Alyftrek

Procedural steps taken and scientific information after the authorisation*

*Due to the Agency`s update of its procedure management systems, an additional document, reflecting the historical lifecycle may be available in the 'Assessment history' section. For the complete product lifecycle procedures, you may need to also refer to **EPAR - Procedural steps taken and scientific information after authorisation (archive)**.

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
Variation type II /	Outcome:	23/07/2026		SmPC	142 mutations were newly identified to be

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

EMA/VR/0000332466	This was an application for a group of variations. C. Safety, efficacy, pharmacovigilance changes - C.4 Change(s) in the summary of product characteristics, labelling or package leaflet due to new quality, preclinical, clinical or pharmacovigilance data. - Accepted C. Safety, efficacy, pharmacovigilance changes - C.4 Change(s) in the summary of product characteristics, labelling or package leaflet due to new quality, preclinical, clinical or pharmacovigilance data. - Accepted A grouped application consisting of: C.4. Update of section 5.1 of the SmPC in order to introduce 143 D-IVA/TEZ/VNZ-responsive FRT mutations, based on results from the nonclinical study report U015 version 3.0; this is an in vitro pharmacological profiling of CFTR mutations in FRT cells using vanzacaftor (VNZ; VX-121), tezacaftor (TEZ; VX-661), and deutivacaftor (D-IVA; VX-561): effects on CFTR processing and trafficking and Cl – transport. C.4. Update of section 5.1 with the R334W mutation based on the extrapolation of published real-world data from a French Compassionate Use study conducted by Burgelet al. with ELX/TEZ/IVA. The Alyftrek SmPC would also align with the Kaftrio SmPC.				responsive to Alyftrek in the FRT assay and added in section 5.1 Table 5 of the Summary of Product Characteristics (SmPC). The R334W mutation is also added in section 5.1, Table 5 of the SmPC based on extrapolation from clinical responsiveness to Kaftrio (ELX/TEZ/IVA). 2 mutations: 1151ins12, Y563C were newly identified as FRT non-responsive mutations as they did not meet the threshold for responsiveness in the FRT assay. While a positive response in the FRT assay is predictive of clinical benefit, there are some mutations previously shown to be non-responsive in the FRT assay where clinical benefit with CFTR modulator therapy has been established. For more information, please refer to the Summary of Product Characteristics.

Variation type IA_IN / EMA/VR/0000349498	Outcome: This was an application for a group of variations. Q.I.a.1 Change in the manufacturing site of a starting material/intermediate used in the manufacturing process of the active substance or change in the manufacturing site (including where relevant quality control testing sites) of the active substance - Q.I.a.1.a) Addition or replacement of a manufacturing site of an active substance or intermediate - Accepted Q.I.a.1 Change in the manufacturing site of a starting material/intermediate used in the manufacturing process of the active substance or change in the manufacturing site (including where relevant quality control testing sites) of the active substance - Q.I.a.1.j) Addition or replacement of a batch control/testing site of the – the active substance or – intermediate of an active substance or – starting material of a biological active substance applying physicochemical and/or microbiological analytical procedures - Accepted	29/05/2026			
Variation type IA_IN / EMA/VR/0000338822	Outcome: Q.II.f.1.b) Extension of the shelf life of the finished product - Q.II.f.1.b.1 As packaged for sale (supported by real time data, fully in line with the stability protocol) - Accepted	30/03/2026		SmPC	

Variation type IB / EMA/VR/0000315339	Outcome: This was an application for a group of variations. B.I.a.1 Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier - B.I.a.1.z Other variation - Accepted A. ADMINISTRATIVE CHANGES - A.4 Change in the name and/or address of: a manufacturer (including where relevant quality control testing sites); or an ASMF holder; or a supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance (where specified in the technical dossier) where no Ph. Eur. Certificate of Suitability is part of the approved dossier; or a manufacturer of a novel excipient (where specified in the technical dossier) - Accepted B.II.d.2 Change in test procedure for the finished product - B.II.d.2.e Update of the test procedure to comply with the updated general monograph in the Ph. Eur. - Accepted	16/01/2026			

Variation type IB / EMA/VR/0000315468	Outcome: B.II.f.1.b Extension of the shelf life of the finished product - B.II.f.1.b.1 As packaged for sale (supported by real time data) - Accepted	17/12/2025		SmPC	
Variation type IB / EMA/VR/0000304508	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.z Other variation - Accepted C.I.z (Type IB) – To update Section 4.4 of the SmPC and Section 2 of the PL to reconcile a discrepancy in the SmPCs for Alyftrek and Kaftrio related to 'Depression and other psychiatric disorders'. In addition, the MAH took the opportunity to implement editorial change to the PI by (1) removing the local representatives in the PL, (2) adding the date of first authorisation and (3) correct translation errors in the FR and DE PI.	14/11/2025		SmPC and PL	To update Section 4.4 of the SmPC and Section 2 of the PL to reconcile a discrepancy in the SmPCs for Alyftrek and Kaftrio related to 'Depression and other psychiatric disorders'. In addition, the MAH took the opportunity to implement editorial change to the PI by (1) removing the local representatives in the PL, (2) adding the date of first authorisation and (3) correct translation errors in the FR and DE PI.
Variation type IB / EMA/VR/0000302870	Outcome: C.I HUMAN AND VETERINARY MEDICINAL PRODUCTS - C.I.z Other variation - Accepted To provide the initial study OECD 308 (VX-121-TX-035: Aerobic Transformation of VX-121 in Aquatic Sediment Systems at 12°C) and interim updated VX-121 Environmental	30/10/2025			

	Risk Assessment (ERA) reports.				
PSUR / EMA/PSUR/0000336139	EURD: PSUSA/00011146/202512 Active substance: deutivacaftor / tezacaftor / vanzacaftor Outcome: Maintenance	09/07/2026			