

Herpes zoster

ZOSTER VACCINE FOR AUSTRALIAN ADULTS: INFORMATION FOR IMMUNISATION PROVIDERS

Disease and epidemiology

- Herpes zoster or ‘shingles’ is a common and usually self-limiting painful rash resulting from reactivation of the same virus that causes chickenpox earlier in life.
- 20–30% of people will have an episode of shingles in their lifetime, most likely after the age of 50 years. Older people (particularly those >60 years of age) are also more likely to have shingles complicated by post-herpetic neuralgia, a chronic neuropathic pain syndrome.

Who should be vaccinated

- The vaccine is registered for use in people aged >50 years as a single dose. The zoster vaccine has been recommended for use in adults aged 60–79 years on the National Immunisation Program but a government decision is pending.

Vaccine

- The vaccine contains a live attenuated varicella-zoster virus, and is only recommended for use in immunocompetent people.
- Vaccination of persons 60–79 years of age is estimated to prevent approximately half the cases of shingles and two-thirds of post-herpetic neuralgia cases in that population. In vaccinated people in whom an episode of shingles occurs, the pain severity and duration is reduced by 60%. Medical therapy (such as analgesics and antivirals) should still be considered for treatment of a shingles episode, regardless of immunisation status.
- Mild reactions at the injection site, such as pain, swelling and redness, are likely to occur in approximately 50% of vaccine recipients. Other side-effects that may occur include headache and fatigue.

The disease

Herpes zoster (also known just as ‘zoster’ or ‘shingles’) is a localised, usually painful, skin eruption that occurs more frequently among older adults and in immunocompromised people. Shingles is the result of the reactivation of latent varicella-zoster virus (VZV). The varicella-zoster virus causes two distinct diseases. The primary (or initial) infection causes varicella (‘chickenpox’). After primary varicella infection, VZV remains latent in the dorsal root or trigeminal ganglia and can then reactivate, usually much later in life, to cause a cutaneous rash at the site supplied by that nerve root. This secondary infection is herpes zoster (‘shingles’).

For information on primary varicella (‘chickenpox’) infection, see the NCIRS fact sheet [Varicella-zoster \(chickenpox\) vaccines for Australian children](#).

Clinical features of shingles

In the majority of patients shingles clinically presents as an acute, self-limiting, vesicular rash, which is often painful and lasts approximately 10–15 days. The rash is usually unilateral (does not cross the midline) and in a dermatomal distribution, with the thoracic or lumbar dermatomes most commonly affected. A prodromal phase occurs 48–72 hours prior to the appearance of the rash in

80% of shingles cases with symptoms of itching, tingling, or severe pain in the affected dermatome, and sometimes headache, photophobia and malaise.

The clinical characteristics of shingles are dependent on:

- the location of the lesions,
- the immune status and age of the patient, and
- whether adequate and timely administration of appropriate therapeutic medication has occurred.

Complications

The most common complication of shingles is post-herpetic neuralgia (PHN). PHN is a chronic neuropathic pain syndrome where pain in the affected region persists longer than 3 months after rash healing.¹ PHN can have a significant impact on quality of life and can be refractory to treatment. Risk factors for the development of PHN include advanced age, severe prodromal pain and severe pain/rash in the acute phase of shingles.^{2,3} Depending on use of antivirals, PHN occurs in 25-50% of shingles cases in people aged >50 years. This age group accounts for 80-85% of PHN cases.^{3,4}

Other common complications of shingles include:

- skin pigmentation changes and scarring
- secondary bacterial infection of the rash
- neurological complications (most commonly nerve palsies)
- pneumonia
- eye involvement, called herpes zoster ophthalmicus, which occurs in ~10–25% of patients
- cutaneous hypersensitivity, or allodynia, which is seen in 5–10% of shingles patients.⁵

Disseminated disease, which can include generalised spread of skin lesions and, in some cases, organ system involvement, occurs rarely and is more likely in people with immunosuppression.

Diagnosis of shingles

Shingles is usually diagnosed on the basis of a clinical assessment, particularly once the rash appears. However, conditions such as HSV infection, eczema herpeticum, impetigo, contact dermatitis and others can be mistaken for shingles. Laboratory confirmation can be obtained by taking a sample from the base of the skin lesions and performing a nucleic acid detection test (such as PCR) or direct-fluorescent antibody test (DFA). Other techniques, such as viral culture, are less sensitive and take longer to complete. Each state and territory within Australia has developed guidelines for reporting shingles cases, using

either clinical and/or laboratory techniques. Providers should consult their state or territory guidelines.

Treatment of shingles

The aim of treatment for shingles is to accelerate the healing of the zoster rash, reduce the duration and severity of pain, and decrease the risk of complications and long-term sequelae of shingles, especially PHN. Aggressive treatment early in the acute phase of shingles using antivirals and analgesics has been shown to reduce the likelihood of PHN in the clinical trial setting.² Antiviral therapy should be initiated within 72 hours for optimal treatment benefit but may still be beneficial if started after this time, particularly if new lesions are still forming or the patient is immunocompromised.⁶ Uncertainties do exist in how to determine which combination of therapies for shingles and PHN is best, and there are few clinical trials that compare treatments or study their use in combination. Despite active treatment a significant number of patients will remain refractory to treatment.

The zoster vaccine has not been studied as a ‘treatment’ for shingles or PHN, and should not be administered for that purpose.

Disease transmission

VZV is usually present in the skin lesions of the shingles rash until the lesions crust over. The transmission of VZV from the skin vesicles of a person with shingles to a susceptible person can occur. However, the rate of infection in susceptible people after exposure to a person with shingles (15.5% of susceptible household contacts infected) is much less than exposure to a person with chickenpox (61–100% of susceptible contacts infected).⁷ During an episode of shingles, household contacts of susceptible people should cover their rash until after their lesions have crusted and should avoid contact with people with impaired immunity.

Epidemiology

Previous primary infection with VZV is an essential prerequisite for the development of shingles. In Australia more than 97% of the population have antibodies to VZV by the age of 30 years, indicating that they’ve been previously infected with the virus. Therefore, almost the entire adult population are at risk of shingles.⁸ Most cases of shingles occur in immunocompetent adults aged >50 years.

The lifetime risk of shingles is estimated to be approximately 20–30% across the population and about half of people who live to 85 years will develop shingles.^{3,9} Approximately 100,000 cases of shingles

occur each year in Australia, with rates estimated at 490 cases per 100,000 population per year across all ages (range 330–830 per 100,000).^{10–12} The annual rate of shingles in the Australian population aged >60 years is not precisely known, but is likely to be similar to that seen in other developed countries, such as the United States, where the incidence of shingles in persons aged >60 years in the placebo arm of the Shingles Prevention Study was 1,112 cases per 100,000 person-years.¹³

A decline in cell-mediated immunity (CMI) appears to be the most important risk factor influencing the development of shingles. Although antibodies to VZV generally persist through life, cellular immunity to the virus declines with age.¹⁴ This correlates with the observation that the risk of developing zoster increases substantially from the age of 50 years. CMI to VZV may be maintained by both ‘exogenous boosting’, from exposure to circulating VZV from chickenpox cases in the community, and/or by ‘endogenous boosting’, the response from either sub-clinical reactivation of VZV or an episode of shingles.⁷ For example, studies have shown that adults with greater contact with children have a lower rate of shingles.¹⁵ Immunosuppressive conditions and treatments that alter CMI also increase the likelihood of developing shingles. For example, shingles is up to 15 times more likely to occur in those immunocompromised due to HIV infection, and occurs in up to 30% of patients following haematopoietic stem cell transplantation (HSCT).^{7,16} Higher rates of shingles are also seen in those who had chickenpox in the 1st year of life or who had congenital varicella infection.

Second or subsequent episodes of zoster do occur in immunocompetent people, although the risk is difficult to estimate. Rates of recurrence are greater in immunocompromised individuals. Shingles appears to be much less common in people who have been vaccinated with the varicella (chickenpox) vaccine than in those naturally infected with VZV. However, continuing studies looking at rates of zoster in populations vaccinated against varicella over future decades are needed. When cases of shingles in people previously vaccinated with the varicella vaccine have occurred, genotyping of the virus has found the rash is usually due to the wild-type VZV, indicating a history of previously undiagnosed varicella infection.^{7,17} Shingles caused by the reactivation of the varicella vaccine strain has been reported to occur, but appears quite rare.

Who should be vaccinated

National Immunisation Program (NIP)

The Pharmaceutical Benefits Advisory Committee (PBAC) recently recommended that Zostavax[®] be included on the National Immunisation Program as a single dose for persons aged 60–79 years, on the basis that the vaccine will be cost-effective in reducing the rate of, and complications from, zoster in that age group.¹⁸ A decision as to whether to proceed with funding of Zostavax[®] under the NIP has not yet been made by the Australian Government. The 9th edition of *The Australian Immunisation Handbook* ([updated Zoster \(Herpes zoster\) chapter](#) available online) recommends that all adults ≥60 years of age, with no contraindications to vaccination, receive 1 dose of Zostavax[®].

In the single large clinical efficacy study of zoster vaccine, known as the Shingles Prevention Study, 38,546 immunocompetent adults ≥60 years of age received either the vaccine or a placebo.¹³ Although persons with significant underlying illnesses were excluded from the large clinical trial, pre-existing morbidities, such as hypertension and arthritis, were frequent (~90% of participants). Therefore, unless a contraindication or precaution exists due to their condition or medical treatment, persons with chronic medical conditions, such as arthritis, hypertension, chronic renal failure, diabetes and other similar conditions, can receive the zoster vaccine.

Other eligible groups

Persons aged 50–59 years

Zostavax[®] is currently registered for use in Australia in adults aged ≥50 years as a single dose.

Data on the safety and immunogenicity of the vaccine in the 50–59 years age group have been obtained from small studies which suggest that the vaccine is likely to be safe and generate a similar immune response in this age group. However, no efficacy studies in this age group have been performed.^{19,20} The incidence of shingles in this age group is increased compared to those <50 years of age; however, the risk of PHN is lower in those 50–59 years than in those aged 60 years or older.

Persons aged ≥80 years

The vaccine is registered for use in persons ≥80 years and the 9th edition of *The Australian Immunisation Handbook* ([updated Zoster \(Herpes zoster\) chapter](#) available online) recommends that all adults ≥60 years of age, with no contraindications to vaccination, receive 1 dose of Zostavax[®]. Overall, the effectiveness of vaccination is reduced in persons ≥80 years of age, but individual

benefit may still be obtained (see ‘Vaccine effectiveness’ below).

Eligible persons with a negative clinical history of chickenpox

Although an adult person may report not having had chickenpox, it is unlikely that they will actually be seronegative for VZV. In Australia, >97% of people for whom the zoster vaccine is recommended will be seropositive to VZV.⁸ In addition, the vaccine is likely to be well tolerated and immunogenic in seronegative people, although the incidence of injection site reactions may be slightly higher.^{20,21} It is NOT necessary to provide laboratory evidence of immunity to VZV in adults >60 years of age prior to administering Zostavax[®].

Eligible persons with a clinical history of shingles

Shingles may recur; however, the likelihood of experiencing a repeat episode is difficult to predict, and has been estimated to range from less than 5% up to rates similar to that for first episodes.^{2,7} In addition, a clinical history of previous shingles may be inaccurately recalled by a patient or the illness may have been mistakenly diagnosed (see ‘Diagnosis of shingles’ above). Based on these factors, it is suggested that people over the age of 60 years with a clinical history of shingles can be vaccinated with the zoster vaccine.⁷ However, no clinical trials of the use of zoster vaccine in individuals with a history of zoster have been performed, and there is no data to determine after what time following an episode of shingles that vaccination should be offered. It is suggested that the vaccine could be given at least 1 year after an episode of shingles.²²

Groups for whom zoster vaccination is NOT recommended

Zoster vaccination is not recommended for use in persons <50 years of age and is not registered for use in this age group.

Zostavax[®] is not indicated for use for therapeutic benefit during an acute shingles episode, nor for the treatment of PHN. In addition, the licensed varicella vaccines (Varilrix[®] and Varivax[®]) are *not* indicated for use for the primary purpose of preventing shingles in older persons (who are likely to have already had varicella) and Zostavax[®] is *not* indicated for use in persons to provide primary protection against varicella infection.

Zostavax[®] vaccination of people who have previously received varicella vaccine is not recommended at this time.

Vaccine

A zoster vaccine, known as Zostavax[®] (CSL Biotherapies/Merck & Co. Inc.) was licensed in Australia in 2006 and has been available via private purchase since early 2008. Zostavax[®] is a live attenuated viral vaccine formulated from the same VZV vaccine strain (Oka-derived) as both currently licensed varicella (chickenpox) vaccines (Varivax[®] and Varilrix[®]) but is of a higher potency, containing, on average, at least 14 times more plaque forming units of vaccine virus per dose. This higher viral potency is required to yield a satisfactory boost in the immune response in older adults.²³ (See ‘Vaccine effectiveness’ below.)

Administration

A single 0.65 mL dose of Zostavax[®] is required and is to be administered by subcutaneous injection only.

Vaccine effectiveness

The Shingles Prevention Study (SPS) demonstrated vaccine efficacy in trial participants (adults aged >60 years) with a significant reduction in the incidence of shingles, PHN and the burden of illness (BOI) associated with shingles (the BOI was a measure used in the clinical trial to describe the total pain, severity and duration of shingles).¹³ Overall, compared with those who received the placebo, vaccinated individuals experienced a reduction in the incidence of shingles by 51.3% and a reduction in the incidence of PHN by 66.5% over a median of over 3 years follow-up.¹³ Longer term follow-up of vaccine participants is continuing. In those that developed shingles despite vaccination, the severity of the shingles episode was also reduced (BOI score decreased by 61%). Thus, the vaccine reduces the likelihood that an individual experiences zoster or PHN, and may reduce the severity of a zoster episode if it occurs.

Zostavax[®] was more efficacious in reducing shingles in people aged 60–69 years compared with those aged >70 years. However, efficacy in reducing the incidence of PHN and the burden of illness of zoster was similar across both age groups.¹³ Furthermore, in people aged >80 years, vaccine efficacy was lower and not statistically significant.⁷ Although participant numbers in this age group were low, this suggests that the vaccine is less likely to provide a clinical benefit in this age group.

Approximately 65% of the participants in the trial received antiviral and pain medication within 72 hours of the onset of the rash (regardless of whether they were in the vaccine or placebo group), suggesting that the overall effect of the vaccine was in addition to any benefit that may have been obtained from timely medical therapy.

People who are vaccinated and develop shingles should still present to their health practitioner for diagnosis and timely prescription of treatment, such as antiviral medication, which is best commenced within 72 hours of rash onset.

A booster dose of Zostavax[®] is not currently recommended. Clinical trial data on the duration of protection from Zostavax[®] is currently limited to an average duration of follow-up of 3.1 years.¹³ The SPS trial data showed an initial decline in vaccine efficacy over the 1st year post vaccination; however, the efficacy from years 2 to 3 post vaccination was stable.¹⁴ Studies assessing the persistence of immunity in the SPS trial participants are ongoing and it is unknown at this stage whether a booster dose will be necessary to prevent lifelong reactivation of VZV.

Vaccine safety

Based on clinical trials, Zostavax[®] is safe and well tolerated among adults >50 years of age.^{13,19,20} The most common side-effects were injection site reactions. One or more injection site reactions (such as swelling, pain, redness) occurred in 48.3% of vaccine recipients compared with 16.6% in placebo recipients in the safety sub-study of the SPS trial. However, the reactions were generally mild and lasted <4 days; no injection site reaction was considered serious.¹³ Injection site reactions appear to be age-related, with reactions more common in vaccine recipients aged 60–69 years than in those aged ≥70 years (58.3% vs 41.3% in the SPS safety sub-study). In a separate small safety trial, 50–59 year olds reported higher rates of injection site reactions (69% of those received a vaccine of similar potency).^{13,19}

Vaccine recipients were significantly more likely to have varicella-like rashes around the injection site compared with placebo recipients, but rates were low overall, with 20 cases (0.1%) in vaccine recipients compared with 7 cases (0.04%) in placebo recipients. Generalised varicella-like rashes were rare, and occurred at similar rates in vaccine and placebo recipients (0.1% in both groups). In clinical trials where rashes were analysed by PCR for VZV, the majority of rashes were due to wild-type virus, with only two subjects found to have rashes due to the Oka/Merck VZV vaccine strain.²⁴

The rate of systemic symptoms was greater in vaccinees (Zostavax[®] 6.3% vs. placebo 4.9%), with the most frequently reported systemic symptoms being headache and fatigue.^{1,24} Fever >38.3°C occurred in <0.1% of subjects overall, with no difference between vaccine and placebo groups. Serious adverse events reported during the SPS were similar between the vaccine and placebo

recipients overall, but slightly higher in vaccine recipients in the safety sub-study (1.9% vs. 1.3%). No temporal or clinical patterns could be determined to suggest the vaccine was the cause of these systemic events.⁷

Adverse events occurring after vaccination should be reported to the Adverse Drug Reactions Advisory Committee (ADRAC), via specific state/territory reporting mechanisms.²² If a varicella- or zoster-like rash occurs after or despite receipt of the zoster vaccine, vaccinees should avoid contact with people with impaired immunity and household contacts of susceptible individuals should cover their rash until the lesions have crusted.

Contraindications/precautions

Zoster vaccination is contraindicated where there has been anaphylaxis following a previous dose of any VZV-containing vaccine, or anaphylaxis following any vaccine component.

As with other live viral vaccines, persons with significantly impaired immunity should NOT receive the zoster vaccine. Immunocompetent people who anticipate alteration of their immunity because of their existing illness, or who may require future immunosuppressive therapy, can be given zoster vaccine under certain conditions, on a case by case basis after seeking appropriate specialist advice. Further information on vaccination of these special risk groups is available.^{7,22} Vaccination of age-eligible household contacts of a person with impaired immunity is suggested. VZV-containing vaccines are contraindicated in pregnancy; however, a non-immune pregnant household contact is *not* a contraindication to zoster or varicella vaccination.

As people eligible to receive zoster vaccine will generally already have antibodies to VZV from primary infection, the zoster vaccine can be given at any time before or after administration of immunoglobulin, or any antibody-containing blood product and is not a precaution to vaccination.^{7,22}

Concomitant administration

Zostavax[®] can be given at the same visit as inactivated influenza vaccine (at separate sites and using separate syringes). A clinical trial of the simultaneous administration of these two vaccines demonstrated that the safety and efficacy profile of both vaccines was similar.²⁵ A clinical trial of the concomitant administration of Zostavax[®] with pneumococcal polysaccharide vaccine (Pneumovax[®]) showed some reduction in the serum antibody levels induced by Zostavax[®], but not Pneumovax[®].²⁶ Concomitant

administration should therefore be avoided where possible. Administer the two vaccines at least 4 weeks apart. However, there is no need to revaccinate if the vaccines are inadvertently administered concomitantly or at an interval of less than 4 weeks apart.

Data on the administration of zoster vaccine with other vaccines routinely recommended for persons aged >50 years, such as tetanus-containing vaccines, are not currently available. However, the simultaneous administration of live attenuated and inactivated vaccines have not generally resulted in impaired immune responses or an increased rate of adverse events, suggesting that zoster vaccine can be given at the same visit as these other vaccines, if required.

As with other live viral vaccines, if Zostavax[®] is to be given around the same time as another live viral parenteral vaccine (e.g. MMR, yellow fever), the vaccines should be given either at the same visit or at least 4 weeks apart.^{7,22}

Other considerations

Universal vaccination of children 18 months of age to prevent primary varicella is recommended in Australia. For further information see the NCIRS fact sheet [Varicella-zoster \(chickenpox\) vaccines for Australian children](#).

References

(References marked with an * are suggestions for further reading)

1. Dworkin RH, Portenoy RK. Proposed classification of herpes zoster pain. *Lancet* 1994;343:1648.
- 2.* Dworkin RH, Johnson RW, Breuer J, et al. Recommendations for the management of herpes zoster. *Clinical Infectious Diseases* 2007;44 Suppl 1:S1-26.
3. Schmader KE. Epidemiology and impact on quality of life of postherpetic neuralgia and painful diabetic neuropathy. *Clinical Journal of Pain* 2002;18:350-354.
4. Yawn BP, Saddier P, Wollan PC, et al. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clinic Proceedings* 2007;82:1341-1349.
5. Arvin AM. Varicella-zoster virus. *Clinical Microbiology Reviews* 1996;9:361-381.
6. Australian Herpes Management Forum (AHMF). Guidelines for clinicians: managing herpes zoster. 2009. Available at: http://www.ahmf.com.au/sites/default/files/Clinical_guidelines/200904/AHMF_Managing_Herpes_Zoster.pdf (accessed July 2009).
- 7.* Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR - Morbidity & Mortality Weekly Report* 2008;57(RR-5):1-30.
8. Gidding HF, MacIntyre CR, Burgess MA, Gilbert GL. The seroepidemiology and transmission dynamics of varicella in Australia. *Epidemiology & Infection* 2003;131:1085-1089.
9. Brisson M, Edmunds WJ, Law B, et al. Epidemiology of varicella zoster virus infection in Canada and the United Kingdom. *Epidemiology & Infection* 2001;127:305-314.
10. Araújo LQ, MacIntyre CR, Vujacich C. Epidemiology and burden of herpes zoster and post-herpetic neuralgia in Australia, Asia and South America. *Herpes* 2007;14 Suppl 2:40A-44A.
11. Gidding HF, Brisson M, MacIntyre CR, Burgess MA. Modelling the impact of vaccination on the epidemiology of varicella zoster virus in Australia. *Australian and New Zealand Journal of Public Health* 2005;29:544-551.
12. MacIntyre CR, Chu CP, Burgess MA. Use of hospitalization and pharmaceutical prescribing data to compare the prevaccination burden of varicella and herpes zoster in Australia. *Epidemiology & Infection* 2003;131:675-682.
- 13.* Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *New England Journal of Medicine* 2005;352:2271-2284.
14. Levin MJ. Veterans zoster trial [presentation]. NCIRS VZV Workshop; Sydney, 2006. Available at: http://www.ncirs.usyd.edu.au/newsevents/vzv_workshop_presentations_nov_06.doc (accessed 12 August 2009).
15. Thomas SL, Wheeler JG, Hall AJ. Contacts with varicella or with children and protection against herpes zoster in adults: a case-control study. *Lancet* 2002;360:678-682.
16. Vafai A, Berger M. Zoster in patients infected with HIV: a review. *American Journal of the Medical Sciences* 2001;321:372-380.
17. Civen RH, Maupin T, Xiao H, et al. A population-based study of herpes zoster (HZ) in children and adolescents post-varicella licensure 2000–2003. 38th National Immunization Conference; Nashville, TN, 2004. Available at: http://cdc.confex.com/cdc/nic2004/techprogram/paper_5427.htm (accessed 12 August 2009).
18. Australian Government Department of Health and Ageing, Pharmaceutical Benefits Advisory Committee (PBAC). PBAC outcomes by meeting.

Positive recommendations made by the PBAC – March 2008. 2008. Available at: <http://www.health.gov.au/internet/main/publishing.nsf/Content/pbacrec-mar08-positive> (accessed 1 September 2009).

19. Tying SK, Diaz-Mitoma F, Padget LG, et al. Safety and tolerability of a high-potency zoster vaccine in adults \geq 50 years of age. *Vaccine* 2007;25:1877-1883.
20. Diaz C, Dentico P, Gonzalez R, et al. Safety, tolerability, and immunogenicity of a two-dose regimen of high-titer varicella vaccine in subjects 13 years of age. *Vaccine* 2006;24:6875-6885.
21. Macaladad N, Marcano T, Guzman M, et al. Safety and immunogenicity of a zoster vaccine in varicella-zoster virus seronegative and low-seropositive healthy adults. *Vaccine* 2007;25:2139-2144.
- 22.*National Health and Medical Research Council (NHMRC). The Australian immunisation handbook. 9th ed. Canberra: Australian Government Department of Health and Ageing; 2008. Available at: <http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook-home> (accessed 4 May 2009).
23. Oxman MN. Vaccination to prevent herpes zoster and postherpetic neuralgia. *Human Vaccines* 2007;3:64-68.
24. Merck Sharpe & Dohme (Australia) Pty Limited. Zostavax[®]. Zoster virus vaccine live (Oka/Merck), MSD, refrigerator stable (ZST/R-I-042008). Product information. TGA approved 12 September 2007. 2008.
25. Kerzner B, Murray AV, Cheng E, et al. Safety and immunogenicity profile of the concomitant administration of ZOSTAVAX and inactivated influenza vaccine in adults aged 50 and older. *Journal of the American Geriatric Society* 2007;55:1499-1507.
26. MacIntyre CR, Egerton T, McCaughey M, et al. Concomitant administration of zoster and pneumococcal vaccines in adults \geq 60 years old [Poster # G-399d]. 48th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Infectious Diseases Society of America (IDSA) 46th Annual Meeting; Washington, DC, 2008.