

Czech Vaccination Society recommendation for vaccination against invasive meningococcal disease

July 4, 2017 (update of recommendation from February 25, 2014)

Meningococcal disease is a purely human transmitted infectious disease caused by the gram-negative diplococcus *Neisseria meningitidis*. The clinical presentation ranges from asymptomatic carriage to severe invasive disease. At present *N. meningitidis* remains the main cause of bacterial meningitis and septicaemia. The invasive meningococcal disease (IMD) has an acute course, which may cause death within the initial 24 - 48 hours after the initial symptoms arise. The disease may be diagnosed late because of its initial non-specific symptoms followed by insufficient response to treatment of a progressed disease. It is a serious disease with mostly fatal consequences if not treated adequately, with risk of permanent sequelae such as limb amputation, deafness or mental retardation. Despite the advances in medicine, IMD are still life threatening and have a high case fatality rate worldwide. In the Czech Republic, the average case fatality rate was 9.4 % over the last decade, ranging from 4.7 % in 2012 to 13.9 % in 2016.

Given the high case fatality rate and severe consequences of IMD not only for patients but also for their families, prevention by vaccination is highly relevant. Currently, the most used vaccine against invasive meningococcal disease in the Czech Republic is conjugated tetravaccine against four serogroups A, C, W, Y. The vaccine is used for children starting at 6 weeks of age and for adults (NIMENRIX) or for children starting at 2 years of age and for adults (MENVEO). The conjugated tetravaccine is currently the most adequate available vaccine to ensure as broad protection as possible especially in case of frequent travelling of young people. Substance W and Y which is included in the vaccine protects against serogroups W and Y which cause the highest case fatality among the all serogroups also in the Czech Republic. The number of cases of IMD caused by these serogroups has recently been on the rise in the Czech Republic, similarly to other countries. The next registered vaccine is a recombinant four-component vaccine against serogroup B (MenB) vaccine BEXSERO for use in infants starting at 2 months of age and in adults. It is the only registered vaccine against the most frequent meningococcal group (approximately 75% of cases) causing disease and death in the Czech Republic. With respect to the serogroup B antigen variability, the vaccination cannot create protection against all serogroup B meningococcal strains. The coverage of this MenB vaccine is expected to be 74% in the Czech Republic.

The meningococcal tetravalent conjugate vaccine A, C, W, Y has proven effective in providing protection not only against IMD caused by the four serogroups but also against carriage of meningococci of these serogroups. The MenB vaccine (BEXSERO) is expected to provide protection against meningococcal carriage, but no data have been available so far.

In the light of the current epidemiological situation in the Czech Republic, when the incidence of invasive meningococcal disease is low (0.4-0.8/100,000 inhabitants in the last 10 years), the importance of individual protection and vaccination of risk groups stands out. The aim is to ensure as complex and long immunity as possible of the vaccinated person. Given the low vaccine coverage rate, the herd immunity effect is not expected to occur. Until

a universally efficient vaccine against all meningococcal serogroups is developed, the combination of conjugated tetravaccine A, C, W, Y and the vaccine MenB is recommended. Administration of both vaccines is recommended in at least a 14-day interval; if necessary they may be concomitantly administered in two different sites. In order to maintain long-term immunity re-vaccination is recommended for both vaccines. In the case of conjugated tetravaccine A, C, W, Y in a five-year interval. In the case of MenB vaccine one re-vaccination in children up to 2 years of age; in children above 2 years of age the interval is not yet determined.

Vaccination is especially recommended for:

- children aged from 2 months to 4 years against serogroup B, administration is preferable not later than at six months of age;
- children between the ages of 13 and 15 years; combination of conjugate tetravaccine A, C, W, Y and MenB vaccine;
- adolescents and young adults, in particular before entering university, boarding school and in light of individual risk assessment (participation at music festivals, mass events, stay in a big group); combination of conjugate tetravaccine A, C, W, Y and MenB vaccine;
- persons travelling or planning a long-term stay in countries with hyperendemic or epidemic situation of meningococcal diseases; combination of conjugate tetravaccine A, C, W, Y and MenB vaccine;
- persons with the following health conditions; combination of conjugate tetravaccine A, C, W, Y and MenB vaccine:
 - patients with anatomic asplenia or splenic dysfunction (hyposplenism/asplenia) or complement deficiency;
 - patients after autologous or allogeneic hematopoietic stem cell transplantation;
 - patients suffering from primary and secondary immunodeficiency including complement deficiency;
 - persons after bacterial meningitis and septicaemia;
 - patients before starting treatment with Eculizumab;
- persons professionally exposed to a risk of infection; combination of conjugate tetravaccine A, C, W, Y and MenB vaccine.

On the basis of surveillance data on invasive meningococcal disease in the Czech Republic and in line with the current knowledge and vaccine availability, the Czech Vaccination Society recommends the following vaccination strategy for the Czech Republic:

MenB vaccine:

- 1) For infants from **2 to 5 months of age**, administration of recombinant MenB vaccine in three doses in at least a 1-month interval and re-vaccination with one dose between 12 and 23 months of age.
- 2) In children **from 6 months to 4 years of age**, administration of two doses of recombinant MenB vaccine in at least a 2-month interval. Re-vaccination will be performed:

- a) in children primary vaccinated at the age of 6 - 11 months with administration of one dose in the second year of life, but not earlier than in 2 months from primary vaccination,
- b) in children primary vaccinated at the age of 12 - 23 months with the administration of one dose between the second and third year of life, but not earlier than 12 - 23 months from primary vaccination.

3) In children **between 4 and 10 years** of age with administration of two doses of recombinant MenB vaccine in at least a 2-month interval based on individual risk assessment (joining a group, nursery school, group exercises with babies, swimming classes for infants and toddlers), in particular prior to joining a group. The need for re-vaccination is not determined.

4) In preadolescents between 13 -15 years of age, adolescents and adults: administration of two doses of recombinant MenB vaccine in at least a 1-month interval based on individual risk assessment, mainly prior to joining a group. The need for re-vaccination is not determined.

The combination of MenB with hexavalent vaccine or pneumococcal conjugated vaccine can lead to a higher frequency of febrile reactions. In order to use these vaccines concomitantly, especially in the age category from 2 to 5 months of age, it is possible to prophylactically use paracetamol. After such prophylaxis, studies show significantly lower frequency of febrile reactions. Immunogenicity of MenB vaccine is not influenced at all; slight decrease has been observed at other components with no clinical significance or practical implications.

Conjugated tetravaccine Y, C, W, Y:

1) Vaccination with one dose of meningococcal conjugated tetravaccine A, C, W, Y is possible in small children, usually **at the age of 2 months -4 years** in the light of individual risk assessment (joining a group, nursery school, group exercises with babies, swimming classes for infants and toddlers), in particular prior to joining a group.

2) In preschool children at the age **between 5 and 6 years** it is possible to vaccinate (re-vaccinate) with one dose of conjugated tetravaccine A, C, W, Y which is recommended to carry out after 5 years from the first conjugated tetravalent vaccine dose administration. Vaccination may be re-vaccination in children who have already been vaccinated with meningococcal conjugated or polysaccharide vaccine and primary vaccination in children who have not been vaccinated yet.

3) in pre-adolescents at the age of 13, but not later than 15 years, administration of one dose of tetravalent conjugate vaccine A, C, W, Y. Vaccination would be re-vaccination in preadolescents who have already been vaccinated with meningococcal conjugate or polysaccharide vaccine in childhood age and primary vaccination in children who have not been vaccinated yet.

4) Vaccination (re-vaccination) with one dose of conjugated tetravaccine A, C, W, Y is possible also **in adults**, in particular young adults (before entering university) in the light of individual risk assessment (participation at music festivals, travelling, participating in a group).