

Research Review

EDUCATIONAL SERIES

Private Market Vaccines in New Zealand – an update

About the Reviewers



Dr Nikki Turner. Nikki is a NZ-trained GP with background experiences also in paediatrics and public health. She has a specialty interest in immunisation both internationally and in NZ.

Nikki currently works as the Director of the Immunisation Advisory Centre, a national public health programme based at The University of Auckland. She also works part time as a GP in Wellington, and is a senior lecturer in the Depts of General Practice and Primary Care at The Universities of Auckland and Otago.



Dr Helen Petousis-Harris. Helen is Senior Lecturer in the Department of General Practice and Primary Health Care at The University of Auckland and the Academic Lead for Immunisation Research and Vaccinology at the

Immunisation Advisory Centre. She has a PhD in Vaccinology and is particularly interested in factors associated with vaccine safety and reactogenicity. Other areas of research activity include social aspects of immunisation, immunisation coverage and epidemiology and clinical aspects of immunogenicity and reactogenicity.



Karin Baty

Karin is a Registered Nurse working as an Immunisation Advisor and Technical Writer for the Immunisation Advisory Centre at The University of Auckland. She recently

completed a Post-Graduate Certificate in Health Sciences which included the paper on human vaccinology and its application in the health sector.



About Research Review

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas.

Research Review publications are intended for New Zealand medical professionals.

Subscribing to Research Review

To subscribe to Research Review publications go to www.researchreview.co.nz

Disclaimer: This publication is an independent review of significant research on effective vaccines available on the private market in New Zealand. It provides summaries and opinions of published data that are the opinion of the writers rather than that of the scientific journal or research group. It is suggested the reader reviews the full trial data before forming a final conclusion on any recommendations.

BREAKING NEWS: Did you know that aside from the free National Immunisation Schedule vaccines there are really effective vaccines available on the New Zealand private market that lead to demonstrable reductions in morbidity, yet many are unaware of their availability? These are excellent vaccines, but they don't come free. Although historically the cost may have put us off discussing them with patients and their families, it is appropriate and important to discuss them as options that are available.

Privately purchased vaccines against rotavirus, meningococcal, varicella, human papillomavirus, pertussis, pneumococcal and herpes zoster disease can provide protection from birth and across the lifespan. The actual needs of and targeted interventions for individuals and families vary depending on age and circumstances.

Suggested vaccines and estimated vaccine costs are listed below:*

- **Infants:** Rotavirus ≈ \$160 (2 dose), meningococcal C conjugate (2 dose) ≈ \$100
 - **High risk infants/childcare attendees ≥ 9 months:** also varicella (2 dose) ≈ \$160
- **Toddlers/Children:** Varicella ≈ \$80 (1 dose), meningococcal ACYW-135 conjugate (1 dose) ≈ \$105
- **Adolescents** (an expensive bunch!): Meningococcal ACYW-135 conjugate ≈ \$105, HPV for boys (3 dose) ≈ \$450
- **High risk adults:** Pertussis ≈ \$30, pneumococcal conjugate followed by polysaccharide ≈ \$250
- **Elderly:** Pneumococcal polysaccharide ≈ \$50, herpes zoster ≈ \$200
- **Non-immune close contacts of high risk individuals:** think varicella, influenza, pertussis.

* All these vaccines are purchased through Healthcare Logistics.

* Small orders, four or less vaccines, incur a handling fee of \$45 + GST.

* Add the cost of staff time to administer the vaccine

This resource aims to raise awareness of Ministry of Health and Immunisation Advisory Centre (IMAC) recommendations for non-funded vaccines. Table 1 provides an outline of vaccines available for private purchase and to whom they may be offered. Following Table 1 each vaccine is briefly described in the context of the New Zealand (NZ) burden of disease, available vaccine brands, recommendations and answers to frequently asked questions.

Table 1: Privately purchased vaccines available in 2013 in NZ and who to offer them to

| Disease | Vaccine brands | Who to offer the vaccine to | | | |
|--|--|-----------------------------|----------|-------------------------|----------------------|
| | | Infants | Children | Adolescents | Adults |
| Rotavirus | Rotarix® | <14 weeks | | | |
| Meningococcal | | | | | |
| Conjugate vaccines^a | Meningitec® (C) | ≥6 weeks – ≤9 months | | | |
| | NeisVac-C™ (C) | ≥8 weeks – ≤9 months | | | |
| Polysaccharide vaccines^a | Menactra® (ACYW-135) | ≥9 months | ✓ | ✓ | ✓ |
| | Mencevax® ACYW Menomune® ACYW-135 | | ≥2 years | ✓ | ✓ |
| Varicella | Varilrix® Varivax® | ≥9 months | ✓ | ✓ | <50 years |
| Herpes zoster | Zostavax® | | | | ≥50 years |
| Human papillomavirus | Gardasil® | | | Boys/Men 12–26 years | Women 20–45 years |
| Pneumococcal | | | | | |
| Conjugate vaccine^b | Prevenar 13® | ≥6 weeks | ✓ | ✓ | ✓ |
| Polysaccharide vaccines^b | Pneumovax® 23 Pneumo 23® | | ≥2 years | ✓ | ✓ |
| | Boostrix® Adacel® (Tdap) Adacel® Polio (Tdap-IPV) | | | | ✓ |

a. IMAC recommends use of the conjugate vaccines in preference to the polysaccharide vaccines.

b. IMAC recommends administration of a single Prevenar 13® dose at least eight weeks before administration of a pneumococcal polysaccharide vaccine for individuals at higher risk of the disease.

Rotavirus vaccine

Rotavirus is the most common cause of gastroenteritis in infants and children worldwide.^{1,2} Transmission occurs through the faecal-oral route, both through close personal contact and fomites. It is highly infectious. There are multiple serotypes that vary considerably over region and time.¹

The symptoms, typically fever, diarrhoea and/or vomiting, vary from asymptomatic or mild^{1,2} to severe and may result in dehydration, hospitalisation, electrolyte imbalance and death.^{1,3} Infants and children in the 4–23-month age group have the highest risk of dehydration and its sequelae.⁴ Almost all children will contract rotavirus in early childhood. NZ data estimates that rotavirus infection leads to hospitalisation of one in every 52 children by three years of age and for every admission there are a further eight children seen in primary care. Death in NZ is very rare.⁵

Available vaccines

Two live, attenuated vaccines against rotavirus, Rotarix[®] and RotaTeq[®], are licensed in NZ and cover the most common NZ serotypes. However, only the Rotarix[®] brand is currently available for private purchase.

Recommendations

Vaccination against rotavirus infection is not currently on the New Zealand National Immunisation Schedule. The vaccine is recommended but not funded by the Ministry of Health for all infants, particularly if they regularly attend an early childhood service or live with a person who is immunocompromised.⁶

Rotarix[®] is approved for use in infants from 6–24 weeks of age, administered as two separate oral doses. The first dose should be administered between 6–14 weeks of age and the second a minimum of four weeks later, but must be given before 24 weeks of age.⁷

Frequently asked questions

How safe are rotavirus vaccines?

Infants may experience fever and mild diarrhoea and/or vomiting during the week after vaccination, but these are likely to be coincidental rather than caused by the vaccine.⁸ The vaccine virus is shed in faeces for up to 10 days post-vaccination; it is important to advise parents and caregivers to observe careful hygiene measures during nappy changes over this period.⁷

Postmarketing surveillance of rotavirus vaccination suggests there may be a small increase^{9,11} of an extra 3–4 cases of intussusception above the background rate of approximately 87 cases per 100,000 person-years within seven days of the first dose.¹⁰

How well do rotavirus vaccines work?

In countries with similar serotype distribution to NZ, both licensed vaccines reduce hospitalised rotavirus disease by around 80%, with the best efficacy against most severe disease.⁸ The vaccine is slightly less effective in lower income countries where there are different patterns of serotype distribution.

Can the first vaccine dose be given after 14 weeks of age?

In view of the slightly increased risk of intussusception after the first dose, the age limits for initiating and completing the vaccine series should be adhered to, with the uppermost age limit for the first dose being 14 weeks and six days of age.⁸ However, there may be occasions when an infant's doctor and parents determine that the risks of wild-type disease and potential benefits of vaccination outweigh the unknown risks of administering vaccine doses outside of the recommended age limits.

Can an infant living with a person who is immunocompromised have rotavirus vaccine?

Yes. Infants living in a household with a pregnant woman or person who is immunocompromised can receive the vaccine.⁴ It is important to advise household contacts to observe careful hygiene measures during nappy changes over this period.⁷

Can Rotarix[®] be used to complete a course of RotaTeq[®] started overseas?

Yes. Rotarix[®] can be used to complete a total of three doses of rotavirus vaccine for infants from overseas who have previously received one or two doses of RotaTeq[®], provided they are less than 24 weeks of age.^{4,12}

Can Rotarix[®] be given at the same time as other vaccines?

Yes. Rotarix[®] can be administered at the same time as routine schedule vaccines.^{4,7} Rotarix[®] can also be administered at any time before or after BCG vaccination.¹³

Meningococcal vaccines

Five serogroups of meningococcal bacteria, groups A, B, C, Y and W-135, are known to cause invasive disease in New Zealand. Of these, serogroups B and C account for most cases of disease.¹⁴ Group B causes around 60% of all disease, and C around 40%, with occasional cases of the other serogroups. Asymptomatic carriage of the bacteria in the nasopharynx increases during infancy and peaks in adolescence, with up to 25% of adolescents being colonised, before declining with age.¹⁵ Carriage generally leads to protection against disease.¹⁶ Transmission occurs through direct contact with saliva and respiratory secretions.¹⁶ Children less than five years of age (particularly infants less than one year of age) and adolescents have the highest risk of developing invasive disease.¹⁴

Available vaccines

Five vaccines against meningococcal disease are licensed in New Zealand. Three of these are conjugate vaccines, Meningitec[®], NeisVac-C[™] and Menactra[®]. Two are polysaccharide vaccines, Mencevax[®] ACYW and Menomune[®] ACYW-135.

Conjugate vaccines generate better quality, longer lasting, circulating antibodies and immune memory that rapidly responds to a booster vaccination producing more circulating antibodies.¹⁷ They are usually more expensive than the polysaccharide vaccines. Meningitec[®] and NeisVac-C[™] protect against meningococcal group C. Menactra[®] protects against groups A, C, Y and W-135.

Polysaccharide vaccines generate shorter-term circulating antibodies without immune memory. Subsequent polysaccharide vaccine doses have been shown to generate fewer circulating antibodies. These vaccines are only used in children from two years of age and in adults.¹⁷ They are usually less expensive than the conjugate vaccines. Mencevax[®] ACYW and Menomune[®] ACYW-135 protect against meningococcal groups A, C, Y and W-135.

There is no vaccine against meningococcal group B available in New Zealand. The MeNZB[™] vaccine is no longer manufactured.

Recommendations

The conjugate vaccines are preferred over the polysaccharide vaccines due to the superior immunity they generate, but they are usually more expensive. For those aged two years and over needing only short-term protection, e.g. for travel, the polysaccharides are a reasonable, less expensive option.

The only Ministry of Health-funded meningococcal vaccine is Menomune[®] ACYW-135 for children 2–18 years of age with functional asplenia or who are pre/post-splenectomy, and adults who are pre/post-splenectomy.

IMAC recommends two privately purchased doses of Menactra[®] for immunocompromised individuals instead of Menomune[®] ACYW-135 or Mencevax[®] ACYW when possible.

Meningococcal vaccination is recommended but not funded by the Ministry of Health for adolescents and young adults living in close proximity to each other, e.g. boarding schools, hostel type accommodation, close contacts of cases of meningococcal

GlaxoSmithKline NZ is proud to support the
2013 WHO World Immunisation Week with this publication.

Protect your world – get vaccinated.

Editorial content is independent.



TAPS DA5312IG/13AP/VAC/00016/13. H&T GSK1154.

disease, individuals with a medical condition that increases their risk of meningococcal infection, military recruits, some laboratory workers and travellers to sub-Saharan Africa or Hajj pilgrims.⁶

During a disease outbreak, individual District Health Boards may elect to fund a particular meningococcal vaccine for a specified population.

When a person requires both Menactra[®] and Prevenar 13[®] vaccinations, Menactra[®] should be administered a minimum of four weeks after the last Prevenar 13[®] dose.¹⁸

Frequently asked questions

How safe are the vaccines?

Polysaccharide and conjugate meningococcal vaccines have excellent safety profiles. The most common vaccine side effects include soreness/pain, redness and/or swelling at the injection site. Temporary fever, headache, fussiness/irritability, drowsiness, nausea/vomiting and/or dizziness could also occur.^{19,22}

How well do the vaccines work?

Protection against invasive meningococcal disease is dependent on circulating antibodies

The initial immune response and duration of protection for both conjugate and polysaccharide vaccines is influenced by the age at vaccination and the meningococcal serogroup in the vaccine. In general polysaccharide vaccines provide up to 85–90% protection²³ and conjugates up to 97% protection.²¹ After receipt of a meningococcal polysaccharide vaccine circulating antibodies wane over 3–5 years in adults and as early as 2–3 years in children aged 2–5 years when vaccinated.^{24,25} Whereas after receipt of meningococcal conjugate vaccine antibodies persist for at least five years in older children, adolescents and adults and up to three years in children aged 1–6 years when vaccinated but wane very rapidly in infants vaccinated before one year of age and in whom a booster vaccination should be administered at 12 months of age.¹⁷

Can children less than two years of age receive Mencevax[®] ACYW or Menomune[®] ACYW-135?

No. Infants and children less than two years of age have a very poor immune response to polysaccharide vaccines and are unlikely to be protected against meningococcal disease.

Can children less than two years of age receive Menactra[®]?

Yes. In the US the vaccine is now licensed from nine months of age; New Zealand licensure is expected to change in the future.

Can adults older than 55 years of age receive Menactra[®]?

Yes. IMAC recommends the vaccine for adults at increased risk of meningococcal disease in this age group. No data are available on the efficacy of the vaccine in this age group; however, no safety concerns are expected.

Can meningococcal vaccines be given at the same time as other vaccines?

Yes. The meningococcal vaccines can be administered at the same time as other vaccines except for Prevenar 13[®]. Menactra[®] should be administered a minimum of four weeks after the last Prevenar 13[®] dose.¹⁸

Varicella (chickenpox) vaccines

Varicella (chickenpox) is commonly seen in NZ children. It is highly infectious.²⁶ Transmission occurs through contact with infected droplets, respiratory secretions and liquid from vesicular lesions.^{26,27} Although rare, some people get chickenpox more than once.²⁸ During infection, the virus establishes latency in sensory-nerve ganglia and years later may reactivate causing herpes zoster, also known as shingles.²⁷

When maternal chickenpox occurs during the first 20 weeks of pregnancy, the foetus may develop congenital varicella syndrome.^{27,29} When it occurs within five days before to two days after delivery, the newborn infant may develop severe disease leading to death.^{27,29}

Available vaccines

Two live, attenuated vaccines against chickenpox, Varilrix[®] and Varivax[®], are licensed in NZ. The combination measles, mumps, rubella and varicella vaccines are not yet available in NZ.

Recommendations

Varicella vaccine is not currently on the National Immunisation Schedule. Two doses of the vaccine are recommended but not funded by the Ministry of Health for:⁶

- Children likely to require solid organ transplantation
- Children infected with human immunodeficiency virus (HIV) with a CD4 cell count $\geq 25\%$
- Adolescents and adults up to 50 years of age³⁰ with no history of varicella disease or vaccination, particularly if they live or work in environments where the risk of disease exposure is high, are non-pregnant women of childbearing age, or are planning international travel
 - *The herpes zoster vaccine Zostavax[®] is recommended instead for adults 50 years of age and over
- Varicella-susceptible individuals who have been exposed to the disease, i.e. post-exposure prophylaxis

IMAC recommends that:

- Infants in the 9–12 months age group at increased risk of exposure to wild-type chickenpox, e.g. those attending early childhood services, with older non-immune siblings, or immunocompromised family members, receive two vaccine doses; the first dose between 9–12 months of age and the second dose at 12 months of age
- All other infants receive a single vaccine dose at 12 months of age⁸
- Non-immune older children and adults receive two vaccine doses with a minimum interval of four weeks between the vaccine doses

*The current level of wild-type chickenpox circulating in the NZ environment boosts immunity and therefore a single varicella vaccine dose administered between 12 months and 12 years of age is likely to provide long-lasting protection against the disease. This advice would change if there was less circulating wild disease.

A single vaccine dose administered within 72–96 hours of exposure may prevent the disease developing or reduce the severity of the disease.^{27,29} Receipt of the vaccine after disease exposure at any age will not make wild-type chickenpox more severe.

Women should delay pregnancy for one month after receiving a live vaccine. However, surveillance of inadvertent vaccination during pregnancy has not identified any foetal safety concerns.³¹

Frequently asked questions

How safe are the vaccines?

Varicella vaccines have an excellent safety profile. The most common vaccine side effects include soreness/pain, redness and/or swelling at the injection site. Temporary fever, headache and tiredness may also occur.³²

Around 5% of healthy vaccine recipients develop a vaccine-related rash 6–43 days post-vaccination, with fewer spots in comparison with wild-type chickenpox.^{27,32} It is possible, but extremely rare, for a vaccine recipient with a vaccine-related rash to transfer the vaccine virus to another person. Vaccine recipients who develop a rash are recommended to avoid contact with pregnant women susceptible to the disease, newborn babies and individuals who are immunocompromised, until the rash has gone. If avoiding contact is not possible, the susceptible person should avoid contact with the rash and observe careful hygiene measures. There is no risk of transmitting the vaccine virus if there is no vaccine-related rash.³³

How well do the vaccines work?

Both varicella vaccines are similar in how well they prevent the disease.

- After a single vaccine dose in children 12 months to 12 years of age, 70–90% will be protected against all chickenpox and more than 95% protected from moderate to severe chickenpox but they may still develop mild disease.³⁴
- After two chickenpox vaccine doses in children 12 months to 12 years of age, 97–99% will be protected against all chickenpox and up to 100% protected from moderate to severe chickenpox.³⁴
- After two vaccine doses in adolescents aged 12 years and over and in adults, 79–91% will be protected against moderate to severe chickenpox.³⁵

Do NZ children need two vaccine doses?

In healthy children aged 12 months to 12 years of age, one vaccine dose protects most children from moderate-to-severe chickenpox and two vaccine doses protect most children from all disease.³⁴ After receiving a single vaccine dose, seven out of 10 children who develop chickenpox will have milder disease than an unvaccinated peer.³⁶



Can someone living with a person who is susceptible to the disease have varicella vaccine?

Yes. A person living in a household with a susceptible pregnant woman, newborn infant or person who is immunocompromised can receive the vaccine. However, if the vaccine recipient develops a rash the susceptible person should avoid contact with the rash and observe careful hygiene measures until the rash has gone.

Can varicella vaccines be given at the same time as other vaccines?

Yes. Varicella vaccine can be administered at the same time as routine schedule vaccines. When varicella vaccine is not administered at the same visit as another live vaccine, e.g. MMR or BCG vaccines, there must be a minimum interval of four weeks between the vaccine doses.¹³

Herpes zoster (shingles) vaccine

During primary varicella infection (chickenpox), the varicella-zoster virus establishes latency in sensory-nerve ganglia. Years later the virus may reactivate, causing herpes zoster (shingles), characterised by a vesicular rash in a dermatomal distribution of the affected nerves causing severe pain that may be prolonged and disabling.²⁷ Shingles more frequently affects adults aged 50 years or older and immunocompromised individuals of any age.^{27,28} It is possible for a person with shingles to transmit the virus to a varicella susceptible person causing chickenpox, but only through direct contact with the vesicular rash.²⁶

Available vaccine

Zostavax® is the live, attenuated vaccine licensed in NZ to prevent shingles. It is 14 times stronger than either of the varicella vaccines, therefore the varicella and herpes zoster vaccines are not interchangeable.³⁸

Recommendations

Vaccination to prevent shingles is not on the National Immunisation Schedule. The vaccine is recommended but not funded for immunocompetent adults aged 50 years and over, irrespective of a known history of chicken pox.³³

When a person requires Zostavax® and a 23-valent pneumococcal polysaccharide vaccine, Pneumovax® 23 or Pneumo 23®, a minimum interval of four weeks between vaccine doses is recommended.³⁹

Frequently asked questions

How safe is Zostavax®?

The vaccine is generally well tolerated. The most common vaccine side effects include soreness/pain, redness, swelling and/or itching at the injection site. Temporary headache and/or arm pain may also occur.⁴⁰

How well does Zostavax® work?

The age at vaccination influences how well the vaccine protects against shingles. The ability of the vaccine to protect against shingles decreases with advancing age, in parallel to the risk of shingles increasing with advancing age. Around 70% of 50–59-year-olds, 51% of 60–69-year-olds, 41% of 70–79-year-olds and 18% of those aged 80 years and over are protected against shingles after vaccination.⁴¹

How long does the vaccine protection last?

Post-licensure studies of the duration of protection are continuing. Although the degree of protection against shingles has been shown to decrease over time after vaccination, significant protection has been shown to persist to at least five years. There are no current recommendations around offering booster doses of Zostavax®.⁴²

Can a person aged 60 years and older who doesn't remember having chickenpox be given Zostavax®?

Yes. A person in this age group who has avoided all exposure to chickenpox over their lifetime can receive the vaccine and is expected to develop some protection against chickenpox.³⁸

Can a person who has already had shingles be given Zostavax®?

A recent episode of shingles boosts immunity reducing, but not excluding the risk of subsequent episodes, and the person is unlikely to benefit from receiving the vaccine. However, a single vaccine dose is recommended for a person who is unable to clearly describe a previous episode of shingles or describes an episode many years earlier.³⁸

Can Zostavax® cause shingles?

Shingles only occurs when latent varicella zoster virus from primary infection reactivates. The vaccine virus has not been detected in any shingles-like rashes that developed in study participants after receiving Zostavax®.^{38,40} If a person develops shingles after receiving the vaccine, it is likely that the vaccine did not boost their immunity enough to prevent the virus reactivating.

Is anyone too old to be given Zostavax®?

No. There is no upper age limit for receiving Zostavax®. The oldest person in the large Shingles Prevention Study was 99 years of age.³⁸

Can someone living with a person who is susceptible to chickenpox receive the vaccine?

Yes. Although none of the study participants developed a vaccine-related rash after receiving Zostavax®, it is known that varicella vaccine may cause a rash. If the vaccine recipient develops a rash after Zostavax®, the susceptible person should avoid contact with the rash and observe careful hygiene measures until the rash has gone.³⁸

Can Zostavax® be given at the same time as other vaccines?

Zostavax® can be given at the same time as other vaccines except for Pneumovax® 23 or Pneumo23®, where a minimum interval of four weeks between vaccine doses is recommended.³⁹ When Zostavax® is not administered at the same visit as another live vaccine, e.g. yellow fever vaccine, there must be a minimum interval of four weeks between the vaccine doses.

Human papillomavirus (HPV) vaccine

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide. HPV genotypes infecting mucous membranes are classified as high- and low-risk depending on their cancer-causing potential. Persistent infection with a high-risk HPV genotype, most commonly HPV 16 and 18, may lead to cervical cancer in women or a range of other types of cancer in both men and women⁴³ including anal, oropharyngeal, penile and vulval/vaginal cancers. Persistent infection with a low-risk HPV genotype, most commonly HPV 6 and 11, can lead to benign or low-grade cervical cell changes, anogenital warts and oropharyngeal/respiratory papillomatosis.⁴⁴ Anal HPV infection has been associated with an increased risk of acquiring HIV infection.⁴⁵

Available vaccine

Two vaccines against HPV genotypes 6, 11, 16 and 18, Cervarix® and Gardasil®, are licensed in NZ. However, only the Gardasil® brand is routinely available for private purchase.

Recommendations

Gardasil® is only funded for girls from 12 years of age to their 20th birthday.

Gardasil® is recommended but not funded by IMAC for adolescent males from 12 through 26 years of age for direct protection against genital warts and anal, oropharyngeal and penile cancers. Vaccination of heterosexual men may provide indirect protection for women against exposure to these HPV types. Offering the vaccine to men who have sex with men is particularly important as this group is particularly vulnerable to HPV and HIV infection.

Gardasil® can be offered to women from 20 through 45 years of age. Although the risk of HPV infection is highest within 5–10 years of sexual debut, there are still gains for older women who may not have acquired persistent HPV infection against all four genotypes.⁴⁶

Frequently asked questions

How safe is Gardasil®?

The most common vaccine side effects include soreness/pain, redness and/or swelling at the injection site. Temporary fever, headache and/or fatigue can also occur.⁴⁶⁻⁴⁹ Dizziness and fainting has been strongly associated with vaccination in adolescents.⁴⁹

How well does Gardasil® work?

After completion of three vaccine doses in males 16–26 years of age, protection was greater than 90% against HPV 6, 11, 16 and 18 external genital lesions and greater than 85% against persistent infection.⁴⁸

After completion of three vaccine doses in females 24–45 years of age, protection against HPV 6, 11, 16 and 18 cervical intraepithelial neoplasias was 93% and external genital lesions 92%.⁴⁶

How long does vaccine protection last?

Ongoing monitoring of how well the vaccine protects against persistent HPV infection and related disease indicates protection will be long-term. There are no recommendations around offering booster doses of Gardasil®.^{50,51}

Can a person who is already sexually active be given Gardasil®?

Yes. A person who is sexually active may benefit from protection against some or all four HPV genotypes in the vaccine as they may not have acquired persistent infection to all types.⁵²

Can a person who has had genital warts or cervical disease be given Gardasil®?

Yes, but Gardasil® does not treat existing HPV infection. A person with a history of genital warts may benefit from future protection against either or both HPV genotypes 6 and 11 in the vaccine. Women with a history of genital warts, cervical surgery or vaginal and vulval neoplasia were around a third less likely to have subsequent HPV-related disease after vaccination.⁵³ Men with a history of genital warts and HPV-related neoplasias would also be expected to benefit from vaccination.

Can Gardasil® be given to a pregnant woman?

It is not recommended that Gardasil® be given during pregnancy. Health providers are advised to ask women about pregnancy before vaccination, but a formal pregnancy test is not required. Surveillance of inadvertent vaccination during pregnancy has not identified any pregnancy or foetal safety concerns.⁵⁴ The vaccine is not live and it is not necessary to delay pregnancy after vaccination.

Can Gardasil® cause HPV infection?

No. Gardasil® is not a live vaccine. It only contains fragments/pieces of human papillomavirus.

Can Gardasil® be given at the same time as other vaccines?

Yes. Gardasil® can be given at the same time as other vaccines.

Pneumococcal vaccines

Twenty serotypes of pneumococcal bacteria were identified as causing disease in NZ between 2006 and 2011. Serotype 19A is now the most common cause of invasive disease overall and has been associated with a significant increase in invasive disease in adults aged 65 years and over during this time.⁵⁵ Asymptomatic carriage of the bacteria in the nasopharynx is highest in young children and declines towards adolescence.⁵⁶ Carriage may lead to protection against the disease or invasive disease associated with pneumonia, meningitis, septicaemia and death. Transmission occurs through direct contact with respiratory droplets.⁵⁶ Children aged less than five and particularly infants less than one year of age, older adults, with an increasing trend from 45 years of age, Pacific Peoples and Māori, have the highest risk of developing invasive disease.⁵⁵ Older adults are at risk from a broader range of serotypes.

Available vaccines

Four vaccines against pneumococcal disease are licensed in NZ. Two of these are conjugate vaccines, Synflorix® and Prevenar 13®. However, Synflorix® is not available for private purchase. Two are polysaccharide vaccines, Pneumovax® 23 and Pneumo 23®.

Conjugate vaccines generate better quality, longer-lasting circulating antibodies and immune memory that rapidly responds to a booster vaccination producing more circulating antibodies.¹⁷ They are usually more expensive than the polysaccharide vaccines. Prevenar 13® protects against 13 pneumococcal serotypes, the same 10 serotypes covered by the National Immunisation Schedule vaccine Synflorix® plus three more serotypes including 19A.

Polysaccharide vaccines protect against a broader range of serotypes but generate shorter-term circulating antibodies without immune memory. Subsequent polysaccharide vaccine doses have been shown to generate less circulating antibodies. These vaccines are not effective in children less than two years of age¹⁷ and may not be very effective in the elderly.⁵⁷ They are usually less expensive than the conjugate vaccines. Pneumovax® 23 and Pneumo 23® protect against 23 pneumococcal serotypes including 19A.

Recommendations

Prevenar 13® is funded for children less than five years of age who meet the criteria for the High Risk Pneumococcal Programme (refer to the Immunisation Handbook 2011, pages 193–4) and for children up to 18 years of age with functional asplenia or who are pre/post-splenectomy. Prevenar 13® is given outside of licensure between 5–49 years of age; however, no safety concerns are expected.⁵⁸

Pneumovax® 23 is funded for children 2–18 years of age with functional asplenia or who are pre/post-splenectomy and adults who are pre/post-splenectomy.

Pneumococcal vaccination is recommended but not funded by the Ministry of Health for children aged five years and over, and for adults:⁶

- With a medical condition that increases their risk of invasive pneumococcal disease or pneumonia
- With Down syndrome
- Who have had an episode of invasive pneumococcal disease
- Are aged 65 years and over

IMAC recommends a single privately purchased dose of Prevenar 13® for immunocompromised individuals administered eight weeks before Pneumovax® 23 or Pneumo 23® when possible.⁵⁹

For children aged two to less than 10 years at the time of vaccination, the Ministry of Health recommends the first revaccination with Pneumovax® 23 or Pneumo 23® three years after the first dose and a second revaccination at age 65 years. For individuals aged 10 years and over at the time of vaccination, the first revaccination is five years after the first dose and a second revaccination at 65 years of age if this is at least five years after the second dose.⁶

Frequently asked questions

How safe are the vaccines?

Polysaccharide and conjugate pneumococcal vaccines have excellent safety profiles. The most common vaccine side effects include soreness/pain, redness and/or swelling at the injection site. Temporary fever, headache, fussiness/irritability and drowsiness may also occur.^{58,60,61}

How well do the vaccines work?

Protection against invasive pneumococcal disease is dependent on circulating antibodies, because the time between bacterial invasion and disease is shorter than the time taken by the immune system to generate antibodies. The immune response to both pneumococcal conjugate and polysaccharide vaccines is influenced by the age at vaccination and health status.^{58,62}

Prevenar 13® is expected to be at least as effective as the original Prevenar® vaccine where, after completion of a primary course and booster dose in infants and young children, the risk of invasive pneumococcal disease was reduced by 97%.^{60,63}

Prevenar 13® covers fewer serotypes than the pneumococcal polysaccharide vaccine. However, in healthy adults aged 50 years and over, Prevenar 13® has been shown to generate an equal or better immune response than pneumococcal polysaccharide vaccine for the 13 serotypes covered by both vaccines and has the potential to provide better protection against invasive disease caused by these serotypes.⁶⁴

The pneumococcal polysaccharide vaccines, Pneumovax® 23 and Pneumo® 23, generate low levels of protection against the 23 serotypes covered by the vaccine.^{17,57,65}

Medical conditions that increase the risk of disease and older age are likely to reduce the effectiveness of both vaccine types and protection against invasive disease.⁵⁸

The duration of protection after pneumococcal conjugate vaccination has not been established¹⁷ and is unlikely to be due to the impact of the vaccine and decreased rate of disease. After receipt of a pneumococcal polysaccharide vaccine, circulating antibodies wane over 5–10 years in adults.⁶⁶ Antibodies begin to wane more quickly in children less than 12 years of age, as early as 21 months after vaccination.⁶⁷

Can children less than two years of age receive Pneumovax® 23 or Pneumo 23®?

No. Infants and children less than two years of age have a very poor immune response to polysaccharide vaccines and are unlikely to be protected against pneumococcal disease.

Can pneumococcal vaccines be given at the same time as other vaccines?

The pneumococcal vaccines can be administered at the same time as routine schedule vaccines except for the following combinations:

- Prevenar 13® and Menactra®: Menactra® should be administered a minimum of four weeks after the last Prevenar 13® dose¹⁸
- Pneumovax® 23 or Pneumo 23® and Zostavax®: Zostavax® should be administered a minimum of four weeks after either Pneumovax® 23 or Pneumo 23®^{68,69}

Pertussis (whooping cough) vaccines

Whooping cough, also known as pertussis, is highly infectious.^{68,69} Immunity against the disease wanes after wild-type disease and after immunisation.^{68,70} Outbreaks occur worldwide on a 3–5-yearly cycle.^{68,69} Transmission occurs through direct contact with respiratory droplets.⁶⁸

Infants less than one year of age (particularly infants too young to have been fully immunised or who have had any one of their immunisations delayed) have the highest risk of catching whooping cough and developing serious complications leading to death.^{68,69,71-73}

The main source of infection for this age group are mothers,⁷¹ followed by siblings, adolescents and other adults in the household, and health care workers.^{69,73}

Available vaccines

Three vaccines against pertussis, Boostrix®, Adacel® and Adacel® Polio, are licensed for use in older children, adolescents and adults in NZ. All pertussis vaccines are combination vaccines including tetanus and diphtheria antigens.

Recommendations

In adolescents and adults, a single dose of pertussis-containing vaccine is expected to boost protection against the disease, whether the person has previously been vaccinated or not.^{70,74}

A pertussis containing vaccine is recommended but not funded by the Ministry of Health for:

- Children aged seven years and over requiring a catch-up tetanus/diphtheria vaccine⁹
- Household and other close contacts of infants less than one year of age^{6,75}
- Health care staff who work with infants less than one year of age^{6,75}
- Early childhood education staff^{6,75}
- Adults with a medical condition for whom prevention of pertussis is important, e.g. individuals with chronic respiratory/lung disease⁷³

During a disease outbreak, individual District Health Boards may elect to fund a particular pertussis-containing vaccine for a specified population.

Adacel[®] Polio (Tdap-IPV) may be used if the adult is planning to travel and will require a poliovirus booster vaccination.

Frequently asked questions

How safe are the vaccines?

The most common vaccine side effects include soreness/pain, redness and/or swelling at the injection site.⁷⁶ After the fourth and sometimes fifth vaccine dose, a self-limiting extensive redness and swelling of the injected limb reflecting a vigorous immune response can occur in children, and less commonly in adolescents and adults.⁷⁷ Temporary fever, headache and muscle aches may also occur.⁷⁸

Non-live vaccines including tetanus, inactivated polio and influenza vaccines have been administered during pregnancy for over 50 years with no evidence of pregnancy, foetal or newborn harm.⁷⁸ Vaccination of breastfeeding women is safe for both the woman and her child and reduces the risk the mother will contract pertussis and infect her child.^{79,80}

How well do the vaccines work?

Around nine in 10 adolescent and adult vaccine recipients will be protected from severe disease and 5–6 in 10 from milder disease during the two years after vaccination.⁸¹ Protection wanes around four and six years after vaccination.^{68,69,74}

When a pregnant woman is vaccinated before 36 weeks gestation, transplacental maternal antibody may provide protection against severe pertussis in the newborn for four to six weeks after birth.^{78,82}

Can a pertussis-containing vaccine be given to a breastfeeding woman?

Yes. Breastfeeding women can be vaccinated without harm for herself or her child.^{79,80}

Should pertussis vaccination be delayed if the person has recently had a tetanus (Td) vaccination?

No. There is no minimum interval between a previous Td vaccination and administration of a pertussis-containing vaccine.

References

1. Marshall GS. Rotavirus disease and prevention through vaccination. *Pediatr Infect Dis J*. 2009;28(4):351-64.
2. Anderson EJ, Weber SG. Rotavirus infection in adults. *Lancet Infect Dis*. 2004;4(2):91-9.
3. Bernstein DI. Rotavirus overview. *Pediatr Infect Dis J*. 2009;28(Suppl 3):S50-3.
4. Centers for Disease Control and Prevention. Prevention of rotavirus gastroenteritis among infants and children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2009;58(RR-02):1-24.
5. Grimwood K, et al. Rotavirus hospitalisation in New Zealand children under 3 years of age. *J Paediatr Child Health*. 2006;42(4):196-203.
6. Ministry of Health. Immunisation handbook 2011. Wellington: Ministry of Health; 2011.
7. GlaxoSmithKline NZ Limited. Rotarix oral vaccine [Homepage on the Internet]. Wellington: Medsafe; 2011 [cited 2012, February 23]. Available from: <http://www.medsafe.govt.nz/profs/Datasheet/R/rotarixvac.pdf>.
8. Soares-Welser K, et al. Vaccines for preventing rotavirus diarrhoea: Vaccines in use (Review). 2012;(2):Art. No.: CD008521.
9. Buttery JP, et al. Intussusception following rotavirus vaccine administration: Post-marketing surveillance in the National Immunization Program in Australia. *Vaccine*. 2011;29(16):3061-6.
10. Velázquez FR, et al. Postmarketing surveillance of intussusception following mass introduction of the attenuated human rotavirus vaccine in Mexico. *Pediatr Infect Dis J*. 2012;31(7):736-44.
11. Yen C, et al. Trends in intussusception hospitalizations among US infants before and after implementation of the rotavirus vaccination program, 2000–2009. *J Infect Dis*. 2012;206(1):41-8.
12. Australian Technical Advisory Group on Immunisation. The Australian immunisation handbook, 9th ed. Canberra: Australian Government Department of Health and Ageing; 2008.
13. Kroger A, et al. General immunization practices. In: Plotkin S, Orenstein W, Offit P, editors. *Vaccines*. 6th ed. London: W.B. Saunders; 2013. pp. 88-112.
14. Lopez L, et al. The epidemiology of meningococcal disease in New Zealand 2011. Wellington: Institute of Environmental Science and Research Ltd (ESR); 2012.
15. Cartwright KAV, et al. The Stonehouse Survey: Nasopharyngeal carriage of meningococci and *Neisseria lactamica*. *Epidemiol Infect*. 1987;99(3):591-601.
16. Stephens DS, et al. Epidemic meningitis, meningococcaemia, and *Neisseria meningitidis*. *Lancet*. 2007;369(9580):2196-210.
17. Blanchard-Rohner G, Pollard AJ. Long-term protection after immunization with protein-polysaccharide conjugate vaccines in infancy. *Expert Rev Vaccines*. 2011;10(5):673-84.
18. Centers for Disease Control and Prevention. Recommendation of the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MenACWY-D) among children aged 9 through 23 months at increased risk for invasive meningococcal disease. *MMWR Morb Mortal Wkly Rep*. 2011;60(40):1391-2.
19. Ball R, et al. Safety data on meningococcal polysaccharide vaccine from the Vaccine Adverse Event Reporting System. *Clin Infect Dis*. 2001;32(9):1273-80.
20. Campaign GMM, et al. Safety and immunogenicity of three doses of a *Neisseria meningitidis* A + C diphtheria conjugate vaccine in infants from Niger. *Pediatr Infect Dis J*. 2000;19(2):144.
21. Keyserling H, et al. Safety, immunogenicity, and immune memory of a novel meningococcal (groups A, C, Y, and W-135) polysaccharide diphtheria toxoid conjugate vaccine (mcv-4) in healthy adolescents. *Arch Pediatr Adolesc Med*. 2005;159(10):907-13.
22. Pichichero M, et al. Comparative trial of the safety and immunogenicity of quadrivalent (A, C, Y, W-135) meningococcal polysaccharide-diphtheria conjugate vaccine versus quadrivalent polysaccharide vaccine in two- to ten-year-old children. *Pediatr Infect Dis J*. 2005;24(11):57-62.
23. Rosenstein NE, et al. Meningococcal vaccines. *Infect Dis Clin North Am*. 2001;15(1):155-69.
24. Gasparini R, Panatto D. Meningococcal glycoconjugate vaccines. *Hum Vaccin*. 2011;7(2):170-82.
25. Granoff DM, et al. Meningococcal vaccines. In: Plotkin S, Orenstein W, Offit P, editors. *Vaccines*. 6th ed. London: W.B. Saunders; 2013. p. 388-418.
26. Tarlow MJ, Walters S. Chickenpox in childhood: A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect*. 1998;36(Suppl 1):39-47.
27. Pace D. Review of varicella zoster virus: From epidemiology to prevention. *Malta Medical Journal*. 2008;20(3):7-11.
28. Hall S, et al. Second varicella infections: Are they more common than previously thought? *Pediatrics*. 2002;109(6):1068-73.
29. Macartney K, McIntyre P. Vaccines for post-exposure prophylaxis against varicella (chickenpox) in children and adults. *Cochrane Database Syst Rev*. 2008;(3):Art. No.: CD001833.
30. Tebruegge M, et al. Does the use of calamine or antihistamine provide symptomatic relief from pruritus in children with varicella zoster infection? *Arch Dis Child*. 2006;91(12):1035-6.
31. Wilson E, et al. Varicella vaccine exposure during pregnancy: Data from 10 years of the pregnancy registry. *J Infect Dis*. 2008;197(Suppl 2):S178-S84.
32. Chaves SS, et al. Safety of varicella vaccine after licensure in the United States: Experience from reports to the Vaccine Adverse Event Reporting System, 1995–2005. *J Infect Dis*. 2008;197(Suppl 2):S170-7.
33. American Academy of Pediatrics. Varicella-zoster infections. In: Pickering L, Baker C, Kimberlin D, Long S, editors. *Red book: 2009 report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009. p. 714-27.
34. Centers for Disease Control and Prevention. Prevention of varicella recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56(RR-04):1-40.
35. Ampofu K, et al. Persistence of immunity to live attenuated varicella vaccine in healthy adults. *Clin Infect Dis*. 2002;34(6):774-9.
36. Chaves SS, et al. Varicella disease among vaccinated persons: Clinical and epidemiological characteristics, 1997–2005. *J Infect Dis*. 2008;197(Suppl 2):S127-31.
37. Hambleton S, Arvin AM. Chickenpox party or varicella vaccine? In: Pollard AJ, Finn A, editors. *Hot topics in infection and immunity in children II*. New York: Springer US; 2005. p. 11-24.
38. Gnann Jr JW. Vaccination to prevent herpes zoster in older adults. *J Pain*. 2008;9(Suppl 1):31-6.
39. Tseng HF, et al. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine*. 2011;29(20):3628-32.
40. Oxman MN, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med*. 2005;352(22):2271-84.
41. U.S. Food and Drug Administration. Package insert: Zostavax (zoster vaccine live) [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2011 [cited 2012 November 22]. Available from: <http://www.fda.gov/downloads/biologicsbloodvaccines/vaccinesapprovedproducts/ucm132831.pdf>.
42. Schmader K, et al. Persistence of the efficacy of zoster vaccine in the Shingles Prevention Study and the Short-Term Persistence Substudy. *Clin Infect Dis*. 2012. 2012, July 24.
43. World Health Organization. The immunological basis for immunization series: Module 19: Human papillomavirus infection. Geneva: World Health Organization; 2011.
44. Chaturvedi AK. Beyond cervical cancer: Burden of other HPV-related cancers among men and women. *J Adolesc Health*. 2010;46(Suppl 4):S20-6.
45. Chin-Hong PV, et al. Anal human papillomavirus infection is associated with HIV acquisition in men who have sex with men. *AIDS*. 2009;23(9):1135-42.
46. Muñoz N, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24–45 years: A randomised, double-blind trial. *Lancet*. 2009;373(9679):1949-57.
47. Agorastos T, et al. Safety of human papillomavirus (HPV) vaccines: A review of the international experience so far. *Vaccine*. 2009;27(52):7270-81.
48. Giuliano AR, et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. *N Engl J Med*. 2011;364(5):401-11.
49. Klein NP, et al. Safety of quadrivalent human papillomavirus vaccine administered routinely to females. *Arch Pediatr Adolesc Med*. 2012;1-9. 2012 Oct 1.
50. Villa L, et al. High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus-like particle vaccine through 5 years of follow-up. *Br J Cancer*. 2006;95(11):1459-66.
51. Saah A, LBP-1.15 An evaluation of the long-term effectiveness, immunogenicity, and safety of Gardasil in previously vaccinated women. *Sex Transm Infect*. 2011;87(Suppl 1):A357-8.
52. Committee on Infectious Diseases. HPV vaccine recommendations. *Pediatrics*. 2012;129(3):602-5.
53. Joura EA, et al. Effect of the human papillomavirus (HPV) quadrivalent vaccine in a subgroup of women with cervical and vulvar disease: Retrospective pooled analysis of trial data. *BMJ*. 2012;344:e1401.
54. Forinash AB, et al. Safety of the HPV bivalent and quadrivalent vaccines during pregnancy. *Ann Pharmacother*. 2011;45(2):258-62.
55. Lim E, Heffernan H. Invasive pneumococcal disease in New Zealand, 2011. *Poruria*: Institute of Environmental Science and Research Ltd (ESR); 2012.
56. Bogaert D, et al. *Streptococcus pneumoniae* colonisation: The key to pneumococcal disease. *Lancet Infect Dis*. 2004;4(3):144-54.
57. Cadeddu C, et al. 23-valent pneumococcal polysaccharide vaccine (PPV23) for the prevention of invasive pneumococcal diseases (IPDs) in the elderly: Is it really effective? *J Prev Med Hyg*. 2012;53(2):101-3.
58. Musher DM, et al. The potential role for protein-conjugate pneumococcal vaccine in adults: What is the supporting evidence? *Clin Infect Dis*. 2011;52(5):633-40.
59. Centers for Disease Control and Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2012;61(40):816-9.
60. Yeung SH, et al. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in infants and toddlers. *Pediatrics*. 2010;126(3):e493-505.
61. Schwarz TF, et al. A randomized, double-blind trial to evaluate immunogenicity and safety of 13-valent pneumococcal conjugate vaccine given concomitantly with trivalent influenza vaccine in adults aged ≥65 years. *Vaccine*. 2011;29(32):5195-202.
62. Laferriere C. The immunogenicity of pneumococcal polysaccharides in infants and children: A meta-regression. *Vaccine*. 2011;29(40):6838-47.
63. Black S, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. *Pediatr Infect Dis J*. 2000;19(3):187-95.
64. Paradiso PR. Pneumococcal conjugate vaccine for adults: A new paradigm. *Clin Infect Dis*. 2012;55(2):259-64.
65. Borrow R, et al. Use of pneumococcal polysaccharide vaccine in children: what is the evidence? *Curr Opin Infect Dis*. 2012;25(3):292-303.
66. Grabenstein JD, Manoff SB. Pneumococcal polysaccharide 23-valent vaccine: Long-term persistence of circulating antibody and immunogenicity and safety after revaccination in adults. *Vaccine*. 2012;30(30):4435-44.
67. Hillman MR, et al. *Streptococcus pneumoniae* polysaccharide vaccine: Age and dose responses, safety, persistence of antibody, revaccination, and simultaneous administration of pneumococcal and influenza vaccines. *Rev Infect Dis*. 1981;3(Suppl 1):S31-42.
68. Halperin S, De Serres G. *Pertussis*. In: Evans A, Brachman P, editors. *Bacterial infections of humans: Epidemiology and control*. New York: Springer; 2009. pp. 577-96.
69. Crowcroft NS, Pebody RG. Recent developments in pertussis. *Lancet*. 2006;367(9526):1926-36.
70. Heinger U. Pertussis immunisation in adolescents and adults. In: Finn A, Pollard A, editors. *Hot topics in infection and immunity in children IV*. New York: Springer; 2008. pp. 72-97.
71. Bechini A, et al. Acellular pertussis vaccine use in risk groups (adolescents, pregnant women, newborns and health care workers): A review of evidence and recommendations. *Vaccine*. 2012;30(35):5179-90.
72. Grant CC, et al. Delayed immunisation and risk of pertussis in infants: Unmatched case-control study. *BMJ*. 2003;326(7394):852-3.
73. Edwards KM. Overview of pertussis: Focus on epidemiology, sources of infection, and long term protection after infant vaccination. *Pediatr Infect Dis J*. 2005;24(6):S104-8.
74. Knuf M, et al. Immunogenicity of a single dose of reduced-antigen acellular pertussis vaccine in a non-vaccinated adolescent population. *Vaccine*. 2006;24(12):2043-8.
75. Keith R. BCG recall, immunisation health target, pertussis immunisation and advice azithromycin dosage, flu update, Pharmax purchase of vaccines, measles update [facsimile 2012 June 25]. Wellington: Ministry of Health; 2012. p. 2.
76. Beytout J, et al. Safety of Tdap-IPV given one month after Td-IPV booster in healthy young adults: A placebo-controlled trial. *Hum Vaccin*. 2009;5(5):315-21.
77. Woo EJ, et al. Extensive limb swelling after immunization: Reports to the Vaccine Adverse Event Reporting System. *Clin Infect Dis*. 2003;37(3):351-8.
78. Mood FR, de Greeff SC. The case for maternal vaccination against pertussis. *Lancet Infect Dis*. 2007;7(9):614-24.
79. Bruhn K, Tillet J. Administration of vaccinations in pregnancy and postpartum. *MCN Am J Matern Child Nurs*. 2009;34(2):98-105.
80. Centers for Disease Control and Prevention. General recommendations on immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(RR-02):1-61.
81. Wei SC, et al. Effectiveness of adolescent and adult tetanus, reduced-dose diphtheria, and acellular pertussis vaccine against pertussis. *Clin Infect Dis*. 2010;51(3):315-21.
82. Van Rie A, et al. Role of maternal pertussis antibodies in infants. *Pediatr Infect Dis J*. 2005;24(5):S62-5.