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Pneumococcal

Pneumococcal meningitis

NOTIFIABLE

Pneumococcal

The disease

Pneumococcal disease is the term used to describe infections caused by the bacterium *Streptococcus pneumoniae* (also known as the pneumococcus).

S. pneumoniae is an encapsulated Gram-positive coccus. The capsule is the most important virulence factor of *S. pneumoniae*; pneumococci that lack the capsule are normally not virulent. Over 90 different capsular types have been characterised. Prior to the routine conjugate vaccination programme, around 69% of invasive pneumococcal infections were caused by the ten (14, 9V, 1, 8, 23F, 4, 3, 6B, 19F, 7F) most prevalent serotypes (Trotter *et al.*, 2010).

Some serotypes of the pneumococcus may be carried in the nasopharynx without symptoms, with disease occurring in a small proportion of infected individuals. Other serotypes are rarely identified in the nasopharynx but are associated with invasive disease. The incubation period for pneumococcal disease is not clearly defined but it may be as short as one to three days. The organism may spread locally into the sinuses or middle ear cavity, causing sinusitis or otitis media. It may also affect the lungs to cause pneumonia or cause systemic (invasive) infections including bacteraemic pneumonia, bacteraemia and meningitis.

Transmission is by aerosol, droplets or direct contact with respiratory secretions of someone carrying the organism. Transmission usually requires either frequent or prolonged close contact. There is a seasonal variation in pneumococcal disease, with peak levels in the winter months.

History and epidemiology of the disease

Invasive pneumococcal disease is a major cause of morbidity and mortality. In 2005/6, 6,346 cases of invasive pneumococcal disease were confirmed in England and Wales (Ladhani *et al.*, 2018). It particularly affects the very young, the elderly, those with an absent or non-functioning spleen and those with other causes of impaired immunity. Recurrent infections may occur in association with skull defects, cerebrospinal fluid (CSF) leaks, cochlear implants or fractures of the skull.

There are three types of pneumococcal vaccine licensed in the UK which provide protection against different serotypes, detailed in Table 25.1. The vaccines are inactivated, do not contain thiomersal and do not contain live organisms so cannot cause the diseases against which they protect.

Vaccine type	Licensed vaccine	Serotypes covered
Pneumococcal polysaccharide vaccine (PPV23)	Pneumococcal Polysaccharide Vaccine®	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F
Pneumococcal conjugate vaccine (PCV13)	Prevenar13®	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
Pneumococcal conjugate vaccine (PCV10)	Synflorix®	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F.

Table 25.1. Pneumococcal vaccines available in the UK.

Pneumococcal polysaccharide vaccine

PPV23 contains purified capsular polysaccharide from each of 23 common capsular types of pneumococcus. Most healthy adults develop a good antibody response to a single dose of PPV23 by the third week following immunisation. Children younger than two years of age show poor antibody responses to immunisation with PPV23 and there is no evidence of effectiveness of PPV23 in this age group (Grabenstein et al., 2017).

In the UK, PPV23 has been recommended for risk groups since 1992 and for all people aged 65 and over since 2003. PPV23 has a moderate short-term effectiveness of 41% against invasive pneumococcal disease (IPD) caused by the vaccine serotypes in adults aged 65 years and over during the first two years after vaccination, with vaccine effectiveness being higher among healthy individuals compared to those with underlying medical conditions (Djennad et al., 2019). There is some evidence for PPV23 offering protection against non-bacteraemia pneumococcal pneumonia (Diao et al., 2016).

The length of protection offered by PPV23 in risk groups and in older adults is variable and serotype-dependent. Post-immunisation antibody levels usually begin to wane after about five years but may decline more rapidly in asplenic patients and children with nephrotic syndrome (Butler et al., 1993).

Pneumococcal conjugate vaccines (PCV)

PCVs have been developed containing polysaccharides from the most common capsular types. Conjugating the polysaccharide to proteins, using similar manufacturing technology to that used successfully for *Haemophilus influenzae* type b (Hib) and meningococcal conjugate vaccines, improves the antibody response in young children. Pneumococcal conjugate vaccines are known to be highly immunogenic in children from two months of age.

In 2006, the UK introduced the 7-valent PCV (PCV7) into the infant immunisation programme, alongside a 12-month catch-up for all children up to 2 years of age. Although PCV7 was licensed as a 3+1 schedule at the time, the UK implemented a reduced 2+1 schedule at 2 months, 4 months and 1 year of age following a review of evidence by the Joint Committee of Vaccination and Immunisation (JCVI), including the results of a clinical

trial demonstrating similar immunogenicity in infants receiving PCV7 at 2, 3 and 4 months or 2 and 4 months of age (Goldblatt et al., 2006). The UK 2+1 PCV7 immunisation programme achieved very high vaccine coverage (>90%) and resulted in a rapid and sustained reduction in IPD due to the PCV7 serotypes and in IPD overall, across all age groups because of the direct and indirect (herd) protection (Miller et al., 2011). The indirect protection was achieved through the prevention of pneumococcal carriage in the vaccinated child’s nasopharynx and onward transmission to others. The large declines in PCV7-type IPD were partially offset by small increases in non-PCV7 type IPD across all age groups. The success of the UK pneumococcal immunisation programme subsequently led to a change in PCV7 licensure allowing the reduced 2+1 schedule to be used worldwide.

In April 2010, PCV13 replaced PCV7, also at a 2+1 schedule, which led to further reductions in the additional serotypes in PCV13; by 2013/14, more than 70% of all IPD cases were due to serotypes not covered by PCV13 (Waight et al., 2015). Since 2013/14 an increase in overall incidence of invasive pneumococcal disease has been observed, largely due to increases in non-PCV13 vaccine serotypes (especially serotypes 8, 12F and 9N) and mainly in older age groups. Eight of the ten most prevalent serotypes currently causing invasive pneumococcal disease are included in PPV23 (Ladhani et al., 2018) (Figure 25.1).

Another vaccine that protects against 10 pneumococcal serotypes (PCV10) is licensed. This vaccine contains pneumococcal polysaccharide that are conjugated to protein D (derived from non-typeable *Haemophilus influenzae*), tetanus toxoid or diphtheria toxoid carrier proteins. PCV10 does not contain serotypes 3, 6A or 19A and is not currently used in the UK immunisation programme.

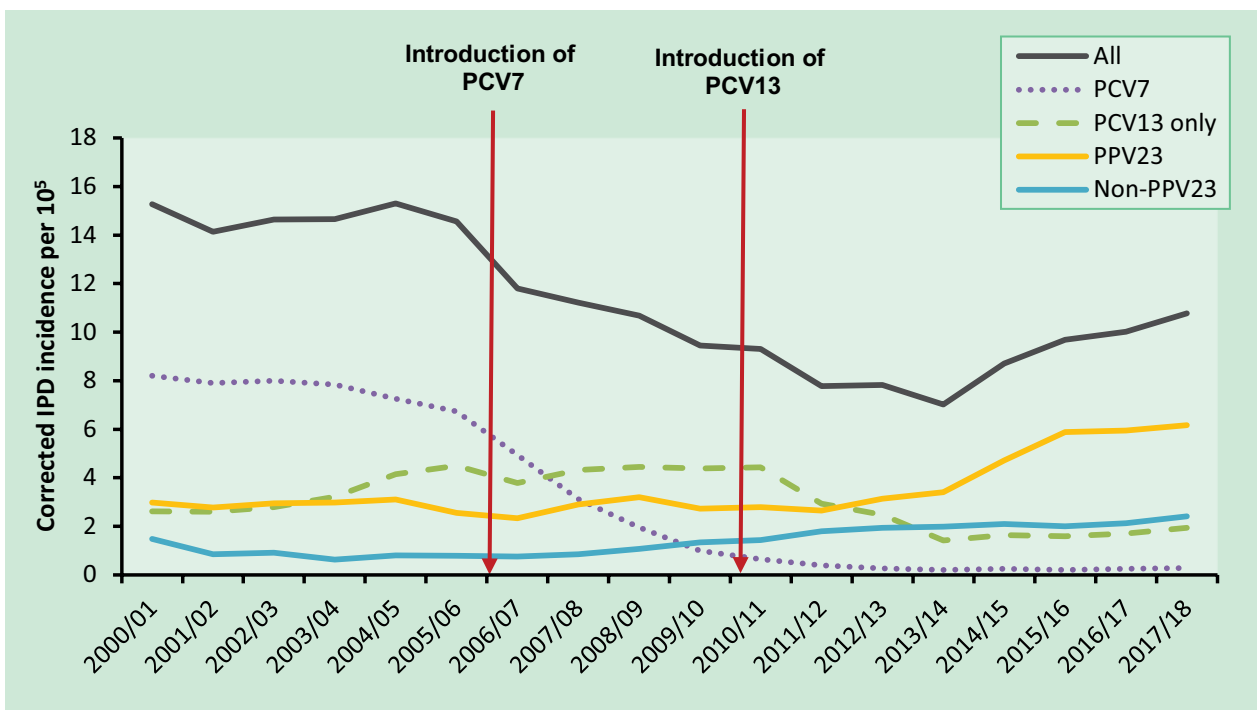


Figure 25.1 Corrected IPD incidence in England between 2000/01 and 2017/2018 by serotype group

Given the success of the programme, both in those vaccinated, and in the wider population (through herd immunity), the JCVI reviewed the infant pneumococcal

vaccination programme in 2017 and 2018. A UK study showed similar immunogenicity after the booster dose when one infant priming dose plus a booster (the 1+1 schedule) were compared to two infant priming doses plus a booster (the 2+1 schedule) (Goldblatt *et al.*, 2017). JCVI recommended that, as the maximum direct and indirect benefit from the PCV13 programme was likely to have been achieved, the UK schedule could change from a 2+1 (with doses given at 8 weeks, 16 weeks and one year of age) to a 1+1 schedule (with doses given at 12 weeks and one year of age) (Choi *et al.*, 2019). This change was implemented in 2020.

Storage

Please see [Chapter 3 Storage, distribution and disposal](#) for information on storage.

Presentation

Information on the presentation of PCV10, PCV13 and PPV23 can be found in the Summary of Product Characteristics (SPCs), available at <https://www.medicines.org.uk/emc>.

PCV10 and PCV13

Storage can cause the vaccine to separate into a white deposit and clear supernatant. The vaccine should be shaken well to obtain a white homogeneous suspension and should not be used if there is any residual particulate matter after shaking.

PPV23

The polysaccharide vaccine should be inspected before being given to check that it is clear and colourless.

Vaccines must not be given intravenously.

Dosage and schedule

PCV13

For children and adults in risk groups, refer to Table 25.2 and the Risk Groups section below.

Routine immunisation for infants under one year of age:

- a single priming dose of 0.5ml of PCV13 at 12 weeks of age
- a booster dose of 0.5ml of PCV13 at one year of age (on or after their first birthday) given at the same time as the Hib/MenC, 4CMenB and MMR vaccines (see [Chapter 11: UK immunisation schedule](#))

Additional PCV13 doses are not recommended for routine immunisation but may be indicated for some risk groups (refer to Table 25.2 and Table 25.3 below).

PPV23

Adults aged 65 years and over, and clinical risk groups aged 2 years or over:

- a single dose of 0.5ml of PPV23

Antibody levels are likely to decline rapidly in individuals with asplenia, splenic dysfunction or chronic renal disease (Giebink *et al.*, 1981; Rytel *et al.*, 1986) and, therefore, re-immunisation with PPV23 is recommended every five years in these groups. Testing of antibody levels prior to vaccination is not required.

Revaccination with PPV23 is currently not recommended for any other clinical risk groups or age groups.

PCV10

Not currently recommended in the UK National Immunisation Programme. See the SPC for potential dosing schedules <https://www.medicines.org.uk/emc>.

Administration

For guidance on administering vaccines please refer to [Chapter 4: Immunisation procedures](#).

Pneumococcal vaccines can be given at the same time as other vaccines such as DTaP/IPV/Hib/HepB, 4CMenB, MMR, MenACWY, Hib/MenC, Rotavirus and influenza. The vaccines should be given at separate sites, preferably in different limbs. If given in the same limb, they should be given at least 2.5cm apart. The site at which each vaccine was given should be noted in the individual's records.

Disposal

Please see [Chapter 3 Storage, distribution and disposal](#).

Individuals with unknown or incomplete vaccination histories

Unless there is a reliable history of previous immunisation, individuals should be assumed to be unimmunised. The full UK recommendations should be followed.

Unimmunised or partially immunised children who present late for vaccination before the age of one year should receive a single priming dose of PCV13, followed by a PCV13 booster at one year of age (on or after their first birthday). If the first PCV13 dose is given very late (such as at 11 months), then a minimum interval of four weeks should be observed before the booster dose to ensure appropriate boosting of the immune response.

An unimmunised or partially immunised child aged between one and under two years of age should have a single dose of PCV13.

Routine immunisation with PCV is not offered after the second birthday.

Any child eligible for PCV vaccination, who has received one or more doses of PCV10 vaccine in another country should be offered an additional dose of PCV13 at least 4 weeks later. This ensures that the infants are protected against the same pneumococcal serotypes as those vaccinated according to the UK national immunisation schedule. These infants should receive one PCV13 dose from 12 weeks of age and a booster at one year of age (on or after their first birthday), allowing an 8-week (ideal) or 4-week (minimum) interval between the two PCV13 doses.

Risk groups

Children and adults in clinical risk groups (Table 25.2) will require additional pneumococcal vaccination depending on their age at presentation (diagnosis), vaccination status and underlying condition (see Table 25.3).

Primary care staff should identify patients for whom vaccine is recommended and use all opportunities to ensure that they are appropriately immunised, for example, when immunising against influenza or at other routine consultations, especially on discharge after hospital admission.

Clinical risk group	Examples (decision based on clinical judgement)
Asplenia or dysfunction of the spleen	This also includes conditions that may lead to splenic dysfunction such as homozygous sickle cell disease and coeliac syndrome.
Chronic respiratory disease (chronic respiratory disease refers to chronic lower respiratory tract disease)	This includes chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema; and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Children with respiratory conditions caused by aspiration, or a neurological disease (such as cerebral palsy) with a risk of aspiration. Asthma is not an indication, unless so severe as to require continuous or frequently repeated use of systemic steroids (as defined in Immunosuppression below).
Chronic heart disease	This includes those requiring regular medication and/or follow-up for ischaemic heart disease, congenital heart disease, hypertension with cardiac complications, and chronic heart failure.
Chronic kidney disease	Nephrotic syndrome, chronic kidney disease at stages 4 and 5 and those on kidney dialysis or with kidney transplantation.
Chronic liver disease	This includes cirrhosis, biliary atresia and chronic hepatitis.
Diabetes	Diabetes mellitus requiring insulin or anti-diabetic medication. This does not include diabetes that is diet controlled.
Immunosuppression	Due to disease or treatment, including patients undergoing chemotherapy leading to immunosuppression, bone marrow transplant, asplenia or splenic dysfunction, complement disorder, HIV infection at all stages, multiple myeloma or genetic disorders affecting the immune system (such as IRAK-4, NEMO). Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age), or for children under 20kg, a dose of 1mg or more per kg per day.
Individuals with cochlear implants	It is important that immunisation does not delay the cochlear implantation.
Individuals with cerebrospinal fluid leaks	This includes leakage of cerebrospinal fluid such as following trauma or major skull surgery (does not include CSF shunts).
Occupational risk	Please see page 9

Table 25.2 Clinical risk groups who should receive the pneumococcal immunisation

Patients age when presenting or first diagnosed with a clinical risk condition	At clinical risk (excluding those with asplenia, splenic dysfunction, complement disorder or severe immunocompromise ¹)		Asplenia, splenic dysfunction, complement disorder or severe immunocompromise ¹	
	PCV13	PPV23	PCV13	PPV23
Infants from birth to one year of age	Routine PCV13 at 12 weeks and one year (on or after first birthday).	PPV23 at 2 years, at least 8 weeks after last PCV dose	Two PCV13 doses at least 8 weeks apart (commencing no earlier than 6 weeks of age) PCV13 booster at one year (on or after the first birthday) Additional PCV13 dose at least 8 weeks later	PPV23 at 2 years, at least 8 weeks after last PCV dose
One year to two years of age	Routine PCV13 booster at one year (on or after first birthday)	PPV23 at 2 years, at least 8 weeks after last PCV dose	Routine PCV13 booster at one year (on or after first birthday) Additional PCV13 dose at least 8 weeks later	PPV23 at 2 years, at least 8 weeks after last PCV dose
Two years to under ten years of age	No further PCV13 required (if unimmunised or partially immunised, give one PCV13 dose)	PPV23 at 2 years, at least 8 weeks after last PCV dose	Asplenia, splenic dysfunction or complement disorder: No further PCV13 required (if unimmunised or partially immunised, give one PCV13 dose) Severely immunocompromised: one PCV13 dose (even if unimmunised or partially immunised)	PPV23 at 2 years, at least 8 weeks after last PCV dose
Children aged over 10 years and adults	No further PCV13 required, irrespective of PCV vaccination history	One PPV23 dose	Asplenia, splenic dysfunction or complement disorder: No further PCV13 required Severely immunocompromised: One PCV13 dose ²	One PPV23 dose, at least 8 weeks after last PCV dose ²

Table 25.3 – Summary of vaccine doses for at-risk patients.

- ¹ Examples of severe immunocompromise include bone marrow transplant patients, patients with acute and chronic leukaemia, multiple myeloma or genetic disorders affecting the immune system (such as IRAK-4, NEMO)
- ² PCV13 or additional PPV23 not needed if individual received PPV23 in the previous 2 years because of a theoretical risk of pneumococcal serotype-specific hypo-responsiveness with re-vaccination.

Timing of vaccination for those requiring splenectomy or commencing immunosuppressive treatment

Because of the high risk of overwhelming infection, particularly for pneumococcal disease, vaccination is recommended for all individuals with asplenia, splenic dysfunction and conditions which may lead to splenic dysfunction, including haemoglobinopathies such as sickle cell disease and coeliac syndrome. See [Chapter 7: Immunisation of individuals with underlying medical conditions](#) for a complete schedule including other vaccines indicated for this group.

Those requiring splenectomy or commencing immunosuppressive treatment should be vaccinated according to the age-specific advice above. Ideally, the vaccines should be given 4-6 weeks before elective splenectomy or initiation of treatment such as chemotherapy or radiotherapy. Where this is not possible, it can be given up to two weeks before treatment. If it is not possible to vaccinate beforehand, splenectomy, chemotherapy or radiotherapy should never be delayed.

If it is not practicable to vaccinate two weeks before splenectomy, immunisation should be delayed until at least two weeks after the operation because functional antibody responses may be better from this time (Shatz *et al.*, 1998). If it is not practicable to vaccinate two weeks before starting chemotherapy/radiotherapy, immunisation should be delayed until at least three months after completion of therapy to maximise vaccine response. Immunisation of these patients should not be delayed if this is likely to result in a failure to vaccinate.

For leukaemia patients, PCV13 should be given from six months after completion of chemotherapy, and for bone marrow transplant patients, PCV13 should be offered 9-12 months following transplantation.

Individuals at occupational risk

There is an association between exposure to metal fume and pneumonia, particularly lobar pneumonia, and between welding and invasive pneumococcal disease (Wong *et al.*, 2010). PPV23 (single 0.5ml dose in those who have not received PPV23 previously) should be considered for those at risk of frequent or continuous occupational exposure to metal fume (such as welders) taking into account the exposure control measures in place. Vaccination may reduce the risk of pneumococcal disease but should not replace the need for measures to prevent or reduce exposure.

Contraindications

There are very few individuals who cannot receive pneumococcal vaccines (see [Chapter 6: Contraindications and Considerations](#)). When there is doubt, appropriate advice should be sought from a consultant paediatrician, local NHS England Screening and Immunisation Team or local Health Protection Team.

The vaccines should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of the vaccines
- a confirmed anaphylactic reaction to any component of the vaccines

Confirmed anaphylaxis is rare. Other allergic conditions, such as rashes, may occur more commonly and are not contraindications to further immunisation. A careful history of the event will often distinguish between true anaphylaxis and other events that are either not due to the vaccine or not life-threatening. In the latter circumstance, it may be possible to continue the immunisation course. Specialist advice must be sought on the vaccines and the circumstances in which they could be given. The risk to the individual of not being immunised must be taken into account. [See Chapter 8: Vaccine Safety and Adverse Events](#) for more information.

Precautions

Minor illnesses, without fever or systemic upset, are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation should be postponed until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Pregnancy and breast-feeding

Pneumococcal vaccines may be given to pregnant women when the need for protection is required without delay. There is no evidence of risk from vaccinating pregnant women or those who are breast-feeding with inactivated viral or bacterial vaccines or toxoids (Plotkin *et al*, 2018).

Premature infants

See [Chapter 11: Immunisation Schedule](#) and [Chapter 7: Immunisation of Individuals with Underlying Medical Conditions](#) for more information.

Immunosuppression and HIV infection

Individuals with immunosuppression and HIV infection (regardless of CD4 count) should be given pneumococcal vaccines according to the recommendations above. The potential benefit of PPV23 in preventing pneumococcal disease outweighs any potential risks in HIV-infected adults.

Adverse reactions

Anyone can report a suspected adverse reaction to the Medical and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme (<http://yellowcard.mhra.gov.uk/>).

Reports of all adverse reactions can be found in the summary of product characteristics available at <https://www.medicines.org.uk>.

PCV13

The safety of the vaccine was assessed in controlled clinical studies and the safety profile of Prevenar13[®] was similar to Prevenar[®]. For Prevenar13[®], the most commonly reported adverse reactions in children 6 weeks to 5 years of age were vaccination-site reactions, fever, irritability, decreased appetite, and increased and/or decreased sleep.

PPV23

Mild soreness and induration at the site of injection lasting one to three days and, less commonly, a low-grade fever may occur. More severe systemic reactions are infrequent. In general, local and systemic reactions are more common in people with higher concentrations of antibodies to pneumococcal polysaccharides.

Management of cases, contacts and outbreaks

Cases of invasive pneumococcal disease (IPD)

Any case of invasive pneumococcal infection or lobar pneumonia believed to be due to *S. pneumoniae* should prompt a review of the patient's medical history to establish whether they are in a recognised risk group and whether they have been appropriately immunised. Unimmunised or partially immunised individuals should be vaccinated upon discharge from hospital whenever possible.

Cases in children under five years of age

Clinicians should ensure that children diagnosed with IPD have completed the recommended national immunisation schedule. Infants who are younger than 12 months of age at the time of IPD and who are unvaccinated or partially vaccinated should complete the recommended immunisation schedule.

Immunised children who subsequently develop IPD caused by one of the pneumococcal vaccine serotypes should be assessed for possible underlying immune deficiency. If the child falls into one of the clinical risk groups in Table 25.2, then additional vaccinations should be offered as recommended in this chapter.

Isolates from all cases of IPD should be referred to the national reference laboratory for serotyping. All new cases of IPD in children aged <5 years, regardless of serotype, will be followed up by Public Health England, Public Health Wales, Health Protection Scotland or the Public Health Agency for Northern Ireland.

Contacts

Close contacts of invasive pneumococcal disease are not normally at an increased risk of pneumococcal infection and therefore antibiotic prophylaxis is not indicated. Clusters of invasive pneumococcal disease should be discussed with local health protection teams.

Outbreaks

Outbreaks of pneumococcal respiratory disease in hospitals and residential care homes need prompt investigation. Control measures including vaccination may be appropriate; these should be agreed in discussion with local health protection or infection control teams. For further information see the UK guidelines for the public health management of clusters of serious pneumococcal disease in closed settings (Health Protection Agency, 2008) available at: <https://www.gov.uk/government/collections/pneumococcal-disease-guidance-data-and-analysis>.

Supplies

- 13-valent PCV (Prevenar 13®) is manufactured by Pfizer (Medical Information website: www.pfizermedicalinformation.co.uk, tel: 01304 616161)
- 23-valent Pneumococcal Polysaccharide Vaccine is manufactured by MSD. MSD vaccines are distributed by AAH Ltd. (Tel: 0344 561 8899)
- 10-valent PCV (Synflorix®) is manufactured by GlaxoSmithKline (Tel: 0800 221 441)

PCV13 to support the routine childhood immunisation programme is centrally supplied, for more information please see [Chapter 3 Storage, distribution and disposal](#).

Information materials

A patient card and information sheet for asplenic and hyposplenic patients are available at:

<https://www.gov.uk/government/publications/splenectomy-leaflet-and-card>

Or in Scotland from:

The Health Protection Team (Immunisation) Health Directorates Scottish Executive Area 3ES
St Andrews House Regent road Edinburgh EH1 3DG

(Tel: 0131 244 2879).

(Fax: 0131 244 2157).

(E-mail: immunisationprogrammes@gov.scot).

Or in Wales a leaflet *A guide for people without a working spleen* and a patient card are available from:

www.publichealthwales.org/HealthInformationResources

In Northern Ireland, '*Splenectomy factsheet for health professionals*', '*Splenectomy patient leaflet*' and a Splenectomy wallet card for patients are available from The Public Health Agency:

<https://www.publichealth.hscni.net/publications/splenectomy-factsheet-health-professionals-0>

<https://www.publichealth.hscni.net/publications/splenectomy-patient-leaflet>

<http://www.publichealth.hscni.net/publications/splenectomy-wallet-card>

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