DATA SHEET

1. PNEUMOVAX® 23

Pneumococcal vaccine polyvalent, MSD, 25 microgram/serotype/0.5 mL
Single Dose Vial/Pre-filled Syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5mL single dose vials/pre-filled syringe contains 25 mcg of each of the following pneumococcal polysaccharide serotypes: 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*

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Single dose vials/pre-filled syringes with a sterile clear colourless solution for intramuscular or subcutaneous administration.

4. CLINICAL PARTICULARS

4.1 Therapeutic 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 Dose and method of 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.

4.2 Dose and method of administration

Dose

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.

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.

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.†[1]

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.

Method of 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.

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

Prefilled syringe:
The prefilled syringe is for single use only. Inject the entire contents of the syringe.

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.

The vaccine is used directly as supplied. No dilution or reconstitution is necessary. Phenol 0.25% added as preservative.

4.3 Contraindications

Hypersensitivity to any component of the vaccine (see *Section 2* and *6.1*).
Epinephrine injection (1:1000) must be immediately available should an acute anaphylactoid reaction occur due to any component of the vaccine.

4.4 Special warnings and precautions for use

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 Dose and method of administration, *Timing of vaccination*.)

Intradermal administration may cause severe local reactions.

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

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.

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.

4.5 Interaction with other medicines and other forms of interaction

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. †[2] 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. Consider administration of the two vaccines separated by at least 4 weeks

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

Immunogenicity following concomitant administration
In a double-blind, controlled clinical trial, 473 adults, 60 years of age or older, were randomised 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 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])). VZV antibody levels 4 weeks postvaccination were increased 1.9-fold (95% CI: [1.7, 2.1]; meeting the pre-specified acceptance criterion) in the concomitant group vs. 3.1-fold (95% CI: [2.8, 3.5]) in the nonconcomitant group. The GMTs for PNEUMOVAX 23 antigens were comparable between the two groups. Concomitant use of ZOSTAVAX and PNEUMOVAX 23 demonstrated a safety profile that was generally similar to that of the two vaccines administered nonconcomitantly.

4.6 Fertility, pregnancy and lactation

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.

Breast-feeding

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.

Fertility

This vaccine has not been evaluated in fertility studies.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable 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.

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/102°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 (≤ 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, thrombocytopenia in patients with stabilised idiopathic thrombocytopenic purpura, haemolytic anaemia in patients who have had other haematologic disorders, leucocytosis

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

Musculoskeletal System: Arthralgia, arthritis, myalgia

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

Skin: Rash, urticaria, erythema multiforme

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions http://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

There is no data available on overdosage.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

PNEUMOVAX 23 is a vaccine which has been shown to produce antibodies to the 23 most prevalent or invasive pneumococcal-types (see section 5.1).

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: pneumococcal vaccines, ATC code: J07 AL

Mechanism of action

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 United States 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.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

No preclinical safety testing was performed using the vaccine.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, water for injection
Preservative: Phenol (0.25%)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life

24 months from date of manufacture

6.4. Special precautions for storage

Store unopened and opened vials/pre-filled syringes at 2°C to 8°C (35.6°F to 46.4°F).

6.5. Nature and contents of container

PNEUMOVAX 23 is supplied as a single dose vial and as a pre-filled syringe of vaccine.

6.6 Special precautions for disposal

All vaccine must be discarded after the expiration date.
Any unused medicinal product or waste material should be dispose of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Merck Sharp & Dohme (New Zealand) Limited
P O Box 99 851
Newmarket
Auckland
NEW ZEALAND
Tel: 0800 500 673

9. DATE OF FIRST APPROVAL

24 May 1978

10. DATE OF REVISION OF THE TEXT

19 May 2017

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SUMMARY TABLE OF CHANGES

Date	Change
19 May 2017	Reformat data sheet;