



Summary of the NACI Statement on the Use of Bivalent Factor H Binding Protein Meningococcal Serogroup B (MenB-fHBP) Vaccine for the Prevention of Meningococcal B Disease

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Abstract

Background: Trumenba™, a bivalent, factor-H binding protein meningococcal serogroup B (MenB-fHBP) vaccine was authorized for use in Canada in October 2017 for the prevention of invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* serogroup B in individuals 10–25 years of age. The National Advisory Committee on Immunization (NACI) provides recommendations regarding the use of meningococcal vaccines to the Public Health Agency of Canada.

Objective: To summarize NACI recommendations regarding the use of MenB-fHBP vaccine in Canada.

Methods: The NACI Meningococcal Disease Working Group developed a predefined search strategy to identify all eligible studies, assessed the quality of these studies, and summarized and analyzed the findings. According to the NACI evidence-based process, the working group then proposed recommendations and identified the grade of evidence that supported them. In light of the evidence, the recommendations were then considered and approved by NACI.

Results: The two serogroup B meningococcal vaccines currently authorized for use in Canada are not interchangeable as they contain different antigens and there are no published studies on the immunogenicity resulting from a vaccination series combining the two products. Following the review of evidence, NACI recommends that MenB-fHBP vaccine may be considered as an option for use in individuals 10 years of age and older in situations when a serogroup B meningococcal vaccine should be offered: 1) during serogroup B meningococcal disease outbreaks or with the emergence of hyperendemic *N. meningitidis* strains that are predicted to be susceptible to the vaccine; 2) for individuals who are close contacts with a case of invasive meningococcal disease caused by serogroup B *N. meningitidis*; 3) for individuals with underlying medical conditions that would put them at higher risk of meningococcal disease than the general population; or 4) for individuals at higher risk of exposure to serogroup B meningococcal isolates than the general population. NACI also recommends that MenB-fHBP vaccine may be considered as an option for individuals 10–25 years of age who are not at higher risk of meningococcal disease than the general population, but who wish to reduce their risk of invasive serogroup B meningococcal disease.

Conclusion: NACI recommends immunization against serogroup B IMD for all individuals who are at a higher risk of disease due to an underlying medical condition or an increased risk of exposure. In addition to providing guidance to public health decision-makers (i.e. provinces/territories making decisions for publicly-funded immunization programs), these NACI recommendations provide information to individuals, vaccine providers and organizations about vaccines that may not currently be included in publicly funded immunization programs. NACI continues to recommend against the use of the serogroup B vaccines in routine universal immunization programs in Canada at this time.

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Introduction

Invasive meningococcal disease (IMD) usually presents as an acute febrile illness with rapid onset and features of meningitis or septicemia (meningococemia), or both, and a characteristic non-blanching rash. Overall case fatality is approximately 10%, and up to a third of survivors may have long term sequelae, which can include hearing loss, neurologic disabilities, and digit or limb amputations. From 2012 to 2016, a total of 353 of 583 (60.5%) reported cases of IMD in Canada were due to serogroup B, with the highest rate being observed in infants younger than one year of age.

The National Advisory Committee on Immunization (NACI) provides recommendations regarding the use of meningococcal vaccines to the Public Health Agency of Canada (PHAC). Trumenba™, a bivalent, factor-H binding protein meningococcal serogroup B (MenB-fHBP) vaccine was authorized for use in Canada in October 2017 for the prevention of IMD caused by *Neisseria meningitidis* serogroup B in individuals 10–25 years of age. The objective of this article is to summarize the NACI recommendations on the use of MenB-fHBP vaccine for the prevention of serogroup B IMD in Canada (1).

Methods

To prepare the NACI *Statement on the Use of Bivalent Factor H Binding Protein Meningococcal Serogroup B (MenB-fHBP) Vaccine for the Prevention of Meningococcal B Disease*, the Meningococcal Disease Working Group (MDWG) identified 10 randomized controlled trials (RCTs) and six observational studies that examined the immunogenicity and 14 studies (11 RCTs and three observational studies) that examined the safety of MenB-fHBP vaccine. Following review and analysis, the MDWG proposed recommendations according to the NACI evidence-based process (2). The MDWG also requested information from one unpublished economic evaluation of MenB-fHBP and reviewed 14 published economic evaluations of protein based meningococcal vaccines against serogroup B IMD. PHAC conducted an analysis of the current epidemiology of serogroup B IMD in Canada. NACI critically appraised the available evidence and approved the specific recommendations brought forward.

Results

Epidemiology

Serogroup B is currently the most common cause of IMD in Canada. Between 2012 and 2016, 60.5% (n=353) of IMD cases were due to serogroup B, with the highest incidence in children younger than one year of age (n=10 cases annually; 2.7 cases per 100,000) followed by children 1–9 years (14 cases annually; 0.9 cases per 100,000) and adolescents 15–19 years (11 cases annually; 0.5 cases per 100,000). In the same time period, 63.8% (n=95) of cases of IMD in individuals 10–25 years were due to serogroup B, representing an incidence of 0.3–0.9 cases per 100,000 population in this age group.

Immunogenicity and effectiveness

In both adolescents (primarily 11–18 years) and young adults (primarily 18–25 years), MenB-fHBP vaccine was found to be immunogenic against both primary and secondary MenB test strains containing a range of fHBP variants that were representative of circulating strains causing invasive meningococcal disease at the time in Europe and the United States. There was limited evidence from two MenB-fHBP vaccine studies on persistence of the immune response up to 48 months post-vaccination in adolescents and 9–11 months in a small study in adults (24–66 years) and no data on the need for booster doses after the primary immunization series. The MDWG did not find any population-level data on the effectiveness of MenB-fHBP vaccine or its effect on meningococcal carriage or herd immunity.

Safety

Immunization with MenB-fHBP vaccine was found to be safe with no associated serious adverse events reported in immunocompetent individuals 10–25 years of age. Most systemic and local adverse events were mild to moderate in intensity and transient in duration (lasting 1–3 days).

Economics

None of the 14 articles (10 peer-reviewed studies and four study reports published by agencies) identified in the literature review included economic assessments of MenB-fHBP vaccine. The economic literature review found that 4CMenB (Bexsero®), which is authorized for use in Canada in individuals two months through 17 years of age, is not cost-effective at commonly used thresholds because of the low incidence of serogroup B IMD and the relatively high vaccine cost. Based on the economic evidence for 4CMenB vaccine and the age distribution of the burden of serogroup B IMD (highest in children younger than 10 years of age), the MDWG concluded that it was unlikely that the MenB-fHBP vaccine would be cost-effective.



Summary of NACI recommendations for the use of MenB-fHBP vaccine for the prevention of invasive meningococcal disease

NACI continues to recommend immunization against serogroup B IMD to all individuals who are at a higher risk of disease due to an underlying medical condition or at an increased risk of exposure. However, the two serogroup B meningococcal vaccines currently authorized for use in Canada are not interchangeable, as they contain different antigens and there are no published studies on the immunogenicity resulting from a vaccination series combining the two products. Therefore, the same vaccine product should be used for all doses in a vaccination series. If, in a person with an incomplete vaccination series, it is unknown what vaccine product they initially received, the initial dose(s) should be discounted and the vaccination series repeated using the same vaccine product for all doses in the new, repeated series.

Recommendations for public health publicly funded immunization programs

Recommendation 1: NACI recommends that the MenB-fHBP vaccine should not be offered in routine universal immunization programs in Canada at this time. (Strong NACI Recommendation).

- NACI concludes there is insufficient evidence to recommend routine universal immunization (Grade I Evidence)

Recommendation 2a: NACI recommends that a serogroup B meningococcal vaccine (MenB-fHBP vaccine or 4CMenB) should be offered in jurisdictions experiencing serogroup B meningococcal disease outbreaks or with the emergence of hyperendemic *N. meningitidis* strains that are predicted to be susceptible to the vaccine. (Strong NACI Recommendation).

- NACI concludes there is fair evidence to recommend vaccine use during outbreaks (Grade B Evidence)

Recommendation 2b: NACI recommends that the MenB-fHBP vaccine may be considered as an option for use in individuals 10 years of age and older in such circumstances. (Discretionary NACI Recommendation).

- NACI concludes there is insufficient evidence of the MenB-fHBP vaccine use in such circumstances (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendation 3a: NACI recommends that a serogroup B meningococcal vaccine (MenB-fHBP or 4CMenB) should be offered, in addition to chemoprophylaxis, for protection of individuals who are close contacts with a case of invasive

meningococcal disease caused by serogroup B *N. meningitidis*. (Strong NACI Recommendation).

- NACI concludes there is insufficient evidence of vaccine effectiveness in close contacts of cases of IMD (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendation 3b: NACI recommends that the MenB-fHBP vaccine may be considered as an option for use in individuals 10 years of age and older who are close contacts with a case of IMD caused by serogroup B *N. meningitidis*. (Discretionary NACI Recommendation).

- NACI concludes there is insufficient evidence of the MenB-fHBP vaccine use in close contacts (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendation 4a: NACI recommends that a serogroup B meningococcal vaccine (MenB-fHBP or 4CMenB) should be offered for the active immunization of individuals with underlying medical conditions that would put them at higher risk of meningococcal disease than the general population to reduce the risk of invasive serogroup B meningococcal disease. (Strong NACI Recommendation).

- NACI concludes there is insufficient evidence of vaccine use in high-risk populations (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendation 4b: NACI recommends that the MenB-fHBP vaccine may be considered as an option for use in high-risk individuals 10 years of age and older, in a three-dose schedule (zero, 1–2, six months), to reduce the risk of invasive serogroup B meningococcal disease. (Discretionary NACI Recommendation).

- NACI concludes there is insufficient evidence of the MenB-fHBP vaccine use in high-risk populations (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendations for individual level decision-making

For individuals wishing to prevent serogroup B IMD or clinicians wishing to advise individual patients about preventing IMD with vaccines that may not be currently included in publicly funded immunization programs. For organizations or decision makers responsible for programs offering vaccine services to various groups including individuals at risk of acquiring IMD.

Recommendation 5a: NACI recommends that a serogroup B meningococcal vaccine (MenB-fHBP or 4CMenB) should be offered for the active immunization of individuals at higher risk of exposure to serogroup B meningococcal isolates than the general population to reduce the risk of invasive serogroup B meningococcal disease. (Strong NACI Recommendation).

- NACI concludes there is insufficient evidence of vaccine use in high-risk populations (Grade I Evidence); therefore, this recommendation is based on expert opinion



Recommendation 5b: NACI recommends that the MenB-fHBP vaccine may be considered as an option for use in such high-risk individuals 10 years of age and older, in a two-dose schedule (zero and six months), to reduce the risk of invasive serogroup B meningococcal disease. (Discretionary NACI Recommendation).

- NACI concludes there is insufficient evidence of the MenB-fHBP vaccine use in high-risk populations (Grade I Evidence); therefore, this recommendation is based on expert opinion

Recommendation 6: NACI recommends that the MenB-fHBP vaccine may be considered as an option for individuals 10–25 years of age who are not at higher risk of meningococcal disease than the general population, in a two-dose schedule (zero and six months), to reduce the risk of invasive serogroup B meningococcal disease. (Discretionary NACI Recommendation).

- NACI concludes there is fair evidence of vaccine immunogenicity to recommend the MenB-fHBP vaccine when given according to the schedule used during clinical trials (Grade B Evidence)

Conclusion

NACI develops evidence-based recommendations for the use of vaccines marketed in Canada in order to support programmatic and clinical decision-making. The *NACI Statement on the Use of Bivalent Factor H Binding Protein Meningococcal Serogroup B (MenB-fHBP) Vaccine for the Prevention of Meningococcal B Disease* provides information and guidance, in addition to that provided in the product monograph, for the use of the newly licenced MenB-fHBP vaccine. Due to the low incidence of serogroup B IMD in the age group for which the MenB-fHBP vaccine is authorized for use, combined with an absence of data for vaccine effectiveness, duration of protection, effect on meningococcal carriage, herd immunity and cost-effectiveness, NACI has concluded that the vaccine should not be offered in routine universal immunization programs in Canada at this time.

Authors' statement

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Conflict of interest

None.

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