Summary of recommendations from the Twenty-fourth Meeting of the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP)

The World Health Organization (WHO) Advisory Committee on Safety of Medicinal Products (ACSoMP) held its 24th meeting on 24–25 November 2025 as a hybrid event with Members participating both in person in Geneva and virtually. Established in 2003, ACSoMP is an independent expert advisory body that provides advice to the Director-General of WHO on pharmacovigilance policies and issues related to the safety of medicinal products.[1]

The November 2025 meeting reviewed progress on previous ACSoMP recommendations and addressed key safety issues related to priority products that may be considered for inclusion or have already been included in WHO clinical guidelines, the Essential Medicines List and the WHO prequalification programme. Discussions covered medicines such as lenacapavir for HIV prevention (PrEP),[2] moxidectin for onchocerciasis, and GLP-1 receptor agonists (GLP-1 RA) which have received conditional recommendations in the newly launched WHO obesity guidelines.[3]

Safety monitoring of moxidectin in mass drug administration

Moxidectin is an oral macrocyclic lactone with potent microfilaricidal activity against *Onchocerca volvulus*. Compared with ivermectin, single-dose moxidectin achieves deeper and more sustained suppression of skin microfilariae, a key reservoir for transmission of onchocerciasis. WHO has not yet issued programmatic recommendations on moxidectin but evidence generation for guideline development and listing in the Essential Medicines List (EML) and the Essential Medicines List for children (EMLc) are underway. The Committee reviewed results from manufacturer safety studies in the Democratic Republic of the Congo (DRC) and Côte d'Ivoire, as well as experiences of roll-out of moxidectin in mass drug administration (MDA) in Ghana.

[1] Terms of Reference for the Advisory Committee on Safety of Medicinal Products (ACSoMP). Geneva: World Health Organization; November 2023 (https://www.who.int/publications/m/item/acsomp-terms-of-reference).

[2] Guidelines on lenacapavir for HIV prevention and testing strategies for long-acting injectable pre-exposure prophylaxis. Geneva: World Health Organization; 2025 (https://www.who.int/publications/i/item/9789240111608). Licence: CC BY-NC-SA 3.0 IGO.

[3] WHO guideline on the use of glucagon-like peptide-1 (GLP-1) therapies for the treatment of obesity in adults. Geneva: World Health Organization; 2025 (https://app.magicapp.org/#/guideline/LrRxrL).

Summary of ACSoMP conclusions and recommendations:

- The risk of serious events such as encephalopathy in recipients infected with Loa loa is well understood on the basis of experience with ivermectin, warranting additional risk minimization measures to prevent such adverse drug reactions (ADRs) in affected patients. Testing for Loa loa is important in regions where the infection is present. National public health programmes (with the support of WHO) should perform mapping of regions where Loa-loa is endemic to support implementation of relevant risk minimization efforts.
- The Committee recommends that countries enhance spontaneous reporting mechanisms or strengthen existing pharmacovigilance (PV) systems in regions targeted for MDA activities, including by supporting community health workers to report and conduct investigations on serious adverse events. Integration of these data into national PV databases and NTD programme systems is essential. Additionally, health care workers should be trained on how to detect, counsel patients and manage Mazzotti and hypersensitivity reactions as well as reporting ADRs.
- Data on efficacy and safety of moxidectin in pregnancy are lacking and, given that pregnancy exposures are highly likely in MDAs, active follow-up of pregnancy exposures is important. The Committee recommends establishing pregnancy exposure registries or leveraging existing registries to follow up actively both moxidectin exposures and pregnancy outcomes.
- The Committee emphasizes the need for targeted research on repeated annual dosing safety, pregnancy and lactation outcomes, drug–drug interactions with other medicines for neglected tropical diseases, and safety in vulnerable groups such as children and elderly persons.
- The Committee looks forward to receiving updated data on safety in pregnancy and other safety data on moxidectin in the future.

Paracetamol during pregnancy and potential association with autism in offspring

The Committee reviewed WHO's approach to evaluating current scientific evidence on the use of paracetamol during pregnancy and its possible association with autism spectrum disorder (ASD) and attention deficit-hyperactivity disorder (ADHD). The Committee discussed the recent umbrella review that assessed the possible association between paracetamol, pregnancy and ASD and ADHD, recognizing the methodological limitations of existing studies and concluded that there is no robust evidence to support a causal link between paracetamol use in pregnancy and the risk of ASD and ADHD. The Committee emphasized the importance of considering the potential risks of untreated pain and fever in pregnancy, noting that these data are also limited. Consideration should be given to the known serious safety risks of alternatives

such as nonsteroidal anti-inflammatory drugs and opioids and the limited data to support efficacy in the case of the opioids.

ACSoMP reinforced the importance of developing a fit-for-purpose communication strategy that educates the public on statistical challenges such as confounding and bias, the evolving definition of outcomes such as ASD and the challenge of assessing the safety of sporadic and often over-the-counter exposures as with paracetamol use. Communications need to be framed in the context of known evidence of benefit and the potential risk of alternative treatments, the potential risks of untreated fever and pain and the importance of always using the lowest most effective dose for the shortest duration of treatment. Engaging with women and their families as well as affected populations is critical in developing a sound communication strategy.

ACSoMP also stressed the need for leadership in developing guidelines on robust post-marketing surveillance studies in pregnancy and the importance of ensuring that methodologies are robust, taking into consideration clear definition of exposures and outcomes while controlling for or addressing for confounding and bias where feasible. Systematic reviews should assess the quality of studies they include in their analysis.

Summary of ACSOMP recommendations:

- The Committee supports WHO's efforts to perform a living systematic review. The PICO questions in the review should assess whether studies looked at timing of exposure, dose, duration and frequency of treatment, the clinical/public health significance of any risk identified and the consistency and comparability of the assessment of outcomes.
- The Committee noted that the studies claiming an association are of poor quality and not conducted according to accepted scientific standards for pharmacoepidemiology.
- The Committee highlighted the need for clear and unambiguous communication with the public, so that pregnant women are not unintentionally driven towards other analgesics with known serious and potentially life-threatening risks for the fetus and neonate.
- The Committee emphasized the need for robust post-marketing surveillance to assess the safety of medicines used in pregnant and breastfeeding women

Teratogenic concerns of topiramate and updates on sodium valproate regional initiatives

The Committee reviewed whether maternal use of the antiseizure medicine topiramate justifies a unique ICD-11 classification for neurodevelopmental disorders following a

recommendation made by ACSoMP in May 2024. While topiramate is associated with a known increased risk of oral clefts in infants born to mothers exposed to the medicine, evidence of neurodevelopmental disorders remains conflicting and less robust than the evidence for sodium valproate.

ACSoMP was also updated on regional initiatives related to safety issues with valproate during pregnancy.

Summary of ACSoMP recommendations:

- The Committee does not recommend proceeding with ICD coding for topiramate-related neurodevelopmental disorders at this point, as evidence is insufficient and inconclusive. Studies show mixed results, lack specificity, and have major confounding. This potential association should be treated as a potential safety signal and monitoring should continue.

Adverse drug reactions causality assessment

This session focused on updating the Committee on the development of a standardized methodology for causality assessment of adverse drug reactions that integrates existing methodologies for assessing adverse reactions, medication errors and substandard or falsified (SF) products.

ACSoMP members were positive about the proposed system and felt that consideration of medication errors would be very important as they may link to other types of errors within a clinic or pharmacy. It was stressed that the proposed method offered an opportunity to address gaps in the current pharmacovigilance system. However, members also observed that the proposed methodology could be difficult to use even in countries with more mature pharmacovigilance systems because obtaining detailed data could be difficult due to data-privacy laws.

ACSoMP members agreed that any tool recommended by the Committee must be appropriate for use in all countries, whatever their socioeconomic status. Members of the Committee expressed broad interest in the proposed system and requested that it be developed further.

Safety surveillance of lenacapavir and cabotegravir in pregnant and breastfeeding women

Currently available safety data from clinical trials and implementation studies for the use of long-acting cabotegravir and lenacapavir as pre-exposure prophylaxis (PrEP) products in pregnant and breastfeeding women were presented to ACSoMP. While current data are reassuring, there is a need for more data to detect rare and uncommon

adverse birth outcomes. The Committee noted that lenacapavir in particular is likely to be used widely in women of child-bearing potential and pregnant women in countries with a high prevalence of HIV.

Summary of ACSOMP recommendations:

- The Committee emphasized the need for post-marketing surveillance of these products, particularly in pregnancy, including support for implementing safety surveillance studies and pregnancy exposure registries in high-prevalence settings as well as reporting of pregnancy exposures to the Antiretroviral Pregnancy Registry.
- The Committee further recommended that longer-term follow-up surveillance and studies be conducted in infants exposed to these medicines *in utero*.
- Concerns about the potential for inappropriate administration or incorrect dosing schedules (i.e. inadvertent administration within 6 months) were raised given the long half-life of the medicines and reports indicating these risks in the WHO database of individual case safety reports, VigiBase. The Committee requested that these potential risks be considered in risk minimization efforts as part of any rollout of these products with clear record-keeping of timing of their exposures in women.
- The Committee recommended that efforts continue to increase collaboration between the different teams in WHO to ensure harmonization and to support the safety monitoring of maternal and newborn health.
- The Committee requested updates on the programmatic safety monitoring and final results of the implementation studies of these products.

NAION as a potential class effect of GLP-1 receptor agonists

GLP-1 Receptor Agonists (GLP-1 RAs) are indicated for the treatment of insufficiently controlled type 2 diabetes as an adjunct to diet and exercise, used either as monotherapy or in combination with other medicinal products to improve glycemic control and reduce the risk of cardiovascular complications or weight-related comorbidities. ACSoMP evaluated whether Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) – a rare condition leading to vision loss – is a class effect of GLP-1 receptor agonists (GLP-1 RAs). Following the ACSoMP meeting in May 2025 the association remains a signal requiring further investigations. Evidence is primarily driven by semaglutide data, while data for other agonists remain limited.

Summary of ACSoMP recommendations:

- The Committee confirms that NAION is a safety signal driven primarily by semaglutide data, and hence a class effect among all GLP-1 RAs cannot yet be determined. The association with semaglutide cannot be ruled out, despite inadequate evidence of a plausible biological mechanism (e.g. rapid glucose reduction). NAION is a very rare, serious and irreversible adverse event.
- A clear communication message must be developed and integrated into the rollout campaign accompanying the *WHO guideline on the use of glucagon-like peptide-1 (GLP-1) therapies for the treatment of obesity in adults* along with warnings on counterfeit use and misuse. This messaging is crucial given the increasing global use of GLP-1 RAs and concerns about unregulated use of these medicines. The message must clearly explain the rarity and potential irreversibility of NAION, encourage patients to report any sudden vision changes promptly, and reinforce the necessity of shared decision-making between the prescriber and the patient.
- Research must address evidence gaps by focusing on mechanistic studies, performing stratified analyses to find populations most at risk, consideration of confounding factors and improving case detections in specialized databases to ensure diagnostic accuracy. It is currently unknown whether stopping the medicine prevents the progression of NAION.