HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PNEUMOVAX 23 safely and effectively. See full prescribing information for PNEUMOVAX 23.

PNEUMOVAX® 23 (pneumococcal vaccine polyvalent)
Sterile, Liquid Vaccine for Intramuscular or Subcutaneous Injection
Initial U.S. Approval: 1983

----------INDICATIONS AND USAGE----------

PNEUMOVAX 23 is a vaccine indicated for active immunization for the prevention of pneumococcal disease caused by the 23 serotypes contained in the vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F). (1.1)

PNEUMOVAX 23 is approved for use in persons 50 years of age or older and persons aged ≥2 years who are at increased risk for pneumococcal disease. (1.1, 14.1)

---------- DOSAGE AND ADMINISTRATION ----------

Single 0.5-mL dose of PNEUMOVAX 23 administered intramuscularly or subcutaneously only. (2.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Clear, sterile solution supplied in a (0.5-mL dose) single-dose vial and a single-dose, prefilled syringe. (3)

----------CONTRAINDICATIONS----------

Severe allergic reaction (e.g., anaphylaxis) to any component of PNEUMOVAX 23. (4.1)

---------- WARNINGS AND PRECAUTIONS----------

- Use caution and appropriate care for individuals with severely compromised cardiovascular and/or pulmonary function in whom a systemic reaction would pose a significant risk. (5.2)

---------- ADVERSE REACTIONS ----------

The most common adverse reactions, reported in >10% of subjects vaccinated with PNEUMOVAX 23 for the first time in a clinical trial, were: injection-site pain/soreness/tenderness (60.0%), injection-site swelling/induration (20.3%), headache (17.6%), injection-site erythema (16.4%), asthenia and fatigue (13.2%), and myalgia (11.9%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme LLC at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

----------DRUG INTERACTIONS----------

In a randomized clinical study, a reduced immune response to ZOSTAVAX® as measured by gpELISA was observed in individuals who received concurrent administration of PNEUMOVAX 23 and ZOSTAVAX compared with individuals who received these vaccines 4 weeks apart. Consider administration of the two vaccines separated by at least 4 weeks. (7.1, 14.3)

---------- USE IN SPECIFIC POPULATIONS ----------

Pediatrics: PNEUMOVAX 23 is not approved for use in children younger than 2 years of age because children in this age group do not develop an effective immune response to capsular types contained in the polysaccharide vaccine. (8.4)

Geriatrics: For subjects aged 65 years or older in a clinical study systemic adverse reactions, determined by the investigator to be vaccine-related, were higher following revaccination (33.1%) than following initial vaccination (21.7%). Routine revaccination of immunocompetent persons previously vaccinated with a 23-valent vaccine, is not recommended. (8.5)

Immunocompromised Individuals: Response to vaccination may be diminished. (5.4, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indications and Use

PNEUMOVAX® 23 is a vaccine indicated for active immunization for the prevention of pneumococcal disease caused by the 23 serotypes contained in the vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A,

12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F). PNEUMOVAX 23 is approved for use in persons 50 years of age or older and persons aged ≥2 years who are at increased risk for pneumococcal disease.

1.2 Limitations of Use

PNEUMOVAX 23 will not prevent disease caused by capsular types of pneumococcus other than those contained in the vaccine.

2 DOSAGE AND ADMINISTRATION

For intramuscular or subcutaneous injection only.

2.1 Preparation

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. If either of these two conditions exists, the vaccine should not be administered.
- Do not mix PNEUMOVAX 23 with other vaccines in the same syringe or vial.
- Use a separate sterile syringe and needle for each individual patient to prevent transmission of infectious agents from one person to another.

  Single-Dose Vial

  Withdraw 0.5 mL from the vial using a sterile needle and syringe free of preservatives, antiseptics, and detergents.

  Single-Dose, Prefilled Syringe

  The package does not contain a needle. Attach a sterile needle to the prefilled syringe by twisting in a clockwise direction until the needle fits securely on the syringe.

2.2 Administration

Administer PNEUMOVAX 23 intramuscularly or subcutaneously into the deltoid muscle or lateral mid-thigh. Do not inject intravascularly or intradermally.

Single-Dose Vial

Administer a single 0.5-mL dose of PNEUMOVAX 23 using a sterile needle and syringe. Discard vial after use.

Single-Dose, Prefilled Syringe

Administer the entire contents of the single-dose, prefilled syringe per standard protocol using a sterile needle. Discard syringe after use.

2.3 Revaccination

The Advisory Committee on Immunization Practices (ACIP) has recommendations for revaccination against pneumococcal disease for persons at high risk who were previously vaccinated with PNEUMOVAX 23. Routine revaccination of immunocompetent persons previously vaccinated with a 23-valent vaccine, is not recommended.

3 DOSAGE FORMS AND STRENGTHS

PNEUMOVAX 23 is a clear, sterile solution supplied in a (0.5-mL dose) single-dose vial and a single-dose, prefilled syringe. *[See Description (11) and How Supplied/Storage and Handling (16).]*

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Do not administer PNEUMOVAX 23 to individuals with a history of anaphylactic/anaphylactoid or severe allergic reaction to any component of the vaccine. *[See Description (11).]*

5 WARNINGS AND PRECAUTIONS

5.1 Persons with Moderate or Severe Acute Illness

Defer vaccination with PNEUMOVAX 23 in persons with moderate or severe acute illness.

5.2 Persons with Severely Compromised Cardiovascular or Pulmonary Function

Caution and appropriate care should be exercised in administering PNEUMOVAX 23 to individuals with severely compromised cardiovascular and/or pulmonary function in whom a systemic reaction would pose a significant risk.

5.3 Use of Antibiotic Prophylaxis

This vaccine does not replace the need for penicillin (or other antibiotic) prophylaxis against pneumococcal infection. In patients who require penicillin (or other antibiotic) prophylaxis against pneumococcal infection, such prophylaxis should not be discontinued after vaccination with PNEUMOVAX 23.

5.4 Persons with Altered Immunocompetence

Persons who are immunocompromised, including persons receiving immunosuppressive therapy, may have a diminished immune response to PNEUMOVAX 23. *[See Use in Specific Populations (8.6).]*

5.5 Persons with Chronic Cerebrospinal Fluid Leakage

PNEUMOVAX 23 may not be effective in preventing pneumococcal meningitis in patients who have chronic cerebrospinal fluid (CSF) leakage resulting from congenital lesions, skull fractures, or neurosurgical procedures.

6 ADVERSE REACTIONS

The most common adverse reactions, reported in >10% of subjects vaccinated with PNEUMOVAX 23 for the first time in a clinical trial, were: injection-site pain/soreness/tenderness (60.0%), injection-site swelling/induration (20.3%), headache (17.6%), injection-site erythema (16.4%), asthenia/fatigue (13.2%), and myalgia (11.9%). *[See Adverse Reactions (6.1).]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Primary Vaccination and Revaccination with PNEUMOVAX 23 in Adults 50 Years of Age or Older

In a randomized, double-blind, placebo-controlled crossover clinical trial, subjects were enrolled in four different cohorts defined by age (50-64 years of age and ≥65 years of age) and vaccination status (no pneumococcal vaccination or receipt of a pneumococcal polysaccharide vaccine 3-5 years prior to the study). Subjects in each cohort were randomized to receive intramuscular injections of PNEUMOVAX 23 followed by placebo (saline containing 0.25% phenol), or placebo followed by PNEUMOVAX 23, at 30-day (±7 days) intervals. The safety of an initial vaccination (first dose) was compared to revaccination (second dose) with PNEUMOVAX 23 for 14 days following each vaccination.

All 1008 subjects (average age, 67 years; 49% male and 51% female; 91% Caucasian, 4.7% African-American, 3.5% Hispanic, and 0.8% Other) received placebo injections.

Initial vaccination was evaluated in a total of 444 subjects (average age 65 years; 32% male and 68% female; 93% Caucasian, 3.2% African-American, 3.4% Hispanic, and 1.1% Other).

Revaccination was evaluated in 564 subjects (average age 69 years; 53% male and 47% female; 90% Caucasian, 3.5% Hispanic, 6.0% African-American, and 0.5% Other).

Serious Adverse Experiences

In this study, 10 subjects had serious adverse experiences within 14 days of vaccination: 6 who received PNEUMOVAX 23 and 4 who received placebo. Serious adverse experiences within 14 days after PNEUMOVAX 23 included angina pectoris, heart failure, chest pain, ulcerative colitis, depression, and headache/tremor/stiffness/sweating. Serious adverse experiences within 14 days after placebo included myocardial infarction complicated with heart failure, alcohol intoxication, angina pectoris, and edema/urinary retention/heart failure/diabetes.

Five subjects reported serious adverse experiences that occurred outside the 14-day follow-up window: 3 who received PNEUMOVAX 23 and 2 who received placebo. Serious adverse experiences after PNEUMOVAX 23 included cerebrovascular accident, lumbar radiculopathy, and pancreatitis/myocardial infarction resulting in death. Serious adverse experiences after placebo included heart failure and motor vehicle accident resulting in death.

Solicited and Unsolicited Reactions

Table 1 presents the adverse event rates for all solicited and unsolicited reactions reported in ≥1% in any group in this study, without regard to causality.

The most common local adverse reactions reported at the injection site after initial vaccination with PNEUMOVAX 23 were pain/tenderness/soreness (60.0%), swelling/induration (20.3%), and erythema

(16.4%). The most common systemic adverse experiences were headache (17.6%), asthenia/fatigue (13.2%), and myalgia (11.9%).

The most common local adverse reactions reported at the injection site after revaccination with PNEUMOVAX 23 were pain/soreness/tenderness (77.2%), swelling (39.8%), and erythema (34.5%). The most common systemic adverse reactions with revaccination were headache (18.1%), asthenia/fatigue (17.9%), and myalgia (17.3%). All of these adverse reactions were reported at a rate lower than 10% after receiving a placebo injection.

Table 1: Incidence of Injection-Site and Systemic Complaints in Adults ≥50 Years of Age Receiving Their First (Initial) or Second (Revaccination) Dose of PNEUMOVAX 23 (Pneumococcal Polysaccharide Vaccine, 23 Valent) or Placebo Occurring at ≥1% in Any Group

	PNEUMOVAX 23 Initial Vaccination N=444	PNEUMOVAX 23 Revaccination* N=564	Placebo Injection† N=1008
Number Followed for Safety	438	548	984‡
	AE Rate	AE Rate	AE Rate
Injection-Site Complaints			
Solicited Events			
Pain/Soreness/Tenderness	60.0%	77.2%	7.7%
Swelling/Induration	20.3%	39.8%	2.8%
Erythema	16.4%	34.5%	3.3%
Unsolicited Events			
Ecchymosis	0%	1.1%	0.3%
Pruritus	0.2%	1.6%	0.0%
Systemic Complaints			
Solicited Events			
Asthenia/Fatigue	13.2%	17.9%	6.7%
Chills	2.7%	7.8%	1.8%
Myalgia	11.9%	17.3%	3.3%
Headache	17.6%	18.1%	8.9%
Unsolicited Events			
Fever§	1.4%	2.0%	0.7%
Diarrhea	1.1%	0.7%	0.5%
Dyspepsia	1.1%	1.1%	0.9%
Nausea	1.8%	1.8%	0.9%
Back Pain	0.9%	0.9%	1.0%
Neck Pain	0.7%	1.5%	0.2%
Upper Respiratory Infection	1.8%	2.6%	1.8%
Pharyngitis	1.1%	0.4%	1.3%

*Subjects receiving their second dose of pneumococcal polysaccharide vaccine as PNEUMOVAX 23 approximately 3-5 years after their first dose.

†Subjects receiving placebo injection from this study combined over periods.

‡The number of subjects receiving placebo followed for injection-site complaints. The corresponding number of subjects followed for systemic complaints was 981.

§Fever events include subjects who felt feverish in addition to subjects with elevated temperature.

In this clinical study an increased rate of local reactions was observed with revaccination at 3-5 years following initial vaccination.

For subjects aged 65 years or older, injection-site adverse reaction rate was higher following revaccination (79.3%) than following initial vaccination (52.9%). The proportion of subjects reporting

injection site discomfort that interfered with or prevented usual activity or injection site induration ≥4 inches was higher following revaccination (30.6%) than following initial vaccination (10.4%). Injection site reactions typically resolved by 5 days following vaccination.

For subjects aged 50-64 years, the injection-site adverse reaction rate for revaccinees and initial vaccinees was similar (79.6% and 72.8% respectively).

The rate of systemic adverse reactions was similar among both initial vaccinees and revaccinees within each age group. The rate of vaccine-related systemic adverse reactions was higher following revaccination (33.1%) than following initial vaccination (21.7%) in subjects 65 years of age or older, and was similar following revaccination (37.5%) and initial vaccination (35.5%) in subjects 50-64 years of age. The most common systemic adverse reactions reported after PNEUMOVAX 23 were as follows: asthenia/fatigue, myalgia and headache.

Regardless of age, the observed increase in post vaccination use of analgesics (≤13% in the revaccinees and ≤4% in the initial vaccinees) returned to baseline by day 5.

Sequential Administration of Prevnar 13 and PNEUMOVAX 23

In a randomized, double-blind, placebo-controlled, multicenter study, healthy adults, 50 years of age and older, received Prevnar 13 followed by PNEUMOVAX 23 either 8 weeks later (Group 1) or 26 weeks later (Group 2). Placebo was administered instead of PNEUMOVAX 23 at 26 weeks (Group 1) or 8 weeks (Group 2). Solicited injection site adverse reactions were evaluated during Days 1 through 5 postvaccination. Solicited systemic adverse reactions and any other adverse reactions were evaluated during Days 1 through 14 postvaccination, and any serious adverse events (SAEs) were collected throughout the study period (through Week 30). *[See Clinical Studies (14.2).]*

Overall, subjects were a mean age of 64.2 years (range: 50 to 97 years). There were more females (n=219, 54.8%) than males (n=181, 45.3%). By race, 84.8% of subjects were White, 9.3% were Black or African-American, and 6.1% were other racial groups; the majority of subjects were not Hispanic or Latino (n=322, 80.5%).

Serious Adverse Reactions

There were 24 SAEs reported in 20 subjects (n=9 [4.5%] Group 1; n=11 [5.5%] Group 2). No SAEs were considered related to vaccination.

Solicited Adverse Reactions

Solicited injection site adverse reactions that occurred during Days 1 through 5 postvaccination with PNEUMOVAX 23, solicited systemic adverse reactions that occurred during Days 1 through 14, and fever that occurred during Days 1 through 5 postvaccination with PNEUMOVAX 23 are presented in Table 2. In this study, 81.4% of subjects in Group 1 and 64.0% of subjects in Group 2 reported at least 1 injection site adverse reaction from Days 1 through 5 postvaccination with PNEUMOVAX 23, and 64.9% of subjects in Group 1 and 54.9% of subjects in Group 2 reported at least 1 systemic adverse reaction from Days 1 through 14 postvaccination with PNEUMOVAX 23.

Table 2: Rates (%) of Solicited Injection Site Reactions Occurring on Days 1 to 5 After PNEUMOVAX 23 and Solicited Systemic Adverse Reactions Occurring on Days 1 to 14 After PNEUMOVAX 23

	Group 1* (Prevnar 13 -> PNEUMOVAX 23 -> Placebo)		Group 2† (Prevnar 13 -> Placebo -> PNEUMOVAX 23)	
	n	(%)	n	(%)
Injection Site Adverse Reactions				
Subjects in population with follow-up	188		164	
Any injection site reaction	153	(81.4)	105	(64.0)
Any Injection site pain‡	149	(79.3)	105	(64.0)
Mild	72	(38.3)	65	(39.6)
Moderate	65	(34.6)	36	(22.0)
Severe§	12	(6.4)	4	(2.4)
Any Injection site swelling	95	(50.5)	48	(29.3)
0 to <2.5 cm	28	(14.9)	19	(11.6)
≥2.5 to <5.1 cm	20	(10.6)	9	(5.5)
≥5.1 to <7.6 cm	20	(10.6)	10	(6.1)
≥7.6 to <10.2 cm	15	(8.0)	2	(1.2)
≥10.2 cm§	12	(6.4)	8	(4.9)
Any Injection site erythema	78	(41.5)	48	(29.3)
0 to <2.5 cm	26	(13.8)	20	(12.2)
≥2.5 to <5.1 cm	12	(6.4)	13	(7.9)
≥5.1 to <7.6 cm	12	(6.4)	6	(3.7)
≥7.6 to <10.2 cm	7	(3.7)	3	(1.8)
≥10.2 cm	19	(10.1)	6	(3.7)
Unknown [missing data]	2	(1.1)	0	(0.0)
Systemic Adverse Reactions				
Subjects in population with follow-up	188		164	
Any systemic adverse reaction	122	(64.9)	90	(54.9)
Myalgia	93	(49.5)	70	(42.7)
Fatigue	59	(31.4)	45	(27.4)
Headache	46	(24.5)	30	(18.3)
Arthralgia	37	(19.7)	25	(15.2)
Subjects with temperature data¶	185		161	
Temperature ≥ 100.4°F	1	(0.5)	0	(0.0)

Every subject is counted a single time for each applicable row and column.

A specific adverse reaction appears in this table only if its incidence in one or more of the columns meets the incidence criterion in the table title, after rounding.

*Group 1: 8-week interval between Prevnar 13 and PNEUMOVAX 23.

†Group 2: 26-week interval between Prevnar 13 and PNEUMOVAX 23.

‡Pain was characterized as mild, moderate or severe. (Mild: awareness of sign or symptom, but easily tolerated. Moderate: discomfort enough to cause interference with usual activity. Severe: incapacitating with inability to work or do usual activity).

§One Group 1 subject with severe pain and swelling greater than 10.2 cm after receipt of PNEUMOVAX 23, went to the Emergency Room for medical attention.

¶Percentages are calculated based on number of subjects with temperature data. Oral temperature was solicited on Days 1 to 5 after PNEUMOVAX 23 vaccination.

6.2 Post-Marketing Experience

The following list of adverse reactions includes those identified during post approval use of PNEUMOVAX 23. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or their causal relationship to product exposure.

General disorders and administration site conditions
- Cellulitis
- Malaise
- Fever (>102°F)
- Warmth at the injection site
- Decreased limb mobility
- Peripheral edema in the injected extremity
- Injection-site necrosis

Digestive System
- Nausea
- Vomiting

Hematologic/Lymphatic
- Lymphadenitis
- Lymphadenopathy
- Thrombocytopenia in patients with stabilized idiopathic thrombocytopenic purpura
- Hemolytic anemia in patients who have had other hematologic disorders
- Leukocytosis

Hypersensitivity reactions including
- Anaphylactoid reactions
- Serum Sickness
- Angioneurotic edema

Musculoskeletal System
- Arthralgia
- Arthritis

Nervous System
- Paresthesia
- Radiculoneuropathy
- Guillain-Barré syndrome
- Febrile convulsion

Skin
- Rash
- Urticaria
- Cellulitis-like reactions
- Erythema multiforme

Investigations
- Increased serum C-reactive protein

7 DRUG INTERACTIONS

7.1 Concomitant Administration with Other Vaccines

In a randomized clinical study, a reduced immune response to ZOSTAVAX® as measured by gpELISA was observed in individuals who received concurrent administration of PNEUMOVAX 23 and ZOSTAVAX compared with individuals who received these vaccines 4 weeks apart. Consider administration of the two vaccines separated by at least 4 weeks. *[See Clinical Studies (14.3).]*

Limited safety and immunogenicity data from clinical trials are available on the concurrent administration of PNEUMOVAX 23 and vaccines other than ZOSTAVAX.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Available human data from clinical trials of PNEUMOVAX 23 in pregnancy have not established the presence or absence of a vaccine-associated risk.

Developmental toxicity studies have not been conducted with PNEUMOVAX 23 in animals.

8.2 Lactation

Risk Summary

It is not known whether PNEUMOVAX 23 is excreted in human milk. Data are not available to assess the effects of PNEUMOVAX 23 on the breastfed infant or on milk production/excretion.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PNEUMOVAX 23 and any potential adverse effects on the breastfed child from PNEUMOVAX 23 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to the disease prevented by the vaccine.

8.4 Pediatric Use

PNEUMOVAX 23 is not approved for use in children less than 2 years of age. Children in this age group do not develop an effective immune response to the capsular types contained in this polysaccharide vaccine.

The ACIP has recommendations for use of PNEUMOVAX 23 in children 2 years of age or older, who have previously received pneumococcal vaccines, and who are at increased risk for pneumococcal disease.

8.5 Geriatric Use

In one clinical trial of PNEUMOVAX 23, conducted post-licensure, a total of 629 subjects who were aged ≥65 years and 201 subjects who were aged ≥75 years were enrolled.

In this trial, the safety of PNEUMOVAX 23 in adults 65 years of age and older (N=629) was compared to the safety of PNEUMOVAX 23 in adults 50 to 64 years of age (N=379). The subjects in this study had underlying chronic illness but were in stable condition; at least 1 medical condition at enrollment was reported by 86.3% of subjects who were 50 to 64 years old, and by 96.7% of subjects who were 65 to 91 years old. The rate of vaccine-related systemic adverse experiences was higher following revaccination (33.1%) than following primary vaccination (21.7%) in subjects ≥65 years of age, and was similar following revaccination (37.5%) and primary vaccination (35.5%) in subjects 50 to 64 years of age.

Since elderly individuals may not tolerate medical interventions as well as younger individuals, a higher frequency and/or a greater severity of reactions in some older individuals cannot be ruled out.

Post-marketing reports have been received in which some elderly individuals had severe adverse experiences and a complicated clinical course following vaccination. Some individuals with underlying medical conditions of varying severity experienced local reactions and fever associated with clinical deterioration requiring hospital care.

8.6 Immunocompromised Individuals

Persons who are immunocompromised, including persons receiving immunosuppressive therapy, may have a diminished immune response to PNEUMOVAX 23.

11 DESCRIPTION

PNEUMOVAX 23 (Pneumococcal Vaccine Polyvalent) is a sterile, liquid vaccine consisting of a mixture of purified capsular polysaccharides from *Streptococcus pneumoniae* types (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F).

PNEUMOVAX 23 is a clear, colorless solution. Each 0.5-mL dose of vaccine contains 25 micrograms of each polysaccharide type in isotonic saline solution containing 0.25% phenol as a preservative. The vaccine is used directly as supplied. No dilution or reconstitution is necessary.

The vial stoppers, syringe plunger stopper and syringe tip cap are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

PNEUMOVAX 23 induces type-specific antibodies that enhance opsonization, phagocytosis, and killing of pneumococci by leukocytes and other phagocytic cells. The levels of antibodies that correlate with protection against pneumococcal disease have not been clearly defined.

14 CLINICAL STUDIES

14.1 Effectiveness

The protective efficacy of pneumococcal vaccines containing six (types 1, 2, 4, 8, 12F, and 25) or twelve (types 1, 2, 3, 4, 6A, 8, 9N, 12F, 25, 7F, 18C, and 46) capsular polysaccharides was investigated in two controlled studies in South Africa in male novice gold miners ranging in age from 16 to 58 years, in whom there was a high attack rate for pneumococcal pneumonia and bacteremia. In both studies, participants in the control groups received either meningococcal polysaccharide serogroup A vaccine or saline placebo. In both studies, attack rates for vaccine type pneumococcal pneumonia were observed for the period from 2 weeks through about 1 year after vaccination. Protective efficacy was 76% and 92%, respectively, for the 6- and 12-valent vaccines, for the capsular types represented.

Three similar studies in South African young adult male novice gold miners were carried out by Dr. R. Austrian and associates using similar pneumococcal vaccines prepared for the National Institute of Allergy and Infectious Diseases, with pneumococcal vaccines containing a 6-valent formulation (types 1, 3, 4, 7, 8, and 12) or a 13-valent formulation (types 1, 2, 3, 4, 6, 7, 8, 9, 12, 14, 18, 19, and 25) capsular polysaccharides. The reduction in pneumococcal pneumonia caused by the capsular types contained in the vaccines was 79%. Reduction in type-specific pneumococcal bacteremia was 82%.

A prospective study in France found a pneumococcal vaccine containing fourteen (types 1, 2, 3, 4, 6A, 7F, 8, 9N, 12F, 14, 18C, 19F, 23F, and 25) capsular polysaccharides to be 77% (95%CI: 51% to 89%) effective in reducing the incidence of pneumonia among male and female nursing home residents with a mean age of 74 (standard deviation of 4 years).

In a study using a pneumococcal vaccine containing eight (types 1, 3, 6, 7, 14, 18, 19, and 23) capsular polysaccharides, vaccinated children and young adults aged 2 to 25 years who had sickle cell disease, congenital asplenia, or undergone a splenectomy experienced significantly less bacteremic pneumococcal disease than patients who were not vaccinated.

In the United States, one post-licensure randomized controlled trial, in the elderly or patients with chronic medical conditions who received a 14-valent pneumococcal polysaccharide vaccine (types 1, 2, 3, 4, 6A, 8, 9N, 12F, 14, 19F, 23F, 25, 7F, and 18C), did not support the efficacy of the vaccine for nonbacteremic pneumonia.

A retrospective cohort analysis study based on the U.S. Centers for Disease Control and Prevention (CDC) pneumococcal surveillance system, showed 57% (95%CI: 45% to 66%) overall protective effectiveness against invasive infections caused by serotypes included in PNEUMOVAX 23 in persons ≥6 years of age, 65 to 84% effectiveness among specific patient groups (e.g., persons with diabetes mellitus, coronary vascular disease, congestive heart failure, chronic pulmonary disease, and anatomic asplenia) and 75% (95%CI: 57% to 85%) effectiveness in immunocompetent persons aged ≥65 years of age. Vaccine effectiveness could not be confirmed for certain groups of immunocompromised patients.

14.2 Immunogenicity

The levels of antibodies that correlate with protection against pneumococcal disease have not been clearly defined.

Antibody responses to most pneumococcal capsular types are generally low or inconsistent in children less than 2 years of age.

Sequential Administration of Prevnar 13 and PNEUMOVAX 23

In a randomized, double-blind, placebo-controlled, multicenter study, healthy adults, 50 years of age and older, received Prevnar 13 followed by PNEUMOVAX 23 either 8 weeks later (Group 1) or 26 weeks later (Group 2). Four hundred subjects were randomized 1:1 into Group 1 or Group 2, all of whom were initially vaccinated with Prevnar 13; of these, 188 subjects received PNEUMOVAX 23 (Group 1) and 185 subjects received placebo (Group 2) at Week 8, and 172 subjects received placebo (Group 1) and 164 subjects received PNEUMOVAX 23 (Group 2) at Week 26.

Opsonophagocytic activity (OPA) titers were measured at prevaccination, at Week 12 and at Week 30 for the 12 shared serotypes contained in both PNEUMOVAX 23 and Prevnar 13 (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F), 2 of the 11 serotypes unique to PNEUMOVAX 23 (22F and 33F), and 1 serotype unique to Prevnar 13 (6A). OPA testing was performed on evaluable serum samples from all subjects at baseline (Day 1) and Week 12, and on sera from a random subset of subjects (approximately 50% of subjects) at Week 30. Estimated GMTs, GMT ratio, and 95% confidence intervals were obtained from a constrained Longitudinal Data Analysis model {1}.

For each of the shared serotypes, Week 12 OPA geometric mean titers (GMTs) in Group 1 were noninferior to those of Group 2, as the lower bounds of the 95% CIs for the OPA GMT ratios were >0.5 for all 12 shared serotypes. For serotypes 22F and 33F, OPA GMTs in Group 1 at Week 12 were superior to those of Group 2 at Week 12, as the lower bounds of the 95% CIs for the OPA GMT ratios were >2.0 for both serotypes.

The OPA GMTs to the 12 shared serotypes and 2 unique serotypes (22F and 33F) when measured 4 weeks after dosing with PNEUMOVAX 23 were generally similar between Group 1 (Week 12) and Group 2 (Week 30 subset).

14.3 Concomitant Administration with Other Vaccines

In a double-blind, controlled clinical trial, 473 adults, 60 years of age or older, were randomized to receive ZOSTAVAX and PNEUMOVAX 23 concomitantly (N=237), or PNEUMOVAX 23 alone followed 4 weeks later by ZOSTAVAX alone (N=236). At four weeks postvaccination, the varicella-zoster virus (VZV) antibody levels following concomitant use were significantly lower than the VZV antibody levels following nonconcomitant administration (GMTs of 338 vs. 484 gpELISA units/mL, respectively; GMT ratio = 0.70 (95% CI: [0.61, 0.80]).

Limited safety and immunogenicity data from clinical trials are available on the concurrent administration of PNEUMOVAX 23 and vaccines other than ZOSTAVAX.

15 REFERENCES

1. Liang KY, Zeger S. Longitudinal data analysis of continuous and discrete responses for pre-post designs. Sankhyā: The Indian Journal of Statistics (Series B) 2000; 62: 134-148.

16 HOW SUPPLIED/STORAGE AND HANDLING

PNEUMOVAX 23 is supplied as follows:

NDC 0006-4943-00 — a box of 10 single-dose vials, color coded with a purple cap and stripe on the vial labels and cartons.

NDC 0006-4837-03 — a box of 10 single-dose, pre-filled Luer-Lok™ syringes with tip caps, color coded with a violet plunger rod and purple stripe on the syringe labels and cartons.

Storage and Handling

- Store at 2-8°C (36-46°F).
- All vaccine must be discarded after the expiration date.

The vial stoppers, syringe plunger stopper and syringe tip cap are not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

- Inform the patient, parent or guardian of the benefits and risks associated with vaccination.
- Tell the patient, parent or guardian that vaccination with PNEUMOVAX 23 may not offer 100% protection from pneumococcal infection.
- Provide the patient, parent or guardian with the vaccine information statements required by the National Childhood Vaccine Injury Act of 1986, with each immunization.
- Instruct the patient, parent or guardian to report any serious adverse reactions to their health care provider who in turn should report such events to the vaccine manufacturer or the U.S. Department of Health and Human Services through the Vaccine Adverse Event Reporting System (VAERS), 1-800-822-7967, or report online at www.vaers.hhs.gov.

Manuf. and Dist. by: Merck Sharp & Dohme LLC
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For patent information: www.msd.com/research/patent

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