

RECOMMENDATIONS

2024 update on meningococcal vaccination recommendations for children and adults

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ABSTRACT

The best protection against invasive infections caused by meningococcus (*Neisseria meningitidis*), which can lead to death or permanent disability, is immunization. Its effectiveness has been demonstrated in many countries that have introduced it into national immunization programmes. After 2 years, there was a need to update the Polish recommendations issued in 2022. The epidemiological data have been updated. Complications of invasive meningococcal disease, recommendations for administering booster doses and the management of an epidemiological outbreak have been added to the recommendations. In Poland, meningococcal vaccination has been recommended in the National Immunization Programme for many years, including for 2024, but is not reimbursed. Insufficient public awareness of the risks of meningococcal infections, multiple vaccinations in the first year of a child's life, involving a large cumulative number of injections, and the cost of the vaccines are other barriers to their acceptance and performance, especially in the youngest children. This publication provides updated management recommendations for physicians implementing meningococcal vaccination in children and adults. This is the result of the work of the expert group established in 2022 under the auspices of the National Consultants in Pediatrics and Family Medicine, who met again in 2024. We recommend starting meningococcal vaccination in the first six months of life with administration of both MenB and MenACWY vaccines at one visit (just after 8 weeks of life), vaccination against MenACWY and MenB of adolescents and young adults – especially those starting college, planning to live in boarding schools or dormitories, or work in the uniformed services, nurseries, kindergartens, or in childcare or health care facilities, or traveling abroad – and use of booster doses of MenB and MenACWY vaccines in patients at high risk of contracting invasive meningococcal disease over the age of 10. We recommend the prophylactic administration of paracetamol to every child under 2 years of age undergoing immunization against MenB, and a proactive vaccination approach. We advocate for the introduction of free-of-charge vaccination for patients

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from risk groups, urgent action to allow reimbursement of meningococcal vaccines, and the development of regulations for managing meningococcal outbreaks.

KEY WORDS:

health policy, sepsis, purulent meningitis, prevention, immunoprophylaxis.

INTRODUCTION

EPIDEMIOLOGY

Invasive meningococcal disease (IMD) is a relatively rare infectious disease, but it develops rapidly and always poses a serious threat to health and life. The American and European regions of World Health Organization report more cases of IMD than measles, and reports from France, Germany and Poland accounted for 49% of the all cases reported in Europe. According to reports by the National Institute of Public Health – National Institute of Hygiene, ca. 200 cases of IMD were reported annually in Poland before the COVID-19 pandemic. During the pandemic, the number of cases decreased [1]. Detailed data on epidemiology, especially the proportion of individual serogroups of *Neisseria meningitidis*, are analysed annually by the National Reference Centre for the Diagnosis of Bacterial Infections of the Central Nervous System (KOROUN).

The results of the KOROUN research consistently show that IMD can occur at any age, but the highest incidence in Poland concerns children under 5 years of age, especially infants in the first year of life which indicates the need to start meningococcal immunization in the first months of life. Among non-infants, the highest number of IMD cases occurs in the second half of life. According to KOROUN data, in all age groups, including the youngest children, the most common cause of IMD is *Neisseria meningitidis* serogroup B (MenB), which has been responsible for the vast majority of cases for years. The remaining cases are caused by serogroups C, W and Y (MenC, MenW and MenY). In 2023, the KOROUN confirmed 100 cases of IMD. In 2023, serogroup B accounted for 77 cases (77%), MenC for 15 (15%), MenW for 6 (6%), and MenY for 2 cases (2%) [2]. It is worth noting that the size of the birth cohort has been steadily decreasing for several years, so the risk of developing IMD should be related to the incidence rate, not the absolute number of cases. The overall mortality rate for all reported cases of IMD was 13%, while the mortality rate calculated only for cases with a known outcome of infection was 22.8% [3]. From 2014 to 2020, an increase in IMD cases caused by MenW was observed in Poland and other European countries. Although the percentage of this serogroup is currently decreasing, diseases caused by MenW may be accompanied by non-specific gastrointestinal symptoms, which may make it additionally difficult to establish a diagnosis, potentially delaying proper treatment [4].

According to KOROUN data, in the years 2013–2017, in all age groups mortality due to IMD caused by MenW was the highest at 38.5%, followed by MenB at 13.5%, and MenC at 11.2% [5].

DIAGNOSIS OF MENINGOCOCCAL DISEASE

Diagnosing IMD at its initial stage, in the office of a family doctor, paediatrician or internist, is a major challenge. The patient may present with fever and seemingly mild symptoms resembling an upper respiratory tract infection or gastroenteritis.

Characteristic symptoms, including petechiae typical for IMD, appear only at an advanced stage of the disease and do not occur in all patients [6]. The rapid clinical course means that the time in which the doctor should diagnose the disease and start treatment is very short. Physicians working exclusively in primary care have limited opportunities to gain experience in diagnosing and managing IMD, which contributes to delaying diagnosis and late referral of the patient to hospital, which may result in treatment failure, increase the risk of early complications and late sequelae, and may be the cause of the patient's death.

COMPLICATIONS AND PERMANENT CONSEQUENCES OF MENINGOCOCCAL DISEASE

Invasive meningococcal disease is associated with a high risk of both direct and long-term consequences. According to a meta-analysis based on data from over 163,000 patients with IMD, the case fatality rate is in the range 4.1–20%, averaging 8.3% (95% confidence interval (CI): 7.5–9.1%) [7]. The highest mortality rate was recorded for group W (12.8%), followed by C (12%), Y (10.8%) and B (6.9%).

The coefficient for serogroup A was not calculated due to the small number of patients included in the analysis [7]. The meta-analysis determined the infant mortality rate at about 9%. The rate decreased to 7% by the age of 7, then increased to 15% for young adults and stabilized in the range of 15–20% among middle-aged and older people [7]. According to data reported by the KOROUN, the mortality rate in Poland is higher, and in 2013–2022 it was 13–31.1% for cases with a known outcome of IMD. Large differences were also found between serogroups depending on the epidemiological year: for serogroup B, the mortality rate was 12.4–19.5%; for serogroup C, 9.7–14.7%; for serogroup W, 38.5–50%; and for serogroup Y, 18.2% or more [2, 3, 8–11].

The World Health Organization predicts that 1 in 5 IMD survivors will develop long-term complications, such as hearing or growth loss, speech disorders, epilepsy, skin scars, paralysis or limb amputation, memory impairment or communication problems [12]. During developing a map of meningococcal complications, 44 different complications of IMD were identified, including 30 somatic or neurological complications and 14 psychological or behavioural disorders [13]. The most frequently observed somatic complications were Raynaud's syndrome (27.7%) and other vascular disorders (15.2%), chronic headache (13.9%), learning difficulties (11.8%), lung diseases (10.8%), and kidney disease (7.3%). Among psychological and behavioural disorders, attention deficit hyperactivity disorder and oppositional defiant behaviour (11.4% each) predominated [13].

The consequences of IMD may occur at different times after disease onset and may be short-term (approx. 40%), medium-term (26%) or long-term (34%) complications [14]. Most somatic complications are observed shortly after onset, while psychological and behavioural disorders are reported over a longer period after the onset of IMD, e.g. anxiety or depressive disorders 16–23 months after IMD among children aged 5–17 years [13]. Complications appeared after 1 month (median) for somatic complications, 8.5 months for neurological complications, and 15.5 months for psychological complications (36.2 months for children under one year of age) [15]. About 15% of convalescents are discharged from hospital with complications, while a year later 40% experience sleep problems, over 30% complain of headaches, 30% have depressive episodes, and 10% have problems with concentration [16, 17]. As a result, one year after suffering from IMD, 13% of patients do not return to their professional work [17]. Having an IMD disturbs both the physical and mental components of health, resulting in the fact that 50% and 30% of convalescents, respectively, are placed in the lowest quartile of the quartile of the quality of life of the general population. The significance of complications is important from an economic point of view, as they account for 75% of the direct costs of IMD [13, 18].

PREVENTION OF INVASIVE MENINGOCOCCAL DISEASE

The most clinically significant (> 90% of infections) are 5 serological groups of *Neisseria meningitidis*: B (MenB) and A, C, W, and Y (MenACWY). Vaccines are available against all 5 serogroups. Immunization is the most effective way to protect against IMD. The vaccines available in Poland (MenB, MenACWY, MenC) are presented in Table 1. According to the National Immunization Programme (PSO) for 2024, meningococcal vaccination is recommended just after the age of 6 weeks (MenACWY) and just after 8 weeks (MenB) of life [19].

EFFECTIVENESS AND SAFETY OF VACCINATIONS

In countries that have introduced universal vaccination against meningococci, a significant reduction in the incidence of IMD has been recorded. The most complete analysis of the effectiveness of meningococcal vaccines used in real clinical practice has been carried out in the United Kingdom. In 1999, universal vaccination of infants against MenC was introduced there, along with temporary vaccinations for children and adolescents up to 18 years of age, which resulted in a rapid and sustained decrease in the incidence of IMD caused by serogroup C [20].

Currently, the MenC/Hib vaccine is given to children as young as 12 months of age, and MenACWY to teenagers (9th and 10th grade students). In 2015, universal vaccination of infants against MenB in the 2 + 1 regimen (at least 8 and 16 weeks of age and a booster dose at the age of 12 months) was introduced, administered simultaneously with the other vaccines recommended in the immunization programme (DTaP-Hib-IPV, MMR, pneumococcal and rotavirus) [21].

EFFICACY OF *IN VITRO* SEROGROUP B MENINGOCOCCAL VACCINES

4CMenB VACCINE (BEXSERO)

Analyses of exMATS and gMATS (Meningococcal Antigen Typing System) of MenB isolates showed that the antigens contained in the 4CMenB vaccine were 83.3–86.6% consistent with the antigens present in MenB isolates responsible for IMD among Polish patients in 2010–2016 [22–25].

MenB-fHbp VACCINE (TRUMENBA)

Studies on the MenB-fHbp vaccine were carried out using the meningococcal antigen surface expression (MEASURE) method, which consists in measuring the correlation of the level of expression of the fHbp protein – a key antigen on the surface of group B meningococcus – with the bactericidal efficacy of antibodies in human serum determined by the hSBA (serum bactericidal assay with human complement) method. The analysis included over 2150 MenB isolates from 7 European countries (excluding Poland), the USA and Canada collected in the years 2000–2014. Overall, 91% of the isolates analysed were sensitive to antibodies induced by vaccination [22, 23].

The MATS, MEASURE, BAST and gMATS methods allow for a rapid assessment of the theoretical protein coverage of MenB vaccines. When interpreting the results, it should be borne in mind that each method retrospectively evaluates theoretical vaccination coverage, which should then be confirmed by observations of actual effectiveness [26].

TABLE 1. Meningococcal vaccines available in Poland

Serogroup dose	Vaccine (date of last SmPC/EMA)	Producer	Age restrictions	Number of doses of the full vaccination schedule according to the age of the first dose
B	Bexsero (4CMenB) (25.02.2022)	GSK vaccines	First 8 week of life, no data > 50 years	Primary vaccinations: • infants aged 2 months to infants aged 2–6 months – 2 doses at least 2 months apart or 3 doses at least 1 month apart • infants and children aged 6 months until the end of the 2nd year – 2 doses at an interval of min. 2 months Single booster dose: • in the case of primary vaccination, started within the first 6 months of life – at 12–15 months of age, with an interval of min. 6 months from the last primary dose • in the case of primary vaccination started at the second half of the first year of life – in the 2nd year of life, with an interval of at least 2 months from the last primary dose • with primary vaccination during second year of life – after 12–23 months • children over 2 years of age, adolescents and adults up to 50 years of age – 2 doses at least 1 month apart
	Trumenba (2rLfHbp) (24.05.2022)	Pfizer Manufacturing Belgium N.V.	First 10 years of life	Primary vaccination: 2 doses 6 months apart or 3 doses – 2 at an interval of min. 1 month, 3rd dose min. 4 months after the 2nd dose Booster dose: • should be considered in subjects at continued increased risk of invasive meningococcal disease
A, C, W, Y	MenQUADFI (10.05.2022)	Sanofi Pasteur	After the 1 st birthday	1 dose
	Menveo (18.01.2022)	GSK Vaccines	Over 2 years	1 dose
	Nimenrix (24.05.2022)	Pfizer Manufacturing Belgium N.V.	After completion of 6 weeks of age	Primary vaccination: • infants from 6 weeks to 6 months of age – 2 doses at 2 months apart • infants from 6 months, children, adolescents and adults – 1 dose Booster dose: • infants from 6 weeks to less than 12 months – 1 dose at the age of 12 months at least 2 months after the previous dose of the vaccine
C	NeisVac-C	Pfizer Manufacturing Belgium N.V.	After completion of 2 months of age	Primary vaccination: • infants from 2 months to 4 months of age – 2 doses at least 2 months apart • infants over 4 months of age, older children, adolescents and adults – 1 dose

SmPC – summary of product characteristics

MenB VACCINATION

4CMenB (Bexsero)

The 4CMenB vaccine is recommended in 35 national clinical recommendations, which is not equivalent to reimbursement. Universal (free) vaccination of infants or infants and adolescents is currently carried out in 13 European countries, and in 17 countries the vaccine

is reimbursed for people at high risk of contracting IMD. Ten years after the vaccine was registered in 2013, a total of over 74 million doses were distributed worldwide, which is why we have data on the effectiveness and safety of the 4CMenB vaccine used in real conditions in general immunization programmes, in outbreaks of disease and vaccination campaigns in endemic territories [27].

Local national recommendations take into account the proportions of individual meningococcal serogroups

in IMD morbidity and mortality in the entire population, in individual age groups and in groups at increased risk of contracting IMD. The introduction of the 4CMenB vaccine to universal immunization was also determined by the significant burden of the disease on the patient, the family, society and the health care system, economic considerations related to the loss of quality of life and productivity, and the adverse impact of complications on further life (limitation of the possibility of self-fulfilment, choice of profession, impaired efficiency and physical fitness, family and social life).

Immunization programmes in the United Kingdom, Italy, Spain, Portugal and South Australia and ad hoc vaccinations conducted to manage outbreaks of infections (Quebec in Canada, several universities in the USA) have proven that the 4CMenB vaccine effectively reduces the incidence of IMD among vaccinated people [21]. A safety assessment carried out in the United Kingdom 20 months after the introduction of universal 4CMenB vaccination (about 1.3 million children were vaccinated) did not identify additional adverse post-vaccination reactions beyond those recorded during clinical trials, and their total number was lower than expected on the basis of experience with the introduction of MenC vaccination [28].

The safety of administering 4CMenB to premature infants was confirmed in an observational study conducted in the United Kingdom. In a group of 133 premature infants hospitalized for reasons unrelated to vaccination born before the 35th week of gestation (median age 26.9 weeks of gestation), the 2 + 1 regimen was used together with DTaP-Hib-IPV, PCV13 and RV vaccination and prophylactic administration of paracetamol. The control group consisted of premature infants who received only DTaP-Hib-IPV, PCV13 and RV. There were no differences between the control group and those vaccinated with additional 4CMenB in terms of the incidence of apnoea, bradycardia, desaturation or the need for respiratory support. The 4CMenB vaccine can be administered to premature infants together with other routine vaccinations with concomitant paracetamol prophylaxis [29]. After the first 3 years of universal vaccination of infants against MenB in the United Kingdom, the percentage of infants vaccinated with the full 4CMenB regimen in the eligible population was 88%. There were no delays in other vaccinations, which proves that parents and doctors accept the administration of 4CMenB together with other vaccinations. Vaccination against MenB has only a direct effect, reducing the number of cases in the vaccinated group (individual protection), without affecting herd protection [30].

MenB-fHbp (Trumenba)

The safety of MenB-fHbp has been evaluated in 11 clinical trials involving 15,227 people aged ≥ 10 years. The most commonly reported adverse reactions were injection site pain after the first dose of vaccine (87%) and muscle pain

(24% of vaccinated subjects). Safety was assessed among 1081 students vaccinated at the time of the outbreak [31–36]. Safety was comparable to that described in clinical trials, and all adverse reactions resolved within a maximum of 7 days [36]. The safety data of the MenB-fHbp vaccine from post-approval observations come from the Vaccine Adverse Event Referral System database of the U.S. Centers for Disease Control and Prevention and the U.S. Food and Drug Administration. Over a period of 4 years (October 29, 2014 – December 31, 2018), 3,018,899 doses of vaccine were administered. During this time, 2106 adverse reactions to vaccination were reported, 97% of which affected people aged 10–25. The most common adverse post-vaccination reactions are fever, headache and, in 27% of cases, local reactions. Two cases of severe local reactions were reported, including erysipelas, which was later classified as an adverse vaccine reaction. There were no reports of meningococcal disease [37].

VACCINATION AGAINST MenACWY

In health policy aimed at the prevention of IMD, it is important not only to protect vaccinated people directly but also to reduce the prevalence of carriage and, indirectly, the disease in the unvaccinated population. The main carriers of meningococci in the population are adolescents [38].

The prevalence of *Neisseria meningitidis* in the European population is estimated at 10%, with the highest prevalence (about 25%) among adolescents and young adults, and in closed and crowded environments (e.g. barracks, boarding schools) it may reach 60–80% [38, 39]. With the introduction of MenB vaccination in the UK in 2015, widespread vaccination against MenACWY was launched (in response to the increase in MenW infections) for teenagers aged 13–18 and those entering higher education. Subsequent programme analyses showed that MenACWY reduced MenW infections among both vaccinated and unvaccinated people.

Conjugated vaccines against MenACWY reduce carriage status, and thus provide herd immunity, which is why a direct effect (individual immunity) and an indirect effect (herd protection) are observed after universal immunization, which was not found after vaccination against MenB [40, 41].

An observational study conducted on a large group of school students in the United Kingdom aged 15–19 years, before and after the start of the MenACWY immunization programme, showed that nasopharyngeal carriage of meningococcal serogroups C, W and Y (combined) decreased by 2.03–0.71%, OR: 0.34 (95% CI: 0.27–0.44, $p < 0.001$), with unchanged carriage of serogroup B [42]. Widespread vaccination of adolescents with the MenACWY conjugated vaccine reduces the spread of meningococci and contributes to the creation of herd protection by reducing the prevalence of carriers, con-

firming the effectiveness of the use of meningococcal vaccines of groups A, C, W and Y for indirect herd protection (herd immunity) [43].

Since 2008, some countries in Europe, South America and Australia have seen a significant increase in the number of cases caused by MenW, which belongs to the hypervirulent clone ST-11. In England, in 2008–2009, infections caused by this clone accounted for only 2% of cases, while in 2014–2015 they increased their share to 24%. Since the incidence was associated with high mortality, it was decided to replace the monovalent vaccine against MenC used in the universal vaccination of adolescents with the MenACWY vaccine [42]. The largest reduction in IMD caused by vaccine serogroups MenW and MenY was recorded among adolescents aged 14–18 years. The actual efficacy of the MenACWY vaccine, assuming a residual effect of the previous programme using the monovalent vaccine against MenC, was estimated at 94% (95% CI: 80–99%). According to the Public Health Institute of England, the introduction of the programme prevented 205–1193 cases of MenW and 60–106 cases of MenY, including in unvaccinated population (indirect effect) [44]. In response to the increase in MenW-ST-11 infections in the Netherlands, since 2018 there has been widespread vaccination against MenACWY with the MenACWY-TT vaccine (Nimenrix) among adolescents aged 14–18 and children aged 14 months. Since 2020, these vaccinations have been part of the routine immunization programme. In 2018–2020, there was a 100% reduction in the incidence of infections caused by serogroups C, W and Y (95% CI: 14–100%) among adolescents aged 14–18 years and by 85% in all age groups covered by the immunization programme (95% CI: 32–97%). A 50% decrease in the number of diseases caused by serogroups C, W and Y in the age groups not covered by the immunization (indirect effect) was also observed (95% CI: 28–65) [45]. In Chile, due to the rapid increase in the number of cases caused by MenW, vaccination against MenACWY in children aged 9 months to 4 years was started in 2012, and in 2014 the vaccine was permanently introduced into the national immunization programme for infants aged 12 months [46, 47]. Seven years after the introduction of the immunization programme, the overall incidence of IMD decreased by 51.3%, and for MenW by 53%. The greatest effects were recorded in the age group covered by the immunization. Among children aged 1–4 years, the incidence of IMD caused by MenW decreased by 92.3%, and mortality from 23% in 2012 to 0% in 2016. The median vaccination rate for the eligible population in 2013–2019 was 94%. No decrease in incidence was observed in non-vaccinated age groups, probably due to the lack of vaccination among adolescents [46, 47]. The following MenACWY conjugate vaccines are available in Poland: Nimenrix, MenQuadfi and Menveo.

Nimenrix (TT) is intended for children aged from 6 weeks. In infants less than 6 months: 2 doses should be

administered with a 2-month interval, while children from 6 months of age, adolescents and adults should receive a single dose. Infants vaccinated from 6 weeks to less than 12 months of age should receive a booster dose at 12 months of age at least 2 months after the previous dose of Nimenrix. In immunocompromised patients and those undergoing immunosuppressive treatment, a reduced immune response can be expected [45].

MenQuadfi (TT) is intended for children after the 1st birthday: a single dose should be administered.

Menveo (CRM) is intended for people aged after the 2nd birthday: a single dose should be administered.

MenACWY AND MenB VACCINES

On October 20, 2023, the US Food and Drug Administration approved the use of the pentavalent meningococcal vaccine (MenACWY-TT/MenB-fHbp, Penbraya, Pfizer Inc.) to prevent the development of IMD caused by serogroups A, B, C, W, and Y among people aged 10–25 years. On October 25, 2023, the Advisory Committee on Immunization Practices recommended that MenACWY-TT/MenB-fHbp be used when MenACWY and MenB are indicated at the same visit in the following groups:

1. Healthy people aged 16–23 (routine management);
2. People aged ≥ 10 years at increased risk of developing IMD, e.g. due to complement deficiencies, use of complement inhibitors, functional or anatomical asplenia. The recommended dose interval for MenACWY-TT/MenB-fHbp is 6 months. MenACWY-TT/MenB-fHbp vaccines can be used as a booster dose for people in high-risk groups if a booster dose of both MenACWY and MenB is indicated during a single visit [48].

RECOMMENDED CLINICAL PRACTICE

Due to the epidemiology of IMD in Poland, it is most important to ensure protection against meningococcal infections in infants in the first half of the first year of life, including premature ones. In Poland, at this time, infants receive numerous mandatory vaccinations [19]. In the first 6 months of life, during the implementation of the basic PSO 2024, the child receives 12 injections. Recommended immunizations, including meningococcal vaccinations, usually require an additional vaccination visit. Studies indicate that vaccination against meningococci should not be postponed unless absolutely necessary, as such action ultimately leads to a reduction in the number of vaccinated children [49]. A strong recommendation from a physician is equally important, as discussed below [50–52]. The optimal solution, used in many countries, is to administer meningococcal vaccines together with highly combined vaccines (“6 in 1” DTaP + IPV + Hib + HBV or “5 in 1” DTaP + IPV + Hib), which allows the administration of meningococcal vaccines during the same visit, and reduces the number of injec-

tions and the risk of possible errors. Unfortunately, despite many years of efforts, highly combined vaccines are still not reimbursed in Poland, and their purchase by parents often limits the possibilities of financing other recommended vaccinations. The situation is further complicated by the fear of both parents and doctors of fever occurring after infant vaccination against MenB. This is the most common reason for postponing this vaccination, despite strong scientific evidence indicating better effects of administering the vaccine as early as possible and for the safety of vaccination [53].

Full immunization, due to the large number of doses administered, is perceived as too expensive, especially if it is started in the first 6 months of life, when it is necessary to administer both meningococcal vaccines (4CMenB and MenACWY) in the 2 + 1 schedule. The cost of meningococcal vaccinations, in addition to low awareness of the need for them, is a significant obstacle for parents, including parents of children at increased risk of developing IMD. These groups include premature infants, patients with asplenia, congenital deficiencies, those treated with complement inhibitors, those with properdin deficiencies, hypogammaglobulinaemia, and those living with human immunodeficiency virus (HIV) [54–57]. The risk of contracting IMD in these groups is up to 10,000 times higher, but due to the chronic disease and the associated costs (direct and indirect), many patients have limited access to meningococcal vaccination.

THE NEED FOR A STRONG RECOMMENDATION OF A HEALTHCARE PROFESSIONAL

Most patients and parents do not see the need for vaccination against meningococci due to insufficient knowledge about IMD and the possibility of its prevention by means of preventive immunization. The attitude of patients and parents is characterized by passive indecision, which means that they expect initiative from health care professionals in the area of preventive activities. The strong recommendation of a health care professional trusted by patients and parents makes the majority of patients and parents agree to meningococcal vaccination. For this reason, vaccination against meningococci should be strongly recommended, and this topic should be actively introduced into the conversation with the patient, which is much more effective than the information about vaccination required by legal regulations [49–52].

RECOMMENDATIONS

VACCINATIONS IN THE FIRST HALF OF THE 1ST YEAR OF LIFE

Infants in the 1st year of life, especially those born prematurely, are at the highest risk of developing IMD. Among the etiological factors of IMD, MenB dominates

in this age group, with a constant proportion of serogroups C and W, which justifies the initiation of both vaccinations (4CMenB, MenACWY) as early as possible, preferably in the first half of the first year of life. For optimal protection against the most common meningococcal serogroups, we recommend both vaccinations (4CMenB and MenACWY) for infants, including those born prematurely. If, due to cost, lack of acceptance or availability of vaccines, it is not possible to administer both vaccines at the same visit, we recommend that vaccination against MenB be initiated, and that MenACWY be administered as soon as possible, which is a prerequisite for full prophylaxis of IMD (this is justified by the possible protection against serogroups other than MenB observed after 4CMenB vaccination) [30, 58, 59].

Parents of all infants, especially those born prematurely, should be offered vaccines highly combined with the acellular pertussis component “6 in 1” (DTaP + Hib + IPV + HBV) or “5 in 1” (DTaP + Hib + IPV) in addition to vaccination against meningococci, which significantly facilitates timely completion of vaccinations with significantly fewer injections (the “5-in-1” vaccine is free of charge for infants born < the 37th week of pregnancy, with a body weight of < 2500 g or permanent contraindications to vaccination with a preparation with a whole-cell pertussis component). The MenB and MenACWY vaccines can be given in one visit to a separate location. The results of the studies confirm the efficacy and safety of administering MenB and MenACWY vaccines together [60–63]. For infants starting 4CMenB vaccination (Bexsero) in the first 6 months of life, 2 schedules were registered: 2 + 1 and 3 + 1.

Due to the similar immunogenicity and efficacy of both vaccination regimens, we recommend the 2 + 1 schedule, which requires that the interval between the first and second dose of the Bexsero vaccine be at least 2 months. For the second dose to be administered earlier (but with an interval not less than 1 month) and in children at risk (including those with congenital asplenia and premature infants), we recommend the 3 + 1 regimen, according to the summary of medical product characteristics (SmPC). Premature infants (at higher risk of developing IMD than full-term infants) should be vaccinated against meningococcal disease according to the calendar age, just like full-term infants. If they are in hospital at the age appropriate for the first dose of vaccination (just after 6 weeks of age for MenACWY and 8 weeks of age for MenB) and are eligible for vaccination, the vaccination should take place in hospital. The hospital should then cover the cost of the vaccines. A full 2- or 3-dose regimen of primary 4CMenB vaccination with a booster dose at the second year of life should always be completed, with an interval of at least 6 months between the primary vaccination and the booster dose [29, 64]. A booster dose of 4CMen B (Bexsero) can be administered simultaneously with the mandatory vaccination against measles,

TABLE 2. Different vaccination schedules for children aged 0–6 months with the use of highly combined vaccines

Scheme 1 Age	Vaccine	Scheme 2 Age	Vaccine
6 weeks	5 in 1/6 in 1 + PCV 10/13 + RV + MenACWY (1)	6 weeks	5 in 1/6 in 1 + PVC 10/13 + RV
		8 weeks	MenB (1) + MenACWY (1) + prophylactic paracetamol
10 weeks	RV + MenB (1) + paracetamol prophylactically	10 weeks	RV
14 weeks	5 in 1/6 in 1 + PCV 10/13 (+ RV*) MenACWY (2)	14 weeks	5 in 1/6 in 1 + PVC 10/13 (+ RV*)
		16 weeks	MenB (2) + MenACWY (2) + paracetamol prophylactically
18 weeks	MenB (2) + paracetamol prophylactically		
22 weeks	5 in 1/6 in 1	22 weeks	5 in 1/6 in 1
13 months	5 in 1/6 in 1 + PVC 10/13 + MenACWY (3)	13 months	MenACWY (3) + MenB (3) + paracetamol prophylactically
14 months	MMR + chickenpox + MenB (3) + paracetamol prophylactically	14 months	5 in 1/6 in 1 + PVC 10/13 MMR + chickenpox

5 in 1 – a high-combination vaccine against diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b with an acellular pertussis component, 6 in 1 – a high-combination vaccine against diphtheria, tetanus, pertussis, polio, hepatitis B and *Haemophilus influenzae* type B with an acellular pertussis component, MenACWY – anti-meningococcal A, C, W, Y conjugate vaccine, MenB – 4CMenB, a recombinant protein vaccine against meningococcal B, MMR – measles, mumps and rubella vaccine, PCV – pneumococcal vaccine, RV – rotavirus vaccine

RV* – the last dose of a 3-dose rotavirus vaccine

*The second regimen can be used with the DTPw vaccine with whole-cell pertussis.

mumps and rubella at the beginning of the second year of life, and the recommended vaccination against chickenpox [29, 61].

For infants initiating vaccination with MenACWY (Nimenrix) in the first 6 months of life, 2 doses of the vaccine are administered with a 2-month interval. The booster dose should be administered at 12 months of age, at least 2 months after the last dose of the vaccine. In infants, the vaccine can be administered simultaneously with a highly-combined vaccine with the acellular pertussis component and the pneumococcal vaccine [45]. In people over 1 year of life, the vaccine can be given at the same time as the measles, mumps and rubella (MMR) and measles, mumps, rubella and varicella (MMRV) vaccines, the pneumococcal, influenza, hepatitis A, hepatitis B, DTaP, DTaP-HBV-IPV/Hib vaccines and the pneumococcal 13-valent conjugate vaccine. Vaccination schedules against meningococci are presented in Table 2.

VACCINATION OF CHILDREN AFTER SIX MONTHS OF AGE

If vaccination against meningococci is not started in the first six months of life, we recommend that it be completed as soon as possible. Children up to the age of 5 are still at a much higher risk of developing IMD than the general population, although lower than that of infants. The frequency of social interaction increases with age (e.g. nursery, kindergarten, older siblings), and so does the percentage of meningococcal carriers. Children attending crèches, kindergartens and other care institutions, as well as their staff, are at increased risk of contracting IMD. We recommend that meningococcal vaccination be planned when evaluating a child for nursery admission. We recommend that each vaccination and well-child check up of children who have not yet been vaccinated

against meningococci should be used as an opportunity to vaccinate against MenB and MenACWY. Both vaccines can be administered simultaneously as well as together with other vaccines [29, 45]. As far as possible, Nimenrix and a vaccine containing a tetanus component, e.g. DTaP-IPV-Hib/HBV, should be administered at the same visit or Nimenrix should be administered at least one month before the tetanus-containing vaccine [45].

Table 3 presents proposed vaccination schedules for MenB and MenACWY to be started after the first six months of life.

VACCINATION OF ADOLESCENTS AND ADULTS

Vaccination of adolescents is important because of the importance of this age group in the transmission of *Neisseria meningitidis*. Meningococcal carriage is found in about 25% of people in this age group, and studies have proven the effectiveness of universal vaccination against MenACWY measured by a decrease in carriage prevalence [38, 39, 41, 43]. We recommend that all adolescents be vaccinated against MenACWY both for individual protection and to improve the epidemiological situation and to protect society as a whole. The goal of vaccination against MenB, for which there is no evidence of a reduction in carriage status, is effective individual prophylaxis [40, 65]. We recommend both meningococcal vaccinations (MenB + MenACWY) for adolescents and young adults starting their studies, planning to stay in boarding schools and dormitories, going abroad and exposed to staying in large groups of people (e.g. in barracks), which increases the risk of *Neisseria meningitidis* infection [56, 66].

Well-child check up carried out in Poland at the age of 10, 14 and 19 are a good opportunity to educate and vaccinate against meningococci. The epidemiology of meningococcal infections in Poland indicates that IMD can

TABLE 3. Recommended meningococcal vaccination schedules in children older than 6 months

Schedule for children aged 6–12 months		
Primary vaccination	First visit	MenACWY + MenB
	Second visit – no earlier than after 2 months	MenB
Booster vaccination	Third visit at 2 years of age – at least 2 months after the second dose of primary vaccination	MenACWY + MenB
Schedule for children aged 12–23 months		
Primary vaccination	First visit	MenB + MenACWY
	Second visit – no earlier than after 2 months	MenB
	Third visit at 3–4 years of age 1 dose with an interval 12–23 months between primary vaccination cycle and booster dose	MenB
Schedule for children over 2 years of age, adolescents and adults		
Vaccination	First visit	MenB + MenACWY
Vaccination	Second visit – no earlier than after 1 month	MenB

4CMenB or MenB-FHbp vaccine according to the age restrictions in the summary of product characteristics, MenACWY – a conjugate vaccine against meningococcal A, C, W, Y, MenB – meningococcal serogroup B vaccine

be contracted at any age (the highest mortality due to IMD concerns people aged 65 years and older); therefore, generally healthy adults and those with co-morbidities benefit individually from vaccination against MenB and MenACWY, while the entire population benefits from reducing carriage status thanks to vaccination against MenACWY. We do not recommend administering additional booster doses to healthy adults vaccinated against MenB and MenACWY in childhood, except for people at significantly increased risk of infection, such as microbiologists who regularly work with meningococcal isolates, or people at risk during an epidemic (outbreak) of meningococcal disease.

Sexually active individuals may benefit further from vaccination with 4CMenB due to observed partial protection against gonococcal infection (*Neisseria gonorrhoeae*)*.

VACCINATION OF PATIENTS AT INCREASED RISK OF DEVELOPING INVASIVE MENINGOCOCCAL DISEASE

Premature infants

Premature birth, i.e. birth between 22–37 weeks of pregnancy, affects 6–12% of newborns worldwide. Premature infants are at increased risk of infections in the neonatal period, and have a 1.5–4-fold increased risk of hospitalization due to infections in infancy, early childhood and adolescence [69, 70]. Epidemiological data indicate an increased risk of hospitalization due to invasive infections (sepsis, pneumonia, meningitis), especially in premature infants with low birth weight, a low Apgar score at the 5th minute of life, or congenital de-

fects [69–71]. Newborns born prematurely are at a higher risk of infections due to reduced maternal antibody transfer, immaturity of the immune system, and more frequent hospitalizations for reasons related to prematurity [69–71]. Premature infants, compared to infants born at full term, are characterized by weaker barrier function of the skin and mucosa, as well as immaturity of the mechanisms of innate immunity (including leukocyte migration and complement function) and acquired immune [70]. Case-control studies and a recent cohort study in England showed an increased tendency of premature infants to severe meningococcal infections (the incidence of IMD among premature infants, especially those born before the 32nd week of gestation, was higher in England than among full-term infants, and premature infants were at higher risk of developing IMD complications). This indicates the need to vaccinate premature infants according to their chronological age and supports the view that they should be included in the group of increased risk of IMD, similarly to other children with immunodeficiencies [57, 72]. Studies indicate that vaccination against IMD with 4CMenB and MenC vaccines is well tolerated even by extremely premature infants [64]. Due to the increased risk of meningococcal infections, we recommend that children born prematurely receive 4CMenB and MenACWY vaccinations in accordance with their calendar (uncorrected) age.

OTHER RISK GROUPS

Patients with functional or anatomical asplenia, complement deficiencies, or hypogammaglobulinaemia, those who have undergone bone marrow stem cell transplantation, and those living with HIV and taking pegcetacoplan, eculizumab or ravulizumab are at many times higher risk of developing IMD [54, 55, 73–75]. Laboratory personnel working with biological material containing *Neisseria meningitidis* bacteria are also at risk of developing

* In the absence of a vaccine against *N. gonorrhoeae*, 4CMenB vaccine provides 33–47% protection against this pathogenic bacterium. Consequently, on 10 November 2023, the UK Joint Committee on Vaccination and Immunization (JCVI) determined that a targeted program for using the 4CMenB vaccine to prevent gonorrhea among people at increased risk of infection should be initiated [67, 68].

TABLE 4. Recommended meningococcal vaccination for the risk groups (preterm infants, children, adolescents and adults)

Risk group	Recommended vaccinations
Prematurity	MenB + MenACWY
Anatomical or functional asplenia	MenB + MenACWY
Complement component disorders	MenB + MenACWY
Living with human acquired immunodeficiency virus (human immunodeficiency virus – HIV) After bone marrow stem cell transplantation	MenB + MenACWY
Taking pegcetacoplan, eculizumab or ravulizumab	MenB + MenACWY
Microbiological laboratory workers at risk of infection	MenB + MenACWY
Traveling to endemic areas	MenB + MenACWY
People living in large population centres (e.g. dormitories, barracks)	MenB + MenACWY
Contact persons in the management of an epidemiological outbreak	MenB or MenACWY*

4CMenB or MenB-fHbp according to the age restrictions in the summary of product characteristics, MenACWY – a conjugate vaccine against meningococcal A, C, W, Y, MenB – vaccine against meningococcal serogroup B

* Depending on the serogroup responsible for the outbreak. If the serogroup is not identified, vaccination against MenB and MenACWY

IMD. Clinical studies of patients aged 2–17 years with complement disfunction, asplenia or spleen disfunction have shown high immunogenicity of vaccination with 2 doses of 4CMenB administered 2 months apart [29, 76]. The MenACWY-TT-084 clinical trial showed a similar response to doses of Nimenrix vaccine administered 2 months apart in children and adolescents aged 2–17 years with anatomical or functional asplenia [45]. Young people and adults living in clusters, uniformed services, recruits, people traveling to endemic areas and people who have recovered from IMD (convalescents) are also at increased risk of contracting IMD. [77, 78].

A person who has had IMD and has not been vaccinated so far should be vaccinated after completing the acute period of IMD (usually after 4–8 weeks) against both MenB and MenACWY. Vaccination schedules appropriate to the age are used. If a person has previously started vaccination against MenB or MenACWY, he or she should receive the missing doses of the appropriate vaccine and complete a full vaccination schedule against missing serogroups according to the age at which he or she finishes the vaccination. In addition, convalescents should undergo diagnostics to detect individual risk factors for IMD (e.g. immune deficiencies, including complement components, and functional asplenia). Table 4 lists the groups at increased risk of IMD. A patient undergoing treatment that reduces immunity (radiotherapy, glucocorticoid therapy, chemotherapy) may not obtain the optimal benefit from vaccination with MenB-fHbp (Trumenba). According to the registration, Trumenba is administered in a basic 2-dose schedule (with an interval of 6 months) or 3-dose schedule (2 doses administered at least 1 month apart, with a third with an interval of at least 4 months after the second dose). A booster dose should be considered in patients with a persistent risk of IMD after each of these dosing regimens [79]. We recommend vaccinating patients from risk groups against MenB and MenACWY. For the vaccines against MenB, Bexsero and Trumenba,

the recommendations are different, so these vaccines should not be administered interchangeably.

Booster doses for people in high-risk groups

In patients aged 10 years and older, regardless of previous vaccination, we recommend that a dose of MenACWY and MenB vaccine be administered and an additional dose of MenB vaccine 4 weeks later [79, 80]. Despite the lack of strong evidence, we recommend that adults belonging to the IMD risk groups receive single booster doses of the MenB and MenACWY vaccines not earlier than 5 years after the end of the primary vaccination.

FEVER PROPHYLAXIS AFTER VACCINATION

We recommend that patients and parents of a vaccinated child be informed that fever is a common occurrence after any vaccination. It is caused by the activation of innate immunity, which reacts to antigens contained in vaccines, but the absence of fever does not mean that the efficacy of the vaccine is weaker. After administration of 4CMenB vaccine to children less than 6 months of age, fever ($> 38.0^{\circ}\text{C}$) occurs more frequently than after other vaccinations (especially if it is administered with other vaccines) [81, 82]. In order to reduce the risk of fever and pain after 4CMenB vaccination, especially when administered concomitantly with other vaccines, we recommend that paracetamol be administered prophylactically to infants, including premature infants and children up to 2 years of age, at the same time as vaccination or shortly after vaccination. The dosage of paracetamol should be adjusted to the child's body weight and age (10–15 mg/kg of body weight *per* dose, maximum 45 mg/kg of body weight *per* day). Prophylaxis should be continued for 24 hours, regardless of the onset of symptoms [29, 83]. If fever or pain symptoms occur after vaccination despite the paracetamol prophylaxis, administration can be ex-

tended to 48 hours. After 48 hours, further antipyretic treatment can only be used after consultation and recommendation from a doctor (after excluding other causes of fever). We also recommend giving paracetamol to premature babies (off-label) [83].

Table 5 provides a dosing regimen for paracetamol that reduces the incidence and severity of fever without a concomitant effect on the immunogenicity of both 4CMenB and other concomitantly administered vaccines. It should be emphasized that only paracetamol has been subjected to clinical trials [82].

FINANCING VACCINATIONS

A significant increase in the percentage of children and adolescents vaccinated against meningococci seems to be impossible without the introduction of at least partial reimbursement of meningococcal vaccines and highly combined vaccines of the “5 in 1” or “6 in 1” type. The introduction of free or partially reimbursed highly combined vaccinations will increase the availability and affordability of meningococcal vaccination, which will reduce the incidence of IMD, as a consequence of treatment costs, sequelae and permanent complications, which also include a reduction in life expectancy (up to 16 years) [84, 85]. We believe that vaccination free of charge against meningococci should be introduced for patients from high-risk groups, including infants born prematurely (for whom the risk of developing IMD is higher than for full-term infants), children staying in orphanages and other care and educational institutions, for IMD survivors, as well as for people eligible for chemoprophylactic in outbreaks – as a part of IMD outbreak management. This is a small group of people characterized by a particularly high risk of IMD on the one hand, and at risk of social exclusion related to the disease or health condition (belonging to a group of increased risk of developing IMD) on the other. Access to free vaccination against meningococci is particularly justified for this group in order to provide equal opportunities and counteract social exclusion. In the first stage, free vaccination against meningococci for the above-mentioned risk groups could cover children, analogously to the mandatory vaccination for risk groups in the PSO for 2024, and ultimately include all age groups. We believe that partial or full reimbursement of both meningococcal vaccines should be introduced for all infants (not only premature infants). Full reimbursement may be considered for children starting vaccination in the first 2 years of life, when the benefits of administering these vaccines are the greatest. Similar solutions are in place in the Czech Republic, among other countries. Vaccination of infants against MenB provides individual protection for children who are particularly vulnerable to developing IMD. Vaccination of adolescents against MenACWY significantly reduces the transmission of meningococci in the population [86]. We recommend reimbursement

TABLE 5. Prophylactic dosage of oral acetaminophen (120 mg/5 ml) after MenB vaccination in children aged 0–6 months

Dose 1	2.5 ml (60 mg) 30 min before or concomitantly with vaccination
Dose 2	2.5 ml (60 mg) 4–6 hours after first dose
Dose 3	2.5 ml (60 mg) 4–6 hours after second dose

of vaccinations for teenagers, as this will reduce the number of carriers, and thus reduce the number of cases in other age groups. These activities will allow both direct and indirect effects of meningococcal vaccination to be achieved [87, 88]. Another very important issue is the reimbursement of meningococcal vaccinations for all children staying in orphanages and other care and educational institutions, especially those exposed to IMD for epidemiological reasons.

EDUCATIONAL ACTIVITIES

In Poland, a significant problem is the low awareness of the risk associated with meningococcal infections. The importance of education for the prevention of meningococcal infections is evidenced by the results of a survey conducted in 2017 by Kantar Millward Brown, which showed that only 63% of young mothers in Poland know about the possibility of immunization of their children against meningococci, and only 19% of pregnant women and those just after childbirth are considering vaccination of their child against meningococcal infections [89]. For this reason, in addition to a strong recommendation to vaccinate during routine medical visits, it is also necessary to carry out and regularly repeat a nationwide educational campaign that builds public awareness of the dangers posed by *Neisseria meningitidis* and the possibilities of preventive vaccination. It should be ensured that subsequent rounds of the above-mentioned educational campaign take into account current data on the epidemiology of IMD, the course of the disease (including the atypical course described for MenW infections), possible complications, long-term consequences, availability of vaccinations, their safety and effectiveness. Long-term, well-planned educational programmes bring better results than *ad hoc* actions. Promotional activities aimed at teenagers and students may also be useful [90]. In this age group, the PSO offers few mandatory vaccinations for 2024, and the fears of young people about vaccination are low. Vaccination against meningococci can be combined with vaccination against human papilloma virus (HPV) (e.g. in the programme for 12–13-year-olds), vaccination against tetanus, diphtheria and pertussis (Tdap in PSO 2024 at the age of 14) or vaccination against tetanus and diphtheria (Td mandatory in PSO 2024 at the age of 19). We believe that annual vaccination against influenza and COVID-19 also provides an opportunity to vaccinate against meningococci. Particular attention should be

paid to the education of midwives who take care of pregnant women and after childbirth and may significantly influence their decisions regarding vaccinations made in the first months of a child's life. Education on vaccination should be extended to the whole family, because meningococcal disease can occur at any age.

MENINGOCOCCAL VACCINATION TO REDUCE OUTBREAKS

We recommend that people exposed to contact with patients with IMD and who qualify for post-exposure chemoprophylaxis simultaneously start vaccination against the meningococcal serogroup that was the cause of the outbreak. If the serogroup that caused the outbreak is unknown, we recommend simultaneous vaccination against MenB and MenACWY. Vaccinations performed during the management or containment of an IMD outbreak should be free of charge. We also recommend using the knowledge acquired during the management of IMD outbreaks to educate local communities and to perform or supplement meningococcal vaccination in people who have not been immunized so far.

CONCLUSIONS

We recommend:

1. Initiation of meningococcal vaccination in the first six months of life with both MenACWY and MenB vaccines (after 6 or 8 weeks of age, respectively).
2. Administration of both MenB and MenACWY vaccines during one visit (vaccination after 8 weeks of age).
3. Vaccination against MenB starting in the first 6 months of life accordance with the scheme: 2 + 1 for the general population of infants, 3 + 1 for infants belonging to groups at increased risk of IMD, including premature infants.
4. Vaccination against MenACWY starting in the first 6 months of life in accordance with the 2 + 1 schedule.
5. Prophylactic administration of paracetamol to every child up to 2 years of age vaccinated against MenB, especially if other vaccines are administered during the same visit.
6. Vaccination of adolescents and young adults with both MenB and MenACWY vaccines, especially those starting their studies, planning to live in dormitories, or work in uniformed services, nurseries, kindergartens, care and educational facilities and health care facilities, or traveling abroad.
7. Administration of both MenB and MenACWY vaccines to patients at increased risk of developing IMD during a single visit.
8. Administering booster doses of the MenACWY and MenB vaccines to patients at increased risk of developing IMD (over 10 years of age).
9. Active (on the doctor's own initiative) and emphatic recommendation of meningococcal vaccination to patients and parents, use of both vaccination and well-child check-up visits for education and vaccination against meningococci. In the case of refusal, patients and parents should be assured of the safety of vaccinations.
10. Introduction of free vaccinations for patients belonging to groups at increased risk of contracting IMD.
11. Urgent action to enable the reimbursement of meningococcal vaccines.
12. Developing regulations governing the management of IMD outbreaks, in particular considering the vaccination of children and adolescents who have not been vaccinated so far and the organization of a free vaccination campaign for people directly exposed to the disease.

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