Summary of Recommendations and Conclusions from the Twenty First (21st) Meeting of the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP)

8-9 May 2025 Virtual

The Advisory Committee on Safety of Medicinal Products (ACSoMP) was established in 2003 to provide independent, authoritative, scientific advice to WHO on medicines' safety issues of global or regional concern. The twenty-first ACSoMP meeting was held virtually from 8-9 May 2025. A summary of the presentations and recommendations is provided below.

Safety of semaglutide (Ozempic®)

The session on semaglutide focused on reviewing and evaluating the evidence regarding the association between semaglutide and nonarteritic anterior ischemic optic neuropathy (NAION) in patients with type 2 diabetes (T2D).

Semaglutide, a GLP-1 receptor agonist approved on December 5, 2017, is used to manage type 2 diabetes (T2D) by enhancing β-cell function, delaying gastric emptying, suppressing glucagon secretion, and promoting weight loss, thereby improving glycaemic control and reducing cardiovascular risk. However, concerns have emerged regarding a potential link between semaglutide and NAION, a serious and typically irreversible cause of sudden vision loss.

A large Danish observational study involving over 424,000 individuals with T2D found a higher incidence rate and increased risk of NAION among semaglutide users. Another Danish study supported this association, although two other recent studies did not find a similar link.

The ACSoMP reviewed the evidence but found it inconclusive due to limitations such as potential biases, confounding factors, unclear mechanisms, and the rarity and diagnostic complexity of NAION.

Recommendations:

The Committee made recommendations on the potential association between semaglutide and NAION as follows:

- The currently available evidence supports that this remains a signal requiring further investigation before any causal relationship can be established. The committee encourages WHO to coordinate with drug regulatory authorities to align recommendations.
- The Risk Management Plan should be updated to include NAION as a potential risk, including any required additional pharmacovigilance activities.

Post meeting notes from the WHO Secretariat: At its June 2025 meeting, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) concluded that

NAION is a very rare side effect of semaglutide (it may affect up to 1 in 10,000 people taking semaglutide). EMA has recommended that the product information for semaglutide medicines be updated to include NAION as a side effect with a frequency of 'very rare'. If patients experience a sudden loss of vision or rapidly worsening eyesight during treatment with semaglutide, they should contact their doctor without delay. If NAION is confirmed, treatment with semaglutide should be stopped.

Update of sodium valproate usage study and other initiatives

The session on valproate use revisited the persistent global concern over the drug's teratogenic and neurodevelopmental risks, particularly in women and girls of childbearing potential. Valproate remains widely used, especially in low- and middle-income countries (LMICs), due to its affordability and broad-spectrum efficacy.

Preliminary results from a study using data from the human data science company IQVIA showed rising global use of anti-seizure medicines, with valproate still prevalent in LMICs. This could be linked to disparities in access to safer alternatives. Details of this study will be published in upcoming months.

Early findings from a WHO survey of national pharmacovigilance centres revealed that while many countries have implemented risk minimization measures (RMMs), their effectiveness varies and is not always measured. Only a minority of countries reported measurable reductions in valproate use or adverse outcomes. The survey also highlighted the need for better integration of RMMs into clinical practice.

A presentation from the Morocco pharmacovigilance centre (Le Centre AntiPoison et de Pharmacovigilance du Maroc (CAPM) outlined plans to implement the WHO protocol on sodium valproate utilization, which aims to evaluate current prescribing patterns and prescriber awareness through both quantitative and qualitative methods. The discussion emphasized the importance of understanding prescriber behaviour, cultural barriers, and the real-world impact of RMMs.

During discussion, the Committee called for improved access to alternative anti-seizure medicines, deeper qualitative research, and the development of a centralized WHO repository of adaptable RMM tools.

Recommendations

In summary, valproate continues to be used among at-risk populations across all WHO regions, with particularly high and increasing use in low- and middle-income countries (LMICs). While overall access to anti-seizure medications is improving, the availability of safer alternatives does not always ensure their accessibility, highlighting the need for targeted strategies to close this gap. The Committee recommends:

- **A Need for Better Data:** More detailed and disaggregated data especially from LMICs is needed to better understand usage patterns. Country- and region-specific factors influencing valproate use should be explored to inform tailored risk minimization strategies.

- **Support for Risk Minimization Measures (RMMs):** The WHO is encouraged to create a repository of effective RMMs (e.g., pregnancy prevention programs, risk acknowledgment forms) that can be adapted by countries. These efforts should be supported by WHO regional and country offices and implemented in collaboration with clinical specialties like neurology, mental health, and maternal health.
- **Monitoring Neurodevelopmental adverse drug reactions:** The Committee requested more detailed data on neurodevelopmental adverse drug reactions (ADR) reporting from VigiBase, particularly from LMICs, and recommended reviewing national clinical guidelines in partnership with the WHO Brain Health Unit.
- **Moroccan Pilot Study:** The Committee endorsed the pilot study and encouraged similar efforts in other countries. Suggestions included exploring barriers women face in risk communication, assessing the accessibility and effectiveness of RMMs, and evaluating how WHO Mental Health Gap Action Programme (mhGAP) recommendations are implemented at the national level.

WHO core variables for suspected adverse drug reactions (ADR) reporting

This session focused on the implementation of WHO's 35 core variables for suspected Adverse Drug Reaction (ADR) reporting, with updates from regional (South-East Asia, SEA) and national (Bhutan) stakeholders. It followed an initial discussion during the ACSoMP meeting in November 2023, where the core variables were introduced to enhance the collection of critical pharmacovigilance data.

A comparative analysis of ADR reporting forms across the SEA region highlighted the importance of these variables for improving data quality and convergence, revealing varying levels of implementation across SEA countries. This comparative analysis is expected to be published soon.

The WHO Collaborating Centre - Uppsala Monitoring Centre (UMC) presented the integration of the core variables into the VigiMobile platform, emphasizing its user-friendly, offline-capable design and addressing challenges such as E2B standard mapping and pregnancy exposure reporting.

Bhutan shared its approach to implementing VigiMobile reflecting the core variables, noting that implementing the core variables would improve data quality and ensure compatibility with global databases. Bhutan's implementation timeline includes full rollout planned by January 2027.

Conclusions

The session concluded that the rationale for standardized reporting using WHO's 35 core variables is well understood and electronic tools, particularly VigiMobile, are solutions to address challenges.