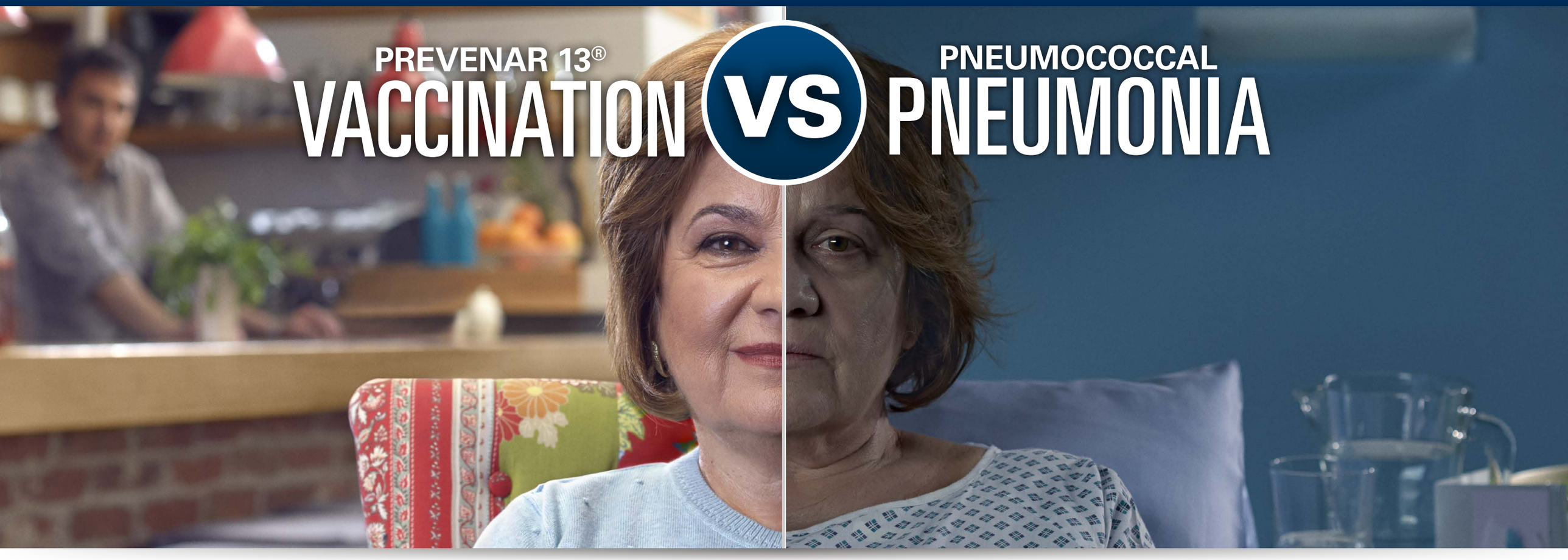


Prevenar 13®: The background

By the end of this eModule you should:

- Understand how Prevenar 13® works
- Understand what evidence supports the use of Prevenar 13® in adults
- Feel confident that you know who is appropriate for Prevenar 13®, and who isn't

Prevenar 13®
Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)

This eModule is provided to you by Pfizer Ltd. It is not intended to replace your guidelines, protocols and SOPs.*

*SOP: Standard operating procedures

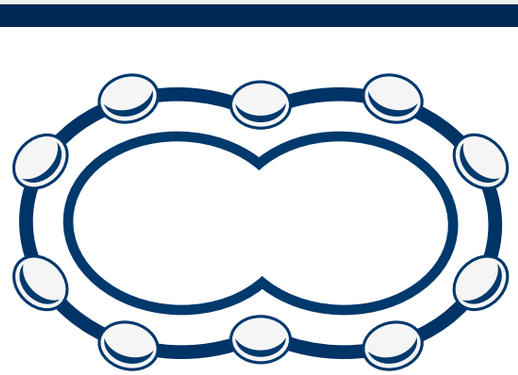
Begin

PP-PNA-GBR-0394 February 2020

How does Prevenar 13® work?

Prevenar 13® helps protect against pneumococcal pneumonia[1]

The bacteria that cause pneumococcal infections such as pneumococcal pneumonia *(Streptococcus pneumoniae)* are **covered by a polysaccharide capsule.**[2,3]



Prevenar 13® contains[13] polysaccharides from the capsules of **13 types of** *Streptococcus pneumoniae*.[1]

Administering the vaccine therefore **introduces these polysaccharides** to the recipient's immune system so it is able to **produce an immune response** against them.[4]

These polysaccharide capsules vary among *Streptococcus pneumoniae*, and this variation is what makes some *Streptococcus pneumoniae* strains more harmful (or pathogenic) than other strains (the various versions or strains are called serotypes).[2]

Prevenar 13® will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine.

Prevenar 13® does not provide 100% protection against vaccine serotypes nor protect against nonvaccine serotypes.

The natural immune response to bacterial polysaccharides is not long-lasting[4-7]

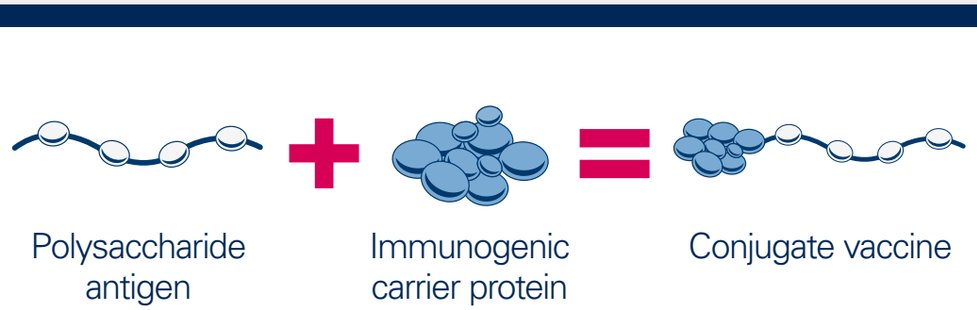
The **level of immune response** against a foreign body (antigen) is dependent on many factors, including how much of a perceived **threat it presents.**[7] This is known as immunogenicity.

Bacterial polysaccharides alone have quite low immunogenicity, and therefore **do not stimulate** the pathways required to develop **immune memory.**[4-7]

This means the body's ability to generate an immune response is **relatively short-lived.**[4-6]

Prevenar 13® is the only pneumococcal conjugate vaccine licensed for adults[1,8]

In conjugate vaccines, the polysaccharide antigens are **bound (or conjugated) to a protein.**[4]



As **proteins** naturally have greater immunogenicity than **polysaccharides**, the protein-polysaccharide mixture is able to stimulate the pathways necessary to develop **immune memory.**[4-6]

Immune memory allows the immune system to **remember** the foreign body (antigen) and **respond to it in the future.**[5] Conjugate vaccines can therefore provide **lasting protection.**[4-6]

Immune memory has been demonstrated with Prevenar 13® in infants, memory B-cell production has not been studied with Prevenar 13® in adults.

The above information is general vaccine information and not all information is specific to pneumococcal vaccines.

What clinical evidence supports the use of Prevenar 13®?

Prevenar 13® offers proven, lasting protection against pneumococcal pneumonia[9]

In a large-scale efficacy trial, which included 84,496 subjects ≥65 years of age:[9]

46%

Prevenar 13® **reduced** the first episode incidence of vaccine-type community-acquired **pneumococcal pneumonia** by **46% vs. placebo** (p<0.001; 49/42,240 vs. 90/42,256)[9]

Prevenar 13® demonstrated **lasting protection**: efficacy of Prevenar 13® vs. placebo persisted throughout the 4-year trial without evidence of waning (post-hoc analysis)[9]

Prevenar 13® will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine.

Prevenar 13® does not provide 100% protection against vaccine serotypes nor protect against nonvaccine serotypes.

Prevenar 13® generates a functional antibody response, regardless of age[1,10-11]

Clinical trials included healthy adults aged ≥18 years, as well as immunocompetent adults with stable underlying comorbidities who were at increased risk for invasive pneumococcal disease[1]

	Functional antibody response in adults aged:		
Serotypes	**18–49 years***	**50–64 years***	**≥70 years†**
1	✓	✓	✓
3	✓	✓	✓
4	✓	✓	✓
5	✓	✓	✓
6A	✓	✓	✓
6B	✓	✓	✓
7F	✓	✓	✓
9V	✓	✓	✓
14	✓	✓	✓
18C	✓	✓	✓
19A	✓	✓	✓
19F	✓	✓	✓
23F	✓	✓	✓

*Pneumococcal vaccination-naïve; †Previously vaccinated with Pneumococcal Polysaccharide Vaccine (PPV)

Prevenar 13® is generally well tolerated[1]

For adults aged 18 years or older, common (reported in at least 1% but less than 10% of participants) or very common (reported in at least 10% of participants) adverse reactions reported in Prevenar 13® clinical trials were:[1]

- Injection-site reactions (redness; swelling and/or hardness; severe tenderness and/or severe pain)
- Severe limitation of arm movement
- Decreased appetite
- Headache
- Diarrhoea
- Vomiting
- Chills
- Fatigue
- Rash
- Joint or muscle pain
- Pyrexia

Other, uncommon, adverse reactions reported were nausea, hypersensitivity reactions (including facial swelling, shortness of breath, narrowing of the airways), and enlarged lymph nodes near the injection site.[1]

The safety profile for Prevenar 13® has been investigated in clinical studies in over **90,000 adults** aged from **18 to 101 years**[1]

Who is appropriate for Prevenar 13®?

Prevenar 13® can be used to help protect adults against pneumococcal pneumonia[1]

In adults, Prevenar 13® is given intramuscularly as a single 0.5 ml dose.[1]

Adults can also receive Prevenar 13® with the flu vaccine (trivalent and quadrivalent)[1]

Very few adults are unable to receive Prevenar 13®[1]

The only individuals for whom Prevenar 13® is contraindicated are those who are:[1]

Hypersensitive (allergic) to:[1]

- **Pneumococcal polysaccharides**
- **Diphtheria toxoid**
  The carrier protein used in Prevenar 13® to boost the immune response to bacterial polysaccharides is a non-toxic version of diphtheria toxoid
- **Aluminium phosphate**
  Aluminium salts are used in many vaccines to stimulate the immune system to respond to the vaccine, enhancing the immune response
- **Sodium chloride, succinic acid, Polysorbate 80 and water for injections**
  These are the other ingredients used in the vaccine

Pregnant[1]

Individuals following a low-sodium diet are not specifically contraindicated to receive Prevenar 13® as the sodium content is less than 1 mmol (23 mg) per dose, essentially ‘sodium free’.[12]

However, certain medical conditions require precautions to be taken[1]

Acute illnesses[1]

Administration of Prevenar 13® should be postponed in **any** individual suffering from an **acute, severe febrile illness (fever).** A minor infection, such as a cold, should not result in the deferral of vaccination.

Bleeding disorders[1]

Individuals with thrombocytopaenia, or any coagulation disorder that would contraindicate intramuscular injection, must not be given Prevenar 13® as an intramuscular injection. It may be given subcutaneously if the potential benefit clearly outweighs the risks.

Can adults receive both Prevenar 13® and PPV?

PPV contains polysaccharides from 11 pneumococcal serotypes that are not contained within Prevenar 13®.[3] It therefore may be appropriate to **administer both vaccines** to the same person for **additional serotype coverage**.[3]

In clinical studies, immune responses for all 13 serotypes were lower when Prevenar 13® was given 1 year after PPV than when it was given to PPV-naïve patients.[1]

Although the clinical significance of this is unknown, it is recommended that if PPV and Prevenar 13® are both administered to the same person, **Prevenar 13® should be given first**.[1]

When Prevenar 13® is administered first, the interval between vaccines should be **at least 2 months**.[3]

If an individual has previously received PPV, the interval before administering Prevenar 13® should be at least **6 months**.[3]

If a patient is **pneumococcal-vaccine naïve:**

Visit 1	→	At least **2 months later**	→	Visit 2
Prevenar 13®				PPV

If a patient has **previously received PPV:**

Visit 1	→	At least **6 months later**	→	Visit 2
PPV				**Prevenar 13®**

Information regarding Prevenar 13® is available for individuals with specific ingredient concerns

Many individuals are concerned about the ingredients of vaccines.
Below are the answers to some frequently asked ingredient queries.

Prevenar 13® **does not contain** any ingredients derived from **nuts**.[13]

Prevenar 13® **does not contain** any ingredients derived from **eggs**.[13] Eggs are also not used in the manufacturing process for Prevenar 13®.

Latex

Prevenar 13® pre-filled syringes are **latex-free**.[1,13]

HG Mercury

Prevenar 13® **does not, and never did, contain** the **mercury**-based preservative **thiomersal**.[13]

No **blood** products are used in the manufacture of Prevenar 13®.[13]

CH_2O

Prevenar 13® **does not contain formaldehyde**, and formaldehyde is not used in the manufacturing process for Prevenar 13®.[13]

Prevenar 13® itself **does not contain** gelatin, or any other material of **animal** origin.[13] However, materials of ovine (sheep), bovine (cow) and caprine (goat) origin are used at an early stage of the manufacturing process.[13]

Prevenar 13® has also received **halal certification**.[13]

Pfizer cannot guarantee that individual vaccines have never come into contact with the allergens listed opposite.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Congratulations!

You have now completed this eModule.

In summary:

- Prevenar 13® is the only pneumococcal conjugate vaccine licensed for adults[1,8]
- Prevenar 13® has been clinically proven to help prevent vaccine type pneumococcal pneumonia in adults vs. placebo[9]
- Prevenar 13® demonstrated lasting protection: efficacy of Prevenar 13® vs. placebo persisted throughout the 4-year trial without evidence of waning (post-hoc analysis)[9]
- Prevenar 13® is **generally well tolerated**[1]
- Very few adults are **unable to receive** Prevenar 13®[1]
  - The **only** individuals for whom Prevenar 13® **is contraindicated** are those who are hypersensitive to any of the ingredients of the vaccine or pregnant[1]

References

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5. Pollard AJ, et al. Maintaining protection against invasive bacteria with protein polysaccharide vaccines. Nat Rev Immunol. 2009;9:213-220.
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10. Jackson LA, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naive adults. Vaccine. 2013;31(35):3577-3584.
11. Jackson LA, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults 70 years of age and older previously vaccinated with 23-valent pneumococcal polysaccharide vaccine. Vaccine. 2013;31(35):3585-3593.
12. Prevenar 13® Patient Information Leaflet. January 2020.
13. Pfizer. Data on File. Ingredients. January 2015.

Prevenar 13®: The background

Back

ABBREVIATED PRESCRIBING INFORMATION FOR ADULT INDICATION

Prevenar 13® suspension for injection
Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)
Presentation: Each 0.5ml dose of Prevenar 13 contains 2.2 micrograms of each of the following polysaccharide serotypes: 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F and 4.4 micrograms of polysaccharide serotype 6B. Each polysaccharide is conjugated to the CRM_{197} carrier protein and adsorbed on aluminium phosphate. 1 dose (0.5 ml) contains approximately 32 µg CRM_{197} carrier protein and 0.125 mg aluminium.
Indications: Active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in adults ≥18 years of age and the elderly. The use of Prevenar 13 should be determined on the basis of official recommendations taking into consideration the risk of invasive disease and pneumonia in different age groups, underlying comorbidities as well as the variability of serotype epidemiology in different geographical areas.
Dosage and Administration: For intramuscular injection.
Adults ≥18 years of age and the elderly: One single dose. The need for revaccination with a subsequent dose of Prevenar 13 has not been established. Regardless of prior pneumococcal vaccination status, if the use of 23 valent pneumococcal polysaccharide vaccine is considered appropriate, Prevenar 13 should be given first. **Special Populations:** Individuals who have underlying conditions predisposing them to invasive pneumococcal disease (such as sickle cell disease or HIV infection) including those previously vaccinated with one or more doses of 23-valent pneumococcal polysaccharide vaccine may receive at least one dose of Prevenar 13. In individuals with an haematopoietic stem cell transplant (HSCT), the recommended immunisation series consists of four doses of Prevenar 13, each of 0.5 ml. The primary series consists of three doses, with the first dose given at 3 to 6 months after HSCT and with an interval of at least 1 month between doses. A fourth (booster) dose is recommended 6 months after the third dose. **Contra-indications:** Hypersensitivity to the active substances, to any of the excipients, or to diphtheria toxoid. As with other vaccines, the administration of Prevenar 13 should be postponed in subjects suffering from acute, severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.
Warnings and Precautions: Do not administer intravascularly. Appropriate medical treatment and supervision must be available in case of anaphylaxis. It should not be given to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, but may be given subcutaneously if the potential benefit clearly outweighs the risks. Prevenar 13 will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine, and will not protect against other microorganisms that cause invasive disease and pneumonia. As with any vaccine, Prevenar 13 may not protect all individuals receiving the vaccine from pneumococcal disease. Individuals with impaired immune responsiveness, whether due to the use of immuno-suppressive therapy, a genetic defect, human immunodeficiency virus (HIV) infection, or other causes, may have reduced antibody response to active immunisation. Safety and immunogenicity data are available for a limited number of individuals with sickle cell disease, HIV infection, or with an HSCT. Safety and immunogenicity data for Prevenar 13 are not available for individuals in other specific immuno-compromised groups (e.g., malignancy, or nephrotic syndrome) and vaccination should be considered on an individual basis.
Adults aged 50 years and older: When Prevenar 13 was given concomitantly with trivalent inactivated influenza vaccine (TIV), the immune responses to Prevenar 13 were lower compared to when Prevenar 13 was given alone, however, there was no long-term impact on circulating antibody levels. The immune responses to Prevenar 13 were noninferior when Prevenar 13 was given concomitantly with quadrivalent inactivated influenza vaccine (QIV) compared to when Prevenar 13 was given alone. As with concomitant administration with trivalent vaccines, immune responses to some pneumococcal serotypes were lower when both vaccines were given concomitantly.
Fertility, Pregnancy & Lactation: There are no data from the use of pneumococcal 13-valent conjugate vaccine in pregnant women. Therefore the use of Prevenar 13 should be avoided during pregnancy. It is unknown whether pneumococcal 13-valent conjugate is excreted in human milk. **Side Effects:** Adverse reactions reported in clinical studies or from the post-marketing experience are listed in this section per system organ class, in decreasing order of frequency and seriousness. **Adults ≥18 years of age, and the elderly:** ***Very common*** (≥ 1/10): Decreased appetite, headaches, diarrhoea, vomiting, rash, chills; fatigue; injection-site erythema; injection-site induration/swelling; injection-site pain/tenderness; limitation of arm movement, arthralgia; myalgia. ***Common*** (≥ 1/100 to < 1/10): Vomiting, pyrexia. ***Uncommon*** (≥ 1/1,000 to < 1/100): Nausea, hypersensitivity reaction including face oedema, dyspnoea, bronchospasm, lymphadenopathy localized to the region of the injection site. ***Additional information in special populations***: Adults with HIV infection have similar frequencies of adverse reactions, except that pyrexia and vomiting were very common and nausea common. Adults with an HSCT have similar frequencies of adverse reactions, except that pyrexia and vomiting were very common. **Legal Category:** POM. **Package Quantities:** Pack of 1 single-dose pre-filled syringe (with separate needle) or pack of 10 single-dose pre-filled syringes. **Cost:** Cost for supply outside the UK routine childhood immunisation programme: Single-dose pre-filled syringe (with separate needle) pack of 1: £49.10; single-dose pre-filled syringe pack of 10: £491.
Marketing Authorisation Numbers: Single-dose pre-filled syringe (with separate needle) pack of 1: EU/1/09/590/002, single-dose pre-filled syringe pack of 10: EU/1/09/590/003. **Marketing Authorisation Holder:** Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.
For full prescribing information and details of other side effects see Summary of Product Characteristics.
Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Last revised: 09/2018. Ref: PN Adult 5_0.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161