Vaxelis™

Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine

VAXELIS™ CLINICAL PROFILER

Before administering VAXELIS™, please read full Prescribing Information. The Patient Product Information also is available.

MERCK SANOFI PASTEUR

VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine)

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About VAXELIS

VAXELIS is the **FIRST-AND-ONLY** hexavalent vaccine approved by the FDA[1]

VAXELIS is the result of the US-based joint-partnership[a] between Merck and Sanofi Pasteur,[1] the vaccines unit of Sanofi, and draws upon both companies' experience in the development, manufacturing and marketing of individual and combination vaccines.

VAXELIS includes antigens for diphtheria, tetanus, pertussis (whooping cough), and poliomyelitis from Sanofi Pasteur and antigens for *H. influenzae* type b and hepatitis B from Merck.[1]

With 2-3 fewer shots needed compared to Pentacel (+hepatitis B) or Pediarix (+hib), VAXELIS may help improve vaccination compliance in the infant series[2-7]

- **According to CDC's ACIP, combination vaccines can improve vaccination coverage rates[8]**
- **Combination vaccines are generally preferred by the CDC over separate injections of the equivalent component vaccines[8]**

VAXELIS is available in a ready-to-use formulation that may help reduce preparation time[9]

VAXELIS will be available through the VFC program

[a]VAXELIS is a hexavalent vaccine codeveloped by Merck and Sanofi Pasteur in a joint venture known as MSP Vaccine Company (MSP) in the United States.

ACIP, Advisory Committee on Immunization Practices; CDC, Centers for Disease Control and Prevention; *H. influenzae, Haemophilus influenzae.*

1. Oliver SE, Moore KL. Licensure of a diphtheria and tetanus toxoids and acellular pertussis, inactivated poliovirus, Haemophilus influenzae type b conjugate, and hepatitis b vaccine, and guidance for use in infants. *MMWR Morb Mortal Wkly Rep*. 2020;69(5):136-139. doi:10.15585/mmwr.mm6905a5. 2. Pentacel. Prescribing Information: Sanofi Pasteur.; 2020. Accessed September 18, 2020. https://www.vaccineshoppe.com/image.cfm?doc_id=13799&image_type = product_pdf. 3. Pentacel. Prescribing Information: Sanofi Pasteur.; 2019. Accessed September 18, 2020. https://www.vaccineshoppe.com/mailing/VSH/PIs%20&%20SDS/PI/dtppv-fplr-sl-dec19.pdf. 4. PEDIARIX. Prescribing Information. GlaxoSmithKline, Inc.; 2019. Accessed September 18, 2020. https://www.gsksource.com/pharma/content/dam/ GlaxoSmithKline/US/en/Prescribing_Information/Pediarix/pdf/PEDIARIX.PDF. 5. Centers for Disease Control and Prevention. Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2020. Accessed September 24, 2020. https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf. 6. Marshall GS, Happe LE, Lunacsek OE, et al. Use of combination vaccines is associated with improved coverage rates. *Pediatr Infect Dis J.* 2007;26(6):496-500. doi:10.1097/INF.0b013e31805d7f17. 7. Kurosky SK, Davis KL, Krishnarajah G. Effect of combination vaccines on completion and compliance of childhood vaccinations in the United States. *Hum Vaccin Immunother.* 2017;13(11):2494-2502. doi:10.1080/21645515.2017.1362515. 8. Centers for Disease Control and Prevention. General best practice guidelines for immunization. Accessed September 16, 2020. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html. 9. Pellissier JM, Coplan PM, Jackson LA, May JE. The effect of additional shots on the vaccine administration process: results of a time-motion study in 2 settings. *Am J Manag Care.* 2000;6(9):1038-1044.

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Indication

VAXELIS™ is a vaccine indicated for active immunization to prevent diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive disease due to *Haemophilus influenzae (H. influenzae)* type b. VAXELIS is approved for use as a 3-dose series in children 6 weeks through 4 years of age (prior to the 5th birthday).

Important Safety Information

Do not administer VAXELIS to anyone with a history of severe allergic reaction to a previous dose of VAXELIS, any ingredient of VAXELIS, or any other diphtheria toxoid, tetanus toxoid, pertussis containing vaccine, inactivated poliovirus vaccine, hepatitis B vaccine, or Hib vaccine.

Do not administer VAXELIS to anyone with a history of encephalopathy within 7 days of a pertussis containing vaccine with no other identifiable cause.

Do not administer VAXELIS to anyone with a history of progressive neurologic disorder until a treatment regimen has been established and the condition has stabilized.

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Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C. diphtheriae*.

Tetanus

Tetanus is an acute disease caused by an extremely potent neurotoxin produced by *C. tetani*.

Pertussis

Pertussis (whooping cough) is a respiratory disease caused by *B. pertussis*.

Poliomyelitis

Polioviruses, of which there are 3 serotypes (Types 1, 2, and 3), are enteroviruses.

Haemophilus influenzae type b Invasive Disease

H. influenzae type b can cause invasive disease such as meningitis and sepsis.

Hepatitis B

Hepatitis B virus is one of several hepatitis viruses that cause systemic infection, with major pathology in the liver.

B. pertussis, Bordetella pertussis; C. diphtheriae, Corynebacterium diphtheriae; C. tetani, Clostridium tetani; H. influenzae, Haemophilus influenzae.

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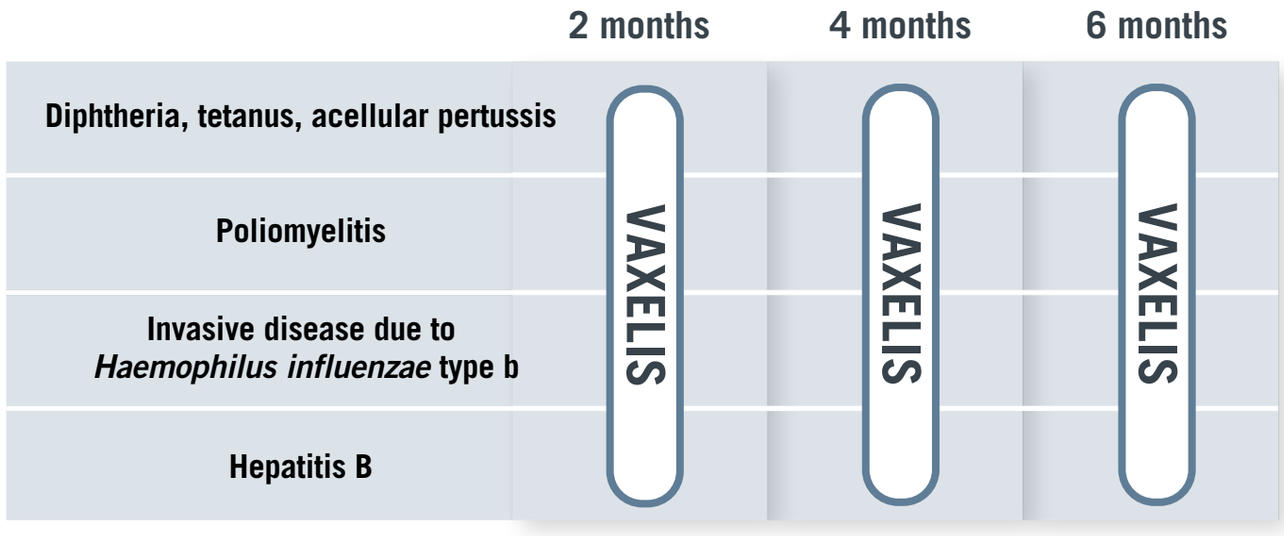
Dosage and Administration

VAXELIS Vaccination Schedule



For intramuscular use only.

The first dose may be given as early as 6 weeks of age. Three doses of VAXELIS constitute a primary immunization course against diphtheria, tetanus, *H. influenzae* type b invasive disease and poliomyelitis.

VAXELIS may be used to complete the hepatitis B immunization series.

A 3-dose series of VAXELIS does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the (pertussis) primary series. [See *Pertussis Vaccination Following VAXELIS* on next page.]

VAXELIS is a suspension for injection available in 0.5 mL single-dose vials and prefilled syringes.

H. influenzae, Haemophilus influenzae.

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Dosage and Administration (*continued*)

Vaccination Schedule

Pertussis Vaccination following VAXELIS

VAXELIS, Pentacel® [(Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine): DTaP-IPV/Hib], Quadracel® [(Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine): DTaP-IPV] and Daptacel® [(Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed): DTaP] contain the same pertussis antigens manufactured by the same process. Children who have received a 3-dose series of VAXELIS should complete the primary and pertussis vaccination series with Pentacel, Quadracel or Daptacel according to the respective prescribing information in the approved package inserts.

Administration of VAXELIS following previous doses of other DTaP-containing Vaccines

VAXELIS may be used to complete the first 3 doses of the 5-dose DTaP series in infants and children who have received 1 or 2 doses of Pentacel or Daptacel and are also scheduled to receive the other antigens in VAXELIS. Data are not available on the safety and immunogenicity of such mixed sequences.

Data are not available on the safety and effectiveness of using VAXELIS following 1 or 2 doses of a DTaP vaccine from a different manufacturer.

Administration of VAXELIS following previous doses of any Hepatitis B Vaccine

A 3-dose series of VAXELIS may be administered to infants born to HBsAg-negative mothers, and who have received a dose of any hepatitis B vaccine, prior to or at 1 month of age.

VAXELIS may be used to complete the hepatitis B vaccination series following 1 or 2 doses of other hepatitis B vaccines, in infants and children born of HBsAg-negative mothers and who are also scheduled to receive the other antigens in VAXELIS. However, data are not available on the safety and effectiveness of VAXELIS in such infants and children.

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Dosage and Administration (*continued*)

Administration of VAXELIS following previous doses of Inactivated Polio Vaccine (IPV)

VAXELIS may be administered to infants and children who have received 1 or 2 doses of IPV and are also scheduled to receive the other antigens in VAXELIS. However, data are not available on the safety and effectiveness of VAXELIS in such infants and children.

Administration of VAXELIS following previous doses of Haemophilus b Conjugate Vaccines

VAXELIS may be administered to infants and children who have received 1 or 2 doses of *H. influenzae* type b Conjugate Vaccine and are also scheduled to receive the other antigens in VAXELIS. However, data are not available on the safety and effectiveness of VAXELIS in such infants and children.

Administration

Just before use, shake the vial or syringe until a uniform, white, cloudy suspension results.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the product should not be administered.

Administer a single 0.5 mL dose of VAXELIS intramuscularly.

In infants younger than 1 year, the anterolateral aspect of the thigh is the preferred site of injection. The vaccine should not be injected into the gluteal area.

VAXELIS should not be combined through reconstitution or mixed with any other vaccine. Discard unused portion.

Important Safety Information (*continued*)

Carefully consider benefits and risks before administering VAXELIS to persons with a history of: fever ≥40.5°C (≥105°F) , hypotonic-hyporesponsive episode (HHE), or persistent, inconsolable crying lasting ≥3 hours within 48 hours after a previous pertussis-containing vaccine; and/or seizures within 3 days after a previous pertussis-containing vaccine.

If Guillain-Barré syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the risk for Guillain-Barré syndrome may be increased following VAXELIS.

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Consider the individual infant's medical status and potential benefits and possible risks of intramuscular vaccination in deciding when to administer VAXELIS to an infant born prematurely.

Vaccination with VAXELIS may not protect all individuals.

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Important Safety Information (*continued*)

The solicited adverse reactions 0-5 days following any dose were irritability (≥55%), crying (≥45%), injection site pain (≥44%), somnolence (≥40%), injection site erythema (≥25%), decreased appetite (≥23%), fever ≥38.0°C (≥19%), injection site swelling (≥18%), and vomiting (≥9%).

The 3-dose immunization series consists of a 0.5 mL intramuscular injection, administered at 2, 4, and 6 months of age.

A 3-dose series of VAXELIS does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the primary series.

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Clinical Trials Experience[1]

- The safety of VAXELIS was evaluated in 6 clinical studies, in which a total of 5,251 infants 43 to 99 days of age at enrollment received at least 1 dose of VAXELIS. Two of these (study 005 and 006) were controlled clinical studies conducted in the US, in which a total of 3,380 infants 46 to 89 days of age at enrollment received at least 1 dose of VAXELIS. The vaccination schedules of VAXELIS, Control vaccines, and concomitantly administered vaccines used in these studies are provided on slide 11. At 15 months of age, participants in Study 005 received a dose of Daptacel and a *H. influenzae* type b conjugate vaccine, whereas participants in Study 006 received a dose of Pentacel. In a non-US study, 294 children received a dose of VAXELIS at 15 months of age.

- Across the 2 studies conducted in the US, among all randomized participants (3,392 in the VAXELIS group and 889 in the Control group), 52.6% were male and 47.4% were female. The race distribution was as follows: 71.7% were White, 11.0% were Black, 4.5% were American Indian or Alaska Native, 3.5% were Asian, and 9.3% were of other racial groups. Most participants (81.8%) were of non-Hispanic or Latino ethnicity. The racial/ethnic distribution of participants who received VAXELIS and Control vaccines was similar.

H. influenzae, Haemophilus influenzae.

1. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020.

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Two Clinical Studies with VAXELIS in the US: Vaccination Schedules[1]

Study	Vaccine	Concomitantly Administered Vaccines
005[a]	VAXELIS at 2, 4, 6 months Daptacel + PedvaxHIB® at 15 months	Rotateq® at 2, 4, 6 months Prevnar 13® at 2, 4, 6, and 15 months
	Control group vaccines: Pentacel at 2, 4, 6 months Recombivax HB® at 2 and 6 months Daptacel + ActHIB® at 15 months	 Rotateq at 2, 4, 6 months Prevnar 13 at 2, 4, 6, and 15 months
006[a]	VAXELIS at 2, 4, 6 months Pentacel at 15 months	Rotateq at 2, 4, 6 months Prevnar 13 at 2, 4, 6, and 15 months
	Control group vaccines: Pentacel at 2, 4, 6, 15 months Recombivax HB® at 2 and 6 months	Rotateq at 2, 4, 6 months Prevnar 13 at 2, 4, 6, and 15 months

ActHIB [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)][2]
Daptacel (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed)
PedvaxHIB [Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)]
Pentacel [Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine] Prevnar 13 (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein])
Recombivax HB (Hepatitis B Vaccine [Recombinant])
RotaTeq (Rotavirus Vaccine, Live, Oral, Pentavalent)
[a]The first dose of Hepatitis B vaccine was administered prior to study initiation (prior to or at 1 month of age).

1. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020. 2. ActHIB® [Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)] Prescribing Information, Sanofi Pasteur.; 2019.

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Immunogenicity – Clinical Trials Experience (Study 005)[1]

- In the US Study 005, infants were randomized to receive 3 doses of VAXELIS at 2, 4, and 6 months of age and Daptacel and PedvaxHIB at 15 months of age, or Control group vaccines (3 doses of Pentacel vaccine at 2, 4, and 6 months of age + Recombivax HB at 2 and 6 months of age and Daptacel and ActHIB at 15 months of age). All subjects received concomitant vaccines: RotaTeq at 2, 4 and 6 months and Prevnar 13 at 2, 4, 6, and 15 months of age. All infants had received a dose of hepatitis B vaccine prior to study initiation, prior to or at one month of age.

- Antibody responses to diphtheria, tetanus, pertussis (PT, FHA, PRN and FIM), poliovirus types 1, 2 and 3, hepatitis B and *H. influenzae* type b antigens were measured in sera obtained one month following the third dose of VAXELIS or Pentacel + Recombivax HB vaccines.

FHA, filamentous hemagglutinin; FIM, fimbriae types 2 and 3; *H. influenzae, Haemophilus influenzae;* PRN, pertactin; PT, pertussis toxin.

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Immunogenicity – Clinical Studies (Study 005)[1]

Antibody Responses One Month Following Dose 3 of VAXELIS or Control Vaccines Administered Concomitantly with Prevnar 13 and RotaTeq in Study 005[a]

	VAXELIS + Prevnar 13 + RotaTeq (N=688 - 810)	Pentacel + Recombivax HB + Prevnar 13 + RotaTeq (N=353 - 400)
Anti-Diphtheria Toxoid		
% ≥ 0.1 IU/mL	82.4[b]	86.3
Anti-Tetanus Toxoid		
% ≥ 0.1 IU/mL	99.9[c]	99.5
Anti-PT		
% vaccine response[d]	98.1[b]	98.5
GMC	109.6[e]	85.4
Anti-FHA		
% vaccine response[d]	87.3[b]	92.0
GMC	46.6[f]	72.3
Anti-PRN		
% vaccine response[d]	79.3[b]	82.0
GMC	55.8[e]	66.8
Anti-FIM		
% vaccine response[d]	90.2[g]	86.2
GMC	235.9[e]	184.4

CI, confidence interval; FIM, fimbriae types 2 and 3; FHA, filamentous hemagglutinin; GMC, geometric mean concentration; LLOQ, lower limit of quantitation; PRN, pertactin; PT, pertussis toxin.

[a]N = The number of participants with available data. [b]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the difference [VAXELIS group minus Control vaccines group] was >-10%). [c]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the difference [VAXELIS group minus Control vaccines group] was >-5%). [d]Vaccine response = if pre-vaccination antibody concentration was <4 x lower limit of quantitation [LLOQ], then the post-vaccination antibody concentration was ≥4 x LLOQ; if pre-vaccination antibody concentration was ≥4 x LLOQ, then the post-vaccination antibody concentration was ≥pre-vaccination levels (pre-Dose 1). [e]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the GMC ratio [VAXELIS group/Control vaccines group] was >0.67). [f]Non-inferiority criterion not met for anti-FHA GMC (lower bound of 2-sided 95% CI for the GMC ratio [VAXELIS group/Control vaccines group] was 0.59 which is below the non-inferiority criterion >0.67). [g]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the difference [VAXELIS group minus Control vaccines group] was >-10%).

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Immunogenicity – Clinical Studies (Study 005)[1] (*continued*)

Antibody Responses One Month Following Dose 3 of VAXELIS or Control Vaccines Administered Concomitantly with Prevnar 13 and RotaTeq in Study 005[a]

	VAXELIS + Prevnar 13 + RotaTeq (N=688 - 810)	Pentacel + Recombivax HB + Prevnar 13 + RotaTeq (N=353 - 400)
Anti-Poliovirus Type 1		
% ≥1:8 dilution	100.0[b]	98.2
Anti-Poliovirus Type 2		
% ≥1:8 dilution	100.0[b]	99.7
Anti-Poliovirus Type 3		
% ≥1:8 dilution	100.0[b]	99.8
Anti-PRP		
% ≥0.15 μg/mL	97.3[b]	92.4
% ≥1.0 μg/mL	85.0[c]	75.3
Anti-HBsAg		
% ≥10 mIU/mL	99.4[c]	98.6

CI, confidence interval; FIM, fimbriae types 2 and 3; GMC, geometric mean concentration; HBsAg, hepatitis B surface antigen; LLOQ, lower limit of quantitation; PRP, polyribosylribitol phosphate.

[a]N = The number of participants with available data.

[b]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the difference [VAXELIS group minus Control vaccines group] was >-5%).

[c]Non-inferiority criterion met (lower bound of 2-sided 95% CI for the difference [VAXELIS group minus Control vaccines group] was >-10%).

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Immunogenicity – Clinical Studies (Study 006)[1]

Lot Consistency Study

- Study 006 was a lot consistency study conducted in the US, where infants were randomized to receive 3 doses of VAXELIS at 2, 4, and 6 months of age and Pentacel at 15 months of age (N=2,406), or control group vaccines (4 doses of Pentacel at 2, 4, 6, and 15 months of age + Recombivax HB at 2 and 6 months of age; N=402). All subjects received concomitant vaccines: RotaTeq at 2, 4 and 6 months and Prevnar 13 at 2, 4, 6, and 15 months of age. All infants had received a dose of hepatitis B vaccine prior to study initiation, from birth up to one month of age.
- Antibody responses to diphtheria, tetanus, pertussis (PT, FHA, PRN and FIM), poliovirus types 1, 2 and 3, hepatitis B and *H. influenzae* type b antigens were measured in sera obtained one month following the third dose of VAXELIS or Pentacel + Recombivax HB.

Results

- VAXELIS was non-inferior to Pentacel + Recombivax HB administered concomitantly at separate sites, as demonstrated by the proportions of participants achieving seroprotective levels of antibodies to diphtheria, tetanus, poliovirus, hepatitis B and PRP antigens, and pertussis vaccine response rates and GMCs, except for GMCs for FHA (lower bound of 2-sided 95% CI for GMC ratio [VAXELIS group/Control group vaccines] was 0.62, which was below the non-inferiority criterion >0.67).

Concomitantly Administered Vaccines[1]

- In Study 006 conducted in the US, the immune responses to Prevnar 13 were measured one month after the third dose.

Results

- Non-inferiority criteria were met for GMCs to 12 of the 13 serotype antigens in Prevnar 13 for participants who received VAXELIS relative to Control vaccines. For serotype 6B, the non-inferiority criterion was not met (lower bound of 2-sided 95% CI for GMC ratio [VAXELIS group/Control vaccines group] is 0.64, which is below the non-inferiority criterion >0.67).

Of the 65 non-inferiority comparisons in these two studies, all were met, but with the following 4 exceptions:

- Non-inferiority criterion—lower bound of 95% CI around GMC ratio >0.67—not met for:
  - Anti-FHA after 6-month doses: 0.59 in study 005 and 0.62 in study 006
  - Anti-pneumococcal serotype 6B after 6-month doses: 0.64 in study 006
  - Anti-PRN after 15-month Pentacel dose: 0.66 in study 006

FHA, filamentous hemagglutinin; FIM, fimbriae types 2 and 3; GMC, geometric mean concentration; *H. influenzae, Haemophilus influenzae*; PRN, pertactin; PRP, polyribosylribitol phosphate; PT, pertussis toxin.

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Percentage of Infants with Solicited Adverse Reactions Occurring within 5 days Following VAXELIS or Control Vaccines Administered Concomitantly at Separate Sites with Prevnar 13 and RotaTeq in Studies 005 and 006[1]

Injection Site Adverse Reactions		VAXELIS + Prevnar 13 + RotaTeq			Pentacel + Recombivax HB + Prevnar 13 + RotaTeq		
		Dose 1 (N=3,370)[a]	Dose 2 (N=3,221)	Dose 3 (N=3,134)	Dose 1 (N=880)	Dose 2 (N=849)	Dose 3 (N=825)
		VAXELIS site			Pentacel or Recombivax HB site		
Injection site erythema	Any	25.8%	31.8%	31.8%	25.0%	25.8%	30.9%
	≥2.5 cm	0.9%	1.0%	1.3%	1.1%	1.1%	1.2%
	>5.0 cm	0.0%	0.1%	0.2%	0.3%	0.2%	0.1%
Injection site pain[b]	Any	53.3%	49.0%	44.9%	55.8%	43.7%	44.4%
	Moderate or severe	16.3%	14.1%	12.5%	19.1%	11.3%	10.8%
	Severe	2.8%	2.5%	2.0%	3.2%	1.9%	1.3%
Injection site swelling	Any	18.9%	22.8%	23.4%	20.8%	20.4%	22.9%
	≥2.5 cm	2.5%	1.6%	1.7%	2.7%	1.3%	0.8%
	>5.0 cm	0.2%	0.2%	0.2%	0.3%	0.1%	0.0%

[a]N = Number of vaccinated participants with safety follow-up. [b]Moderate: cries and protests when injection site is touched; Severe: cries when injected limb is moved or the movement of the injected limb is reduced.

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Percentage of Infants with Solicited Adverse Reactions Occurring within 5 days Following VAXELIS or Control Vaccines Administered Concomitantly at Separate Sites with Prevnar 13 and RotaTeq in Studies 005 and 006[1] (*continued*)

Systemic Adverse Reactions		VAXELIS + Prevnar 13 + RotaTeq			Pentacel + Recombivax HB + Prevnar 13 + RotaTeq		
		Dose 1 (N=3,370)[a]	Dose 2 (N=3,221)	Dose 3 (N=3,134)	Dose 1 (N=880)	Dose 2 (N=849)	Dose 3 (N=825)
		VAXELIS site			Pentacel or Recombivax HB site		
Fever	≥38°C	19.2%	29.0%	29.3%	14.6%	18.0%	17.8%
	≥38.5°C	5.3%	11.5%	13.2%	3.4%	6.5%	8.1%
	≥39.5°C	0.2%	0.7%	1.5%	0.1%	0.2%	0.9%
Crying	Any	52.0%	49.5%	45.1%	50.6%	47.0%	40.6%
	>1 hour	18.6%	19.8%	16.7%	20.6%	16.8%	14.1%
	>3 hours	3.6%	3.8%	3.4%	4.4%	4.0%	2.9%
Decreased Appetite[b]	Any	28.9%	24.2%	23.2%	25.8%	20.5%	20.1%
	Moderate or severe	7.0%	5.5%	4.8%	6.8%	3.9%	5.0%
	Severe	0.5%	0.5%	0.5%	0.6%	0.2%	0.0%

[a]N = Number of vaccinated participants with safety follow-up. [b]Moderate: missed 1 or 2 feeds/meals completely; Severe: refuses ≥3 feeds or refuses most feeds.

1. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020.

Vaxelis™
Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine

Percentage of Infants with Solicited Adverse Reactions Occurring within 5 days Following VAXELIS or Control Vaccines Administered Concomitantly at Separate Sites with Prevnar 13 and RotaTeq in Studies 005 and 006[1] (*continued*)

Systemic Adverse Reactions		VAXELIS + Prevnar 13 + RotaTeq			Pentacel + Recombivax HB + Prevnar 13 + RotaTeq		
		Dose 1 (N=3,370)[a]	Dose 2 (N=3,221)	Dose 3 (N=3,134)	Dose 1 (N=880)	Dose 2 (N=849)	Dose 3 (N=825)
		VAXELIS site			Pentacel or Recombivax HB site		
Irritability[b]	Any	61.8%	58.9%	55.2%	61.7%	56.3%	51.6%
	Moderate or severe	24.6%	23.4%	20.1%	25.7%	19.2%	16.8%
	Severe	2.5%	3.8%	2.9%	2.2%	2.7%	2.2%
Somnolence[c]	Any	56.3%	47.8%	40.8%	55.2%	44.1%	38.8%
	Moderate or severe	15.0%	11.5%	8.5%	14.5%	9.4%	8.2%
	Severe	1.5%	1.1%	1.0%	1.7%	0.6%	1.1%
Vomiting[d]	Any	13.1%	11.5%	9.5%	11.3%	9.7%	6.9%
	Moderate or severe	3.5%	2.6%	2.1%	2.8%	3.1%	1.0%
	Severe	0.4%	0.2%	0.1%	0.5%	0.6%	0.1%

[a]N = Number of vaccinated participants with safety follow-up. [b]Moderate: requiring increased attention; Severe: inconsolable. [c]Moderate: not interested in surroundings or did not wake up for a meal; Severe: Sleeping most of the time or difficult to wake up. [d]Moderate: 2-5 episodes per 24 hours; Severe: ≥6 episodes per 24 hours or requiring parenteral hydration. A subject with the same adverse reactions at both the Pentacel and Recombivax HB injection site, was counted once and was classified according to the highest intensity grading. Fever is based upon actual temperatures recorded with no adjustments due to the measurement route. Following Doses 1-3 combined, the proportion of temperature measurements that were taken by rectal, axillary, or other routes were 91.7%, 8.1%, and 0% respectively, for VAXELIS group, and 90.3%, 9.7%, and 0%, respectively, for Pentacel + Recombivax HB vaccines group.

1. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020.

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VAXELIS suspension for intramuscular injection

Approval date[1]	December 21, 2018
Dosage[2]	The 3-dose immunization series consists of a 0.5-mL intramuscular injection, administered at 2, 4, and 6 months of age.
How Supplied[2a]	VAXELIS is supplied in a single-dose vial (NDC 63361-243-58) in packages of 10 vials (NDC 63361-243-10). VAXELIS is supplied as a single-dose, prefilled syringe with Luer lock connection and a tip cap, without needle, 0.5 mL (NDC 63361-243-88) in packages of 10 (NDC 63361-243-15). The vial stopper, syringe plunger stopper, and syringe tip cap are not made with natural rubber latex.
Storage and Handling[2]	• VAXELIS should be stored at 2°C to 8°C (36°F to 46°F). • DO NOT FREEZE. Product that has been exposed to freezing should not be used. Do not use after expiration date shown on the label. Discard unused portion.
Catalog Price[b]	Prefilled Syringes or Vials: • $128.27 per dose, plus $4.50 Federal Excise Tax • $1282.67 per carton of 10 doses, plus $45.00 Federal Excise Tax

[b]Catalog Price as of January 1, 2021; subject to change without notice. Catalog price does not necessarily reflect the actual price paid by consumers, payers, or dispensers.

[a]Please note: The NDCs above are the billable NDCs that appear on the carton and the unit of use, when NDC is required by the payer.

1. U.S. Food and Drug Administration. December 21, 2018 Approval Letter - VAXELIS. Accessed November 16, 2020. https://www.fda.gov/media/119466
2. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020.

Vaxelis™
Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine

Billing Codes and National Drug Codes for VAXELIS™

Included are lists of codes that may be relevant for VAXELIS and its administration. This information is current as of November 2020. The information provided here is compiled from sources believed to be accurate, but Merck and Sanofi Pasteur make no representation that it is accurate. Consult the relevant manual and/or other guidelines for a description of each code to determine the appropriateness of a particular code and for information on additional codes. This information is subject to change. Merck and Sanofi Pasteur caution that payer coding requirements vary and can frequently change, so it is important to regularly check with each payer as to payer-specific requirements. You are solely responsible for determining the appropriate codes and for any action you take in billing.

The information provided here is not intended to be definitive or exhaustive, and is not intended to replace the guidance of a qualified professional advisor. Merck and Sanofi Pasteur and their agents make no warranties or guarantees, expressed or implied, concerning the accuracy or appropriateness of this information for your particular use given the frequent changes in public and private payer billing. The use of this information does not guarantee payment or that any payment received will cover your costs. Diagnosis codes should be selected only by a health care professional.

Vaxelis™
Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine

Billing Codes

CPT® Code[1]	*Vaccine product*
90697	Diphtheria, tetanus toxoids, acellular pertussis vaccine, inactivated poliovirus vaccine, *Haemophilus influenzae* type b PRP-OMP conjugate vaccine, and hepatitis B vaccine (DTaP-IPV-Hib-HepB), for intramuscular use
	Administration of vaccine
90460	Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified HCP; first or only component of each vaccine or toxoid administered (Bill 1 unit for the first component of VAXELIS)
AND	
+90461	Immunization administration through 18 years of age via any route of administration, with counseling by physician or other qualified HCP; each additional vaccine or toxoid component administered (list separately in addition to code for primary procedure) (Bill 5 units; 1 unit for each additional component within VAXELIS)
OR	
90471	Immunization administration 1 injected vaccine (single or combination vaccine/toxoid) (Assuming VAXELIS is administered first during child's visit, bill 1 unit)
+90472	Immunization administration; each additional injected vaccine (single or combination vaccine/toxoid) (Assuming VAXELIS is administered subsequent to other vaccine[s] during child's visit, bill 1 unit)
ICD-10-CM[2]	Z23[a] Encounter for immunization

CPT is a registered trademark of the American Medical Association.

The use of this information does not guarantee payment or that payment received will cover your costs. Diagnosis codes should be selected only by a health care professional.

CPT, Current Procedural Terminology; HCP, health care provider; ICD-10-CM, International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Clinical Modification.

[a]Z23 is reported for all vaccine-related encounters for all vaccines given, and in addition to any health exam ICD-10-CM codes.[2]

1. American Academy of Pediatrics. Commonly administered pediatric vaccines. Accessed October 15, 2020. https://www.aap.org/enus/Documents/coding_vaccine_coding_table.pdf. 2. Centers for Disease Control and Prevention. ICD-10-CM Tabular list of diseases and injuries. Accessed October 15, 2020. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD10CM/2020/icd10cm_tabular_2020.pdf.

National Drug Codes and Immunization Registry Codes

Supplied Packages	National Drug Codes[1a]	
	NDC Unit of Use	NDC Carton
10 single-dose vials	N463361024358 ML0.5	N463361024310 ML0.5
10 single-dose prefilled syringes	N463361024388 ML0.5	N463361024315 ML0.5

CVX Code[2]	146
MVX Code[2]	PMC

The use of this information does not guarantee payment or that payment received will cover your costs. Diagnosis codes should be selected only by a health care professional.

[a]Please note: The NDCs above are the billable NDCs that appear on the carton and the unit of use, when NDC is required by the payer.

CVX Code, indicates the product used in a vaccination; MVX Code, indicates the manufacturer of a vaccine.

This coding information is provided for informational purposes only.

1. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020. 2. Medicare NCCI 2020 Coding Policy Manual. Chapter XI Medicine evaluation and management services CPT codes 90000-99999 for national correct coding initiative policy manual for Medicare services. Accessed October 30, 2020. https://www.supercoder.com/exclusives/cci-policy-manual/Chapter11_CPTCodes90000-99999_Final_11_12_19.pdf.

VAXELIS™ is the FIRST-AND-ONLY FDA-approved pediatric hexavalent combination vaccine[1]

VAXELIS is the result of the US-based joint-partnership between Merck and Sanofi Pasteur[1]

VAXELIS is to be administered as a 3-dose series at 2, 4, and 6 months of age and is available as single-dose vials and prefilled syringes[2]

With 2-3 fewer shots needed compared to Pentacel (+hepatitis B) or Pediarix (+hib), VAXELIS may help improve vaccination compliance in the infant series[3-8]

The immunogenicity and safety of VAXELIS on the US immunization schedule were evaluated in 2 US clinical trials[2]

VAXELIS will be available through the Vaccines For Children (VFC) program.

Before administering VAXELIS™, please read full Prescribing Information. The Patient Product Information also is available.

1. Oliver SE, Moore KL. Licensure of a diphtheria and tetanus toxoids and acellular pertussis, inactivated poliovirus, Haemophilus influenzae type b conjugate, and hepatitis b vaccine, and guidance for use in infants. *MMWR Morb Mortal Wkly Rep.* 2020;69(5):136-139. doi:10.15585/mmwr.mm6905a5. 2. VAXELIS™ (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) Prescribing Information, MSP Vaccine Company.; 2020. 3. Pentacel. Prescribing Information: Sanofi Pasteur.; 2020. Accessed September 18, 2020. https://www.vaccineshoppe.com/image.cfm?docid=13799&image_type=product_pdf. 4. Pentacel. Prescribing Information: Sanofi Pasteur.; 2019. Accessed September 18, 2020. https://www.vaccineshoppe.com/mailing/VSH/PIs%20&%20SDS/PI/dtppv-fplr-sl-dec19.pdf. 5. PEDIARIX. Prescribing Information. GlaxoSmithKline, Inc.; 2019. Accessed September 18, 2020. https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Pediarix/pdf/PEDIARIX.PDF. 6. Centers for Disease Control and Prevention. Recommended child and adolescent immunization schedule for ages 18 years or younger, United States, 2020. Accessed September 24, 2020. https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf. 7. Marshall GS, Happe LE, Lunacsek OE, et al. Use of combination vaccines is associated with improved coverage rates. *Pediatr Infect Dis J.* 2007;26(6):496-500. doi:10.1097/INF.0b013e31805d7f17. 8. Kurosky SK, Davis KL, Krishnarajah G. Effect of combination vaccines on completion and compliance of childhood vaccinations in the United States. *Hum Vaccin Immunother.* 2017;13(11):2494-2502. doi:10.1080/21645515.2017.1362515.

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