AUSTRALIAN PRODUCT INFORMATION

PNEUMOVAX® 23

Pneumococcal Vaccine Polyvalent

Pneumococcal purified capsular polysaccharides

Solution for Injection

1 NAME OF THE MEDICINE

Pneumococcal purified capsular polysaccharides

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

PNEUMOVAX 23 (Pneumococcal Vaccine Polyvalent) is a sterile, liquid vaccine for intramuscular or subcutaneous injection. It consists of a mixture of 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). The 23-valent vaccine accounts for at least 90% of pneumococcal blood isolates and approximately 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	19F*	19A*	20	22F	23F*	33F				

* These serotypes most frequently cause drug-resistant pneumococcal infections

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

The manufacture of this product includes exposure to bovine derived material. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

For the full list of excipients, see **Section 6.1 List of Excipients.**

3 PHARMACEUTICAL FORM

PNEUMOVAX 23 (Pneumococcal Vaccine, Polyvalent) is a sterile, liquid vaccine for intramuscular or subcutaneous injection.

PNEUMOVAX 23 is a clear, colourless solution for injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

PNEUMOVAX 23 is indicated for immunisation of individuals in the following situations:

- All individuals over the age of 65 years;
- Individuals with asplenia, either functional or anatomical, including sickle cell disease, in persons more than 2 years of age; where possible the vaccine should be given at least 14 days before splenectomy;
- Immunocompromised patients at increased risk of pneumococcal disease (e.g. patients with HIV infection before the development of AIDS, nephrotic syndrome, multiple myeloma, lymphoma, Hodgkin's disease and organ transplantation);
- Aboriginal and Torres Strait Islander people over 50 years of age;
- Immunocompetent persons at increased risk of complications from pneumococcal disease because of chronic illness (e.g. chronic cardiac, renal or pulmonary disease, diabetes mellitus, alcoholism and cirrhosis);
- Patients with cerebrospinal fluid leaks.

In Australia, the National Health and Medical Research Council (NHMRC) currently recommends the vaccination of tobacco smokers with the 23-valent polysaccharide pneumococcal vaccine.

PNEUMOVAX 23 is indicated for immunisation only 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.

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

4.2 DOSE AND METHOD OF 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 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 **Section 4.1 Therapeutic Indications**).

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.

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

In Australia, recommendations for revaccination are available in the Australian Immunisation Handbook.

Method of Administration
Do not inject intravenously. Intradermal administration should be avoided.

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.

PNEUMOVAX 23 vials and pre-filled syringes are for use in a single individual on one occasion only.

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

Single-Dose Vial

For Syringe Use Only: 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.

4.3 CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Immunocompromised patients

Effectiveness of PNEUMOVAX 23 in immunocompromised patients is not proven, but the high risk for disease and the potential benefits and safety of the vaccine justify vaccination.

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 **Section 4.2 Dose and Method of Administration**).

If the vaccine is used in persons receiving intensive immunosuppressive therapy, (e.g. in patients with Hodgkin's disease) the expected serum antibody response may not be obtained and potential impairment of future immune responses to pneumococcal antigens may occur.

Treatments with proven efficacy, such as penicillin prophylaxis, should be continued despite vaccination or revaccination with PNEUMOVAX 23.

General

Intradermal administration may cause severe local reactions.

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

Caution and appropriate care should be exercised in administering PNEUMOVAX 23 to individuals with severely compromised cardiac 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.

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

Use in renal impairment

See **Section 4.2 Dose and Administration, Revaccination**.

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 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.

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.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

In Australia, the National Health & Medical Research Council (NHMRC) advises that influenza vaccine can be administered concurrently with pneumococcal polysaccharide vaccine.

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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

(Category B2)

Animal reproduction studies have not been conducted with PNEUMOVAX 23. It is also not known whether PNEUMOVAX 23 can cause foetal harm when administered to pregnant women or can affect reproduction capacity. PNEUMOVAX 23 should be given to pregnant women only if clearly needed.

Use in lactation

It is not known whether this drug 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trial Experience

A clinical trial was undertaken to evaluate immunogenicity and safety of revaccination at 3-5 years following primary vaccination. Enrolled were 1008 subjects ≥ 50 years of age. The results were analysed separately for subjects ≥ 65 years of age (primary analysis), and 50-64 years (secondary analysis).

In this study, the overall injection-site adverse experience rate was higher after revaccination than after primary vaccination. For subjects ≥ 65 years of age, the rate was 52.9% following primary vaccination and 79.3% after revaccination. For subjects 50-64 years of age, the rates were similar (72.8% and 79.6%, respectively). The injection site reactions occurred within the 3 days monitoring period and typically resolved by day 5.

The study also analysed a composite endpoint including one or more of the following:

moderate pain, severe pain and/or large induration at the injection site. In both age groups, revaccination resulted in a higher reported rate of the composite endpoint than following

primary vaccination. Among subjects ≥ 65 years of age, the composite endpoint was reported by 10.4% of subjects following primary vaccination and 30.6% following revaccination. For subjects 50-64 years of age, the endpoint was reported by 18.9% after primary vaccination and 35.5% after revaccination.

The rate of overall systemic adverse experiences was similar after primary vaccination and revaccination, regardless of age. For subjects ≥ 65 years of age, the rates were 32.1% and 39.1%, respectively. For subjects 50-64 years of age, the rates were 48.8% and 47.4%, respectively. A generally small increase in post-vaccination analgesic use was observed in the four study groups (range from < 1% to 13%) and returned to baseline by day 5.

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.

Post-Marketing Experience
Cellulitis-like reactions have been reported in post-marketing experience. These cellulitis-like reactions were reported with primary vaccination or revaccination at a median onset time of 1 day after 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.

Tabulated Summary of Adverse Events
Table 2 below summarizes 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).

Table 2
Frequencies of the Adverse Events that were Reported in Clinical Trials and/or Post-Marketing Surveillance

Adverse events:	**Frequency:**
Blood and the lymphatic system disorders:	
Haemolytic anaemia* Leukocytosis Lymphadenitis Lymphadenopathy Thrombocytopenia**	Not known
Immune system disorders:	
Anaphylactoid reactions Angioneurotic oedema Serum sickness	Not known
Nervous system disorders:	
Febrile convulsions Guillain-Barré Syndrome Headache Paraesthesia Radiculoneuropathy	Not known
Gastrointestinal disorders:	
Nausea Vomiting	Not known
Skin and subcutaneous tissue disorders:	
Rash	Not known

Urticaria Erythema multiforme	
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
Extensive Swelling of the Vaccinated Limb	Rare[#]
Asthenia Chills Fever Injected limb mobility decreased Malaise Peripheral oedema[†]	Not known
Investigations:	
C-reactive protein increased	Not known

* In patients who have had other haematologic disorders.
** In patients with stabilized idiopathic thrombocytopenic purpura.
[#] With short onset time from vaccine administration; defined by clinical review of cases reporting the preferred terms of extensive swelling of the vaccinated limb, injection site cellulitis and cellulitis, all of which described cellulitis-like reactions."
[†] In the injected extremity.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

No specific information is available on the treatment of overdose.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

Epidemiology
Invasive pneumococcal disease (e.g. bacteraemia or meningitis) and pneumonia cause high morbidity and mortality in spite of effective antimicrobial control by antibiotics. Vaccination offers an effective means of further reducing the morbidity and mortality of this disease.

Risk factors
In addition to the very young and persons 65 years of age or older, patients with certain chronic conditions and disease states are at increased risk of developing pneumococcal infection and severe pneumococcal illness. Examples of such patients include individuals

with asplenia, immunocompromised patients, cirrhotic patients, immunocompetent patients with chronic cardiac, renal or pulmonary disease, and patients with cerebrospinal fluid leaks.

A case-control study has shown an increased risk of pneumococcal infection among cigarette smokers, suggesting that smoking is an important risk factor for invasive pneumococcal disease among immunocompetent adults.

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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

Clinical trials

Efficacy

The protective efficacy of pneumococcal vaccines containing 6 and 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.

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

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

In the United States, two postlicensure randomised 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 nonbacteraemic pneumonia. However, these studies may have lacked sufficient statistical power to detect a difference in the incidence of laboratory-confirmed, nonbacteraemic pneumococcal pneumonia between the vaccinated and nonvaccinated study groups.

A meta-analysis of nine randomised controlled trials of pneumococcal vaccine concluded that pneumococcal vaccine is efficacious in reducing the frequency of nonbacteraemic pneumococcal pneumonia among adults in low risk groups but not in high-risk groups. These studies may have been limited because of the lack of specific and sensitive diagnostic tests for nonbacteraemic 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.

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.

Only one case-control study did not document effectiveness against bacteraemic disease, possibly due to study limitations including small sample size and incomplete ascertainment of vaccination status in patients. 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.

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. 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 bacteraemic pneumococcal disease than patients who were not vaccinated.

Duration of Immunity
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 (see **Section 4.2 Dose and Method of Administration**).

Immunogenicity of PNEUMOVAX 23
It has been established that the purified pneumococcal capsular polysaccharides 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.

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 < 2 years whose immune systems are immature.

Immunogenicity following concomitant administration with zoster virus vaccine
In a double-blind, controlled clinical trial, 473 adults, 60 years of age or older, were randomized to receive ZOSTAVAX and PNEUMOVAX 23 concomitantly (N=237), or PNEUMOVAX 23 alone followed 4 weeks later by ZOSTAVAX alone (N=236). At four weeks postvaccination, the 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.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Not applicable.

Distribution

Not applicable.

Metabolism

Not applicable.

Excretion

Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

sodium chloride
phenol
water for injection

6.2 INCOMPATIBILITIES

Please refer to Section 4.5 Interactions with Other Medicines and Other Forms of Interactions for further information.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store unopened and opened vials and pre-filled syringes at 2°C to 8°C. All vaccine must be discarded after the expiration date.

6.5 NATURE AND CONTENTS OF CONTAINER

PNEUMOVAX 23 (pneumococcal vaccine, polyvalent) is supplied as follows:

- Carton of single-dose injection vial of vaccine (25 microgram/0.5 mL), in packs of 1* or 10*
- Carton of single-dose injection pre-filled syringe of vaccine (25 microgram/0.5 mL) in packs of 1 or 10

**Currently not supplied*

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Not applicable.

CAS number

Not applicable.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (Schedule 4)

8 SPONSOR

Merck Sharp & Dohme (Australia) Pty Limited
Level 1, Building A,
26 Talavera Road
Macquarie Park NSW 2113

Distributor

Seqirus (Australia) Pty Ltd.,
63 Poplar Road, Parkville, 3052
Victoria, Australia

9 DATE OF FIRST APPROVAL

22 July 1991

10 DATE OF REVISION

28 August 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.8	Replace “Cellulitis-like reactions at injection site” with “Extensive Swelling of the Vaccinated Limb”

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