Recommendations for Use of MenACWY-CRM (Menveo®) In Infants at Increased Risk for Meningococcal Disease

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National Center for Immunization & Respiratory Diseases
Meningitis and Vaccine Preventable Diseases Branch

Infant and Toddler Meningococcal Vaccines

- **Indication for MenACWY-CRM (Menveo®, Novartis Vaccines) as a four dose primary series in infants (2, 4, 6, and 12 months) approved by FDA on August 1, 2013**
  - Previously approved for children and adults aged 2 through 55 years
- **Two other meningococcal vaccines previously licensed for use in this age group**

Vaccine	Carrier protein	2	4	6	9	12
Menactra® (MenACWY-D), sanofi pasteur	Diphtheria toxoid					
MenHibrix® (HibMenCY), GSK	Tetanus toxoid					
Menveo® (MenACWY-CRM), Novartis	CRM_{197}					

ACIP Recommendations

- **In October 2012, ACIP recommended vaccination of infants aged 2 through 23 months at increased risk for meningococcal disease**
- **No recommendation for routine vaccination of infants**
  - Recognition that all infants aged <1 year have higher rates of disease
  - Epidemiology in infants makes disease prevention difficult in this age group
    - High proportion of serogroup B disease
    - Highest rates of disease prior to 6 months of life

Defining Infants at Increased Risk

- **Complement component deficiencies**
  - C3, C5-C9, properdin, factor H, factor D
- **Functional or anatomic asplenia**
  - Includes infants with sickle cell disease
- **Infants who are in defined risk group for a community or institutional outbreak**
- **Infants traveling to an area where meningococcal disease is hyperendemic or epidemic**
  - Travel to the Hajj, living in the Meningitis Belt

Average Annual Cases of Meningococcal Disease in Children <5 Years, United States, 2010-2012

Age	Serogroup B	Serogroup C	Serogroup Y	Serogroup W	Serogroup C, Y, W (Incidence)
0-2 months	15	1	3	0	4 (0.44)
3-5 months	16	1	6	2	9 (0.88)
6-8 months	11	2	2	2	6 (0.61)
9-11 months	4	1	3	1	5 (0.47)
1 year	15	4	5	2	11 (0.28)
2 years	9	4	1	1	6 (0.12)
3 years	6	3	1	0	4 (0.09)
4 years	4	2	1	0	3 (0.06)
Total	80	18	22	8	48 (0.23)

Average annual cases and incidence of meningococcal disease
NNDSS cases from 2010-2012; serogroup missing for 15% of cases in children <5

IMMUNOGENICITY AND SAFETY SUMMARY

Immunogenicity of MenACWY-CRM

- **Demonstrated immune response at age 7 months (post-dose 3)**
  - Lower response to serogroup A
- **≥89% of infants achieved protective antibody titers to all four serogroups at 13 months (post-dose 4)**
- **Immunogenic when administered as a two dose series at 7 and 12 months**
- **Antibody levels wane by 40 months of age (28 months post-dose 4), particularly for serogroups A and C**

Co-administration with Routine Childhood Vaccines

- **4 dose infant series (2, 4, 6, and 12 months)**
  - Concomitant DTaP-IPV-Hib or DTaP-IPV-HBV, PCV
  - No interference observed for DTaP, IPV, Hib, HBV antigens or for PCV after 12 month dose
- **2 dose older infant series (7-9 and 12 months)**
  - Concomitant MMRV at 12 months
  - No interference observed with MMRV antigens

Co-administration with PCV7

- **Seroresponse to pneumococcal serotypes 6B and 23F somewhat diminished when co-administered with MenACWY-CRM at 2, 4, and 6 months**
  - Serotypes 6B and 23F did not meet statistical criteria for non-inferiority after dose 3 (at 7 months of age)
  - Other 5 serotypes met non-inferiority criteria
- **Statistical criteria for non-inferiority was met post-dose 4 for both pneumococcal serotypes 6B and 23F**
- **No data available on co-administration with PCV13**
- **Data shared with Meningococcal and Pneumococcal WGs**
  - Consensus was that MenACWY-CRM may be co-administered with PCV13, including in asplenic children

Safety of MenACWY-CRM

- **MenACWY-CRM is well-tolerated**
  - Reported adverse events similar between infants receiving MenACWY-CRM + routine childhood vaccines and infants receiving routine childhood vaccines alone
- **11 serious adverse events considered possibly related to vaccine**
- **No deaths attributed to vaccine**

VACCINE CONSIDERATIONS AND PROPOSED RECOMMENDATIONS

Considerations for MenACWY-CRM

- **MenACWY-CRM is an additional option for vaccinating infants 2 through 23 months of age at increased risk for meningococcal disease**
- **No preference for licensed vaccine formulations with exceptions:**
  - HibMenCY (MenHibrix®) not recommended for infants who are traveling to the meningitis belt or Hajj
  - MenACWY-D (Menactra®) not recommended for infants 9 through 23 months with functional or anatomic asplenia to avoid potential interference with PCV13
- **Guidance for use of MenACWY-CRM in infants at increased risk will be integrated with guidance for HibMenCY in infants 2 through 23 months and MenACWY-D in 9 through 23 months**

Meningococcal Vaccines for Children Aged 2 through 23 Months at Increased Risk

Vaccine	Primary Vaccination	Booster Doses	Indicated for:	Not indicated for:
MenACWY-D (Menactra)	• 9, 12 months	• 3 yrs after 1^0 series, then every 5 years	• Complement deficiencies • Outbreaks • Travel	• Asplenia
HibMenCY-TT (MenHibrix)	• 2, 4, 6, and 12-15 months	• 3 yrs after 1^0 series, then every 5 years (using MenACWY-D or –CRM)	• Complement deficiencies • Asplenia • Outbreaks	• Travel • Booster dose
MenACWY-CRM (Menveo)	• 2, 4, 6, and 12 months	• 3 yrs after 1^0 series, then every 5 years	• Complement deficiencies • Asplenia • Outbreaks • Travel	

Vaccines for Children – Recommended Vaccination Schedule and Intervals

Age Group	Vaccine	Routine Recommendations	Dosing Schedule
2 mos – 10 years	MCV4-Crm (Menveo, Novartis)	High-risk only¶	**Primary:** • Age 2 through 6 months: 4 doses at 2, 4, 6, and 12 months • Age 7 through 23 months: 2 doses should be given with the second dose given in the second year of life • Age 2 through 10 years: 1 or 2 doses **Booster (for persons who remain at risk¶):** • 1st booster 3 years after primary series for children who received primary series prior to age <7 years, then every 5 years • Every 5 years for children who received primary series after 7th birthday
	MCV4-D (Menactra, Sanofi)	High-risk only*	**Primary:** • Age 9 through 23 months: 2 dose series with 12 weeks between doses • Age 2 through 10 years: 1 or 2 doses **Booster (for persons who remain at risk¶):** • 1st booster 3 years after primary series for children who received primary series prior to age <7 years, then every 5 years • Every 5 years for children who received primary series after 7th birthday
	HibMenCY-TT (MenHibrix, GSK)	High-risk only§	**Primary:** • Age 2 through 23 months: 4 dose series with doses at 2, 4, 6, and 12-15 months **Booster (for persons who remain at risk¶):** • Use MCV4-D or MCV4-Crm (see above)

Proposed Recommendations: Background Statement

- **Infants 2 through 23 months of age at increased risk* for meningococcal disease should be vaccinated with an age and formulation appropriate meningococcal conjugate vaccine**
- **MenACWY-CRM is an additional option for vaccinating infants 2 through 23 months of age at increased risk for meningococcal disease**

*Infants at increased risk for meningococcal disease include those with recognized persistent complement component deficiencies, those with functional or anatomic asplenia (including sickle cell disease), healthy infants who are part of the risk group for a meningococcal disease outbreak for which vaccination is recommended, and infants traveling to or residing in areas with hyperendemic or epidemic meningococcal disease

Guidance for Use

- Those who remain at increased risk for meningococcal disease should receive a booster dose 3 years after the primary series and additional boosters every 5 years thereafter
- If MenACWY-CRM is used to achieve protection against serogroup A and W meningococcal disease, a quadrivalent vaccine should be used to complete the series.

Proposed Recommendations for Vote

- **MenACWY-CRM can be used for protection against serogroups A, C, W, and Y in increased risk infants aged 2 through 23 months**
  - Infants aged 2 through 8 months who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic are recommended to receive MenACWY-CRM prior to travel to provide protection against meningococcal serogroups A and W
  - MenACWY-CRM may be co-administered with PCV13, including in asplenic children

Thank you

- ACIP Meningococcal Vaccines Work Group
- Lorry Rubin
- Amanda Cohn
- Nancy Messonnier
- Thomas Clark
- Elizabeth Briere
- Ismael Ortega-Sanchez
- Lucy McNamara

DISCUSSION AND VOTE

Proposed Recommendations for Vote

- **MenACWY-CRM can be used for protection against serogroups A, C, W, and Y in increased risk infants aged 2 through 23 months**
  - Infants aged 2 through 8 months who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic are recommended to receive MenACWY-CRM prior to travel to provide protection against meningococcal serogroups A and W
  - MenACWY-CRM may be co-administered with PCV13, including in asplenic children