Casgevy

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 /	C.I HUMAN AND VETERINARY MEDICINAL	24/07/2025		SmPC and PL	SmPC new text The following warning has been

[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/0000258214	PRODUCTS - C.I.4 Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data - Accepted Update of sections 4.4 and 5.3 of the SmPC in order to update information on off-target editing based on (1) Results of in silico analysis to nominate genetic variants and (2) Interim study report presenting results from genotyping of subjects and off-target editing in drug product from subjects in clinical Studies 111 and 121. In addition, the MAH took the opportunity to make editorial changes to the PI.				added to section 4.4 of the SmPC: The risk of unintended, off target editing in an individual's edited CD34+ cells cannot be ruled out. A search spanning the human genome identified off-target editing at a single variant site. The variant was identified in 3.3% (3/91) of patient samples analyzed (edited CD34+ cells). The currently identified off target site is located in an intron of a gene not expressed in haematopoietic cells so no ill effects are expected (see section 5.3). And the following information has been added to section 5.3: During preclinical development, the potential for off target editing was assessed at over 5000 sites, including those nominated based on human genetic variation. No off target editing was observed in edited CD34+ cells from healthy donors and patients. A post marketing non clinical study (Study U270) evaluated 33 additional candidate off target editing sites nominated based on the presence of genetic variation. No off target editing was observed at 32 of these sites in edited CD34+ cells from patients. One site had off target editing due to a minor variant allele present in 3 of 91 patient samples (3.3%). The off target editing was observed at a low fraction of alleles (≤ 1%) and included a balanced inversion (<0.25%). This variant leads to a canonical TGG protospacer adjacent motif in the intronic region of the gene encoding for carbamoyl-phosphate synthetase 1 (CPS1). Gene editing in this minor allele is not expected to have any ill effects in patients as the off target site is within an intron and CPS1 is not

					expressed in haematopoietic cells. For more information, please refer to the Summary of Product Characteristics.
Variation type IB / EMA/VR/0000258235	This was an application for a group of variations. B.I.a.2 Changes in the manufacturing process of the active substance - B.I.a.2.z Other variation - Accepted B.I.b.2 Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - B.I.b.2.e Other changes to a test procedure (including replacement or addition) for the active substance or a starting material/intermediate - Accepted 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.a The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer - Accepted	25/04/2025	N/A		

	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.a The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer - Accepted				
PSUR / EMA/PSUR/0000248449	- -				Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing exagamglogene autotemcel remains unchanged and therefore recommends the maintenance of the marketing authorisation(s).