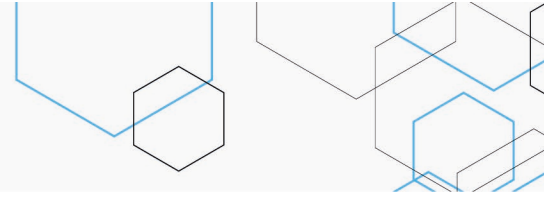


# Meningococcal ACWY (conjugate) vaccine for adolescents aged 11–12 years in the National Vaccination Schedule



**Technology:** Meningococcal ACWY (conjugate) Vaccine.

**Indication:** Prevention of meningococcal disease caused by the bacterium *Neisseria meningitidis* (*N. meningitidis*), serogroups A, C, W-135, and Y.

**Applicant:** Secretariat of Health Surveillance of the Ministry of Health of Brazil.

**Background:** Meningococcal Disease (MD) is caused by the bacterium *N. meningitidis*, transmitted through the respiratory tract, and it is more common in children and adolescents. It usually presents clinically as some syndromes such as meningitis and meningococcal septicaemia, and results in high morbidity and mortality. Some infected people do not have any symptoms but can still spread the disease to others. The incidence and prevalence of MD vary across the world, influenced even by the serogroups of *N. meningitidis*. In Brazil, the main circulating serogroups are B, C, W and Y. Vaccination is considered the best strategy for MD prevention and vaccines are specific to each serogroup. Currently, there are unconjugated meningococcal polysaccharide vaccines and meningococcal polysaccharide-protein conjugate vaccines. These vaccines can be monovalent, such as the meningococcal C (conjugate) vaccine, or multivalent, such as the meningococcal ACWY (conjugate) vaccine. Conjugate vaccines can induce immunological memory for a longer time and prevent nasopharyngeal colonization by *N. meningitidis* among those vaccinated. This Technical Report provides an evaluation of the meningococcal ACWY (conjugate) vaccine versus the meningococcal C (conjugate) vaccine available in the Brazilian Public Health System - SUS for the prevention of MD in adolescents. The report aims to address the demand of the Secretariat of Health Surveillance of the Ministry of Health of Brazil (SVS/MS in Portuguese), by the Technical Note No. 25/2019-CGPNI/DEIDT/SVS/MS (General Coordination of the National Immunization Programme/Department of Immunization and Communicable Diseases/Secretariat of Health Surveillance/Ministry of Health of Brazil).

**Question:** Is meningococcal ACWY (conjugate) vaccine effective and safe compared with meningococcal C (conjugate) vaccine in adolescent patients aged 11-12 years for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis*, serogroups A, C, W and Y?

**Scientific evidence:** MenACWY-TT and MenC-TT vaccines elicited high MenC rSBA titers, high MenC-PS-specific IgG concentrations, and high number of MenC-PS and TT-specific (IgG and IgA) memory B cells in young people aged 10, 12 and 15 years. Despite decreasing between the first month and one year after the booster dose, rSBA titers as well as specific IgG concentrations and the number of memory B cells remained elevated, suggesting protective response against MenC, mainly among adolescents aged 12 and 15 years. However, non-inferiority of rSBA titers to MenACWY-TT vaccine versus MenC-TT vaccine was not demonstrated one year after the booster dose. MenACWY-TT vaccine also elicited high rSBA titers against MenA, MenW and MenY, and high specific IgG concentrations against MenA-PS, MenW-PS and MenY-PS, mainly among adolescents aged 12 and 15 years. Although these titers and concentrations also decreased between the first month and one year after the booster dose, they remained higher elevated, suggesting protective responses against MenA, MenW and MenY. Meningococcal ACWY (conjugate) vaccines were shown to be safe, with few mild to moderate adverse events, mainly local and related to the administration of the dose. It should be noted that the safety findings of these vaccines were based on indirect evidence.

**Budget impact analysis:** A budget impact model was developed to estimate the costs associated with the expansion of the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years in the scope of SUS, and a complete market share over a five-year time horizon (2021 to 2025). In a scenario where all adolescents aged 11 years would receive the vaccine, the incremental budget impact was estimated to be approximately BRL 148 million in the first year and BRL 744 million after five years. In a scenario that considers a vaccination coverage of 37.8%, the incremental budget impact was estimated to be approximately BRL 91



**International recommendations:** The New Zealand's Pharmaceutical Management Agency (PHARMAC) recommends that meningococcal ACWY (conjugate) vaccine should be publicly funded for individuals aged between 13 and 25 years, who meet the eligibility criteria related to health status or perform daily activities that provide the opportunity for frequent and close social interactions. Recommendations on the use of meningococcal ACWY (conjugate) vaccine for adolescent patients from the National Institute for Health and Care Excellence (NICE), the All Wales Medicines Strategy Group (AWMSG) and the Scottish Medicines Consortium (SMC) were not identified. Nonetheless, this vaccine have been introduced in the UK national immunization programme in 2015, replacing meningococcal C (conjugate) vaccine, due to the increase in meningococcal serogroup W disease in England and Wales. Recommendations on the use of meningococcal ACWY (conjugate) vaccine for adolescents from the Canadian Agency for Drugs and Technologies in Health (CADTH) have also not been identified. However, in 2012, through a rapid review, CADTH presented a study suggesting that a booster dose of meningococcal vaccines at age 12, after routine vaccination at 12 months, would be beneficial. Beside this, using meningococcal C (conjugate) vaccine would be the most cost-effective option, while using meningococcal ACWY (conjugate) vaccine would be more effective reducing the burden of disease by 78% for a cost of US\$ 31,000 per QALY. CADTH also reported in this review two Canadian recommendations for routine administration of meningococcal conjugate vaccines in adolescents, which may be either monovalent or quadrivalent vaccines depending on the burden of disease and the availability of financial resources. Recommendations on the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years from the Pharmaceutical Benefits Scheme (PBS) were not identified, but since 2019 MenACWY-TT vaccine (Nimenrix®) is funded for adolescents aged 14–16 years by the Australian Government Department of Health.

**Technology horizon scanning:** No other vaccines in clinical development (phase 3 or 4 clinical trials) were identified for the treatment of meningococcal disease.

**Initial Recommendation:** Conitec, at its 87<sup>th</sup> Ordinary Meeting, on June 3, 2020, decided that the subject matter should be made available in a public consultation with a preliminary recommendation against the expansion of the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years in the National Vaccination Schedule. The following aspects were considered: the need for evidence to demonstrate the effectiveness or immunogenicity of the meningococcal ACWY (conjugate) vaccine over the years after the single or booster dose in adolescents; currently in Brazil, the *N. meningitidis* serogroup W incidence is low, despite mortality associated with it has been higher than for other serogroups; both the unit cost of the meningococcal ACWY (conjugate) vaccine and the estimated incremental budget impact associated with the expansion of its use in the scope of SUS.

**Public consultation:** The Public Consultation No. 23/2020 was held from June 24 to July 13, 2020. A total of 1,074 contributions were received, of which 239 were technical-scientific contributions, and 835 were experience or opinion contributions of patients, relatives, friends or caregivers of patients, health professionals or people interested in the subject. In general, the participants of the public consultation disagreed with Conitec's preliminary recommendation, demonstrating society's perception that the meningococcal ACWY (conjugate) vaccine is already part of the National Vaccination Schedule and its 'exclusion' would create grounds for discontent. The reason for this is its acquisition and distribution in order to meet a need of the National Immunization Programme to avoid shortage of meningococcal C (conjugate) vaccine. Some contributions included additional studies showing that immunogenicity and effectiveness of the meningococcal ACWY (conjugate) vaccine persist for more than one year, and that although the *N. meningitidis* serogroup W incidence is considered to be low in Brazil, this serogroup has increased in some states of the country, and mortality associated with it has been higher than for other serogroups. Finally, these were important contributions, providing additional evidence and supporting the studies carried out for the preparation of this Recommendation Report.



**Final Recommendation:** The Conitec's members present at the 90<sup>th</sup> Ordinary Meeting, on September 2, 2020, unanimously decided to recommend the expansion of the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years in the National Vaccination Schedule. After analysing the Public Consultation, the members of Conitec's plenary session considered that the questions raised about the epidemiology of meningococcal disease in Brazil – especially regarding the increase of serogroup W and mortality associated with it in some Brazilian regions, and the immunogenicity and effectiveness of meningococcal ACWY (conjugate) vaccine for a period exceeding one year, including the possible differences among the carrier proteins – were addressed in the presentations of the General Coordination of the National Immunization Programme (CGPNI) and the contributions of the Public Consultation No. 23/2020. Therefore, the members of CONITEC's plenary session decided to recommend the expansion of the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years in the National Vaccination Schedule. The Deliberation Record No. 550/2020 was signed.

**Decision:** To expand the use of meningococcal ACWY (conjugate) vaccine for adolescents aged 11-12 years in the National Vaccination Schedule, in the scope of SUS, according to Ordinance No. 46, published in the Official Gazette of the Federal Executive No. 189, Section 1, page 861, on October 1, 2020.

