PRODUCT MONOGRAPH

PNEUMOVAX® 23

(pneumococcal vaccine, polyvalent, MSD Std.)

Solution for injection

Active Immunizing Agent Against Infections Caused by Pneumococci

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Date of Revision: June 9, 2014

Global Trade Identification No.:
0 67055 04355 0 (1 x 0.5 mL)
0 67055 04734 3 (10 x 0.5 mL)

Control No: 175674 **Date of Approval: January 16, 2015**

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION 3
SUMMARY PRODUCT INFORMATION 3
DESCRIPTION 3
INDICATIONS AND CLINICAL USE 4
CONTRAINDICATIONS 6
WARNINGS AND PRECAUTIONS 6
ADVERSE REACTIONS 8
DRUG INTERACTIONS 10
DOSAGE AND ADMINISTRATION 11
OVERDOSAGE 12
ACTION AND CLINICAL PHARMACOLOGY 12
STORAGE AND STABILITY 14
DOSAGE FORMS, COMPOSITION AND PACKAGING 14

PART II: SCIENTIFIC INFORMATION 16
PHARMACEUTICAL INFORMATION 16
CLINICAL TRIALS 16
REFERENCES 19

PART III: CONSUMER INFORMATION 22

PNEUMOVAX® 23

(pneumococcal vaccine, polyvalent, MSD Std.)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular or subcutaneous injection	Solution Each 0.5 mL dose contains 25 µg of capsular polysaccharide from each of 23 types of pneumococci: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F	Phenol *For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING section.*

DESCRIPTION

PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.), is a sterile, liquid vaccine for intramuscular or subcutaneous injection. It consists of a mixture of highly purified capsular polysaccharides from the 23 most prevalent or invasive pneumococcal types of *Streptococcus pneumoniae*, including the six serotypes that most frequently cause invasive drug-resistant pneumococcal infections among children and adults in the United States[1] (see DOSAGE FORMS, COMPOSITION AND PACKAGING). The 23-valent vaccine accounts for at least 90% of pneumococcal blood isolates and at least 85% of all pneumococcal isolates from sites which are generally sterile as determined by ongoing surveillance of United States data.[2] Canadian population based surveillance for invasive pneumococcal disease in metropolitan Toronto-Peel region found that 92% of cases were caused by serotypes contained in PNEUMOVAX® 23. Similarly, the Sentinel Health Unit Surveillance System (SHUSS) study documented 94% of cases being caused by serotypes contained in PNEUMOVAX® 23.[3]

INDICATIONS AND CLINICAL USE

PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) is indicated for vaccination against pneumococcal disease caused by those pneumococcal types included in the vaccine. Effectiveness of the vaccine in the prevention of pneumococcal pneumonia and pneumococcal bacteremia has been demonstrated in controlled trials in South Africa, France and in case-controlled studies.

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

If it is known that a person has not received any pneumococcal vaccine or if earlier pneumococcal vaccination status is unknown, then persons in the categories listed below should be administered pneumococcal vaccine; however, if a person has received a primary dose of pneumococcal vaccine, before administering an additional dose of vaccine, please refer to the Revaccination section.

Vaccination with PNEUMOVAX® 23 is recommended for selected individuals as follows:

Immunocompetent persons:

- Routine vaccination for persons 50 years of age or older[1,4]
- Persons aged ≥ 2 years with chronic cardiovascular disease (including congestive heart failure and cardiomyopathies), chronic pulmonary disease (including chronic obstructive pulmonary disease and emphysema), or diabetes mellitus[1,4]
- Persons aged ≥ 2 years with alcoholism, chronic liver disease (including cirrhosis) or cerebrospinal fluid leaks[1,4]
- Persons aged ≥ 2 years with functional or anatomic asplenia (including sickle cell disease and splenectomy)[1,4]
- Persons aged ≥ 2 years living in special environments or social settings (including Aboriginals)
- In Canada, the National Advisory Committee on Immunization (NACI) currently recommends the vaccination of smokers with the 23-valent polysaccharide pneumococcal vaccine.[4]

Immunocompromised persons:

- Persons aged ≥ 2 years, including those with HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure or nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and those who have received an organ or bone marrow transplant.[1,4] For selected groups, see INDICATIONS AND CLINICAL USE, Timing of Vaccination.

According to NACI guidelines, children aged 2 years to < 5 years of age who are at increased risk of invasive pneumococcal disease (IPD) should receive pneumococcal conjugate vaccine, with pneumococcal polysaccharide vaccine being used as a booster dose in this age group to increase the serotype coverage. Children at increased risk of IPD include those who attend child

care centres, are Aboriginal, have sickle cell disease and other sickle cell hemoglobinopathies, have other types of functional or anatomic asplenia, HIV infection, immunocompromising conditions (e.g., primary immunodeficiencies; malignancies; conditions resulting from immunosuppressive therapy, solid organ transplantation, or use of long-term systemic corticosteroids; nephrotic syndrome), chronic medical conditions (e.g., chronic cardiac and pulmonary disease such as bronchopulmonary dysplasia, diabetes mellitus, chronic renal disease or CSF leak) and children with cochlear implants or those receiving cochlear implants. Pneumococcal polysaccharide vaccine should be given to all individuals ≥ 5 years of age who have not received the conjugate vaccine previously and who are at higher risk of IPD.[4]

Timing of Vaccination
Pneumococcal vaccine should be given at least two weeks before elective splenectomy, if possible.

For planning cancer chemotherapy or other immunosuppressive therapy (e.g., for patients with Hodgkin's disease or those who undergo organ or bone marrow transplantation), pneumococcal vaccination should be administered at least two weeks prior to the initiation of immunosuppressive therapy. Vaccination during chemotherapy or radiation therapy should be avoided. Based on literature reports, pneumococcal vaccine may be given as early as several months following completion of chemotherapy or radiation therapy for neoplastic disease.[5,6] In Hodgkin's disease, immune response to vaccination may be impaired for two years or longer after intense chemotherapy (with or without radiation). During the two years following the completion of chemotherapy or other immunosuppressive therapy, antibody responses improve in some patients as the interval between the end of treatment and pneumococcal vaccination increases.[5]

Persons with asymptomatic or symptomatic HIV infection should be vaccinated as soon as possible after their diagnosis is confirmed.

Revaccination
Revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not routinely recommended.[1] However, revaccination once is recommended for persons ≥ 2 years of age who are at highest risk of serious pneumococcal infection and those likely to have a rapid decline in pneumococcal antibody levels, provided that at least five years have passed since receipt of a first dose of pneumococcal vaccine.[1,4]

The highest risk group includes persons with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (e.g., organ or bone marrow transplantation), and those receiving immunosuppressive chemotherapy (including long-term systemic corticosteroids)[1] (see INDICATIONS AND CLINICAL USE, Timing of Vaccination).

For children ≤ 10 years of age at the time of initial immunization and at highest risk of severe pneumococcal infection (e.g., children with functional or anatomic asplenia, including sickle cell disease or splenectomy or conditions associated with rapid antibody decline after initial vaccination including nephrotic syndrome, renal failure or renal transplantation), the United States Advisory Committee on Immunization Practices (ACIP) and NACI recommend that a single revaccination may be considered three years after the initial dose.[1,4]

For children > 10 years of age at the time of initial immunization and at highest risk of severe pneumococcal infection (as described above) the ACIP and NACI recommend that a single revaccination may be considered five years after the initial dose.[1,4]

If prior vaccination status is unknown for patients in the high risk group, patients should be given pneumococcal vaccine.[1]

All persons ≥ 65 years of age who have not received vaccine within 5 years (and were < 65 years of age at the time of vaccination) should receive another dose of vaccine.[1]

Because data are insufficient concerning the safety of pneumococcal vaccine when administered three or more times, revaccination following a second dose is not routinely recommended.[1,4]

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine.

According to the Canadian National Advisory Committee on Immunization, anaphylactic reaction to polysaccharide pneumococcal vaccine is a contraindication to re-immunization with that product.[4]

WARNINGS AND PRECAUTIONS

General

In case of severe hypersensitivity or anaphylactoid reaction to the vaccine, refer to NACI recommendations regarding the management of these reactions in the Canadian Immunization Guide.[4]

Epinephrine injection (1:1000) must be immediately available should an acute anaphylactoid reaction occur due to any component of the vaccine.

For planning cancer chemotherapy or other immunosuppressive therapy (e.g., for patients with Hodgkin's disease or those who undergo organ or bone marrow transplantation), the timing of the vaccination is critical (see INDICATIONS AND CLINICAL USE, Timing of Vaccination).

If the vaccine is administered to patients who are immunosuppressed due to either an underlying condition or medical treatment (e.g., immunosuppressive therapy such as cancer chemotherapy or radiation therapy), the expected serum antibody response may not be obtained and potential impairment of future immune responses to pneumococcal antigens may occur[7] (see INDICATIONS AND CLINICAL USE, Timing of Vaccination).

Intradermal administration may cause severe local reactions.

Caution and appropriate care should be exercised in administering PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) to individuals with severely compromised cardiovascular and/or pulmonary function in whom a systemic reaction would pose a significant risk.

Any febrile respiratory illness or other active infection is reason for delaying use of PNEUMOVAX® 23, except when, in the opinion of the physician, withholding the agent entails even greater risk.

In patients who require penicillin (or other antibiotic) prophylaxis against pneumococcal infection, such prophylaxis should not be discontinued after vaccination with PNEUMOVAX® 23.

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.

Routine revaccination of immunocompetent persons previously vaccinated with a 23-valent vaccine is not recommended.[1] However, revaccination once is recommended for persons aged ≥ 2 years who are at highest risk for serious pneumococcal infections and those likely to have a rapid decline in pneumococcal antibody levels (see INDICATIONS AND CLINICAL USE, Revaccination).

As with any vaccine, vaccination with PNEUMOVAX® 23 may not result in complete protection in all recipients and lack of effect following PNEUMOVAX® 23 vaccination has been reported through post-market surveillance.

Special Populations

Pregnant Women:
Animal reproduction studies have not been conducted with PNEUMOVAX® 23. It is also not known whether PNEUMOVAX® 23 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. PNEUMOVAX® 23 should be given to a pregnant woman only if clearly needed.

Nursing Women:
It is not known whether this vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PNEUMOVAX® 23 is administered to a nursing woman.

Pediatrics (< 2 years of age):
PNEUMOVAX® 23 is not recommended for use in children less than 2 years of age. Safety and effectiveness in children below the age of 2 years have not been established. Children in this age group respond poorly to the capsular types contained in this vaccine (see ACTIONS AND CLINICAL PHARMACOLOGY, Immunogenicity).

Geriatrics:
Persons 65 years of age or older were enrolled in several clinical studies of PNEUMOVAX® 23 that were conducted pre- and post-licensure. In the largest of these studies, the safety of PNEUMOVAX® 23 in adults 65 years of age and older (n=629; median age of 72 years) was compared to the safety of PNEUMOVAX® 23 in adults 50 to 64 years of age (n=379; median age of 58 years). All subjects in this study were ambulatory and had an expected prevalence of age associated chronic diseases. The clinical data did not suggest an increased rate or severity of adverse reactions among subjects ≥ 65 years of age compared to those 50 to 64 years of age. However, 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 frail elderly individuals with multiple co-morbid conditions had severe adverse experiences and a complicated clinical course following vaccination (see ADVERSE REACTIONS).

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The following adverse experiences have been reported with PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) in clinical trials and/or post-marketing experience: Injection site reactions, consisting of pain, soreness, erythema, warmth, swelling, local induration, decreased limb mobility and peripheral edema in the injected extremity. Rarely, cellulitis-like reactions were reported. These cellulitis-like reactions, reported in post-marketing experience, show short onset time from vaccine administration. Local reactions may be accompanied by systemic signs and symptoms including fever, leukocytosis and an increase in the laboratory value for serum C-reactive protein.

The most common adverse experiences reported in clinical trials were fever (≤ 38.8°C), injection site reactions including soreness, erythema, warmth, swelling and local induration.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another vaccine. Adverse drug reaction information from clinical trials is useful for identifying vaccine-related adverse events and for approximating rates.

In a clinical trial, an increased rate of self-limited local reactions has been observed with revaccination at 3–5 years following primary vaccination. It was reported that the overall injection-site adverse experiences rate for subjects ≥ 65 years of age was higher following revaccination (79.3%) than following primary vaccination (52.9%). The reported overall injection-site adverse experiences rate for re-vaccinees and primary vaccinees who were 50 to 64 years of age were similar (79.6% and 72.8% respectively). In both age groups, re-vaccinees reported a higher rate of a composite endpoint (any of the following: moderate pain, severe pain, and/or large induration at the injection site) than primary vaccinees. Among subjects ≥ 65 years of age, the composite

endpoint was reported by 30.6% and 10.4% of revaccination and primary vaccination subjects, respectively, while among subjects 50–64 years of age, the endpoint was reported by 35.5% and 18.9% respectively. The injection site reactions occurred within the 3 day monitoring period and typically resolved by day 5. The rate of overall systemic adverse experiences was similar among both primary vaccinees and re-vaccinees within each age group. The most common systemic adverse experiences were asthenia/fatigue, myalgia and headache. Among subjects ≥ 65 years of age, asthenia/fatigue and myalgia were reported more frequently following revaccination than primary vaccination. The observed generally small increase (≤ 13%) in post-vaccination use of analgesics returned to baseline by day 5.

Other Adverse Experiences reported in Clinical Trials and/or in Post-Marketing Experience include

Body as a Whole

Cellulitis
Asthenia
Fever
Chills
Malaise

Digestive System

Nausea
Vomiting

Hematologic/Lymphatic System

Lymphadenitis
Lymphadenopathy
Thrombocytopenia in patients with stabilized idiopathic thrombocytopenic purpura[8]
Hemolytic anemia in patients who have had other hematologic disorders
Leukocytosis

Hypersensitivity reactions including:

Anaphylactoid reactions
Serum sickness
Angioneurotic edema

Musculoskeletal System

Arthralgia
Arthritis
Myalgia

Nervous System

Headache
Paresthesia
Radiculoneuropathy
Guillain-Barré Syndrome
Febrile convulsion

Skin

Rash
Urticaria
Erythema multiforme

Special Populations:

Geriatrics:
Post-marketing reports have been received in which some frail elderly individuals with multiple co-morbid conditions had severe adverse experiences and a complicated clinical course following vaccination.

DRUG INTERACTIONS

Use with Other Vaccines

It is recommended that pneumococcal vaccine may be administered at the same time as influenza vaccine (by separate injection in the other arm) without an increase in side effects or decreased antibody response to either vaccine.

In contrast to pneumococcal vaccine, influenza vaccine is recommended annually, for appropriate populations.[4]

PNEUMOVAX® 23 and ZOSTAVAX® (zoster vaccine live, attenuated [Oka/Merck]) should not be given concurrently because concomitant use in a clinical trial resulted in reduced immunogenicity of ZOSTAVAX®. In this trial, the immunogenicity of PNEUMOVAX® 23 was not affected by ZOSTAVAX®.

DOSAGE AND ADMINISTRATION

Dosing Considerations

The healthcare provider should determine the current health status and previous vaccination history of the vaccinee (see INDICATIONS AND CLINICAL USE, Revaccination).

The healthcare provider should question the patient, parent or guardian about reactions to a previous dose of PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) or other pneumococcal vaccine.

Recommended Dose and Dosage Adjustment

The recommended dose of PNEUMOVAX® 23 is a single 0.5 mL injection given subcutaneously or intramuscularly (see Administration).

Administration

DO NOT INJECT INTRAVENOUSLY OR INTRADERMALLY.

Vials

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. PNEUMOVAX® 23 is a clear, colourless solution. The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol 0.25% has been added in the vaccine as a preservative.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of infectious agents from one person to another.

Proper aseptic technique should be used for withdrawal of each dose from the multi-dose vial.

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

Administer a single 0.5 mL dose of PNEUMOVAX® 23 subcutaneously or intramuscularly (preferably in the deltoid muscle or lateral mid-thigh), with appropriate precautions to avoid intravascular administration.

Prefilled Syringe

The prefilled syringe is for single use only. Inject the entire contents of the syringe (0.5 mL).

OVERDOSAGE

There are no data with regard to overdose.

For management of a suspected overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Infections caused by *Streptococcus pneumoniae* are a major cause of morbidity and mortality all over the world[9] and a major cause of pneumonia, bacteremia, meningitis, and otitis media.[3]

Strains of drug-resistant *S. pneumoniae* have become increasingly common in the United States and in other parts of the world. In some areas as many as 35% of pneumococcal isolates have been reported to be resistant to penicillin. Many penicillin-resistant pneumococci are also resistant to other antimicrobial drugs (e.g., erythromycin, trimethoprim-sulfamethoxazole and extended-spectrum cephalosporins), therefore emphasizing the importance of vaccine prophylaxis against pneumococcal disease.[1]

According to the results of a Canadian National Survey among 1,089 clinical isolates of *S. pneumoniae* obtained from 39 laboratories across Canada between October 1994 and August 1995, the prevalence of antimicrobial resistance has increased in Canada in just a few years.[10]

Immunogenicity

It has been established that the purified pneumococcal capsular polysaccharides induce antibody production and that such antibody is effective in preventing pneumococcal disease.[11,12] Clinical studies have demonstrated the immunogenicity of each of the 23 capsular types when tested in polyvalent vaccines.

Studies with 12-, 14-, and 23-valent pneumococcal vaccines in children two years of age and older and in adults of all ages showed immunogenic responses.[12-16] Protective capsular type-specific antibody levels generally develop by the third week following vaccination.[15]

Bacterial capsular polysaccharides induce antibodies primarily by T-cell-independent mechanisms. Therefore, antibody response to most pneumococcal capsular types is generally poor or inconsistent in children aged < 2 years whose immune systems are immature.[1]

ADDITIONAL RELEVANT INFORMATION

Epidemiology

Pneumococcal infection causes approximately 40,000 deaths annually in the United States.[1]

In Canada, population-based surveillance for invasive pneumococcal disease in metropolitan Toronto-Peel region (population 3.4 million) revealed an overall incidence of 11.8–16.1 cases per 100,000 population in 1995-1997.[3] At least 500,000 cases of pneumococcal pneumonia are estimated

to occur annually in the United States; *S. pneumoniae* accounts for approximately 25–35% of cases of community-acquired bacterial pneumonia in persons who require hospitalization.[1]

Pneumococcal disease accounts for an estimated 50,000 cases of pneumococcal bacteremia annually in the United States. Some studies suggest the overall annual incidence of bacteremia to be approximately 15 to 30 cases/100,000 population with 50 to 83 cases/100,000 for persons 65 years of age and older and 160 cases/100,000 for children less than two years of age. The incidence of pneumococcal bacteremia is as high as 1% (940 cases/100,000 population) among persons with acquired immunodeficiency syndrome (AIDS). In the United States, the risk of acquiring bacteremia is lower among whites than among persons in some other racial/ethnic groups (i.e., blacks, Alaskan Natives, and American Indians). Despite appropriate antimicrobial therapy and intensive medical care, the overall case-fatality rate for pneumococcal bacteremia is 15%–20% among adults,[17] and among elderly patients this rate is approximately 30–40%. An overall case-fatality rate of 36% was documented for adult inner-city residents who were hospitalized for pneumococcal bacteremia.[1]

The SHUSS (Sentinel Health Unit Surveillance System), an active population-based surveillance for laboratory-confirmed disease conducted in nine health units within eight Canadian provinces, revealed an overall incidence of 15.1 cases of invasive pneumococcal disease per 100,000 population.[3] The age-specific incidence was greatest in children < 5 years of age (55.3 cases per 100,000) and in persons ≥ 65 years of age (46.4 cases per 100,000). Ninety-four percent of cases were caused by serotypes contained in the 23-valent pneumococcal vaccine.[3]

In the United States, pneumococcal disease accounts for an estimated 3,000 cases of meningitis annually. The estimated overall annual incidence of pneumococcal meningitis is approximately 1 to 2 cases per 100,000 population. The incidence of pneumococcal meningitis is highest among children 6 to 24 months and persons aged ≥ 65 years; rates for blacks are twice as high as those for whites or Hispanics. Recurrent pneumococcal meningitis may occur in patients who have chronic cerebrospinal fluid leakage resulting from congenital lesions, skull fractures, or neurosurgical procedures.[1]

Invasive pneumococcal disease (e.g., bacteremia or meningitis) and pneumonia cause high morbidity and mortality in spite of effective antimicrobial control by antibiotics.[17] These effects of pneumococcal disease appear due to irreversible physiologic damage caused by the bacteria during the first 5 days following onset of illness,[11,18] and occur irrespective of antimicrobial therapy.[18,19] The incidence of penicillin resistance in many areas of the world has been steadily increasing. The National Centre for Streptococcus (NCS) in Edmonton, a voluntary passive surveillance reporting system, found that 7.8% of isolates submitted between 1992 and 1995 had diminished susceptibility to penicillin.[3] During 1996 to 1997, this proportion had increased to 10.2%. In a similar study, SHUSS identified 7.4% of isolates having diminished susceptibility to penicillin in 1996.[3] Vaccination offers an effective means of further reducing the mortality and morbidity of this disease.

Risk Factors

In addition to the very young and persons 65 years of age or older, patients with certain chronic conditions are at increased risk of developing pneumococcal infection and severe pneumococcal illness.

Patients with chronic cardiovascular diseases (e.g., congestive heart failure or cardiomyopathy), chronic pulmonary diseases (e.g., chronic obstructive pulmonary disease or emphysema), or chronic liver diseases (e.g., cirrhosis), diabetes mellitus, alcoholism or asthma (when it occurs with chronic bronchitis, emphysema, or long-term use of systemic corticosteroids) have an increased risk of pneumococcal disease. In adults, this population is generally immunocompetent.[1]

Patients at high risk are those who have a decreased responsiveness to polysaccharide antigen or an increased rate of decline in serum antibody concentrations as a result of: immunosuppressive conditions (congenital immunodeficiency, human immunodeficiency virus [HIV] infection, leukemia, lymphoma, multiple myeloma, Hodgkin's disease, or generalized malignancy); organ or bone marrow transplantation; therapy with alkylating agents, antimetabolites, or systemic corticosteroids; chronic renal failure or nephrotic syndrome.[1,20]

Patients at the highest risk of pneumococcal infection are those with functional or anatomic asplenia (e.g., sickle cell disease[21] or splenectomy), because this condition leads to reduced clearance of encapsulated bacteria from the bloodstream. Children who have sickle cell disease or have had a splenectomy are at increased risk for fulminant pneumococcal sepsis associated with high mortality.[1]

STORAGE AND STABILITY

Store unopened and opened vials at 2–8°C.

All vaccines must be discarded after the expiration date.

Five-dose vial: After first opening of the multi-dose vial, immediate use is recommended. If not used immediately, the vaccine should be stored in a refrigerator (2°C–8°C). If not used within 48 hours, it should be discarded.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

Vials

PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) is supplied as a sterile, clear, colourless liquid in a single-dose vial. A five-dose vial can be made available for mass immunization programs.

The vaccine should be used directly as supplied; no dilution or reconstitution is necessary.

Prefilled Syringe

PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) is also supplied as a sterile,

clear, colourless liquid in a 1.5 mL glass syringe.

Inject the entire contents of the syringe (0.5 mL).

Composition

Each single dose (0.5 mL) contains:

Active Ingredients

Purified capsular polysaccharides from the following 23 serotypes of *Streptococcus pneumoniae* (Danish nomenclature):	
1, 2, 3, 4, 5, 6B*, 7F, 8, 9N, 9V*, 10A, 11A, 12F, 14*, 15B, 17F, 18C, 19A*, 19F*, 20, 22F, 23F*, 33F	25 µg of each serotype

*These serotypes most frequently cause drug-resistant pneumococcal infections[1]

Other Ingredients

Excipients	
Sodium chloride	0.9% (w/w)
Phenol	0.25% (w/w)
Water for injection	to volume

Packaging

Vials

PNEUMOVAX® 23 is supplied in 3 mL single-dose Type I glass vials containing one 0.5 mL dose of liquid vaccine. Available in packages of 1 and 10 single-dose vials.

For mass immunization progams, PNEUMOVAX® 23 can also be supplied in 4 mL multi-dose Type I glass vials containing five 0.5 mL doses of liquid vaccine. Available in packages of 1 five-dose vial.

Prefilled Syringe

PNEUMOVAX® 23 is also supplied in 1.5 mL Type I glass barrel syringes with a round flange, rubber plunger stopper and plastic tip cap. Each syringe contains 0.5 mL dose of liquid vaccine.

The container closure systems of PNEUMOVAX® 23 are free of latex.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Pneumococcal vaccine, polyvalent, MSD Std.

Product Characteristics

PNEUMOVAX® 23 (pneumococcal vaccine, polyvalent, MSD Std.) is a sterile, liquid vaccine for intramuscular or subcutaneous injection. It consists of a mixture of highly purified capsular polysaccharides from the 23 most prevalent or invasive pneumococcal types of *Streptococcus pneumoniae*, including the six serotypes that most frequently cause invasive drug-resistant pneumococcal infections among children and adults in the United States (see Table 1).[1]

Table 1: 23 Pneumococcal Capsular Types Included in PNEUMOVAX® 23

Pneumococcal Types (Danish Nomenclature)
1 2 3 4 5 6B* 7F 8 9N 9V* 10A 11A 12F 14* 15B 17F 18C 19A* 19F* 20 22F 23F* 33F

*These serotypes most frequently cause drug-resistant pneumococcal infections[1]

PNEUMOVAX® 23 is manufactured according to methods developed by Merck Research Laboratories. Each 0.5 mL dose of vaccine contains 25 μg of each polysaccharide type dissolved in isotonic saline solution containing 0.25% phenol as a preservative.

CLINICAL TRIALS

Efficacy

The protective efficacy of pneumococcal vaccines containing 6 or 12 capsular polysaccharides was investigated in two controlled studies of young, healthy gold miners in South Africa, in whom there was a high attack rate for pneumococcal pneumonia and bacteremia.[15] Capsular type-specific attack rates for pneumococcal pneumonia were observed for the period from 2 weeks through about 1 year after vaccination. Protective efficacy was 76% and 92%, respectively, in the two studies for the capsular types represented.

In similar studies carried out by Dr. R. Austrian and associates, using similar pneumococcal vaccines prepared for the National Institutes of Allergy and Infectious Diseases, the reduction in pneumonia caused by the capsular types contained in the vaccines was 79%.[22] Reduction in type-specific pneumococcal bacteremia was 82%.

A prospective study in France found pneumococcal vaccine to be 77% effective in reducing the incidence of pneumonia among nursing home residents.[23]

In the United States, two postlicensure randomized controlled trials, in the elderly or patients with chronic medical conditions, who received a multivalent polysaccharide vaccine, did not support the efficacy of the vaccine for nonbacteremic pneumonia.[24,25] However, these studies may have lacked sufficient statistical power to detect a difference in the incidence of laboratory-confirmed, nonbacteremic pneumococcal pneumonia between the vaccinated and nonvaccinated study groups.[1,26]

A meta-analysis of nine randomized controlled trials of pneumococcal vaccine concluded that pneumococcal vaccine is efficacious in reducing the frequency of nonbacteremic pneumococcal pneumonia among adults in low risk groups but not in high-risk groups.[27] These studies may have been limited because of the lack of specific and sensitive diagnostic tests for nonbacteremic pneumococcal pneumonia. The pneumococcal polysaccharide vaccine is not effective for the prevention of acute otitis media and common upper respiratory diseases (e.g., sinusitis) in children.[1]

More recently, multiple, case-control studies have shown pneumococcal vaccine is effective in the prevention of serious pneumococcal disease, with point estimates of efficacy ranging from 56% to 81% in immunocompetent persons.[1,28-33]

Only one case-control study did not document effectiveness against bacteremic disease possibly due to study limitations, including small sample size and incomplete ascertainment of vaccination status in patients.[34] In addition, case-patients and persons who served as controls may not have been comparable regarding the severity of their underlying medical conditions, potentially creating a biased underestimate of vaccine effectiveness.[1,26]

A serotype prevalence study, based on the Centers for Disease Control pneumococcal surveillance system, demonstrated 57% overall protective effectiveness against invasive infections caused by serotypes included in the vaccine in persons ≥ 6 years of age, 65–84% 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% effectiveness in immunocompetent persons aged ≥ 65 years of age.[1] Vaccine effectiveness could not be confirmed for certain groups of immunocompromised patients; however, the study could not recruit sufficient numbers of unvaccinated patients from each disease group.

In an earlier study, 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.[1,35]

Duration of Immunity

Following pneumococcal vaccination, serotype-specific antibody levels decline after 5–10 years.[1] A more rapid decline in antibody levels may occur in some groups (e.g., children).[1] Limited published data suggest that antibody levels may decline more rapidly in the elderly > 60 years of age.[36,37] The Advisory Committee on Immunization Practices states that these findings indicate that revaccination may be needed to provide continued protection[1] (see INDICATIONS AND CLINICAL USE, Revaccination).

The results from one epidemiologic study suggest that vaccination may provide protection for at least nine years after receipt of the initial dose.[29] Decreasing estimates of effectiveness with increasing interval since vaccination, particularly among the very elderly (persons aged ≥ 85 years) have been reported.[30]

REFERENCES

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PART III: CONSUMER INFORMATION

PNEUMOVAX® 23
(pneumococcal vaccine, polyvalent, MSD Std.)

This leaflet is part III of a three-part "Product Monograph" published when PNEUMOVAX® 23 was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PNEUMOVAX® 23. Contact your doctor or pharmacist if you have any questions about the vaccine.

ABOUT THIS VACCINE

What the vaccine is used for:
PNEUMOVAX® 23 is an injectable vaccine to help prevent infections, such as pneumonia and bacteremia (severe infection in the blood), caused by certain types of pneumococcal bacteria.

The vaccine can be administered routinely to persons 50 years of age or older. The vaccine can also be administered to persons 2 years of age and older if:

- they have chronic illnesses (e.g., heart disease, lung disease, liver disease or diabetes mellitus), alcoholism or cerebrospinal fluid leaks.
- they do not have a spleen or have a spleen that does not function properly.
- they have HIV infection, Hodgkin's disease, lymphoma, multiple myeloma, leukemia, generalized malignancy, chronic renal failure or nephrotic syndrome, are receiving cancer chemotherapy or other immunosuppressive therapy (including corticosteroids) or have organ or bone marrow transplantation.
- they are living in special environments or social settings with an increased risk of pneumococcal infection.

A second dose of the vaccine may be recommended at a later date if you are at high risk for a pneumococcal infection.

What it does:
Your doctor has recommended or administered PNEUMOVAX® 23 to help protect you or your child against pneumococcal infections caused by the most common types of pneumococci.

Pneumococcal infection is a leading cause of death throughout the world and is a major cause of pneumonia, swelling of the coverings on the brain and spinal cord (meningitis), middle ear infections (otitis media), and a severe infection in the blood (bacteremia). These problems are more likely to occur in older people and those with certain diseases that make them more susceptible to a pneumococcal infection.

When it should not be used:
PNEUMOVAX® 23 should not be used by anyone who:

- is allergic to any of the ingredients in the vaccine. A list of ingredients can be found below.
- has had an allergic reaction from a previous dose of the vaccine.

What the medicinal ingredient is:
Each dose of vaccine contains 25 micrograms of each of 23 types of polysaccharide from bacteria known as pneumococci. These have been highly purified to make them suitable for you or your child to be given them as an injection. The 23 types of pneumococcal polysaccharide in the vaccine are types 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F.

What the important nonmedicinal ingredients are:
PNEUMOVAX® 23 also contains the following inactive ingredients: phenol, sodium chloride and water for injection.

What dosage forms it comes in:
PNEUMOVAX® 23 is supplied as a single-dose vial containing 0.5 mL of liquid vaccine. A multi-dose vial containing five 0.5 mL doses can be made available for mass immunization programs.

PNEUMOVAX® 23 is also supplied as prefilled syringes containing 0.5 mL of liquid vaccine.

WARNINGS AND PRECAUTIONS

Before you or your child receive PNEUMOVAX® 23, it is very important to tell your healthcare provider:

- if you or your child are allergic to any component of the vaccine; and
- about any medical problem you or your child have or have had, including any allergies.

Use in children
PNEUMOVAX® 23 can be used in children 2 years of age and older. It is not recommended for use in children below 2 years of age.

Use in pregnancy
It is not known whether the vaccine is harmful to an unborn baby when administered to a pregnant woman. Tell your doctor if you are pregnant. Your doctor will decide if you should receive PNEUMOVAX® 23.

Use in breast-feeding
Tell your doctor if you are breast-feeding or intend to breast-feed. Your doctor will decide if you should receive PNEUMOVAX® 23.

Use in elderly
Individuals 65 years and older may not tolerate medical interventions as well as younger individuals. Therefore, a higher number and/or a greater severity of reactions in some older individuals cannot be ruled out. Severe side effects after vaccination have been reported in some frail elderly people who have other serious medical problems.

Can I drive or operate machinery following vaccination with PNEUMOVAX® 23?
There is no information to suggest that PNEUMOVAX® 23 affects your ability to drive or operate machinery.

What other important information about PNEUMOVAX® 23 should I know?

As with other vaccines, PNEUMOVAX® 23 may not fully protect all those who receive it.

INTERACTIONS WITH THIS VACCINE

PNEUMOVAX® 23 has been administered at the same time as influenza vaccines with satisfactory results. Your doctor will decide the vaccination schedule.

PNEUMOVAX® 23 should not be given at the same time as ZOSTAVAX® (zoster vaccine live, attenuated [Oka/Merck]). For more information, talk to your doctor.

PROPER USE OF THIS VACCINE

Usual dose:
PNEUMOVAX® 23 is given by intramuscular or subcutaneous injection.

The dose of the vaccine is the same for everyone.

A second dose of PNEUMOVAX® 23 is not routinely recommended. However, for persons at the highest risk of serious pneumococcal infection, a second dose of the vaccine may be recommended. Your doctor will decide if and when you need a second dose of PNEUMOVAX® 23.

Overdose:

In case of overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Any vaccine may have unintended or undesirable effects, so-called side effects. The most common side effects reported with PNEUMOVAX® 23 are soreness, redness, swelling, warmth and hardening at the injection site and fever.

Other side effects may also occur rarely (e.g., fatigue, chills, feeling unwell, nausea, vomiting, enlarged and/or inflamed lymph glands, arthritis, headache, allergic reaction, joint pain, muscle pain, altered skin sensation, hives or rash, pain, decreased ability to move limb, and seizures in children due to fever), and some of these may be serious.

Tell your health care provider or get emergency help right away if you get any of the following problems after vaccination because these may be signs of an allergic reaction or other serious conditions:

- difficulty breathing
- wheezing
- rash
- hives

Reactions at the site where you get the shot may be more common and intense after a second shot than after the first shot.

Your doctor has a more complete list of side effects.

Tell your doctor promptly about any of these or any other unusual symptoms. If the condition persists or worsens, seek medical attention.

This is not a complete list of side effects. For any unexpected effects while taking PNEUMOVAX® 23, contact your doctor or pharmacist.

HOW TO STORE IT

Store refrigerated at 2–8°C.

All vaccines must be discarded after the expiration date.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For health care professionals:
If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in **your province/territory.**

For the General Public:
Should you experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada.

By toll-free telephone: 1-866-844-0018
By toll-free fax: 1-866-844-5931
By e-mail: caefi@phac-aspc.gc.ca
Web: http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php

Mail:

The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road, A/L 6502A
Ottawa, ON K1A 0K9

or at Merck Canada Inc. by one of the following 2 ways:

- Call toll-free at 1-800-567-2594
- Complete an Adverse Events following Immunization (AEFI) Form and:
  - Fax toll-free to 1-800-369-3090, or
  - Mail to: Merck Canada Inc.
    Pharmacovigilance
    P.O. Box 1005
    Pointe-Claire – Dorval, QC H9R 4P8

NOTE: Should you require information related to the management of the side effects, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada or Merck do not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
http://www.merck.ca
or by contacting the sponsor, Merck Canada Inc., at:
1-800-567-2594.

This leaflet was prepared by Merck Canada Inc.

Last revised: June 9, 2014

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