Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

PNEUMOVAX 23 solution for injection in pre-filled syringe Pneumococcal Polysaccharide Vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The 0.5 mL dose of vaccine contains 25 micrograms of each of the following 23 pneumococcal polysaccharide serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F.
Excipient(s) with known effect
Sodium less than 1 mmol (23 mg) per dosage unit.
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe.

The vaccine is a clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

PNEUMOVAX 23 is recommended for active immunisation against pneumococcal disease in children aged from 2 years, adolescents and adults.

See section 5.1 for information on protection against specific pneumococcal serotypes.

4.2 Posology and method of administration

The immunisation schedules for PNEUMOVAX 23 should be based on official recommendations.

Posology

Primary vaccination: Adults and children of 2 years of age or older- one single dose of 0.5 millilitre by intramuscular or subcutaneous injection. PNEUMOVAX 23 is not recommended for use in children below 2 years of age as the safety and efficacy of the vaccine have not been established and the antibody response may be poor.

Special dosing:
It is recommended that pneumococcal vaccine should preferably be given at least two weeks before elective splenectomy or the initiation of chemotherapy or other immunosuppressive treatment. Vaccination during chemotherapy or radiation therapy should be avoided.

Following completion of chemotherapy and/or radiation therapy for neoplastic disease, immune responses to vaccination may remain diminished. The vaccine should not be administered any sooner than three months after completion of such therapy. A longer delay may be appropriate for patients who have received intensive or prolonged treatment (see section 4.4).

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

Re-vaccination:
One single dose of 0.5 millilitre by intramuscular or subcutaneous injection.

The specific timing of, and need for, re-vaccination should be determined on the basis of available official recommendations.

See section 5.1 for information on immune responses following re-vaccination.

Re-vaccination at an interval of less than three years is not recommended because of an increased risk of adverse reactions. The rates of local and, in persons aged ≥ 65 years, some systemic reactions have been shown to be higher after re-vaccination than after primary vaccination when three to five years have elapsed between doses. See section 4.8.

There are very limited clinical data regarding administration of more than two doses of PNEUMOVAX 23.

Adults
Healthy adults should not be re-vaccinated routinely.

Re-vaccination may be considered for persons at increased risk of serious pneumococcal infection who were given pneumococcal vaccine more than five years earlier or for those known to have a rapid decline in pneumococcal antibody levels. For selected populations (e.g., asplenics) who are known to be at high risk of fatal pneumococcal infections, re-vaccination at three years may be considered.

Children
Healthy children should not be re-vaccinated routinely.

Children of 10 years of age and over
May be considered for re-vaccination according to the adult recommendation (see above).

Children between the ages of 2 and 10 years
Should only be considered for re-vaccination after 3 years if they are at high risk of pneumococcal infection (e.g., those with nephrotic syndrome, asplenia or sickle cell disease).

Method of administration

A dose of 0.5 mL from a single-dose of PNEUMOVAX 23 is to be injected intramuscularly (IM) or subcutaneously (SC).

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Delay the use of the vaccine in any significant febrile illness, other active infection or when a systemic reaction would pose a significant risk except when this delay may involve even greater risk.

PNEUMOVAX 23 should never be injected intravascularly, and precautions should be taken to make sure the needle does not enter a blood vessel. Also, the vaccine should not be injected intradermally, as injection by that route is associated with increased local reactions.

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 after a first or second dose. Accordingly, such patients may not be as well protected against pneumococcal disease as immunocompetent individuals.

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

For patients receiving immunosuppressive therapy, the time to recovery of the immune response varies with the illness and the therapy. Significant improvement in antibody response has been observed for some patients during the two years following the completion of chemotherapy or other immunosuppressive therapy (with or without radiation), particularly as the interval between the end of treatment and pneumococcal vaccination increased (see section 4.2).

As with any vaccine, adequate treatment provisions including epinephrine (adrenaline) should be available for immediate use should an acute anaphylactic reaction occur.

Required prophylactic antibiotic therapy against pneumococcal infection should not be stopped after pneumococcal vaccination.

Patients at especially increased risk of serious pneumococcal infection (e.g., asplenics and those who have received immunosuppressive therapy for any reason), should be advised regarding the possible need for early antimicrobial treatment in the event of severe, sudden febrile illness.

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

A clinical study of primary vaccination and revaccination was conducted in 629 adults ≥65 years of age and 379 adults 50 to 64 years of age. The data obtained suggested that the rates of injection site and systemic adverse reactions among subjects ≥65 years of age were not higher than the rates amongst subjects 50 to 64 years of age. It should be noted that, in general, 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 (see section 4.2).

Sodium
This medicinal product contains less than 1 mmol (23 mg) sodium per dosage unit and is considered to be essentially sodium-free.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interactions

Pneumococcal vaccine can be administered simultaneously with influenza vaccine as long as different needles and injection sites are used.

The concomitant use of PNEUMOVAX 23 and ZOSTAVAX resulted in reduced immunogenicity of ZOSTAVAX in a small clinical trial (see section 5.1). However, data collected in a large observational study did not indicate increased risk for developing herpes zoster after concomitant administration of the two vaccines.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal studies are insufficient with respect to effects on reproductive toxicity (see section 5.3). The vaccine should not be used during pregnancy unless clearly necessary (the potential benefit must justify any potential risk to the foetus).

Breast-feeding
It is unknown whether this vaccine is excreted in human milk. Caution should be exercised when it is administered to a nursing mother.

Fertility
The 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

a. Summary of the safety profile

A clinical study of primary vaccination and revaccination was conducted in 379 adults 50 to 64 years of age and 629 adults ≥65 years of age. The rate of overall injection site adverse reactions in the older revaccination group was comparable to the rate observed in the younger revaccination recipients. Injection site reactions occurred within 3 days of vaccination and typically resolved by day 5. The rate of systemic and vaccine related systemic reactions in the older revaccination group was comparable to the rate observed in the younger revaccination recipients. The most common systemic adverse events overall were as follows: asthenia/fatigue, myalgia and headache. Symptomatic treatment resulted in complete recovery in most cases.

b. Tabulated list of adverse reactions

The table below summarises the frequencies of the adverse reactions 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 reactions	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 Urticaria	Not known
Musculoskeletal and connective tissue 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
Injection site cellulitis[†]	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 stabilised idiopathic thrombocytopenic purpura
† with short onset time from vaccine administration
†† in the injected extremity

c. Paediatric population

A clinical study was conducted to evaluate the safety and immunogenicity of Pneumococcal polysaccharide vaccine in 102 individuals, including 25 subjects 2 to 17 years of age, 27 subjects 18 to 49 years of age, and 50 subjects 50 years of age and older. The type and severity of injection-site and systemic adverse reactions reported among children 2 to 17 years of age were comparable to those reported among adults 18 years of age and older. However, the proportions of subjects reporting injection-site and systemic adverse reactions were higher among subjects 2 to 17 years of age than those 18 years of age and older.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: pneumococcal vaccines, pneumococcus, purified polysaccharides antigen, ATC code: J07AL01

The vaccine is prepared from purified pneumococcal capsular polysaccharide antigens derived from the 23 serotypes that account for approximately 90% of invasive pneumococcal disease types. The following pneumococcal capsular polysaccharides are included: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F.

Immunogenicity
The presence of type-specific humoral antibodies is generally thought to be effective in preventing pneumococcal disease. A ≥2-fold increase in antibody level following vaccination was associated with efficacy in clinical trials of polyvalent pneumococcal polysaccharide vaccines. However, the concentration of anti-capsular antibody required to protect against pneumococcal infection caused by any specific capsular type has not been established. Most persons aged ≥2 years (85 to 95%) respond to vaccination by making antibody to most or all of the 23 pneumococcal polysaccharides in the vaccine. Bacterial capsular polysaccharides induce antibodies primarily by T-cell-independent mechanisms and elicit poor or inconsistent antibody responses in children aged <2 years.

Antibodies can be detected by the third week following vaccination but may decline as soon as 3 to 5 years after vaccination and a more rapid decline may occur in some groups (e.g., children and the elderly).

Immune responses to eight of the polysaccharides in PNEUMOVAX 23 have been compared following administration of a single dose of vaccine or placebo. Four groups of subjects were entered as defined by age (50-64 years and ≥65 years) and by prior vaccination status (no prior vaccination or 1 vaccination 3-5 years previously).

- Prior to vaccination, antibody levels were higher in the revaccination group than in the primary vaccination group.
- In the primary and revaccination groups the geometric mean antibody levels for each serotype increased from pre- to post-vaccination.
- The ratios in geometric mean antibody concentrations by serotype at day 30 between those who were revaccinated and those who were given primary vaccination ranged from 0.60-0.94 in the ≥65 years group and from 0.62-0.97 for the group aged between 50-64 years.

The clinical relevance of the lower antibody responses observed on revaccination compared to primary vaccination is not known.

Concomitant administration

In a double-blind, controlled clinical trial, 473 adults, 60 years of age or older, were randomised to receive a single dose of ZOSTAVAX either concomitantly (N=237), or nonconcomitantly (N=236) with 23-valent Pneumococcal polysaccharide vaccine. At four weeks post-vaccination, the VZV-specific immune responses following concomitant use were not similar to the VZV-specific immune responses following nonconcomitant administration. However in a US effectiveness cohort study of 35,025 adults ≥60 years old, no increased risk of herpes zoster (HZ) was observed in individuals who received ZOSTAVAX and 23-valent pneumococcal polysaccharide vaccine concomitantly (N=16,532) as compared to individuals receiving ZOSTAVAX one month to one year after 23-valent pneumococcal polysaccharide vaccine (N=18,493) in routine practice. The adjusted hazard ratio comparing the incidence rate of HZ in the two groups was 1.04 (95% CI, 0.92, 1.16) over a median follow-up of 4.7 years. The data do not indicate that concomitant administration of the two vaccines alters the effectiveness of ZOSTAVAX.

Efficacy

The efficacy of polyvalent Pneumococcal polysaccharide vaccine was established for pneumococcal pneumonia and bacteraemia in randomised controlled trials that were conducted among novice gold miners in South Africa. The protective efficacy against pneumococcal pneumonia, the primary endpoint in these studies, was 76.1% with a 6-valent vaccine and 91.7% with a 12-valent preparation. In trials conducted in populations for which the vaccine is indicated (see section 4.1), vaccine effectiveness was reported to be 50 to 70% (e.g., persons with diabetes mellitus, chronic cardiac or pulmonary disease, and anatomic asplenia).

One study found that vaccination was significantly protective against invasive pneumococcal disease caused by several individual serotypes (e.g., 1, 3, 4, 8, 9V, and 14). For other serotypes, the number of cases detected in this study were too small to draw conclusions about serotype specific protection.

The results from one epidemiologic study suggest that vaccination may provide protection for at least 9 years after receipt of the initial dose of vaccine. Decreasing estimates of effectiveness have been reported with increasing interval after vaccination, particularly among the very elderly (persons aged ≥85 years).

The vaccine is not effective for the prevention of acute otitis media, sinusitis and other common upper respiratory tract infections.

5.2 Pharmacokinetic properties

Since Pneumovax 23 is a vaccine, pharmacokinetic studies were not performed.

5.3 Preclinical safety data

No preclinical safety testing was performed using the vaccine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Sodium chloride
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

28 months.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C)
Do not freeze.

6.5 Nature and contents of container

0.5 mL solution in pre-filled syringe (glass) with a plunger stopper (bromobutyl elastomer) and tip cap (isoprene bromobutyl blend-polyisoprene or styrene-butadiene rubber) without needle.
0.5 mL solution in pre-filled syringe (glass) with a plunger stopper (bromobutyl elastomer) and tip cap (isoprene bromobutyl blend-polyisoprene or styrene-butadiene rubber), with 1 separate needle.
0.5 mL solution in pre-filled syringe (glass) with a plunger stopper (bromobutyl elastomer) and tip cap (isoprene bromobutyl blend-polyisoprene or styrene-butadiene rubber), with 2 separate needles.

Pack size of 1 or 10.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

The normal appearance of the vaccine is a clear, colourless solution.
Parenteral products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. In the event of either being observed, discard the medicinal product.
The vaccine should be used directly as supplied; no dilution or reconstitution is necessary.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Merck Sharp & Dohme Ireland (Human Health) Limited
Red Oak North
South County Business Park
Leopardstown
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1286/055/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

January 2020