CSL Vifor

Point – Level 3
29 Market Street
Maidenhead, SL6 8AA, UK

July 2026

Avacopan Vifor, previously known as Tavneos (avacopan)▼: Updated requirements for liver monitoring and stopping rules to mitigate risk of drug-induced liver injury and vanishing bile duct syndrome

Dear Healthcare Professional,

Vifor Fresenius Medical Care Renal Pharma France in agreement with the Medicines Healthcare Products Regulatory Agency (MHRA), would like to inform you of the following important updates to the product information of avacopan:

Summary

- **Following additional cases of drug-induced liver injury (DILI) and vanishing bile duct syndrome (VBDS) with avacopan, including cases with fatal outcome, the requirements for liver function monitoring and for permanent discontinuation have been updated.**
- **Updated requirements for monitoring liver function (new text underlined):**
  - **Before treatment initiation: Liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin levels must be obtained.**
  - **During treatment: Liver function must be monitored <u>at least every 2 weeks</u> <u>for the first 3 months</u> after the start of therapy, followed by every 4 weeks for the next 3 months of treatment, and as clinically indicated thereafter.**
- **Updated requirement for permanent discontinuation of treatment:**
  - **Permanent discontinuation of treatment must be considered if:**
    - **ALT or AST > 8 × the upper limit of normal (ULN);**
    - **ALT or AST > 5 × ULN for more than 2 weeks;**
    - **ALT or AST > 3 × ULN and total bilirubin > 2 × ULN or international normalised ratio (INR) > 1.5;**
    - **ALT or AST > 3 × ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (> 5%);**
    - **<u>alkaline phosphatase (ALP) ≥ 2 times ULN, when the source of increased ALP levels is the liver;</u>**
    - **<u>presence of clinical symptoms of vanishing bile duct syndrome (VBDS) such as jaundice or pruritus;</u>**
    - **an association between avacopan and hepatic dysfunction has been established.**
  - **<u>Treatment must be immediately and permanently discontinued if VBDS is suspected.</u>**
- **This safety communication is issued independently of the ongoing MHRA review of the benefits and risks of avacopan that is being undertaken under the Human**

CSL Vifor

Point – Level 3
29 Market Street
Maidenhead, SL6 8AA, UK

Medicines Regulations 2012 Section 68 which states that the licensing authority, may revoke, vary or suspend a UK marketing authorisation if the licensing authority considers that the application, or the material supplied with it, is incorrect or no longer supports a positive benefit–risk balance for the product.

- **No new patients should be started on avacopan whilst the MHRA review of the benefits and risks of avacopan is ongoing.**

Background on the safety concern

Avacopan, 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 risk of hepatotoxicity, including events of drug-induced livery injury (DILI) and vanishing bile duct syndrome (VBDS), is a known risk and reflected in the current UK-product information (PI) of avacopan. VBDS is a severe type of liver injury characterised by cholestasis and progressive loss of intrahepatic bile ducts. The current PI includes information on hepatotoxicity including fatal cases, criteria for permanent discontinuation (section 4.2) and liver monitoring (section 4.4).

DILI and VBDS have been reported in the post marketing setting and were previously included with frequency not known (section 4.8). Based on a recent review of available data, including cases of DILI and VBDS reported globally, as well as fatalities, the requirements for liver monitoring and criteria for permanent discontinuation (‘stopping rules’) have been updated.
Review of cumulatively reported cases showed that most cases of liver injury occurred within the first 3 months after initiation of avacopan, mostly between 1 and 2 months; only a few cases had a time to onset between 3 and 6 months. Almost all VBDS events occurred within 3 months after initiation of treatment. The available data therefore justify more intensive liver monitoring requirements for all populations treated with avacopan during the first 3 months of treatment.

The product information of avacopan will be updated in line with this new safety information.

Call for reporting

Avacopan Vifor▼is subject to additional monitoring. This will allow quick identification of new safety information.

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme

Please report:

- all suspected adverse drug reactions (ADRs) that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

CSL Vifor

Point – Level 3
29 Market Street
Maidenhead, SL6 8AA, UK

You can report via:

- the Yellow Card website (https://yellowcard.mhra.gov.uk/)
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

Suspected adverse reactions should also be reported to Vifor Fresenius Medical Care Renal Pharma France Medical Information on Tel: 0044(0)1276 853 633 or by email at medicalinfo_uk@viforpharma.com.

Company contact point
Should you have any questions or require additional information, please contact Kate Higgs, Senior Medical Scientist (kate.higgs@viforpharma.com or 07710855305).

Alternatively, please contact the Medical Information department as described above.

Yours sincerely

Signed by:
Marie Li
0B82AB5FD0A34F3...
Marie Li
Head of Medical Affairs, UK and Ireland