The Tavneos® Dilemma: Science, Integrity, and the Patient Interests

A position statement from Vasculitis International on the ongoing review of TAVNEOS® (avacopan)

Recent developments around TAVNEOS® (avacopan) have raised serious questions — about scientific integrity, about regulatory responsibility, and about what happens to patients when both are at stake simultaneously. At the heart of this debate lie two separate issues.

The first question: data integrity and scientific accountability

The first concerns data integrity: the FDA has formally concluded that certain patient outcomes in the ADVOCATE trial were re-adjudicated after unblinding in a way that changed the primary endpoint from non-significant to statistically significant. That is a grave finding, and we do not minimise it. What has been described is not a procedural irregularity. According to the FDA's formal findings, unblinded personnel selectively identified patients for re-adjudication after the initial analysis had already failed to reach statistical significance — and did so in a way that changed the outcome of the primary endpoint. The reliability of clinical trial data is the foundation on which medicine rests. Where that foundation is compromised, those responsible must be held to account — clearly and visibly, and regardless of the therapeutic value of the product involved.

A separate question: benefits, risks, and clinical reality

The second issue is entirely distinct, even if the EMA's current procedure treats it as derivative: how do the benefits and risks of avacopan balance out in clinical practice? The EMA has initiated its review primarily on the basis of data integrity concerns, and its starting position is that if the ADVOCATE study cannot be relied upon, the evidentiary basis for the effectiveness claim is undermined — and with it, the benefit-risk balance. That logic is procedurally coherent.

Post-marketing surveillance has nonetheless generated new and independent safety signals that stand entirely apart from the data integrity question. Cases of drug-induced liver injury with fatal outcomes have been identified, including vanishing bile duct syndrome — a progressive condition not anticipated at the time of authorisation. It should be noted that rates and severities of hepatotoxicity observed in Europe and North America have remained in line with the primary trial report; elevated rates have been reported primarily in Japan. These are not labelling issues; they are findings that the CHMP must assess on their own merits, regardless of what the data integrity review concludes.

By the same token, four years of real-world clinical use have generated evidence about therapeutic value that also exists independently of the trial. That evidence — including the significance of glucocorticoid reduction for patients' daily lives, and the absence of equivalent alternatives — deserves equal weight in any genuine benefit-risk assessment. Vasculitis International therefore urges the EMA to treat this evaluation as a substantive and independent exercise in its own right — one grounded in all available evidence, including post-marketing data and the lived experience of patients.

These two principles — scientific accountability and patient access to treatment — must each be protected. The tension arises because they may converge in a single potential outcome: the withdrawal of the medicine from the market.

Regulatory logic and clinical reality do not always align

Since its introduction, avacopan has been used in thousands of patients across Europe. In practice, many clinicians regard it as a meaningful addition to the vasculitis treatment landscape — not least because real-world clinical experience consistently points to a significant reduction in glucocorticoid use. That observation is moreover supported by trial data that remains unaffected by the integrity concerns. The re-adjudication issue relates solely to the week 52 superiority conclusion on the primary endpoint.

The non-inferiority findings at both six and twelve months, and the four key secondary endpoints — reduced relapse risk, reduced steroid toxicity, better recovery of quality of life, and better recovery of kidney function — were not subject to re-adjudication and have not been called into question. It matters greatly that this evidence remains intact — though perhaps not equally to everyone involved in these decisions.

For clinicians, reduced steroid exposure is a welcome outcome, measurable in laboratory values and fracture risk statistics. For patients, it is something far more immediate. The side effects of long-term prednisone use — the moon face, the mood swings, the weight gain, the progressive bone loss — are not abstract risks to be managed; they are daily lived realities that affect identity, self-image, and quality of life in ways that rarely appear in clinical endpoints. That gap between clinical and patient perception is itself a form of evidence — and one that belongs in any serious benefit-risk assessment. It becomes even more significant when considered against the therapeutic landscape in which patients and clinicians must make their choices.

The treatment toolbox for ANCA-associated vasculitis remains narrow, relying heavily on a small number of agents each carrying their own risks and limitations. In that setting, every available option has potential value — not as a comfort, but as a clinical reality that regulators must weigh alongside trial methodology.

Consequences that fall on patients

Withdrawing a medicine from the market is not a neutral regulatory act. It is a decision that directly and immediately affects patients, for whom withdrawal does not mean switching to an equivalent alternative, but accepting a step back in disease management with real consequences for their glucocorticoid burden. Such a decision should only be reached following a full, transparent, and independent assessment of all available evidence, including real-world data from clinical practice.

The role of patient representatives in this process

In earlier correspondence, Vasculitis International formally requested that patient representatives be actively involved in the EMA's review process. We renew that request here. Data from clinical trials, however rigorously assessed, do not capture the full picture. The lived experience of patients — the weight of treatment burden, the significance of reduced steroid exposure, the daily reality of limited therapeutic options — must also be part of the evidentiary picture.

The debate around TAVNEOS® reflects a broader question that regulatory science has not yet fully resolved: how do we uphold strict standards of scientific integrity while ensuring that consequential decisions remain grounded in patient reality? There is no simple answer. But one principle must be clear: addressing potential misconduct and safeguarding patient access to treatment are not the same problem, and they should not be treated as a single decision.

The responsibility now lies with the EMA and the CHMP to weigh all available evidence and reach a balanced conclusion — one that is fully aware of its consequences for patients who depend on the treatments available to them.

As Vasculitis International, we have confidence in the EMA's capacity to navigate this process with the independence, scientific rigour, and sense of responsibility that patients are right to expect. We also stand ready, as patient representatives, to contribute what data alone cannot provide: the perspective of those for whom these decisions are not procedural, but personal.

May 2026 Peter Verhoeven Chair, Vasculitis International