SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

PNEUMOVAX® 23 (Pneumococcal Vaccine Polyvalent, MSD) Solution for Injection

COMPOSITION

Each 0,5 mL dose of vaccine contains 25 µg of each polysaccharide type dissolved in isotonic saline solution containing 0,25 % *m/v* phenol as preservative.

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 drug-resistant pneumococcal infections

PHARMACOLOGICAL CLASSIFICATION

A.30.1 Antigens

PHARMACOLOGICAL ACTION

PNEUMOVAX 23 (pneumococcal vaccine, polyvalent, MSD), consists of a mixture of highly purified capsular polysaccharides from the 23 most prevalent or invasive pneumococcal types of *Streptococcus pneumoniae*.

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.

Protective capsular type-specific antibody levels generally develop by the third week following vaccination.

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 younger than 2 years whose immune systems are immature.

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 is a high attack rate for pneumococcal pneumonia and bacteraemia. 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.

Following pneumococcal vaccination, serotype-specific antibody levels decline after 5 to 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 older than 60 years of age. These findings indicate that re-vaccination may be needed to provide continued protection (see **INDICATIONS, Re-vaccination**).

INDICATIONS

PNEUMOVAX 23 is indicated for vaccination against pneumococcal disease caused by those pneumococcal types included in the vaccine.

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 **Re-vaccination** section.

PNEUMOVAX 23 is recommended for the prevention of pneumococcal pneumonia and pneumococcal systemic infections caused by the serotypes included in the vaccine, in high-risk subjects from 2 years of age.

Elderly patients from 65 years of age.

Immunocompetent patients with chronic illness (e.g. cardiovascular disease, pulmonary disease, diabetes mellitus, alcoholism, cirrhosis, cerebrospinal fluid leaks).

Immunocompromised patients: anatomic or functional asplenia (including patients to be splenectomised), sickle cell disease, Hodgkin's disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome and organ transplantation.

Special groups: persons living in a social or working environment with an identified increased risk of pneumococcal infection or its complications (e.g. hospitalised elderly people or those in institutional care).

It should be noted that this vaccine is not indicated for recurrent upper respiratory tract infections, particularly otitis media and sinusitis.

Immunocompromised persons

Persons 2 years of age and older, 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 **INDICATIONS, Timing of Vaccination**).

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

Timing of Vaccination

Pneumococcal vaccine should be given at least 2 weeks before elective splenectomy. 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 2 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 2 years or longer after intensive chemotherapy (with or without radiation).

Re-vaccination

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

However, re-vaccination once is recommended for persons 2 years and older 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 5 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), 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 **INDICATIONS, Timing of Vaccination**).

For children 10 years and younger at re-vaccination 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 re-vaccination may be considered 3 years after the previous dose.

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 and older who have not received vaccine within 5 years (and were younger than 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 3 or more times, re-vaccination following a second dose is not routinely recommended.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine.

Paediatric Use

PNEUMOVAX 23 is not recommended for use in children < 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.

WARNINGS

Use of this vaccine at the same time as other vaccines that contain endotoxins may provoke a febrile reaction.

INTERACTIONS

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.

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.

PREGNANCY AND LACTATION

Safety in pregnancy and during lactation has not been demonstrated.

DOSAGE AND DIRECTIONS FOR USE

Do not inject intravenously or intradermally.

The vaccine is used directly as supplied. No dilution or reconstitution is necessary. All vaccine must be discarded after the expiration date.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. PNEUMOVAX 23 is a clear, colourless solution.

Pre-filled Syringe

The pre-filled syringe is for single use only. Inject the entire contents of the syringe.

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.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side Effects

The following adverse experiences have been reported with PNEUMOVAX 23.

Injection site reactions consisting of pain, soreness, erythema, warmth, swelling, local induration, decreased limb mobility and peripheral oedema 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.

In a clinical trial, an increased rate of self-limited local reactions has been observed with re-vaccination at 3 to 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 re-vaccination (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 re-vaccination and primary vaccination subjects, respectively, while among subjects 50 to 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 (≤ 13 %) in post-vaccination use of analgesics returned to baseline by day 5.

The table below summarises the frequencies of the adverse events that were reported with PNEUMOVAX 23 in clinical trials and/or post-marketing surveillance, using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000), not known (cannot be estimated from available data).

Adverse Event	Frequency
Blood and the lymphatic system disorders	
Lymphadenitis, lymphadenopathy, thrombocytopenia in patients with stabilised idiopathic thrombocytopenic purpura, haemolytic anaemia in patients who have had other haematologic disorders, leukocytosis	Not known
Immune system disorders	
Anaphylactoid reactions, serum sickness, angioneurotic oedema	Not known
Nervous system disorders	
Headache, paraesthesia, radiculo-neuropathy, Guillain-Barré Syndrome, febrile convulsion	Not known
Gastrointestinal disorders	
Nausea, vomiting	Not known
Skin and subcutaneous tissue disorders	
Erythema multiforme, rash, urticaria	Not known

Musculoskeletal, connective tissue and bone disorders	
Arthralgia, arthritis, myalgia	Not known
General disorders and administration site conditions	
Fever (≤ 38,8 °C) Injection site reactions: • erythema • induration • pain • soreness • swelling • warmth	Very common
Cellulitis	Rare
Asthenia, fever, malaise, chills	Not known

Special Precautions

Adrenaline injection (1:1 000) must be immediately available should an acute anaphylactoid reaction occur due to any component of the vaccine.

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 **INDICATIONS, Timing of Vaccination**).

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 doctor, 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.

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 data did not suggest an increased rate 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Not applicable; vaccine is supplied as a single-dose pre-filled syringe.

IDENTIFICATION

PNEUMOVAX 23 is a clear, colourless liquid. The vaccine is used directly as supplied. No dilution or reconstitution is necessary.

PRESENTATION

PNEUMOVAX 23 is available in a pack containing 1 or 10 single-dose, pre-filled 1,5 mL glass syringes containing 0,5 mL liquid vaccine.

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

STORAGE INSTRUCTIONS

Store at 2 to 8 °C.

Keep out of reach of children.

REGISTRATION NUMBER

T/30.1/0544

NAME AND ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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