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Health Technology Briefing
March 2026

VX-522 for treatment of CFTR genotype cystic fibrosis unresponsive to CFTR modulator treatment

Company/Developer	Vertex Pharmaceuticals

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 40895	NICE ID: Not Available	UKPS ID: 675243

Licensing and Market Availability Plans

In phase I/II clinical development.

Summary

VX-522 is in development for treatment of cystic fibrosis in patients with cystic fibrosis transmembrane conductance regulator (CFTR) genotype which are not responsive to CFTR modulator therapy. Cystic fibrosis is a rare, chronic and life-shortening genetic disease caused by a faulty gene that affects the movement of salt and water in and out of cells. It is a progressive, multi-system disease that affects the lungs, liver, gastrointestinal tract, pancreas, sinuses, sweat glands and reproductive tract. In the lungs, it leads to the build-up of abnormally thick, sticky mucus that can cause chronic lung infections and inflammation, resulting in progressive lung damage and premature death. It is an inherited condition, and symptoms include recurring chest infections, wheezing, coughing, shortness of breath, damage to the airways and jaundice. Current therapies are not effective in some patients with CFTR mutations, and only control symptoms rather than addressing the cause of the disease, meaning patients have limited therapeutic options available.

VX-522 is given via oral inhalation using a nebuliser. VX-522 uses mRNA to deliver instructions to cells in the lung which produce a functional version of the CFTR protein. By providing instructions to make a working version, VX-522 may help improve symptoms of the disease. If licensed, VX-522 may offer an option for patients who have few treatments available.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Patients with cystic fibrosis and a cystic fibrosis transmembrane conductance regulator (CFTR) genotype not responsive to CFTR modulator therapy.[1]

Technology

Description

VX-522 is an inhaled messenger RNA (mRNA) therapy. It delivers a full-length copy of CFTR mRNA to lung cells using a lipid nanoparticle.[2] Once inside the target lung cells, the mRNA is designed to produce functional copies of the CFTR protein.[3]

In a phase I/II trial (NCT05668741), participants receive ascending doses of VX-522 via oral inhalation using as nebuliser.[1]

Key Innovation

There is currently a disparity in treatment options for patients with cystic fibrosis who are genetically ineligible for or intolerant of CFTR modulator therapy.[4] In patients unresponsive or ineligible for CFTR modulator therapy, treatment is largely focused on management of symptoms such as use of airway clearance techniques or mucoactive agents.[5] CFTR modulators work by correcting the malfunctioning protein made by the CFTR gene, whereas VX-522 delivers mRNA directly to lung cells which use the instructions in the mRNA to create a functional CFTR protein.[2,6] VX-522 could work for any person with cystic fibrosis, including those with nonsense (also known as “x” or “stop”) and other rare mutations that do not respond to CFTR modulators.[2] VX-522 is one of the only inhalable mRNA therapeutics in clinical development, which may offer advantages over intravenous mRNA therapies which can accumulate in the liver and have limited internalisation in target tissues.[7] Additionally, mRNA therapies such as VX-522 are associated with favourable safety profiles and can produce high levels of intracellular CFTR protein.[7] If licensed, VX-522 would offer a therapeutic option for patients who have limited treatment options available.

Regulatory & Development Status

VX-522 does not have marketing authorisation in the UK/EU for any indication.

VX-522 is not in phase II/III clinical development for any other indication.

Patient Group

Disease Area and Clinical Need

Cystic fibrosis is a life-limiting autosomal recessive disease caused by mutations in the CFTR gene, which encodes an ion channel involved in the transport of chloride and bicarbonate this affects the movement of salt and water in and out of cells.[8,9] Insufficient or poorly functioning CFTR protein leads to a problem with the balance of salt and water in the body. This causes a thick, sticky mucus to develop in different parts of the body, especially in the lungs.[10] The symptoms of cystic fibrosis include: recurring chest infections, wheezing, coughing, shortness of breath and damage to the airways. Cystic fibrosis is a progressive condition, meaning symptoms worsen over time. Eventually the condition can be fatal if it leads to a serious infection or if the lungs stop working properly.[11]

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In the UK, 11,148 people have a diagnosis of cystic fibrosis, 63% of which are aged 16 years and older. By December 2022, 71% of cystic fibrosis patients were receiving CFTR modulator therapy.[12] In England (2024-25), there were 7,658 finished consult episodes (FCEs) and 6,113 admissions for cystic fibrosis (ICD-10 code E84), resulting in 3,008 day cases and 32,728 FCE bed days.[13]

Recommended Treatment Options

There are no treatment options recommended by the National Institute for Health and Care Excellence (NICE) for cystic fibrosis unresponsive to CFTR modulator therapies.

Clinical Trial Information

Trial	NCT05668741; 2023-504786-23-00; A Phase 1/2 Dose Escalation Study Evaluating the Safety, and Tolerability and Efficacy of VX-522 in Subjects 18 Years of Age and Older With Cystic Fibrosis and a CFTR Genotype Not Responsive to CFTR Modulator Therapy **Phase I/II:** Recruiting **Locations:** 6 EU countries, UK, US and two other countries **Primary completion date:** December 2026
Trial Design	Sequential assignment, open-label.
Population	Number (estimated) = 39; subjects with cystic fibrosis and CFTR gene mutations on both alleles that are not responsive to CFTR modulator therapy; aged 18 to 65 years.
Intervention(s)	• VX-522 mRNA therapy • VX-522 mRNA therapy with ivacaftor
Comparator(s)	No comparator
Outcome(s)	Primary outcome: safety and tolerability as assessed by number of participants with adverse events and serious adverse events. [Time frame: day 1 to week 8] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of VX-522 is not yet known.

Relevant Guidance

NICE Guidance

- NICE guideline. Cystic fibrosis: diagnosis and management. (NG78). October 2017.
- NICE quality standard. Cystic fibrosis. (QS168). May 2018.
- NICE medtech innovation briefing. (MIB219). CFHealthHub for managing cystic fibrosis during the COVID-19 pandemic. (MIB219). July 2020.

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NHS England (Policy/Commissioning) Guidance

- NHS England. NHS England commissioning statement: Arrangements for access to cystic fibrosis transmembrane conductance regulator (CFTR) modulators for licensed and off-label use in patients with cystic fibrosis. July 2025.
- NHS England. 2023 Commissioning Statement: Ivacaftor, tezacafor/ivacaftor, lumacaftor/ivacaftor and elexacaftor/tezacaftor/ivacaftor for cystic fibrosis. 210508Pa.
- NHS England. 2019/20 NHS Standard Contract for Prescribed Specialised Services Commissioning for Quality and innovation (PSS CQUIN). PSS3 Cystic Fibrosis Supporting Self-care PSS CQUIN indicator.
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- NHS England. A01/P/c. Clinical Commissioning Policy: Ivacaftor for Cystic Fibrosis (G551A mutations). July 2015.
- NHS England. 2014 NHS Clinical Commissioning Policy: Inhaled Therapy for Adults and Children with Cystic Fibrosis. A01/P/b.
- NHS England. 2014 NHS Clinical Commissioning Urgent Policy Statement: Ivacaftor and tezacaftor/ivacaftor for cystic fibrosis: "off-label" use in patients with named rarer mutations. 200809P.

Other Guidance

- Cystic Fibrosis Trust. Standards for the clinical care of children and adults with cystic fibrosis in the UK. 2024.[14]
- Southern KW, Castellani C, Lammertyn E, Smyth A, VanDevanter D, van Koningsbruggen-Rietschel S et al. Standards of care for CFTR variant-specific therapy (including modulators) for people with cystic fibrosis. 2023.[15]

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

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