May 21, 2026
Pharmaceuticals and Medical Devices Agency, Japan

Investigation Results on Avacopan

Product Overview

Brand name: Tavneos Capsules 10 mg (Kissei Pharmaceutical Co., Ltd.)
Nonproprietary name: Avacopan
Indications: Microscopic polyangiitis, granulomatosis with polyangiitis
Estimated number of patients using the product: Approximately 8,503
(February 2025 – January 2026)

Overview

Avacopan (hereinafter referred to as “the drug”) is a compound that exhibits selective C5a receptor (C5aR) antagonistic activity, and is considered to suppress neutrophil priming via C5a–C5aR signaling, thereby mitigating the amplification of ANCA-mediated vasculitis induced by neutrophils. It is a therapeutic agent for microscopic polyangiitis and granulomatosis with polyangiitis.

At the time of initial marketing approval in September 2021, warnings had already been provided in the package insert stating that hepatic impairment may occur under “Clinically significant adverse reactions,” and that liver function tests should be performed regularly before and during treatment under “Important precautions.” However, since the start of marketing in June 2022, multiple reports of serious hepatic impairment, including vanishing bile duct syndrome, leading to death have been reported. Accordingly, on May 1, 2026, the package insert was revised to add vanishing bile duct syndrome to the section on hepatic impairment under “Clinically significant adverse reactions.” Furthermore, based on accumulated reports, the necessity for additional safety measures was examined, and as a result of the investigation based on expert evaluation, the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”) concluded that revision of the precautions for use of the drug was necessary.

Investigation Results

As a result of deliberation including consultation with expert advisors, PMDA determined that this revision falls under an urgent safety measure for the following reasons:

- Although warnings regarding hepatic impairment had been provided since approval, adverse event reports of serious hepatic impairment, including vanishing bile duct syndrome, have been received.
- Of the 20 cases reported to have resulted in death with hepatic impairment, a causal relationship with the drug could not be ruled out in 2 cases.

Based on the above, it is appropriate to inform healthcare professionals that serious cases of hepatic impairment, including fatal cases, have accumulated domestically. In addition, in order to enable early detection of hepatic impairment and prevent aggravation, a new “Warnings” section will be established as shown in the Appendix. Furthermore, the following should be added to the precautions for use and thoroughly communicated:

- Liver function tests should be performed before initiation of treatment and during treatment at frequencies corresponding to the elapsed time since treatment initiation.
- Specific findings of hepatic function for which treatment should be interrupted or discontinued should be clearly specified, and appropriate measures should be taken in the event of hepatic impairment.

The expert advisors in the specialized consultation for this investigation were appointed in accordance with the “PMDA Regulations for the Implementation of Expert Consultations” (Notification No. 8 dated December 25, 2008), based on declarations, etc., from the experts regarding this drug.

Appendix

Revised description is underlined.

Current	Revision
(N/A)	**1.Warnings** Serious hepatic dysfunction, including vanishing bile duct syndrome, may occur, and fatal cases have been reported. Patients should be carefully monitored through periodic hepatic function tests before and during treatment with this drug. If serious hepatic dysfunction is observed during treatment with this drug, appropriate measures, such as discontinuation of treatment with this drug, should be taken.
8. IMPORTANT PRECAUTIONS Since hepatic dysfunction may occur, patients should be closely monitored through hepatic function tests before the start of treatment with this drug and periodically during treatment.	**8. IMPORTANT PRECAUTIONS** Since hepatic dysfunction may occur, careful attention should be paid to the following points. In most cases, hepatic dysfunction has been reported in the first 3 months of treatment with this drug.
(N/A)	Patients should be closely monitored through hepatic function tests before the start of treatment with this drug, at least once every 2 weeks during the first 3 months of treatment, at least once every 4 weeks during the next 3 months of treatment, and periodically during treatment thereafter.
	If ALT or AST >3 times upper limit of normal is observed during treatment with this drug, treatment should be interrupted and patients should be assessed immediately. In addition, treatment with this drug should be discontinued in the following cases: - ALT or AST >8 times upper limit of normal - ALT or AST >5 times upper limit of normal for more than 2 weeks - Total bilirubin >2 times upper limit of normal - ALP ≥2 times upper limit of normal - Presence of signs or symptoms of hepatic dysfunction such as jaundice and pruritus Treatment with this drug should be discontinued immediately if vanishing bile duct syndrome is suspected.

N/A: Not Applicable. No corresponding language is included in the current PRECAUTIONS.