TAVNEOS

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
PSUSA/10967 /202403	Periodic Safety Update EU Single assessment - avacopan	14/11/2024	15/01/2025	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10967/202403.
II/0015	Update of sections 4.5 and 5.2 of the SmPC based on final results from study CL020_168; this is an open-label, phase 1 study to evaluate the effect of	31/10/2024	15/01/2025	SmPC and PL	The current variation is based on the results from study CL020_168, which was an open-label, Phase 1 study with the primary study objective to evaluate the effect of

[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).

	repeated oral doses of avacopan on the pharmacokinetics of a single dose of simvastatin in healthy volunteers; the Package Leaflet is updated accordingly. The updated RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				repeated oral doses of avacopan given under fed conditions for nine days on the PK of a single dose of simvastatin in 32 healthy volunteers. The co-administration of avacopan with simvastatin, a sensitive CYP3A4 substrate, increased the total systemic exposure (AUC) of simvastatin by 3.5-fold and Cmax by 3.2-fold. No new safety signals were observed. The results are adequately presented in the SmPC with the information that dose reductions or monitoring of adverse events may be necessary. The updated RMP version 2.1 is acceptable. For more information, please refer to the Summary of Product Characteristics.
IA/0017/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	16/09/2024	n/a		
IB/0014/G	This was an application for a group of variations.	17/07/2024	15/01/2025	SmPC	

	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) 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				
PSUSA/10967 /202309	Periodic Safety Update EU Single assessment - avacopan	25/04/2024	27/06/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10967/202309.
II/0013	Submission of the analysis of 2 selected pharmacodynamic (PD) markers in the avacopan clinical studies CL003_168 and CL010_168: serum anti-proteinase 3 antibody (anti-PR3) titres and serum anti-myeloperoxidase antibody (anti-MPO) titres. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	30/05/2024	n/a		The MAH submitted an analysis to reevaluate data from the avacopan Phase 2 study CL003_168 and Phase 3 study CL010_168. The goal was to assess the pharmacodynamic effect of avacopan relative to a prednisone taper, in the presence of a background treatment of cyclophosphamide or rituximab, on circulating anti-PR3 and anti-MPO antibodies. There were no meaningful differences in terms of reducing anti-PR3- and anti-MPO levels in subjects with AAV between prednisone taper/SOC and avacopan treated subjects. Further, there were no notable differences in reduction of ANCA titres between patients achieving sustained remission and those who did not. This indicates that the correlation between ANCA titre and clinical response is low, and that ANCA titre is no reliable marker for disease activity. For more information, please refer to the Summary of Product Characteristics.
IA/0011/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name	31/10/2023	11/01/2024	Annex II and PL	

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer A.7 - Administrative change - Deletion of manufacturing sites				
PSUSA/10967 /202303	Periodic Safety Update EU Single assessment - avacopan	26/10/2023	n/a		PRAC Recommendation - maintenance
II/0010	B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	12/10/2023	n/a		
II/0007	Update of sections 5.1 of the SmPC in order to correct a recently identified calculation error that occurred in the conversion of various non-prednisolone glucocorticoids to their prednisolone-equivalent doses in the pivotal Phase 3 Study CL010_168 (ADVOCATE). Furthermore minor revisions were made to section 4.4. (deletion of the term "viral" from the warning on live viral vaccines to have also not viral vaccines within the scope of the warning), and revised white blood cell count units (L instead of µL)).	06/07/2023	11/01/2024	SmPC	Higher non-study supplied prednisone-equivalent levels were observed in both treatment arms of study CL010_168. The difference in total cumulative glucocorticoid use between the arms was smaller in the presented data (3846.9 mg in the comparator group vs 1675.5 mg in the avacopan group, 2.3-fold higher in the comparator group) than compared to the data presented in the original application (3654.5 mg in the comparator group vs 1348.9 mg in the avacopan group, 2.7-fold higher in the comparator group). Although this indicates that the glucocorticoid-sparing effect of avacopan is not as large as previously indicated, it is still considered to be clinically

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				relevant. For more information, please refer to the Summary of Product Characteristics.
IA/0008	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	10/05/2023	11/01/2024	SmPC	
PSUSA/10967 /202209	Periodic Safety Update EU Single assessment - avacopan	14/04/2023	n/a		PRAC Recommendation - maintenance
IB/0006	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	06/03/2023	n/a		
IB/0004	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	25/11/2022	11/01/2024	SmPC, Labelling and PL	
PSUSA/10967 /202203	Periodic Safety Update EU Single assessment - avacopan	27/10/2022	n/a		PRAC Recommendation - maintenance
IA/0001	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	17/03/2022	n/a		