NOTIFICATION TO THE CHMP/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 20 OF REGULATION (EC) 726/2004

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This notification is a referral under Article 20 of Regulation (EC) 726/2004 to the Committee for Human Medicinal Products (CHMP) made by the European Commission (EC):

Product(s) Name(s)	Tavneos
Active substance(s)	Avacopan
Pharmaceutical form(s)	All
Strength(s)	All
Route(s) of Administration	All
Marketing Authorisation Holder(s)	Vifor Fresenius Medical Care Renal Pharma France

Background

Tavneos is a centrally authorised medicinal product containing the active substance avacopan. It was granted a marketing authorisation in the EU in January 2022 as an orphan medicinal product. By the specific and selective blockade of the human complement 5a receptor (C5aR1 or CD88), avacopan reduces the pro-inflammatory effects of C5a, which include neutrophil activation, migration, and adherence to sites of small blood vessel inflammation, vascular endothelial cell retraction and permeability. Tavneos, in combination with a rituximab or cyclophosphamide regimen, is indicated for the treatment of adult patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

The marketing authorisation application for Tavneos included one phase III clinical study (ADVOCATE, also known as Study CL010_168) and two supportive phase II clinical studies (CL002_168 and CL003_168). The ADVOCATE study was considered the pivotal study for the assessment of the clinical efficacy of Tavneos in its therapeutic indication. In this study, avacopan+background therapy was non-inferior to prednisone+background therapy at week 26 (despite a lower dose of glucocorticoids in the avacopan arm) with respect to induction of remission and reached superiority at week 52 for sustained remission. The absolute difference at week 52 was modest, but statistically robust and of clinical relevance. On this basis, it was considered that the ADVOCATE study had met its primary objective, and that the efficacy of Tavneos in its therapeutic indication was established.

At the time of the assessment of the marketing authorisation application, hepatoxicity was an identified risk for Tavneos, in particular in combination with cyclophosphamide/azathioprine (CYC/AZA, mycophenolate mofetil). Precautions were included in the product information, and a post-authorisation safety study (PASS) was initiated to further characterise the safety profile of Tavneos (results expected in 2031). Further, the last two periodic safety update report single assessments (PSUSAs) resulted in updates to the product information to include the adverse reactions drug-induced liver injury (DILI) and vanishing bile duct syndrome (VBDS), and to specify the frequency of the recommended monitoring of liver functions.

Issues to be considered

The European Commission (EC) has been informed by the EMA that in January 2026, the Agency became aware of new information which raised questions regarding the data integrity of the ADVOCATE study, the pivotal trial supporting the marketing authorisation. The new information specifically pertains to the company's handling of the database for the ADVOCATE study prior to the regulatory approval of Tavneos. This has raised serious questions as to whether amendments to the study data have taken place, whether such actions (if any) were consistent with the pre-specified protocol and statistical analysis plan for the study, and whether this new information could potentially impact the assessment of the results and the reliability of the ADVOCATE study that was previously conducted based on the information available to EMA at the time of the granting of a marketing authorisation to Tavneos by the EC.

In view of the above-referred information, the marketing authorisation holder (MAH) has been requested to submit preliminary observations regarding the data integrity of the ADVOCATE study. It is considered that in light of the emerging information as well as the preliminary observations shared by the MAH, a more comprehensive assessment of this matter is warranted, taking into account all available data, to determine whether there is an impact on the benefit-risk balance of Tavneos in its authorised indication.

In view of the above, the EC initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the Agency/CHMP to assess the above concerns and whether there is an impact on the benefit-risk balance for the centrally authorised medicinal product Tavneos. The EC requests the Agency to give its opinion by 30 April 2026 on whether the marketing authorisation for this product should be maintained, varied, suspended or revoked.

In addition, the EC requests the Agency/CHMP to give its opinion, as soon as possible, as to whether temporary measures are necessary to ensure the safe and effective use of this medicinal product.

Signed Date

Olga Solomon
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Medecins: policy, authorisation and monitoring
Health and Food Safety Directorate General