Introduction

Within the framework of its competence in defining the vaccination schedule for Belgium, the Superior Health Council (SHC) has reviewed the previous advisory report and the vaccination schedule for the vaccination of children and adolescents against meningococcal disease.

Epidemiology

The last epidemic wave of invasive meningococcal disease occurred between 1997 and 2001, during which period the recorded incidence increased by 54% (from 2.4 to 3.7 per 100,000). This increase was mainly due to the rise in infections caused by serotype C. As a result, vaccination programmes included systematic vaccination against serotype C as of 2002.

From 2002, the incidences of invasive meningococcal disease (of all serotypes) confirmed annually by the National Reference Centre (*Centre National de Référence*) (NRC, Sciensano) declined significantly and the number of cases reported has stabilised since 2008. The overall incidence was estimated at 1.7 cases per 100,000 population between 2009-2010 in a KCE study pairing hospitalisation data with those of the NRC (the NRC does not receive data in every case).

In 2018, the NRC recorded 116 cases, and 8 deaths were identified through mandatory reporting. The mortality rate of invasive meningococcal disease was 9.7% in Europe in 2017 (and 7.0% in Belgium in 2004-2010). The NRC recorded 42 cases, including 9 deaths, in Belgium during the first quarter of 2019.

The number of cases of type C meningococcal disease has fallen significantly since the introduction of the vaccine in 2002, dropping from 179 cases in 2001 to 5 in 2018. In 2018, serotype C only represented 4% of cases of invasive meningococcal disease. The NRC diagnosed 3 cases during the first quarter of 2019.
A downward trend was also observed in the number of cases of type B meningococcal disease since the start of the 2000s, which declined from 164 cases in 2000 to approximately 60 cases per year since 2014. In 2018, 59 cases of invasive type B meningococcal disease were reported (i.e. 51% of all cases) and 20 cases were recorded for the first quarter of 2019.

While the proportion of serotypes W and Y was approximately 15.8% in Belgium for the period 2011-2017, it reached 41% in 2018. Type Y meningococcal disease has increased since 2011: 3 cases were diagnosed in 2005, 9 in 2011 and 29 in 2018. The NRC diagnosed 7 cases during the first quarter of 2019. Type W has also increased since 2015, with 8 cases diagnosed in 2015 and 19 cases in 2018. In 2018, 13 cases of meningococcal disease due to serotype W clonal complex 11 were reported. This hypervirulent clonal complex has been emerging in Europe for several years, and has been responsible for epidemics in the Netherlands and the United Kingdom. According to the preliminary data for 2019, 12 cases of type W meningococcal disease were recorded from January to mid-April 2019, of which four were due to clonal complex 11.

The most affected age groups differ according to the serotype involved. Serotype B mainly affects children under 5 years of age, who represented 47% of the cases linked to this serotype in 2018, and even more specifically, children under the age of 1, with 22% of the cases involving the latter. Amongst children under the age of 1, 45% of cases (5 cases) were aged under 6 months. This serotype also affects adolescents. 12% of the cases of serotype B affected 15-19 year olds in 2018. The 5 cases of invasive serotype C infection recorded in 2018 were aged 1, 4, 22, 23 and 72 years.

Serotype Y is mainly found in 3 age groups: 0-9 year olds, who represented 34% of cases connected with this serotype in 2018, of which 4 cases were in children under 14 months of age (14%), 15-19 year olds (17% of cases), and 65-85 year olds (31% of cases). Serotype W mainly affected 2 age groups in 2018 with 21% of cases in children under 5 years of age, of which 4 cases were in infants under 14 months (21.0%) and 26% of cases were in adolescents aged 15-19 years.

Vaccines

The following vaccines are available in Belgium for vaccination against meningococcal disease.

1. Vaccines against serotype C meningococcal disease

- Neisvac-C®

  Registered for immunisation from the age of 2 months. Conjugated with tetanic anatoxin.

2. Vaccine against serotype A, C, W, Y meningococcal disease

- Menveo®

  Registered for immunisation from the age of 2 years, conjugated with protein CRM197.

- Nimenrix®

  Registered for immunisation from the age of 6 weeks, conjugated with tetanic anatoxin.

3. Vaccine against serotype B meningococcal disease

- Bexsero®

  Registered for immunisation from the age of 2 months. The Bexsero® vaccine contains 4 cell wall-associated protein antigens of meningococcus B: Neisseria adhesin A (NadA), factor-*H binding protein* (fHbp), *Neisseria heparin binding antigen* (NHBA) and an outer membrane vesicle (OMV).

- Trumenba® (will be available in August 2019)

  This vaccine is composed of two recombinant antigenic variants (A05 and B01) of factor H-binding protein (fHBP). The vaccine is registered for the prevention of invasive MenB infections in individuals over the age of 10 years.

Recommendations and vaccination schedule

1. Vaccination against serotype ACWY meningococcal disease

Based on the current increased incidence of serotype Y and serotype W meningococcal infections (especially Wcc11) in Belgium and in other countries as the Netherlands and the UK (JCVI 2015; Knol et al., 2018; Krone et al., 2019), on the age distribution, the potential herd effect on unimmunized individuals (especially infants and adults), the waning immunity (decline in protective antibody levels

over time) against serotype C meningococcal infections in adolescents previously vaccinated during infancy (Khatami et al., 2011), the SHC recommends to move from the serotype C meningococcal vaccine to the meningococcal ACWY conjugate vaccine in the SHC basic vaccination schedule for children aged 15 months and to add meningococcal ACWY vaccination with the conjugate vaccine in adolescents aged 15-16 years, to be co administered with Tdap (+ catch up vaccination in 15-19 year olds until 2024).

2. Vaccination against meningococcal B disease

The SHC confirms that the type B meningococcal vaccine Bexsero® has proven efficacy in children under the age of 2 and has no major side effect (JCVI 2018). Vaccination may therefore be considered on an individual basis for children aged 2 months- 5 years, aged 15-19 and at risk groups, following the vaccination schedule 2+1 (Martinon-Torres et al., 2017; Martinon-Torres et al., 2018).

For children under the age of 1 :

- The best schedule is at 8 and 16 weeks, given the high % of cases before the age of 6 months (together with routine vaccination and prophylactic paracetamol) with a booster dose between 11 and 14 months (SHC 9125).
- Alternative schedules: at 10 and 18 weeks (type B meningococcal vaccine alone, no prophylactic paracetamol) with a booster dose between 11 and 14 months or at 12 and 20 weeks of age with a booster dose between 11 and 14 months.

For other age groups : (SHC 9125)

Age group (1st dose)	Primary vaccination	Interval between doses	Booster
6 to 11 months	2 doses	min 2 months	during 2nd year, one dose at least 2 months after last dose 1st vaccination
12 to 23 months	2 doses	min 2 months	one dose at least 12 to 23 months after primary vaccination
2 to 5 years	2 doses	min 2 months	
Adolescents (aged 11 to 19)	2 doses	1min 1 month	

Vaccination with Trumenba® can be considered on an individual basis for 15-19 year olds (2 injections at least 6 months apart, a booster dose should be considered for individuals at continuing risk of invasive meningococcal disease) and at-risk groups.

From a public health perspective, the SHC doesn't, at this point in time, recommend that type B meningococcal vaccination should be included in the SHC basic vaccination schedule. The reasons are the following:

- the current low incidence of the disease;
- the need for early vaccination at the age of 2 months, together with the routine vaccines, as the first peak in the incidence is under the age of 6 months. Given the fact that this schedule involves a high risk of fever, prophylactic paracetamol is recommended;

- including type B meningococcal vaccination requires a high degree of acceptance from parents and vaccinators, as this implies giving 3 shots (+ paracetamol) during a single visit. Furthermore, the SHC is concerned that the vaccination coverage of other vaccine-preventable diseases in the basic vaccination schedule could fall in the event of 3 shots being given;
- the poor cost-effectiveness of the vaccine (expensive price and rare disease);
- there is no herd immunity (protein vaccine, no effect on carrying in adolescents).

The Council also undertakes to regularly reassess its position according to the available data regarding epidemiology, efficacy and carrying.

Side effects

The most commonly reported side effects are:

- Neisvac-C®
  Pain, erythema or induration at the injection site, that can last for several days. Sometimes fever, headache, myalgia, rash, drowsiness and irritability.
- Menveo®, Nimenrix®
  Erythema, induration and pain at the injection site, that can last for several days. General reactions (shivers, fever) usually benign.
- Bexsero®
  Pain, erythema or induration at the injection site, that can last for several days. Fever, headache, irritability, drowsiness. Rare: Kawasaki disease. In infants, side effects (such as fever, irritability, local sensitivity) are more frequently observed in the event of co-administration with routine vaccines and can be prevented with prophylactic paracetamol without any effect on the response to the C4MenB vaccine antigens or other routine vaccine antigens (Prymula et al., 2014).
- Trumenba® (will be available in August 2019)
  The most common side effects with Trumenba® (which may affect more than 1 in 10 people) are the following: pain, redness or swelling at the injection site, headache, tiredness, chills, diarrhoea, nausea (feeling sick), and muscle or joint pain.

For a full description, please refer to the FAMHP (Federal Agency for Medicines and Health Products) patient information leaflet and the general information of the CBIP (Belgian Centre for Pharmacotherapeutic Information).

https://www.famhp.be/en/human_use/medicines/medicines/pil

https://www.cbip.be/fr/chapters/13?frag=11668

Composition of the working group

President of the Superior Health Council and of the Board: NEVE Jean
President of the standing working group "Vaccination": VAN LAETHEM Yves
President of the ad hoc working group "Meningococcal disease": TUERLINCKX David
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