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Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2800

vanzacaftor/tezacaftor/deutivacaftor film-coated tablets (Alyftrek®)

Vertex Pharmaceuticals (Europe) Ltd.

06 February 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) is accepted for restricted use within NHSScotland.

Indication under review: for the treatment of cystic fibrosis (CF) in people aged 6 years and older who have at least one F508del mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

SMC restriction: patients aged 6 years and older who have at least one F508del mutation in the CFTR gene.

Vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) offers an additional treatment choice in the therapeutic class of CFTR modulators.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) is a cystic fibrosis transmembrane conductance regulator (CFTR) modulator, which increases the quantity and function of CFTR at the cell surface, resulting in increased CFTR activity. Vanzacaftor/tezacaftor/deutivacaftor should only be prescribed by healthcare professionals with experience in the treatment of CF. It is taken with fat-containing food once daily. Refer to the Summary of Product Characteristics (SPC) for dosing information and monitoring requirements.[1]

1.2. Relevant comparator(s)

Other CFTR modulators include elexacaftor/tezacaftor/ivacaftor (Kaftrio®), which, following SMC collaboration with NICE on TA988, is accepted for use within NHSScotland in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in patients aged 2 years to less than 6 years (granules in sachet) and 6 years and older (film-coated tablets) who have at least one F508del mutation in the CFTR gene (SMC 2713).[2]

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

Vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) was compared with elexacaftor/tezacaftor/ ivacaftor (Kaftrio®) in two phase III, randomised, double-blind, non-inferiority studies (SKYLINE 102 and SKYLINE 103).[3]

Both studies included patients ≥12 years of age. SKYLINE 102 included patients with CF who were heterozygous for F508del and a minimal function mutation. SKYLINE 103 included patients who were homozygous for F508del (F/F); heterozygous for F508del and a gating mutation (F/G) or a residual function mutation (F/RF); or responsive to a triple combination (elexacaftor/tezacaftor/ivacaftor) and no F508del mutation (non-F/TCR).

In both studies patients received elexacaftor/tezacaftor/ivacaftor (Kaftrio®) during a 4-week run-in period and were then randomised in a 1:1 ratio to receive elexacaftor/ tezacaftor/ ivacaftor (Kaftrio®) or vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) for 52 weeks. The primary endpoint was absolute change from baseline in percent predicted Forced Expiratory Volume in one second ($ppFEV_1$) through week 24.[3]

In both studies vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) was non-inferior to elexacaftor/tezacaftor/ivacaftor (Kaftrio®) in absolute change from baseline in $ppFEV_1$ through week 24, with an LS mean treatment difference of 0.2 percentage points in SKYLINE 102 (1-sided P<0.001 for non-inferiority; 95% CI: -0.7, 1.1) and SKYLINE 103 (1-sided P<0.001 for non-inferiority; 95% CI: -0.5, 0.9). Non-inferiority was demonstrated in both studies as the lower bound of the 95% confidence interval for the treatment difference was greater than the pre-specified non-inferiority margin of -3.0 percentage points. [3] In addition, the studies demonstrated that vanzacaftor/tezacaftor/ deutivacaftor (Alyftrek®) had a similar safety profile to elexacaftor/tezacaftor/ ivacaftor (Kaftrio®).

The company provided evidence for vanzacaftor/tezacaftor/deutivacaftor (Alyftrek®) in children aged six to 11 years (n=78), with at least one elexacaftor/tezacaftor/ivacaftor responsive CFTR variant, from a phase III single arm study (RIDGELINE-105).[4] Following a 4-week run-in period with elexacaftor/tezacaftor/ivacaftor, patients received vanzacaftor/ tezacaftor/deutivacaftor for 24 weeks with a 4-week safety follow-up or, for those who completed the study, had the opportunity to participate in an open-label extension study. The primary endpoint was safety and tolerability from day 1 up to week 28. Secondary efficacy endpoints included absolute change in sweat chloride concentration and absolute change in ppFEV$_1$ through week 24. The study found that vanzacaftor/ tezacaftor/ deutivacaftor was safe and well tolerated and maintained ppFEV$_1$ from elexacaftor/tezacaftor/ ivacaftor baseline with further improved CFTR function. Nearly all patients had sweat chloride <60 mmol/L and more than half had normal levels (<30 mmol/L). The safety profile of vanzacaftor/ tezacaftor/deutivacaftor in children aged six to 11 years was similar to that seen in patients aged 12 years and older.[4]

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

SMC is unable to publish the estimated patient numbers as these were commercial in confidence.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHSScotland.

*Other data were also assessed but remain confidential.**

References

1. Electronic Medicines Compendium. Summary of Product Characteristics. Alyftrek® 125 mg/50 mg/10 mg film-coated tablets. Last updated: March 2025. Accessed: May 2025. Available: https://www.medicines.org.uk/emc/product/100699/smpc#gref.

2. Scottish Medicines Consortium. ivacaftor-tezacaftor-elexacaftor (Kaftrio®) SMC 2713. Published: July 2024. Accessed: June 2025. https://scottishmedicines.org.uk/medicines-advice/ivacaftor-tezacaftor-elexacaftor-kaftrio-c19-smc2713/.

3. Keating C, Yonker LM, Vermeulen F, Prais D, Linnemann RW, Trimble A*, et al.* Vanzacaftor–tezacaftor–deutivacaftor versus elexacaftor–tezacaftor–ivacaftor in individuals with cystic fibrosis aged 12 years and older (SKYLINE Trials VX20-121-102 and VX20-121-103): results from two randomised, active-controlled, phase 3 trials. The Lancet Respiratory Medicine. 2025;13(3):256-71.

4. Hoppe JE, Kasi AS, Pittman JE, Jensen R, Thia LP, Robinson P*, et al.* Vanzacaftor–tezacaftor–deutivacaftor for children aged 6–11 years with cystic fibrosis (RIDGELINE Trial VX21-121-105): an analysis from a single-arm, phase 3 trial. The Lancet Respiratory Medicine. 2025;13(3):244-55.

This assessment is based on data submitted by the applicant company up to and including 27 January 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.