

Australian Technical Advisory Group on Immunisation (ATAGI) Statement

Updated recommendations for revaccination of adults with 23-valent pneumococcal polysaccharide vaccine (23vPPV), Pneumovax 23[®]

December 2011

Summary

- In April 2011, following an increase in the reported number of adverse events after immunisation, the Therapeutic Goods Administration (TGA) issued interim advice to health professionals advising against administering a second or subsequent dose of **Pneumovax 23[®]** the 23-valent pneumococcal polysaccharide vaccine (23vPPV).
- ATAGI has reviewed available evidence on the safety, efficacy and effectiveness of the 23vPPV and its place within the National Immunisation Program (NIP).
- There is a definite modest level of protection against invasive pneumococcal disease (IPD) afforded by 23vPPV for adults, including older adults, especially those without underlying chronic medical conditions. Data on the field effectiveness of revaccination with 23vPPV are not available, although antibody responses have been observed.
- Systemic and local reactions after 23vPPV are common. Local reactions, including severe injection site reactions, occur more commonly in repeat dose recipients compared with first dose recipients.
- The TGA has advised that [revaccination with 23vPPV](#) can be undertaken with the approved Product Information.
- ATAGI has revised its recommendations for the use of 23vPPV for **non-Indigenous adults aged ≥65 years** under the NIP.

Following the review, ATAGI's revised revaccination recommendations are:

- A dose of 23vPPV should be given to adults at 65 years of age. Every effort should be made to provide a dose to anyone aged >65 years who has not previously received a dose of 23vPPV.
- For non-Indigenous adults aged ≥65 years, a **second dose** (a single revaccination) of 23vPPV, to be given ≥5 years after the first dose, is recommended for those who have a condition that predisposes them to an increased risk of invasive pneumococcal disease (see **Table A**).
- **A second dose is no longer recommended for those without any of these predisposing conditions.**
- Recommendations for the use of 23vPPV in those < 65 years, including for Aboriginal and Torres Strait Islander (Indigenous) adolescents and adults, are unchanged from the 9th edition of the Australian Immunisation Handbook.

Background

In April 2011 the Therapeutic Goods Administration (TGA) issued interim advice to health professionals^a advising against administering a second or subsequent dose of **Pneumovax 23**[®], the 23-valent pneumococcal polysaccharide vaccine (23vPPV). This followed an increase in the reported number of severe injection site reactions after immunisation with **Pneumovax 23**[®] from some Australian jurisdictions in March and April 2011 and a recall of a batch of the vaccine. The TGA has concluded that the increased reporting of adverse events following immunisation (AEFI) with 23vPPV was not related to a vaccine batch issue and was a result of two factors:

1. an increased rate of revaccination occurring in adults aged >65 years for whom a revaccination dose of 23vPPV five years after an initial dose was recommended; and
2. increased reporting following the publicity of the batch recall.

Further information is available on the [TGA website](#).

As part of the investigation into the increased AEFI reports, ATAGI and its Pneumococcal Working Party have revised their recommendations on the use of 23vPPV in the NIP, based on a review of available evidence on the safety, efficacy and effectiveness of the 23vPPV.

Review of vaccine safety

Available evidence indicates that local and systemic reactions after a primary dose of 23vPPV are common (more than half reporting some local reactions and up to one-third reporting systemic reactions after a first dose), although the frequency varies among different study populations and possibly with age.¹⁻³

Several, though not all, older and/or smaller studies suggested a higher propensity for injection site reactions following repeat doses of a pneumococcal polysaccharide vaccine given within 1–4 years after the first dose, compared with a primary dose. Larger and more recent studies using 23vPPV indicate that both local and systemic AEFI occur more commonly after a repeat dose of 23vPPV compared with the first dose of 23vPPV in adults, particularly more severe injection site reactions, which may occur in up to approximately 20% of re-vaccinees.¹⁻³ In these studies, the repeat doses were given at least 5 years after the previous dose. Nevertheless, the injection site reactions are mostly non-serious and self-limiting. In another study, hospitalisation coded as cellulitis/abscess within 3 days of pneumococcal vaccination was used as a proxy measure for very severe local reactions. Repeat doses given within 5 years of the first dose were significantly more likely to be associated with such hospitalisations.⁴ Other studies showed that more severe local reactions were associated with higher antibody levels prior to receiving the repeat dose.^{2,3,5,6} This may partly explain the differing propensity to local reactions associated with the interval between the repeat and the primary dose.

^a <http://www.tga.gov.au/safety/alerts-medicine-pneumovax-110416.htm>

Review of vaccine efficacy and effectiveness

Most of the studies of the clinical efficacy or effectiveness of pneumococcal polysaccharide vaccines have reported results based on a single dose of 23vPPV (a repeat dose in some) and on outcomes observed within a relatively short period of several years or less.

A Cochrane review in 2008 based on meta-analysis of randomised controlled trials (RCTs) found strong evidence that the pneumococcal polysaccharide vaccine is efficacious against invasive pneumococcal disease (IPD)^b (vaccine efficacy 74%; 95% CI 56–85%) overall and is similarly efficacious against IPD in the subgroup of otherwise healthy adults (without chronic disease) in high income countries.⁷ A vaccine efficacy estimate of 52% (95% CI 39–63%) against IPD was derived from the cohort and case-control studies included in the same meta-analysis. The vaccine efficacy against all-cause pneumonia was lower, at 29%, with a wide confidence interval (3–48%).⁷

Evidence from more recent controlled trials and observational studies in the general elderly population that were not included in the meta-analysis is consistent with the review findings. There was a modest effectiveness of 23vPPV against IPD, and lesser and less certain effectiveness against presumptive pneumococcal pneumonia without bacteraemia.⁸⁻¹³

Estimates of the effectiveness of 23vPPV at population level in England and Wales have recently been published in summary form.^c For adults aged ≥65 years, vaccine effectiveness against IPD within 2 years of vaccination was 48% (95% CI 32–60%) but waned over 2 to 5 years, becoming insignificant beyond 5 years. In adults aged 65-74 years who have no clinical risk factors for pneumococcal disease, the effectiveness of 23vPPV was higher (65% within 2 years; 95% CI: 23–84%) and was maintained for longer.

There is a lack of specific studies on the clinical effectiveness of a revaccination dose of 23vPPV, although antibody responses to a revaccination dose of 23vPPV have been shown in adults, including the elderly.^{1,3,14,15}

Blunting of antibody response (sometimes referred to as “immune hyporesponsiveness”) to repeat doses of pneumococcal vaccines may occur; however, the evidence on this is not consistent, and the interval between the 23vPPV doses may be a factor. Whether immune hyporesponsiveness has any significant detrimental outcome on vaccine effectiveness remains unknown.

Conclusion

There is a definite modest level of protection afforded by 23vPPV against IPD for adults, including older adults, especially those without underlying chronic medical conditions. Data on field effectiveness are not available regarding revaccination with 23vPPV, especially for persons aged ≥70 years, although antibody responses have been observed. Systemic and local reactions after 23vPPV are very common and reactions, especially severe injection site reactions, occur more frequently in repeat dose recipients compared with first dose recipients.

Evidence supports the conclusion that the benefits of a first dose of 23vPPV outweigh the risks of severe adverse reactions. For second doses of 23vPPV, the benefit–risk ratio appears to be greatest for older adults with a higher risk of IPD who received their first 23vPPV dose >5 years previously.

^b i.e. clinical disease where *S. pneumoniae* has been detected at anatomical sites that are normally sterile (e.g. pneumococcal meningitis, or pneumonia with pneumococcal bacteraemia/ septicaemia)

^c http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_128704.pdf

ATAGI Recommendations

ATAGI has revised its recommendations on the use of 23vPPV for non-Indigenous adults under the NIP, based on its effectiveness in elderly adults, uncertainty regarding the benefit of revaccination and the increased risk of AEFI documented with a repeat dose of 23vPPV.

Table B summarises these recommendations regarding revaccination doses of 23vPPV.

Recommendations for the use of 23vPPV in adults:

- A single dose of 23vPPV should be given to Australian adults at 65 years of age. Every effort should be made to provide a dose to anyone aged >65 years who has not previously received a dose of 23vPPV.
- For non-Indigenous adults aged >65 years who do not have any condition that predisposes them to an increased risk of IPD (see **Table A**), a repeat dose of 23vPPV is no longer recommended.
- For adults aged ≥65 years who have a condition that predisposes them to an increased risk of IPD (see **Table A**), a second dose (a single revaccination) of 23vPPV is recommended. This dose is to be given ≥5 years after the first dose. (The recommendation for this population subgroup is unchanged.)

Other recommendations remain unchanged, as per the current (9th) edition of the Australian Immunisation Handbook:

- For non-Indigenous adults aged <65 years who have any predisposing medical conditions to IPD or who are tobacco smokers (see **Table A**), a second dose (first revaccination) of 23vPPV is recommended to be given 5 years after the first dose, and a third dose (second revaccination) of 23vPPV is to be given at age 65 years or 5 years after the previous 23vPPV dose, whichever is later.
- Recommendations for the first or revaccination doses of 23vPPV for Aboriginal and Torres Strait Islander (Indigenous) adolescents and adults remain unchanged, as per the current (9th) edition of the Australian Immunisation Handbook.
- The minimum recommended interval between any 2 doses of 23vPPV is 5 years.

This document does not address recommendations on the use of pneumococcal vaccines in children. Please refer to the [Pneumococcal Disease webpage](#) of the *Immunise Australia Program* website^d and the *provider guidelines* on the *Program* providing a supplementary dose of the 13-valent pneumococcal conjugate vaccine.^e

ATAGI will continue to monitor and review evidence pertaining to the use of pneumococcal vaccines. Further advice will be provided as required.

^d <http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-pneumococcal>

^e <http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/pneumo-gsupp-cnt>

Table A: Risk factors predisposing adolescents and adults to IPD

A. Underlying chronic medical conditions that predispose to IPD:

- asplenia, either functional (including sickle-cell disease) or anatomical; where possible, the vaccine should be given at least 14 days before splenectomy,
- conditions associated with increased risk of IPD due to impaired immunity, eg. HIV infection before the development of AIDS, acute nephrotic syndrome, multiple myeloma, lymphoma, Hodgkin’s disease and organ transplantation,
- chronic illness associated with increased risk of IPD, including chronic cardiac, renal, or pulmonary disease, diabetes, alcohol-related problems,
- CSF leak.

B. Tobacco smokers

Table B: Revaccination with 23vPPV for people ≥15 years of age

Primary dose 23vPPV (First dose) given to	First 23vPPV revaccination (Second dose)	Second 23vPPV revaccination (Third dose)
Non-Indigenous adults ≥65 years without any underlying chronic medical conditions who are not tobacco smokers	No ¹	No
Non-Indigenous adults ≥65 years with underlying chronic medical conditions or smoker	5 years after 1 st dose	No
Non-Indigenous adults <65 years with underlying chronic medical conditions or smoker	5 years after 1 st dose	Either 5 years after first revaccination (2 nd dose) or at 65 years of age, whichever is later
Indigenous adults aged ≥50 years	5 years after 1 st dose	No
Indigenous adults aged <50 years with underlying chronic medical conditions or smoker	5 years after 1 st dose	Either 5 years after first revaccination (2 nd dose) or at 50 years of age, whichever is later
Asplenic individuals	5 years after 1 st dose	Either 5 years after first revaccination (2 nd dose) or at 50 years of age (for Indigenous adults), or at 65 years of age (for non-Indigenous adults), whichever is later

1. ATAGI had previously recommended a repeat dose of 23vPPV for Non-Indigenous adults ≥65 years without any underlying chronic medical conditions who are not tobacco smokers

References

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