EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 June 2026

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 8 – 11 June 2026

PRAC concludes evaluation of new data regarding potential risk of neurodevelopmental disorders in children born to men treated with valproate

PRAC concludes evidence of potential risk of neurodevelopmental disorders in children born to men treated with valproate is inconsistent

Committee recommends updating product information to reflect available data

EMA's safety committee, the PRAC, has completed its review of a safety signal for valproate and related substances, and concluded that based on the evaluation of new data, the evidence on neurodevelopmental disorders (NDDs) in children born to men treated with valproate is inconsistent and the causal role of valproate is uncertain. In light of this uncertainty, the committee recommended maintaining existing precautionary measures for male patients. These measures were put in place in 2024 to address a potential increased risk of NDDs in children born to men treated with valproate during the three months before conception.

In addition, PRAC recommended that the medicines' product information be updated to reflect the most recent data related to NDDs.

Valproate medicines are used to treat epilepsy and bipolar disorder. In some EU Member States, they are also authorised to prevent migraine headaches. NDDs are problems with development that begin in early childhood, such as autism spectrum disorders, intellectual disability, communication disorders, attention deficit/hyperactivity disorders and movement disorders.

In January 2024, the assessment of the findings of a post authorisation safety study (PASS)[1], which used data from multiple registry databases in Denmark, Norway and Sweden suggested an increased risk of NDDs in children born to men treated with valproate in the three months before conception

[1] https://www.ema.europa.eu/en/documents/other/valproate-prac-non-interventional-imposed-pass-final-study-report-assessment-report-emea-h-n-psr-j-0043_en.pdf

compared with men treated with the epilepsy medicines lamotrigine or levetiracetam. At that time, while PRAC acknowledged that the PASS data had limitations, it concluded that NDDs are a potential risk in children born to men treated with valproate during the three months before conception, and recommended precautionary measures for men taking the medicine.

At the time, PRAC requested the marketing authorisation holders to carry out a larger study, specifically designed to address some of the limitations of the PASS study. This study is currently ongoing and is expected to conclude in 2028.

The latest safety signal was started in July 2025 after the publication of a Danish nationwide registry-based study, which did not suggest an increased risk of NDDs in children born to men treated with valproate. In assessing this signal, PRAC reviewed all the latest evidence. While findings from one study[2] suggested a possible link between valproate and NDDs, most studies[3] (so-called retrospective observational studies) investigating this issue have not found an increased risk of NDDs. Differences in how these studies were designed, such as which patients were included and how patients' underlying health conditions were accounted for, may explain why findings vary.

Overall, PRAC could not conclude whether a potential risk of NDDs in children of fathers treated with valproate before conception is due to valproate or other factors, such as the fathers' underlying medical condition. The committee concluded that the available evidence is inconsistent, and a causal link with the medicine is uncertain.

In light of remaining uncertainties and pending the results of the ongoing study in 2028, PRAC agreed that the precautionary measures introduced in 2024 should remain in place. The committee also recommended updating the product information, as well as the healthcare professional guide and the guide for male patients, to ensure that healthcare professionals and patients have access to the most up-to-date information.

Further information can be found in the assessment report, which will be published in due course on the EMA website.

[2] Botton J, Rios P, Drouin J, Miranda S, Zureik M, Weill A, Dray-Spira R. Paternal exposure to valproate during spermatogenesis and risk of neurodevelopmental disorders in children: national study based on the French EPI-MÈRES Register. EPI-PHARE (ANSM-Cnam). Saint-Denis, 6 November 2025, 61 pages.

[3] Meng LC, van Gelder MMHJ, Chuang HM, Lai HY, Chen LK, Hsiao FY, Nordeng HME. Valproate Use by Fathers and Risk of Neurodevelopmental Disorders in Children. NEJM Evid. 2026 Mar;5(3):EVIDoa2500254. doi: 10.1056/EVIDoa2500254. Epub 2026 Feb 24. PMID: 41733407.

Razaz N, Soderling J, Tomson T, Werenberg Dreier J, Christensen J, Bjørk MH, Igland J. Risk of neurodevelopmental disorders associated with paternal use of valproate during spermatogenesis. J Neurol Neurosurg Psychiatry. 2026 Mar 4:jnnp-2025-337441. doi: 10.1136/jnnp-2025-337441. Epub ahead of print. PMID: 41781215.

New safety information for healthcare professionals

Ixchiq: use should be restricted to people at high risk of chikungunya infection

The PRAC has recommended that the chikungunya vaccine Ixchiq should be restricted to individuals with a high risk of becoming infected with the chikungunya virus.

The committee also endorsed a direct healthcare professional communication (DHPC) to inform healthcare professionals of the updated recommendations.

Ixchiq is used to protect people 12 years of age and older against chikungunya disease. It contains a strain of the chikungunya virus that has been attenuated (weakened).

This restriction of the indication follows a routine EMA review of available safety data which evaluated the impact of serious adverse events reported with the vaccine (including aseptic meningitis; inflammation of the membranes around the brain and spinal cord) on the benefit-risk balance of Ixchiq. Some of these events resulted in hospitalisation and death.

Known serious side effects linked to the vaccine mainly occur in people aged 65 years and older and in people with multiple underlying chronic medical conditions, although young otherwise healthy adults have also been affected.

In addition, serious or prolonged chikungunya-like adverse reactions have been observed, sometimes leading to a deterioration of the person's general condition, including malaise and decreased appetite, exacerbation of pre-existing diseases, brain disorders like encephalopathy and encephalitis, aseptic meningitis or confusion.

Healthcare professionals are reminded that the vaccine should only be given to individuals 12 years of age and older who are at high risk of acquiring chikungunya infection and after careful consideration of the potential benefits and risks. It is contraindicated in patients whose immune system is weakened because of disease or medical treatment, and it should not be co-administered with other vaccines.

The PRAC's recommendation will be sent to the EMA's human medicines committee (the CHMP), which will adopt the Agency's opinion.

As for all medicines, the safety of Ixchiq is closely monitored and the recommendations for use will be updated if new relevant information becomes available.

Tavneos (avacopan): reinforced liver function monitoring requirements and stopping rules to mitigate risk of serious liver injury

PRAC has endorsed a DHPC to inform healthcare professionals of its recommendations to reinforce liver function monitoring requirements and stopping rules for Tavneos (avacopan) to mitigate the known risk of drug-induced liver injury (DILI) and vanishing bile duct syndrome (VBDS). VBDS is a rare condition where the small bile ducts inside the liver are gradually damaged and disappear over time.

Tavneos is used to treat adults with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), two rare inflammatory conditions of the blood vessels.

The updated recommendations follow further characterisation of the risk of DILI and VBDS in light of recent reports of serious liver injury, including cases with a fatal outcome.

Before starting treatment with Tavneos, liver function tests, including hepatic transaminases and total bilirubin (key indicators of liver function), must be performed. During treatment, liver function must be monitored at least every two weeks after the start of therapy for the first three months, followed by every four weeks for the next three months of treatment, and as clinically indicated thereafter.

Treatment with Tavneos must be stopped if blood levels of alkaline phosphatase (ALP, another indicator of liver function) are over twice the normal limit when the source of increased ALP is the liver, or when there are clinical symptoms of VBDS such as jaundice (yellowish appearance of the skin and the whites of the eyes) or itching. If VBDS is suspected, treatment must be immediately and permanently stopped. This is in addition to stopping rules already included in the product information.

EMA is also conducting a review of Tavneos, prompted by questions regarding data integrity of the main study. More information is available on the EMA website.

The DHPCs for Ixchiq and Tavneos will be disseminated to healthcare professionals by the marketing authorisation holders, according to an agreed communication plan, and published on the Direct healthcare professional communications page and in national registers in EU Member States.

PRAC statistics: Month Year

[infographic]

Glossary:

Safety signal assessments. A safety signal is information which suggests a new potentially causal association, or a new aspect of a known association between a medicine and an adverse event that warrants further investigation. Safety signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. More information can be found under 'Signal management'.

Periodic safety update reports, abbreviated as PSURs, are reports prepared by the marketing authorisation holder to describe the worldwide safety experience with a medicine in a defined period after its authorisation. PSURs for medicinal products that contain the same active substance or the same combination of active substances but have different marketing authorisations and are authorised in different EU Member States, are jointly assessed in a single assessment procedure. More information can be found under 'Periodic safety update reports: questions and answers'.

Risk management plans, abbreviated as RMPs, are detailed descriptions of the activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines. Companies are required to submit an RMP to EMA when applying for a marketing authorisation. RMPs are continually updated throughout the lifetime of the medicine as new information becomes available. More information is available under 'Risk-management plans'.

Post-authorisation safety studies, abbreviated as PASSs, are studies carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC assesses the protocols (aspects related to the organisation of a study) and the results of PASSs. More information can be found under 'Post-authorisation safety studies'.

Referrals are procedures used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral related to safety of medicines, the PRAC is requested by a Member State or the European Commission to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. More information can be found under referral procedures.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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