Australian Government
Department of Health

Australian Technical Advisory Group on Immunisation

Submission to the National Health and Medical Research Council (NHMRC) on proposed amendments to the infant pneumococcal vaccination schedule recommendations in the Australian Immunisation Handbook

Summary

The Australian Technical Advisory Group on Immunisation (ATAGI), which advises the Australian Government on clinical recommendations for vaccinations, is proposing changes to the vaccination schedule used for the 13-valent pneumococcal conjugate vaccine (13vPCV; Prevenar 13) for Australian children. The changes are being proposed to improve protection in children beyond 12 months of age in whom an increasing number of episodes of invasive pneumococcal disease (IPD) have been observed, despite being fully vaccinated according to the current recommendation.

The total number of 13vPCV doses will remain unchanged. The current recommendation of three doses for the majority of children and four doses for specified at-risk groups will be continued. The main change proposed is to move the third dose of the 13vPCV vaccine (currently given at 6 months of age) to 12 months of age for those children who are recommended to receive three doses. Children who are currently recommended to receive four doses will continue to receive a dose at 6 months of age due to their increased risk of IPD. However, it is proposed that the fourth dose is given at 12 months of age rather than the currently recommended 12–18 months of age.

In addition to improving protection in vaccinated children, the proposed changes are expected to lead to considerable improvement in disease control in older unvaccinated populations through better indirect (herd) protection. Following on from this change, revised schedules are proposed for catch-up doses in those who miss 13vPCV doses at the recommended schedule points. Moving the current third dose from 6 months to 12 months of age may reduce protection between the ages of 6 and 12 months, but any increase in disease as a result is estimated to be low and expected to disappear with time.

Rationale

Most children in Australia are currently recommended to receive three doses of a vaccine against pneumococcal disease at 2, 4 and 6 months of age. The vaccine, called the 13-valent pneumococcal conjugate vaccine (13vPCV; Prevenar 13), has been highly effective in reducing pneumococcal disease in children. Despite this, ATAGI now considers there to be clear evidence to suggest that a dose of 13vPCV in the second year of life (booster dose) is critical to further increase both direct

and indirect benefits of the childhood 13vPCV program for all Australians. The main reasons for this conclusion are:

- Cases of 13vPCV vaccine failures in toddlers older than 12 months continue to occur at higher rates than seen in other countries that provide a booster dose of 13vPCV during the second year of life. These vaccine failures were children diagnosed with IPD due to serotypes covered in 13vPCV who had received three infant doses of 13vPCV (at 2, 4, 6 months of age). Although not all children who are vaccinated will be protected, the evidence shows that some children in Australia who have received three doses of 13vPCV in accordance with the current schedule are not being adequately protected beyond the first year of life.
- Other countries that provide a dose of 13vPCV during the second year of life are seeing greater benefits from herd immunity than is currently being achieved in Australia. This is reflected in a lower number of IPD cases due to vaccine serotypes among unvaccinated children and adults. The experience in other countries shows that by providing better protection during the second year of life, Australia also has the potential to reduce the risk of unvaccinated individuals getting IPD due to the serotypes in the 13vPCV.

ATAGI proposes changes to the childhood pneumococcal vaccination schedule so that children currently recommended to receive three infant doses of 13vPCV (at 2, 4 and 6 months of age) instead receive two infant doses (at 2 and 4 months of age) followed by a second year of life booster dose at 12 months of age. It is expected that this change will significantly improve both the direct and indirect protection provided by the childhood 13vPCV program.

Any potential decline in direct protection in infancy due to shifting the third infant dose to the second year of life will have the greatest impact on children with an increased risk of IPD. For children with at-risk conditions for pneumococcal disease and for Aboriginal and Torres Strait Islander children living in the Northern Territory (NT), Queensland (QLD), South Australia (SA) and Western Australia (WA), the current four-dose schedule (three infant doses at 2, 4 and 6 months of age with a second year of life booster) is to be continued. Regarding the timing of the booster dose, 12 months of age is preferred to 12–18 months in order to shorten the interval between the completion of the primary course and the booster dose. Implementing a nationally consistent schedule point for the fourth dose (i.e. at 12 months of age) is expected to contribute to higher vaccination rates through consistent promotion of the infant pneumococcal vaccine schedule.

Recommendations

1. ATAGI is seeking NHMRC endorsement on the following recommendation changes for 13vPCV use in children (Table 1)

***Table 1*:** Comparison of current and proposed ATAGI recommendations for 13vPCV schedules in children

Cohort		Schedule in current recommendation*	Schedule in proposed recommendation
Children <u>without</u> underlying medical conditions associated with increased risk of IPD	All children in ACT, NSW, TAS or VIC	3+0 (2, 4 and 6 months)	2+1 (2, 4 and 12 months)
	Non-Indigenous children in NT, QLD, SA or WA		

Cohort		Schedule in current recommendation*	Schedule in proposed recommendation
	Aboriginal and Torres Strait Islander children in NT, QLD, SA or WA	3+1 (2, 4, 6 and 12–18 months)	3+1 (2, 4, 6 and 12 months)
All children with underlying medical conditions associated with increased risk of IPD (Attachment A)		3+1 (2, 4, 6 and 12 months)	3+1 (2, 4, 6 and 12 months)

* See *The Australian Immunisation Handbook* Chapter 4.13 Pneumococcal disease, section 4.13.7 'Recommendations'. http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-13

a) All children, except those specified in (b) below, should receive three doses of 13vPCV at 2, 4 and 12 months of age (called '2+1' schedule) instead of the current schedule with doses at 2, 4 and 6 months of age (called '3+0' schedule).

b) The following population groups at increased risk of pneumococcal infection should continue to receive four doses of 13vPCV at 2, 4, 6 and 12 months^ of age (called '3+1' schedule):

   i. Aboriginal and Torres Strait Islander children living in the NT, QLD, SA and WA

   ii. Children with underlying medical conditions associated with an increased risk of IPD (i.e. any condition in Attachment A).

^ Note the preferred schedule point for the fourth (last) 13vPCV dose is age 12 months rather than 18 months.

2. ATAGI is seeking NHMRC endorsement on the following recommendations for catch-up use of 13vPCV in children (Tables 2a & 2b)

Schedules for catch-up doses of 13vPCV for children aged <5 years who have not received any pneumococcal conjugate vaccine (PCV) doses or who have only received incomplete courses of PCVs are covered in Tables 2a (for all children with medical condition(s) increasing IPD risk and Aboriginal and Torres Strait Islander children in NT, QLD, SA or WA) and 2b (for all other children).

Table 2a: Catch-up schedule for 13vPCV for Aboriginal and Torres Strait Islander children living in NT, QLD, SA or WA ONLY, and all children with any medical condition(s)* associated with an increased risk of invasive pneumococcal disease (IPD), aged <5 years

Number of doses given previously	Age at presentation	Age when previous dose of any PCV† was given			Recommendations‡
		1st dose	2nd dose	3rd dose	Number of further dose(s) required
No previous doses	<12 months	–	–	–	4§
	12–59 months	–	–	–	2
1 previous dose	<12 months	Any age	–	–	3§
	12–59 months	<12 months	–	–	2§
		≥12 months	–	–	1
2 previous doses	<12 months	Any age	Any age	–	2§
	12–59 months	<12 months	<12 months	–	2§
			≥12 months	–	1
		≥12 months	≥12 months	–	None

Number of doses given previously	Age at presentation	Age when previous dose of any PCV† was given			Recommendations‡
		1st dose	2nd dose	3rd dose	Number of further dose(s) required
3 previous doses	<12 months	Any age	Any age	Any age	1§
	12–59 months	<12 months	<12 months	Any age	1
			≥12 months	≥12 months	None

* Recommendations for vaccination of haematopoietic stem cell transplant (HSCT) recipients differ: a separate table for revaccination following HSCT in children and adults will be included in upcoming updates to *The Australian Immunisation Handbook*.

† Prior PCV doses may have been given as 7vPCV (e.g. from overseas), 10vPCV or 13vPCV. Use 13vPCV as the vaccine formulation for catch-up doses, regardless of which formulation of PCV the child received previously.

‡ Where possible, align doses with the standard schedule points at 2, 4 and 6 months of age for infants. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

§ The last dose should be given after the child reaches 12 months of age (as a booster dose) with a minimum interval of 2 months after the previous dose of PCV.

Table 2b: Catch-up schedule for 13vPCV for all other children aged <5 years (not covered in Table 2a)

Number of doses given previously	Age at presentation	Age when previous dose of any PCV* was given			Recommendation†
		1st dose	2nd dose	3rd dose	Number of further dose(s) required
No previous doses	<12 months	–	–	–	3‡
	12–59 months	–	–	–	1
1 previous dose	<12 months	<12 months	–	–	2‡
	12–59 months	<12 months	–	–	1
		≥12 months	–	–	None
2 previous doses	<12 months	<12 months	<12 months	–	1‡
	12–59 months	<12 months	<12 months	–	1
			≥12 months	–	None
3 previous doses	<12 months	<12 months	<12 months	<12 months	1‡
	12–59 months	<12 months	<12 months	<12 months	None§
		Any age	Any age	≥12 months	None

* Prior PCV doses may have been given as 7vPCV (e.g. from overseas), 10vPCV or 13vPCV. Use 13vPCV as the vaccine formulation for catch-up doses, regardless of which formulation of PCV the child received previously.

† Where possible, align doses with the standard schedule points at 2 months and 4 months of age for infants aged <5 months. The minimum interval between dose(s) is 1 month if aged <12 months, and 2 months if aged ≥12 months.

‡ The last dose should be given after the child reaches 12 months of age (as a booster dose) with a minimum interval of 2 months after the previous dose of 13vPCV.

§ For children currently aged 13–59 months without an at risk condition who have previously completed 3 scheduled doses of 13vPCV in infancy, a 13vPCV booster dose may be given to maximize protective benefit for the individual, although it is not routinely recommended. If a child is to have this extra 13vPCV dose it should be given at least 2 months after the previous dose of 13vPCV.

3. Research evidence

Recommendation 1: 13vPCV infant schedule

ATAGI has been monitoring the number of notified IPD cases due to serotypes in 13vPCV occurring in three-dose recipients since the introduction of 13vPCV in mid-2011. By December 2015, it had become clear that the number of breakthrough cases in children receiving the 3+0

schedule had steadily increased each year over the first 4 years of 13vPCV use on the National Immunisation Program (NIP). In 2015 alone, there were 41 cases of 13vPCV breakthrough disease, 5 more than the previous year. Breakthrough cases were predominantly due to serotypes 19A (57%) and 3 (27%). The majority (94%) of cases occurred in children aged 12 months or older (Table 3).

Table 3: Age groups and serotypes of 13vPCV (3+0 dose) vaccine failures up to 31 December 2015

Serotype	Age group (months)					
	<12	12–<24	24–<36	36–<48	48–<60	Total
1	–	–	1	–	–	1
3	3	15	8	3	–	29
6A	–	–	1	–	–	1
7F	–	1	–	–	–	1
19A	2	38	14	6	2	62
19F	2	9	3	–	–	14
Total	**7 (6%)**	**63 (58%)**	**27 (25%)**	**9 (8%)**	**2 (2%)**	**108 (100%)**

ATAGI has taken two approaches to evaluate this apparent increase.

1. Comparison of cases during the 13vPCV program with cases during the 2006–2012 7vPCV (the vaccine against pneumococcal disease used prior to 2011) program: 3+0 dose breakthrough cases during the 7vPCV era were relatively stable at an average of 4.6 per year, primarily due to serotype 19F.
2. Review of experience in countries with similar longevity of pneumococcal conjugate vaccine use and high quality surveillance but using alternate schedules for 13vPCV (3+1 in the USA and 2+1 in the UK): Published and unpublished data (provided in confidence by Public Health England [UK] and Centers for Disease Control and Prevention [USA]) were reviewed. The comparison across all three schedules showed better protection in children aged 1 year and older following schedules that included a booster dose in the second year of life. This is because immunity wanes following completion of the primary series; administration of a booster dose results in vigorous antibody responses that enhance the degree and duration of protection. This higher level of immunity achieved by second year of life boosting has also been associated with improved herd protection of older age groups.

Based on these considerations, the 2+1 schedule (doses at ages 2, 4 and 12 months) is the preferred option for the majority of the population (all children in ACT, NSW, TAS and VIC and non-Indigenous children in NT, QLD, SA and WA) as it is *rapidly implementable* given the number of total doses recommended would remain unchanged. Also, comparison of US and UK data suggested that the incremental benefit of a 3+1 schedule over the 2+1 schedule in preventing vaccine-type disease was minimal and likely to decrease over time.

Historical background to the 3+0 schedule

The 3+0 schedule was introduced for non-Indigenous children without specific underlying medical conditions associated with increased risk of IPD in 2005. This decision was based on a lack of evidence of incremental benefit from a fourth dose in clinical trials and the much higher incidence of pneumococcal meningitis in the first year of life (i.e. focused on direct protective effects).

In 2011, 13vPCV replaced 7vPCV in the childhood pneumococcal vaccination program under the NIP. After considering the evidence available at the time, the schedule of three primary doses (at 2, 4 and 6 months of age) without a second year of life booster dose (i.e. a 3+0 schedule) was maintained for non-Indigenous children without specific underlying medical conditions associated with increased risk of IPD.

A fourth dose (booster) of 13vPCV replaced the 23-valent pneumococcal polysaccharide vaccine (23vPPV) recommended for Aboriginal and Torres Strait Islander children living in the NT, QLD, SA and WA, and the fourth 13vPCV dose was also recommended to children with underlying at-risk conditions for IPD.

Impact of the use of 13vPCV in the 3+0 schedule in Australia on incidence of IPD in the population

The introduction of 13vPCV resulted in a large reduction in the number of cases of IPD due to vaccine serotypes in all age groups.[3] The rates of IPD due to the additional serotypes in 13vPCV that were not in the 7vPCV (13v-non7v serotypes) declined by 70% in children <2 years of age and by 49% in adults ≥65 years of age from 2009 to 2014.

The number of cases of meningitis due to 13vPCV serotypes in children between 6 and 12 months of age decreased from 10 cases in the 3 years before 13vPCV introduction to none in 2012–2014, confirming that the 3+0 schedule provided strong direct protection for infants against IPD.

Potential impact of a change in the childhood 13vPCV schedule from 3+0 to 2+1

a) Against breakthrough cases of IPD

In a comparable period of 13vPCV use, the rate of breakthrough IPD in children ≥12 months of age was substantially higher in Australian children (rate of 3.4 cases per 100,000) than in children in the UK (2+1 schedule, rate of 0.7 cases per 100,000).[4] Extrapolation of 13vPCV breakthrough IPD case counts in the UK, following adjustment for birth cohort size, provides a crude estimate of expected breakthrough cases if a 2+1 schedule were to be used, instead of the current 3+0 schedule, in Australia (Table 4).

Table 4: Breakthrough cases of 13vPCV IPD in the UK and Australia* – observed case counts from both populations, and imputed figures for the anticipated Australian experience using a 2+1 schedule based on UK incidence data

Schedule	Age <12 months		Age ≥12 months		Total	
	Severe IPD†	All IPD	Severe IPD†	All IPD	Severe IPD†	All IPD
AUS (observed, 3+0 schedule)	1	7	24	101	25	108
UK (observed, 2+1 schedule)	19	41	18	28	37	69
AUS (imputed, 2+1 schedule‡)	8	18	8	12	16	30
AUS (difference between imputed and observed)	+7	+11	–16	–89	–9	–78

* Observation periods: for UK 2011–2014; for Australia 2012–2015

† Includes pneumococcal meningitis and pneumonia with empyema/effusion

‡ Crude extrapolation to estimate number expected if 2+1 schedule was used instead of 3+0 schedule in this period by accounting for the difference in birth cohort sizes of 700,000 in the UK and 300,000 in Australia $[n \times 3/7]$, rounded to nearest whole number

Had a 2+1 schedule been used during the past 4 years for 13vPCV, it is estimated that a total of 78 additional cases of IPD in vaccinated children would have been averted. Among children aged ≥12 months, 89 fewer cases of breakthrough IPD would have occurred over the 4-year period if a 2+1 schedule was used, with 16 (4 per year) being more severe disease (i.e. either pneumococcal meningitis or pneumonia with empyema).

Whereas a shift to a 2+1 schedule could have averted an estimated 89 cases among children aged ≥12 months, crude estimates suggest this may have been offset by 11 more breakthrough disease cases in infants between the ages of 6 months and 12 months (seven of these being severe disease) over 4 years. This translates to two additional cases of severe IPD per year in children <12 months of age among 300,000 children who would have received two doses by 6 months of age. It should be noted that these estimates do not consider the potential for improved herd protection following administration of a routine booster dose, which would be anticipated to reduce transmission and hence the number of cases across the age spectrum (see below).

b) Against population IPD incidence

Although the reductions in incidence of IPD due to vaccine serotypes at population level following 13vPCV introduction is considerable in Australia, the impact in terms of proportional reduction in IPD incidence has been substantially greater in the UK (using a 2+1 schedule) over a similar period of vaccine use.

In the 2–4 years age group, the reduction in IPD due to 13v-non7v serotypes in Australia was statistically significantly less than that observed in the UK, after 5 years of 13vPCV use. The decline in 13v-non7v serotypes was also less in all adult age groups, especially in the 15–44 years age group. Among individual serotypes, only 19A IPD had significant reductions across all age groups in Australia, while in the UK, significant reductions were also seen in serotypes 7F and 3.

When age-specific reductions in IPD incidence rates in the UK (using a 2+1 schedule) were used to impute incidence rates in Australia, it was estimated that, had the 2+1 schedule been used in Australia over the same time period, a total of approximately 270 fewer cases of 13vPCV serotype IPD would have been observed in the fifth year after 13vPCV introduction.

Recommendation 2: 13vPCV catch-up schedule

The recommended catch-up schedules for 13vPCV vaccinations for children who are unvaccinated or only partially vaccinated were revised using the same principles as for routine vaccinations (i.e. using 2+1 or 3+1 schedules in respective populations). ATAGI has focused on simplifying catch-up schedules, considering feedback received from providers, in order to improve compliance.

In clinical trials, among pneumococcal vaccine naïve toddlers, a single dose of 13vPCV at age 24–72 months provided sufficient antibody responses for protection against IPD for each individual 13vPCV type. It is expected that toddlers aged 12–24 months without at-risk conditions would also develop adequate levels of antibodies for protection against vaccine-type IPD following a single 13vPCV dose. For children with increased risk of IPD, including Aboriginal and Torres Strait Islander children in NT, QLD, SA and WA, an additional dose is recommended due to the higher disease burden and the possibility of lower antibody responses.

4. Additional key information

Benefits/Harms

There are two key benefits from the proposed changes to the infant pneumococcal schedule:

1. Moving the third dose to 12 months of age will lead to an even greater reduction in IPD incidence in the second year of life with substantially fewer cases of breakthrough IPD overall.
2. A nationally consistent four-dose schedule for those with increased risk of IPD will support program delivery by enabling nationally consistent messaging and promotion for eligible cohorts and decreasing variation in practice in the national program.

There are two potential concerns that may arise from the proposed amendments to the infant pneumococcal vaccine schedule:

1. While there would be an overall decrease in breakthrough cases, there is a potential risk of vaccine-type IPD in children aged 6 to 12 months due to these children having received only two doses at 2 and 4 months (down from three doses). This risk is estimated to be small when considering the UK data; however, it is acknowledged that there are limitations in simplistic imputation of UK data to the Australian context.
2. While it is possible that children who are recommended to receive four doses (i.e. a 3+1 schedule that maintains a three-dose primary course in infancy) may miss the third dose provided at 6 months of age, it is not possible to quantify this risk. Moreover, this potential risk should be balanced against the existing risk that such children do not receive their currently recommended booster dose.

ATAGI recommends maintaining a 3+1 schedule for those children at highest risk of IPD and considers this is the best strategy to mitigate the risk of breakthrough IPD at the population level.

Overall, ATAGI's review of the evidence showed that the incremental benefit for all children of a 3+1 schedule over a 2+1 schedule in preventing vaccine-type disease would be low and the longer process required to change from a 3+0 to a 3+1 schedule would lead to significant delays in timely implementation of the booster dose. ATAGI will continue to closely monitor IPD surveillance data to identify any trends.

ATAGI has also considered the implication of adding a vaccination at the 12 month schedule point, where:

- Two vaccinations are currently administered to children without underlying risk factors (including both Aboriginal and Torres Strait Islander children and non-Indigenous children in some states [ACT, NSW, VIC, and TAS]);
- Three vaccinations are administered in Aboriginal and Torres Strait Islander children in NT, QLD, SA and WA; and
- Up to six vaccinations are administered to children in specific locations of Australia (e.g. Far North Queensland) and children with underlying at-risk conditions.

The proposed move to a 2+1 schedule would affect those children currently receiving two vaccinations at the 12 month schedule point. Children in the other cohorts above already receive a dose of 13vPCV at the 12 or 18 month schedule point.

5. Preference and values

Over 90% of children aged 12 months of age are fully vaccinated which shows that parents value immunisation as a means of protecting their children's health. Parents place a high value on preserving their children's health and wellbeing and also to contributing to protecting the community's wellbeing through 'community immunity'.

Amending the infant pneumococcal vaccination schedule is anticipated to result in additional protection for individuals and the wider community, including those who are not vaccinated, which is considered consistent with parental and societal expectations of the NIP.

6. Resources and other considerations

Product information for 13vPCV is available at: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2010-PI-07066-3&d=20170808161146224 83

The Pharmaceutical Benefits Advisory Committee (PBAC) has considered the use of 13vPCV in infants, including safety, efficacy and cost effectiveness: http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2010-07/Pneumococcal_PREVENAR-13_PSD_Wyeth.pdf

Practical information

The third dose of 13vPCV could be administered concomitantly with the other two NIP-funded vaccines given at 12 months of age: the first dose of mumps-measles-rubella (MMR) vaccine and the *Haemophilus influenzae* b–meningococcal C (Hib-MenC) combined vaccine.

It is important to ensure timeliness of the 13vPCV booster dose at age 12 months to avoid any potential compromise to protection by lengthening the window between the second dose and the booster dose.

Education and communication to providers needs to be managed carefully to ensure a smooth transition and to minimise any confusion around the new schedule requirements. The change needs to be communicated to the public with the rationale clearly explained.

The eligibility for a 2+1 schedule would be defined as all children that reach 6 months of age after the schedule change comes into effect. Accordingly a cut-off birth date would be specified to identify eligible children.

The Australian Immunisation Handbook would be updated in 2018 with the revised recommendations for catch-up doses in children who present without having completed the age appropriate course of 13vPCV. For those children at increased risk of IPD due to underlying medical conditions who are identified after 6 months of age, a corresponding 3+1 schedule would still be recommended.

References

1. Ingels H, Lambertsen L, Harboe ZB, Marquart HV, Konradsen H, Christensen JJ, Heilmann C. Recurrent invasive pneumococcal disease in children: epidemiological, microbiological, and clinical aspects from a Danish 33-year nationwide survey (1980-2013). *Scand J Infect Dis* 2014;46:265-71.

2. Alsina L, Basteiro MG, de Paz HD, Inigo M, de Sevilla MF, Trivino M, Juan M, Munoz-Almagro C. Recurrent invasive pneumococcal disease in children: underlying clinical conditions, and immunological and microbiological characteristics. *PLoS ONE* 2015;10:e0118848.

3. Jayasinghe S, Menzies R, Chiu C, Toms C, Blyth CC, Krause V, McIntyre P. Long-term Impact of a "3 + 0" Schedule for 7- and 13-Valent Pneumococcal Conjugate Vaccines on Invasive Pneumococcal Disease in Australia, 2002–2014. *Clinical Infectious Diseases* 2017;64:175-83.

4. Oligbu G, Collins S, Andrews N, Sheppard C, Fry N, Slack M, Burrow R, Ladhani SN. Characteristics and serotype distribution of childhood cases of invasive pneumococcal disease following pneumococcal conjugate vaccination in England and Wales, 2006-14. *Clinical Infectious Diseases* 2017.

Attachment A

Conditions associated with an increased risk of invasive pneumococcal disease (IPD) in children and adults, by severity of risk

Category A: Conditions associated with the *highest* increased risk of IPD

- functional or anatomical asplenia, including:
  - sickle cell disease or other haemoglobinopathies
  - congenital or acquired asplenia (e.g. splenectomy), splenic dysfunction
- immunocompromising conditions, including:
  - congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency (Note: children who require monthly immunoglobulin infusion are unlikely to benefit from vaccination)
  - immunosuppressive therapy (including corticosteroid therapy ≥2 mg/kg per day of prednisolone or equivalent for more than 1 week) or radiation therapy, where there is sufficient immune reconstitution for vaccine response to be expected
  - haematological and other malignancies
  - solid organ transplant
  - haematopoietic stem cell transplant (HSCT)
  - HIV infection (including AIDS)
  - chronic renal failure, or relapsing or persistent nephrotic syndrome
- proven or presumptive cerebrospinal fluid (CSF) leak
- cochlear implants
- intracranial shunts

Category B: Conditions associated with an increased risk of IPD

- chronic cardiac disease
  - particularly cyanotic heart disease or cardiac failure in children
  - excluding hypertension only (in adults)
- chronic lung disease, including:
  - chronic lung disease in preterm infants
  - cystic fibrosis
  - severe asthma in adults (requiring frequent hospital visits and use of multiple medications)
- diabetes mellitus
- Down syndrome
- alcoholism
- chronic liver disease
- preterm birth at <28 weeks gestation
- tobacco smoking
- history of previous IPD (in children[1,2]) (Note: further work required to confirm this in adults).

Source: *The Australian Immunisation Handbook*, Chapter 4.13 Pneumococcal disease (pages 326–327 in hard copy, 10th edition 2013)