Amvuttra

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0015	Extension of indication to include treatment of wild-type or hereditary transthyretin-mediated amyloidosis in adult patients with cardiomyopathy (ATTR-CM), based on primary analysis results from study HELIOS-B (ALN-TTRSC02-003); a Phase 3, Randomized, Double-blind, Placebo-controlled,	25/04/2025	05/06/2025	SmPC and PL	Please refer to Scientific Discussion 'Amvuttra-H-C-005852-II-0015'.

[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).

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	Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients With Transthyretin Amyloidosis With Cardiomyopathy (ATTR Amyloidosis With Cardiomyopathy). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. An updated version 1.5, dated 10 April 2025. and a final update version 2.0. of the RMP have also been submitted. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0014	Update of section 4.2 of the SmPC in order to add the option for administration by patient and/or caregiver, based on an updated Notified Body Opinion report. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial changes in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	06/02/2025	05/06/2025	SmPC, Labelling and PL	Section 4.2 of the SmPC was updated in order to add the option for administration of the product by patient and/or caregiver. This was based on an updated Notified Body Opinion report. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial changes in the PI. For more information, please refer to the Summary of Product Characteristics.

PSUSA/11021 /202406	Periodic Safety Update EU Single assessment - vutrisiran	16/01/2025	n/a		PRAC Recommendation - maintenance
II/0013/G	This was an application for a group of variations. Update of section 5.3 of the SmPC in order to reflect non-clinical information on the carcinogenicity of vutrisiran, based on final results from studies NCS-21-00440 and TTRSC02-GLP18-003; these are 2-year carcinogenicity studies in CD-1 mice and Sprague Dawley rats, respectively. In addition, the MAH took the opportunity to submit Amended Report 1 of the embryo-foetal development toxicity study no. TTRSC02-GLP18-013 in rats to correct an error in the statistical analysis. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/11/2024	05/06/2025	SmPC	The SmPC section 5.3 has been updated to reflect new non-clinical information available on carcinogenicity of vutrisiran in rats and mice. The studies concluded that carcinogenic potential of vutrisiran is considered low if all toxicity data are taken into account. The package leaflet has been updated accordingly. For more information, please refer to the Summary of Product Characteristics.
IB/0011/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	14/06/2024	n/a		

IB/0010/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	17/04/2024	n/a		
IB/0009	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	06/02/2024	n/a		
PSUSA/11021 /202306	Periodic Safety Update EU Single assessment - vutrisiran	11/01/2024	n/a		PRAC Recommendation - maintenance
IB/0006	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	18/12/2023	n/a		

	authorisation, including the RMP - Other variation				
IB/0008	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	14/12/2023	n/a		
IA/0007/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	24/11/2023	n/a		
PSUSA/11021 /202212	Periodic Safety Update EU Single assessment - vutrisiran	06/07/2023	n/a		PRAC Recommendation - maintenance
IA/0004/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	07/03/2023	n/a		

IB/0002	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	10/01/2023	19/12/2023	SmPC	Product information section 6.3 is updated to reflect the shelf-life extension of the finished product Amvuttra 25 mg solution for injection in pre-filled syringe (EU/1/22/1681/001) as packaged for sale from 24 months to 36 months.
IA/0001	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	18/10/2022	n/a		