

Name of Medicine

PNEUMOVAX[®] 23

Pneumococcal vaccine polyvalent, MSD

25 mcg/serotype/0.5 mL

Single Dose Vial

Presentation

Single dose vials with a sterile clear colourless solution for intramuscular or subcutaneous administration.

Inactive ingredients: Sodium chloride, water for injection

Preservative: Phenol (0.25%)

Therapeutic Class

PNEUMOVAX 23 is a vaccine which has been shown to produce antibodies to the 23 most prevalent or invasive pneumococcal-types (see Actions).

Indications

PNEUMOVAX 23 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 bacteraemia 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 (see Dosage and Administration, *Revaccination*).

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

Immunocompetent persons

- routine vaccination for persons 50 years of age or older
- 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
- persons aged ≥ 2 years with alcoholism, chronic liver disease (including cirrhosis) or cerebrospinal fluid leaks
- persons aged ≥ 2 years with functional or anatomic asplenia (including sickle cell disease and splenectomy)
- persons aged ≥ 2 years living in special environments or social settings (including Alaskan Natives and certain American Indian populations).

Immunocompromised persons

- persons aged ≥ 2 years, including those with HIV infection, leukaemia, lymphoma, Hodgkin's disease, multiple myeloma, generalised malignancy, chronic renal failure or nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and those who have received an organ or bone marrow transplant (for selected groups, see Dosage and Administration, *Timing of Vaccination*).

PNEUMOVAX 23 may not be effective in preventing infection resulting from basilar skull fracture or from external communication with cerebrospinal fluid.

Dosage and Administration

Do not inject intravenously or intradermally.

Parenteral medicine 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.

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.

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.

Store unopened and opened vials at 2-8°C (35.6-46.4°F). The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol 0.25% added as preservative. All vaccine must be discarded after the expiration date.

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), the interval between vaccination and initiation of immunosuppressive therapy should be at least two weeks. Vaccination during chemotherapy or radiation therapy should be avoided. Pneumococcal vaccine may be given several months following completion of chemotherapy or radiation therapy for neoplastic disease. In Hodgkin's disease, immune response to vaccination may be suboptimal for two years or longer after intensive chemotherapy (with or without radiation).

For some patients, during the two years following the completion of chemotherapy or other immunosuppressive therapy (with or without radiation), significant improvement in antibody response has been observed, particularly as the interval between the end of treatment and pneumococcal vaccination increased.

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

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 adverse

effects or decreased antibody response to either vaccine.^{†1} In contrast to pneumococcal vaccine, influenza vaccine is recommended annually, for appropriate populations.

PNEUMOVAX 23 and ZOSTAVAX[®] 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.

Revaccination

Revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not routinely recommended.

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.

The highest risk group includes persons with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), HIV infection, leukaemia, lymphoma, Hodgkin's disease, multiple myeloma, generalised 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). (See Dosage and Administration, *Timing of Vaccination*.)

For children ≤ 10 years of age at revaccination 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), it is recommended that revaccination may be considered three years after the previous dose.^{†2}

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

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.

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.

Contraindications

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

Warnings and Precautions

If the vaccine is used in persons receiving immunosuppressive therapy, the expected serum antibody response may not be obtained and potential impairment of future immune responses to pneumococcal antigens may occur. (See Dosage and Administration, *Timing of Vaccination*.)

¹ † The Advisory Committee on Immunisation Practices (ACIP)

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Intradermal administration may cause severe local reactions.

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.

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.

As with any vaccine, vaccination with PNEUMOVAX 23 may not result in complete protection in all recipients.

Pregnancy

It is not known whether PNEUMOVAX 23 can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. PNEUMOVAX 23 should be given to pregnant women only if clearly needed.

Nursing Mothers

It is not known whether this vaccine is excreted in human milk. Caution should be exercised when PNEUMOVAX 23 is administered to a nursing mother.

Paediatric Use

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.

Use in the Elderly

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) was compared to the safety of PNEUMOVAX 23 in adults 50 to 64 years of age (n=379). The 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.

Adverse Effects

The following adverse experiences have been reported with PNEUMOVAX 23 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 oedema in the injected extremity.

Very 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 ($\leq 38.8^{\circ}\text{C}/102^{\circ}\text{F}$), injection site reactions including soreness, erythema, warmth, swelling and local induration.

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 as follows: asthenia/fatigue, myalgia and headache. The observed generally small increase ($\leq 13\%$) 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

Haematologic/Lymphatic System: Lymphadenitis, lymphadenopathy, thrombocytopaenia in patients with stabilised, idiopathic thrombocytopaenic purpura, haemolytic anaemia in patients who have had other haematologic disorders, leukocytosis

Hypersensitivity reactions including: Anaphylactoid reactions, serum sickness, angioneurotic oedema

Musculoskeletal System: Arthralgia, arthritis, myalgia

Nervous System: Headache, paresthesia, radiculoneuropathy, Guillain-Barré Syndrome, febrile convulsion

Skin: Rash, urticaria

Overdosage

There is no data available on Overdosage.

Actions

PNEUMOVAX 23 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 medicine-resistant pneumococcal infections among children and adults in the United States (see Table 1). 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 U.S. data.

Table 1 23 Pneumococcal Capsular Types included in PNEUMOVAX 23																						
Danish Nomenclature											Pneumococcal Types											
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 medicine-resistant pneumococcal infections*

It has been established that the purified pneumococcal capsular polysaccharides in PNEUMOVAX 23, induce antibody production and that such antibody is effective in preventing pneumococcal disease. 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.

Pharmacokinetics

Following pneumococcal vaccination, serotype-specific antibody levels decline after 5-10 years. A more rapid decline in antibody levels may occur in some groups (e.g. children). Limited published data suggest that antibody levels may decline more rapidly in the elderly >60 years of age. These findings indicate that revaccination may be needed to provide continued protection,^{†3} (see Dosage and Administration, *Revaccination*).

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

Pharmaceutical Precautions

Store unopened and opened vials at 2-8°C (35.6-46.4°F). The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol 0.25% added as preservative. All vaccine must be discarded after the expiration date.

Medicine Classification

Prescription Medicine

Package Quantities

PNEUMOVAX is supplied as single dose vials.

Further Information

There is no further information.

³ † *The Advisory Committee on Immunisation Practices (ACIP)*

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