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

Draft scope

Draft 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 • 2 copies of the *CFTR* gene with *F508del* mutations • 1 copy of the *CFTR* gene with a *F508del* mutation and 1 copy with another mutation
Comparators	• Ivacaftor–tezacaftor–elexacaftor • Established clinical management including: o best supportive care o physiotherapy o antibiotics o supplemental feeding o exercise o mannitol dry powder for inhalation o inhaled mucolytics o nebulised hypertonic saline o anti-inflammatory agents o bronchodilators o vitamin supplements o pancreatic enzymes For people with 2 copies of the *CFTR* gene with *F508del* mutations or who have a copy of the *CFTR* gene with an *F508del* mutation and a copy of the *CFTR* gene with one 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: • Tezacaftor–ivacaftor For people with 2 copies of the *CFTR* gene with *F508del* mutations • Lumacaftor–ivacaftor For people with one copy of the *CFTR* gene with a *F508del* mutation and one copy of the *CFTR* gene with an *R117H* or gating mutation • Ivacaftor monotherapy

Outcomes	The outcome measures to be considered include: • mortality • change in the percentage of predicted forced expiratory volume • forced vital capacity • lung function, including transplantation • body mass index • respiratory symptoms • pulmonary exacerbations, including frequency and severity of acute infections • sweat chloride • lung clearance index 2.5 • pulmonary bacterial colonisation • need for hospitalisation and other treatments including antibiotics • 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. 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. 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. 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:** Ivacaftor–tezacaftor–elexacaftor, tezacaftor–ivacaftor and lumacaftor–ivacaftor for treating cystic fibrosis (2024) NICE technology appraisal guidance 988 Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis (2013) NICE technology appraisal guidance 276 Mannitol dry powder for inhalation for treating cystic fibrosis (2012) NICE technology appraisal guidance 266 **Related NICE guidelines:** Cystic fibrosis: diagnosis and management (2017) NICE guideline NG78 **Related quality standards:** Cystic fibrosis (2018) NICE quality standard 168
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 45. Cystic fibrosis services (adults and children)

Questions for consultation

Where do you consider vanzacaftor–tezacaftor–deutivacaftor will fit into the existing care pathway for cystic fibrosis?

Please select from the following, will vanzacaftor–tezacaftor–deutivacaftor be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would vanzacaftor–tezacaftor–deutivacaftor be a candidate for managed access?

Do you consider that the use of vanzacaftor–tezacaftor–deutivacaftor 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 vanzacaftor–tezacaftor–deutivacaftor 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 is considering evaluating this technology through its cost comparison evaluation process.
Please provide comments on the appropriateness of appraising this topic through this 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-technology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.

- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

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]