacaftor<br>• Established clinical management including but not limited to: antibiotics, inhaled mucolytics (including mannitol dry powder for inhalation, hypertonic saline and dornase alfa), anti-inflammatory agents, bronchodilators<br><br>For people with specific mutations, treatment may include:<br>• Tezacaftor–ivacaftor<br>• Lumacaftor–ivacaftor<br>• Ivacaftor monotherapy |

| | |
|---|---|
| **Outcomes** | The outcome measures to be considered include:<br>• mortality<br>• predicted forced expiratory volume<br>• percentage of predicted forced vital capacity<br>• lung function<br>• lung transplantation<br>• body mass index<br>• respiratory symptoms<br>• pulmonary exacerbations, including frequency and severity of acute infections<br>• sweat chloride<br>• lung clearance<br>• pulmonary bacterial colonisation<br>• need for hospitalisation<br>• pancreatic function<br>• inflammation<br>• liver function<br>• adverse effects of treatment<br>• 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.<br>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account |

| | |
|---|---|
| **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 technology appraisals:**<br>Ivacaftor–tezacaftor–elexacaftor, tezacaftor–ivacaftor and lumacaftor–ivacaftor for treating cystic fibrosis (2024) NICE technology appraisal guidance 988<br>Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis (2013) NICE technology appraisal guidance 276<br>Mannitol dry powder for inhalation for treating cystic fibrosis (2012) NICE technology appraisal guidance 266<br>**Related NICE guidelines:**<br>Cystic fibrosis: diagnosis and management (2017) NICE guideline NG78<br>**Related quality standards:**<br>Cystic fibrosis (2018) NICE quality standard 168 |
| **Related National Policy** | The NHS Long Term Plan (2019) NHS Long Term Plan<br>NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 45. Cystic fibrosis services (adults and children) |

**References**

1. The Cystic Fibrosis Trust (2023), UK CF Registry: 2022 Annual Data Report [accessed 29 August 2024]

2. The Cystic Fibrosis Trust. What is cystic fibrosis? [accessed 29 August 2024]

3. The Cystic Fibrosis Trust. What causes cystic fibrosis? [accessed 29 August 2024]