4.24 ZOSTER (herpes zoster)

4.24.1 Virology

Varicella-zoster virus (VZV) is a DNA virus that is a member of the herpesvirus family. Primary infection with VZV is known as varicella or ‘chickenpox’. Herpes zoster (HZ), or ‘shingles’, is caused by reactivation of latent VZV, which typically resides in the dorsal root or trigeminal nerve ganglia following primary infection.

4.24.2 Clinical features

Reactivation of VZV causing HZ is thought to be particularly due to a decline in cellular immunity to the virus, and presents clinically as a unilateral vesicular rash in a dermatomal distribution in the majority of cases. A prodromal phase occurs 48 to 72 hours prior to the appearance of the lesions in 80% of cases. Associated symptoms may include headache, photophobia, malaise, and an itching, tingling or severe pain in the affected dermatome. In the majority of patients, HZ is an acute and self-limiting disease, with the rash lasting 10 to 15 days. However, complications can occur, especially with increasing age.

Post-herpetic neuralgia (PHN), the most frequent debilitating complication of HZ, is a neuropathic pain syndrome that persists or develops after the dermatomal rash has healed. PHN is most commonly defined as the persistence of pain for longer than 3 months after the onset of the rash (although definitions can vary by the period of persistent pain). Other complications may occur, depending on the site of reactivation. These include ophthalmic disease (such as keratitis and chorioretinitis), neurological complications (such as meningoencephalitis and myelitis), secondary bacterial skin infection, scarring and pneumonia. Rarely, disseminated HZ may develop, with widespread vesicular rash, and visceral, central nervous system and pulmonary involvement. Disseminated disease is more common in persons who are immunocompromised. Dermatomal pain without the appearance of rash is also documented (zoster siné herpétique).

Antiviral therapy, if initiated within 3 days of the onset of HZ, has been shown to reduce the severity and duration of HZ and may reduce the risk of developing PHN. However, despite medical therapy, PHN may persist for years and can be refractory to treatment.

4.24.3 Epidemiology

HZ occurs most commonly in persons of older age (particularly rising in incidence after the age of 50 years), with immunocompromise, and following a history of varicella in the 1st year of life. The lifetime risk of reactivation of VZV causing HZ is estimated to be approximately 20 to 30% and it affects half of those who live to 85 years. Second attacks of HZ occur in approximately 5% of immunocompetent persons, but are more frequent in persons who are immunocompromised. The rate of HZ cases reported annually in Australia, in all ages, is approximately 490 cases per 100 000 population, with estimates ranging from 330 to 830 per 100 000 population depending on data source. In comparison, approximately 1000 cases per 100 000 population are estimated to occur in persons aged ≥50 years. Among persons aged ≥50 years, HZ incidence rises with age from an estimated rate of 652 per 100 000 person-years in persons aged 50–59 years to 1450 per 100 000 person-years in persons aged 70–79 years. A similar incidence for HZ (1112 cases per 100 000 person-years) in persons ≥60 years of age has been estimated with active surveillance among unimmunised participants in the large efficacy study of zoster vaccine in the United States. Persons who are immunocompromised have an increased risk of HZ. For example, rates of HZ are up to 15 times higher in those who are immunocompromised due to HIV infection, and in the 1st year following haematopoietic stem cell transplantation (HSCT) up to 30% of patients may develop HZ.

Overall, an estimated 13 to 26% of patients with HZ develop complications. Complications occur more frequently with increasing age and with immunocompromise. PHN is the most common complication of HZ but occurs very infrequently in children and young adults. In persons who
develop HZ. PHN occurs in approximately 1 in 5 cases in those aged >80 years, compared with approximately 1 in 10 cases in those aged 50–59 years.\textsuperscript{22,27,28} The population-based incidence of PHN is 3 times higher in persons 70–79 years of age (235 per 100 000) than in persons 50–59 years of age (73 per 100 000).\textsuperscript{22}

Modelling studies of the impact of universal childhood vaccination programs for varicella have predicted that a rise in the incidence of HZ could occur, based on the assumption that exposure to wild-type VZV circulating in the community boosts immunity.\textsuperscript{29} However, to date, multiple studies and surveillance data do not demonstrate any consistent changes in overall HZ incidence in the United States, which has a universal varicella vaccination program that commenced in 1995.\textsuperscript{30–32} Australian data show an increase in HZ GP consultation rates over time, commencing prior to varicella vaccine introduction, which is likely to be due to the increasing age of the population. Age-standardised HZ hospitalisation rates have not declined since introduction of varicella vaccine, and the use of zoster vaccine has not yet been extensive enough in any country to expect an impact on HZ epidemiology.\textsuperscript{33–35} In the United States, the incidence of HZ in children <10 years of age has declined, indicating that HZ rates are lower in varicella vaccine recipients.\textsuperscript{31}

\subsection*{4.24.4 Vaccine}

Zostavax is a live attenuated vaccine formulated from the same VZV vaccine strain (Oka/Merck) as the registered varicella (chickenpox) vaccine Varivax, but is of higher potency (on average, at least 14 times greater). The higher viral titre in Zostavax is required to elicit a boost in immune response in adults who usually remain seropositive to VZV following primary infection, but have declining cellular immunity with increasing age.\textsuperscript{36} Zostavax is used for the prevention of HZ in persons >50 years of age. It is important to note that the registered varicella vaccines are not indicated for use in preventing HZ in older people and Zostavax is not indicated for use in younger people who have not been previously immunised or infected with VZV. Zostavax is not indicated for use for therapeutic benefit during an acute HZ episode, nor for the treatment of PHN.

A single large, randomised, double-blind, placebo-controlled efficacy study of the frozen formulation of Zostavax (known as the ‘Shingles Prevention Study’ [SPS]) was conducted among 38 546 adults aged ≥60 years and demonstrated that Zostavax significantly reduced the likelihood of developing both HZ and PHN.\textsuperscript{23} Vaccination reduced the incidence of HZ by 51.3\%, the incidence of PHN by 66.5\%, and the burden of illness associated with HZ by 61.1\% over a median of more than 3 years follow-up.\textsuperscript{23} The vaccine was more efficacious in reducing HZ in persons aged 60–69 years than in those aged 70–79 years (64\% compared with 41\% efficacy). However, efficacy against PHN was similar in both age groups.\textsuperscript{25} Efficacy against HZ in the ≥80 years age group was lower (18\% and not statistically different to placebo). However, there were fewer participants of this age in the SPS.\textsuperscript{37} In those who developed HZ despite vaccination, the severity of pain associated with the episode was also reduced.\textsuperscript{38} Another randomised controlled study in >22 000 50–59-year olds demonstrated a reduction in the incidence of HZ after an average follow-up period of 1.3 years (range 0–2 years), with a vaccine efficacy for preventing HZ of 69.8\%.\textsuperscript{39} In these clinical trials many participants were treated with antiviral and pain medication for their HZ, suggesting that the effect of the vaccine was in addition to any benefit obtained from medical therapy.\textsuperscript{25,39} Efficacy of a single dose of zoster vaccine appears to decline over time. Data from one short-term follow-on study of participants in the SPS showed a decline in vaccine efficacy; however, estimates remained statistically significant through to the fifth year post vaccination, with uncertain efficacy beyond that point.\textsuperscript{40,41} A longer-term study of SPS participants suggested that vaccine protection remained significant against HZ up to 8 years post vaccination; however, methodological limitations in that study limit interpretation of this result.\textsuperscript{42} The need for revaccination following a single dose of zoster vaccine has not yet been determined.

The Shingles Prevention Study, together with other smaller studies, demonstrated that Zostavax is safe and generally well tolerated among adults ≥50 years of age.\textsuperscript{23,39} In the SPS, the most common adverse events were injection site reactions, with Zostavax more likely to result in erythema, pain
and swelling at the injection site than placebo (48% versus 17%, respectively). Varicella-like rashes at the injection site were also more common in vaccine recipients; however, varicella-like rash not localised to the injection site did not occur more often. Varicella- or zoster-like rashes that were PCR-positive for VZV were mostly due to wild-type VZV. Fever was no more common in vaccine recipients; however, the rate of vaccine-related systemic symptoms was higher (Zostavax 6.3% versus placebo 4.9%), with the most frequently reported systemic symptoms being headache and fatigue. Mild to moderate adverse events, particularly injection site reactions, were higher in vaccine recipients aged 50–59 years than in those aged ≥60 years.

In Australia, a refrigerated form of Zostavax is registered on the basis of comparable immunogenicity and safety to the frozen vaccine formulation that was used in the SPS. Zostavax was registered for use in persons 50–59 years of age based on a study that demonstrated similar immunogenicity in this age group compared with those ≥60 years of age, and has since been shown to reduce the incidence of HZ in this population. A study of the simultaneous administration of Zostavax with inactivated influenza vaccine (given separately and at different injection sites) demonstrated comparable immunogenicity and safety to giving the vaccines at different times. A study of the simultaneous administration of Zostavax with 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; 23vPPV) reported no effect on the immunogenicity of Pneumovax 23 but suggested that the immunogenicity of Zostavax (indicated by VZV antibody levels) was reduced when the vaccines were administered simultaneously compared with administration 4 weeks apart. However, VZV antibody levels have not been shown to directly correlate with clinical protection and a large observational study from the United States reported that concomitant administration of Zostavax and 23vPPV did not affect the effectiveness of Zostavax against HZ.

- **Zostavax** – Seqirus Pty Ltd/Merck Sharp & Dohme (Australia) Pty Ltd (live attenuated Oka/Merck strain of varicella-zoster virus). Lyophilised powder in a monodose vial with separate diluent. Each 0.65 mL reconstituted dose contains ≥19 400 plaque-forming units of attenuated varicella-zoster virus; 41.05 mg sucrose; 20.53 mg hydrolysed porcine gelatin; 8.55 mg urea; 0.82 mg monosodium glutamate; residual components of MRC-5 cells; traces of neomycin and bovine serum albumin.

### 4.24.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light. Zostavax must be reconstituted by adding the entire contents of the diluent container to the vial and shaking until the powder is completely dissolved. Reconstitute immediately upon removal from the refrigerator. Reconstituted vaccine must be used within 30 minutes.

### 4.24.6 Dosage and administration

The dose of Zostavax is 0.65 mL, to be given by SC injection. Zostavax must never be given where varicella (chickenpox) vaccine is indicated. Zoster vaccine is only registered for use in adults ≥50 years of age.

### Co-administration with other vaccines

Zostavax can be given at the same time as influenza vaccine, using separate syringes and injection sites.

Zostavax can be given at the same time as pneumococcal polysaccharide vaccine, using separate syringes and injection sites (refer to 4.24.4 Vaccine above).
Zostavax can be administered at the same visit as, or at any time following receipt of, other inactivated vaccines (e.g. tetanus-containing vaccines), if required.

If administration of both Zostavax and another live parenteral vaccine (e.g. MMR or yellow fever) is indicated, the vaccines should be given either on the same day or at least 4 weeks apart. (Refer also to 4.22 Varicella.)

4.24.7 Recommendations

Zoster vaccine recommendations are based on the risk of HZ and PHN in relation to vaccine efficacy by age, as listed below. It is important to review a person’s medical history and medication use prior to vaccination as zoster vaccine is contraindicated in persons who are immunocompromised (refer to 4.24.9 Contraindications and 4.24.10 Precautions).

Adults aged ≥70 years

A single dose of zoster vaccine is recommended for adults aged ≥70 years who have not previously received a dose of zoster vaccine.

Routine vaccination of persons aged 70–79 years is expected to obtain the greatest benefits against HZ and its complications. Although the vaccine efficacy against HZ is lower in this age group compared with younger ages, persons ≥70 years of age experience a greater risk of disease.22,23,28 (Refer also to 4.24.3 Epidemiology and 4.24.4 Vaccine above.)

In persons aged ≥80 years vaccination is less efficacious but may still provide some clinical benefit to the vaccinated individual37 (refer to 4.24.4 Vaccine above).

Adults aged 60–69 years

A single dose of zoster vaccine is recommended for adults aged 60–69 years who have not previously received a dose of zoster vaccine.

In this age group the incidence of both HZ and PHN is high and the efficacy of the vaccine has been demonstrated; however, the exact duration of vaccine efficacy is not known and it is possible that protection following a single vaccine dose wanes with time (refer to 4.24.4 Vaccine above). The need for revaccination is not yet determined.

Adults aged 50–59 years

Routine use of zoster vaccine in persons aged 50–59 years is not recommended.

Although the incidence of HZ in persons 50–59 years of age is higher than in younger age groups,19,22 and zoster vaccine is efficacious in 50–59-year olds,39 the likelihood of developing PHN and other complications of HZ is lower in this age group than in those ≥60 years of age.27,51 Persons aged 50–59 years who wish to protect themselves against HZ can be vaccinated; however, the exact duration of vaccine efficacy is not known and it is possible that protection following a single vaccine dose wanes with time (refer to 4.24.4 Vaccine above). The need for revaccination is not yet determined.

Persons aged <50 years

Zoster vaccination is not recommended for use in persons <50 years of age and is not registered for use in this age group. There have been very limited studies of the safety and immunogenicity of zoster vaccine in this age group (refer to 4.24.4 Vaccine above).

Persons with a history of a previous episode of HZ

Persons with a history of a previous episode of HZ can be given zoster vaccine. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis. In addition, the risk of a repeat episode of zoster has been estimated at approximately 5% in immunocompetent persons.17,18,51 Persons with a history of HZ were excluded from the SPS, so no data on the efficacy
of the vaccine in those with a history of HZ is available. The safety and immunogenicity of zoster vaccine in persons with a history of HZ has been studied in one small clinical trial; the vaccine was well tolerated and immunogenic. Injection site reactions were more common in vaccine recipients than in placebo recipients, but similar to vaccine recipients in the SPS. Systemic adverse events were similar between groups. The length of time following an episode of HZ after which it would be reasonable to vaccinate has not been established. However, it is suggested that the vaccine could be given at least 1 year after the episode of HZ.

**Persons previously vaccinated with varicella vaccine**

Zoster vaccination of persons who have previously received varicella vaccine is not recommended at this time. There have been limited studies of the safety and immunogenicity of zoster vaccine in this setting, and the currently available data are insufficient to suggest a benefit from vaccination. It is not yet known whether, in the future, populations vaccinated with varicella vaccine will experience rates of HZ sufficient to warrant zoster vaccination. Preliminary information suggests that the incidence of HZ in persons who have previously received varicella vaccine is lower than in those infected with wild-type varicella.

**Household contacts of persons who are immunocompromised**

Vaccination is recommended for persons ≥50 years of age who are household contacts of a person who is, or is expected to become, immunocompromised. Based on evidence that the rate of VZV-like rashes after vaccination is extremely low, it is unlikely that transmission of vaccine-associated virus to a susceptible contact would occur. If a vaccinated person develops a varicella- or zoster-like rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash. The efficacy of the HZ vaccine is less than 100%, and rashes in vaccinated persons may be due to reactivation of wild-type VZV. If household contacts (<50 years of age) of a person who is immunocompromised have not been previously infected with VZV or immunised with varicella vaccine, they should receive varicella vaccine (refer to 4.22 Varicella).

**Serological testing before and after zoster vaccination**

Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the zoster vaccine (with the exception of certain immunocompromised persons, refer below). Most older people in Australia are seropositive to VZV due to previous primary varicella infection. Limited data from small studies of the administration of high-dose VZV-containing vaccine (comparable to Zostavax) to healthy VZV seronegative adults, compared with previously infected adults, suggest that the vaccine was well tolerated and immunogenic in seronegative persons, although the incidence of self-limited injection site reactions may be slightly higher. If a healthy adult eligible for zoster vaccine has laboratory evidence of a lack of immunity to VZV, and does not have a history of age-appropriate varicella vaccination, they may be vaccinated with either 2 doses of varicella vaccine (preferred; refer to 4.22 Varicella) or 1 dose of zoster vaccine as an alternative.

Laboratory testing to check for an immune response after zoster vaccination is not recommended. Zoster vaccine boosts both humoral (IgG) and cellular immune responses; however, confirmation of such immune responses is neither necessary nor predictive of protection against the development of zoster.
4.24.8 Pregnancy and breastfeeding

VZV-containing vaccines are contraindicated in pregnant women, although women of child-bearing age are not eligible for zoster vaccination. Pregnancy should be avoided for 28 days after vaccination (refer to 4.22 Varicella).

A non-immune pregnant household contact is not a contraindication to zoster vaccination.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.24.9 Contraindications

Anaphylaxis to vaccine components

Zoster vaccine is contraindicated in persons who have had:

- anaphylaxis following a previous dose of any VZV-containing vaccine
- anaphylaxis following any vaccine component.

Persons who are immunocompromised

In persons who are or have recently been immunocompromised, the safety of administering zoster vaccine should always be considered on a case-by-case basis (refer also to 4.24.11 Adverse events below). If there is uncertainty around the level of immunocompromise and when vaccine administration may be safe, vaccination should be withheld and expert advice sought from the treating physician and/or an immunisation specialist.

Live attenuated zoster vaccine is contraindicated in persons with current or recent severe immunocompromise due to either a primary or acquired medical condition, or due to medical treatment. This includes persons receiving high-dose systemic immunosuppressive therapy, such as chemotherapy, radiation therapy, oral corticosteroids (\(\geq 20\) mg per day of prednisone equivalent dose for \(\geq 14\) days), or biologic or targeted synthetic disease modifying anti-rheumatic drugs (bDMARDs or tsDMARDs); persons suffering from malignant conditions of the reticuloendothelial system (such as lymphoma, leukaemia, Hodgkin’s disease, even if not receiving active treatment); persons with AIDS or symptomatic HIV infection; and any person with similar immunocompromise due to a disease or treatment (refer to Table 4.24.1 Recommendations for use of zoster vaccine in persons on immunosuppressive therapy and 3.3.3 Vaccination of immunocompromised persons).

Persons with less severe immunocompromise than described above (e.g. those on low-dose corticosteroids or selected conventional synthetic DMARDs [csDMARDs], or with asymptomatic HIV infection) may be considered for vaccination on a case-by-case basis after seeking appropriate specialist advice (refer to 4.24.10 Precautions below and 3.3 Groups with special vaccination requirements). For example, zoster vaccine can be given to patients receiving certain csDMARDs in low doses (i.e. methotrexate \(\leq 0.4\) mg/kg per week, azathioprine \(\leq 3.0\) mg/kg per day or mercaptopurine \(\leq 1.5\) mg/kg per day), either on their own or in combination with low-dose corticosteroids \(\leq 20\) mg per day of prednisone equivalent dose).\(^{55,56}\) At these doses, it is likely that the level of immunocompromise is not severe. In addition, most adults \(>50\) years of age have had previous wild-type VZV infection, and thus have immune memory to VZV, which also mitigates any risk of vaccine virus replication. However, if the extent of immunocompromise is unclear seek expert advice prior to vaccination. Serological confirmation of previous VZV infection prior to vaccination may also be appropriate in certain patients receiving immunosuppressive therapy (refer to 4.24.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above).

Persons whose treatment with high-dose systemic immunosuppressive therapy has ceased may be vaccinated if an appropriate time interval has passed (refer to Table 4.24.1 Recommendations for use of zoster vaccine in persons on immunosuppressive therapy and 3.3.3 Vaccination of immunocompromised persons).

Table 4.24.1: Recommendations for use of zoster vaccine in persons on immunosuppressive therapy

<table>
<thead>
<tr>
<th>Immunosuppressive therapy</th>
<th>Treatment regimen</th>
<th>Potential timing of vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-dose corticosteroid monotherapy (≥20 mg per day of prednisone or equivalent)</td>
<td>Therapy for less than 14 days</td>
<td>Immunise 1 month prior to treatment initiation OR any time after treatment cessation</td>
</tr>
<tr>
<td></td>
<td>Therapy for 14 days or longer</td>
<td>Immunise 1 month prior to treatment initiation OR at least 1 month after treatment cessation</td>
</tr>
<tr>
<td>csDMARDs</td>
<td>Azathioprine &gt;3.0 mg/kg per day</td>
<td>Immunise 1 month prior to treatment initiation OR at least 3 months after treatment cessation</td>
</tr>
<tr>
<td></td>
<td>6-mercaptopurine &gt;1.5 mg/kg per day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methotrexate &gt;0.4 mg/kg per week</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All other csDMARDs* All regimens</td>
<td></td>
</tr>
<tr>
<td>T-cell inhibitors (e.g. tacrolimus, cyclosporine)</td>
<td>All regimens</td>
<td></td>
</tr>
<tr>
<td>Other unspecified immunosuppressants (e.g. chemotherapy§)†</td>
<td>All regimens</td>
<td></td>
</tr>
<tr>
<td>bDMARDs or tsDMARDs (e.g. monoclonal antibodies)</td>
<td>All regimens</td>
<td>Immunise 1 month prior to treatment initiation OR at least 12 months after treatment cessation‡</td>
</tr>
</tbody>
</table>

* Does not include sulfasalazine which is considered safe at any dose.
† This does not include persons who have received haemopoietic stem cell transplantation (HSCT) who should not receive zoster vaccine until at least 24 months post HSCT (refer also to 3.3 Groups with special vaccination requirements).
‡ In some cases immunosuppression that absolutely contraindicates live attenuated vaccines can persist for a year or more after the last dose of therapy. Live attenuated vaccines should preferably not be given to any patient who has previously received biologic immunotherapies, unless this has been approved by the treating physician after evaluation of the delay since last treatment and in some cases an assessment of immunological recovery.
§ For patients who have recently received chemotherapy and/or radiotherapy waiting at least 6 months rather than 3 months may be appropriate. An individual patient risk benefit assessment is required.

Management of immunocompromised persons who inadvertently receive zoster vaccine

If an immunocompromised person is inadvertently vaccinated with zoster vaccine, they should be promptly assessed and appropriate management discussed with an infectious diseases and/or immunisation expert. The relevant state or territory health authority and the TGA should be notified. (For mechanisms for reporting to the TGA, refer to 2.3.2 Adverse events following immunisation.)

It is important to establish the person’s degree of immunocompromise and risk of vaccine-associated adverse effects. Management of the patient may include the need for specific clinical investigations (including, but not limited to, VZV testing from any rash or other affected sites) and/or pre-emptive or therapeutic use of antiviral medication.
4.24.10 Precautions

Persons with HIV infection

Vaccination with zoster vaccine is not recommended for persons with AIDS or symptomatic HIV infection (refer to 3.3 Groups with special vaccination requirements, Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes) or significant immunocompromise due to other diseases and/or treatment (refer to 4.24.9 Contraindications above).

Persons with asymptomatic HIV infection who are on antiretroviral therapy and who have a very low or undetectable viral load and CD4+ count ≥350 per µL can be vaccinated. Where there is a strong indication to vaccinate, some experts suggest a CD4+ count of >200 per µL is safe; expert advice should be sought from the treating physician and/or an immunisation specialist. (Refer also to 3.3.3 Vaccination of immunocompromised persons, ‘HIV-infected persons’). Serological confirmation of previous VZV infection is recommended prior to vaccination (refer to 4.24.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above).

Although asymptomatic HIV-infected persons are likely to have a higher relative risk of developing HZ in the future, it is possible that both the efficacy and the safety of zoster vaccination may be reduced in such recipients, as compared with uninfected persons.

Persons anticipating future significant immunocompromise

Immunocompetent persons who anticipate future alteration of their immune status because of an existing illness can be given zoster vaccine on a case-by-case basis after seeking appropriate specialist advice. This may include persons with conditions such as anticipated solid organ transplantation, solid tumours that will require future chemotherapy or radiation therapy, and inflammatory diseases (e.g. rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, psoriasis) who, at the time, may have minimal alteration to their immune system, but can anticipate significant immunocompromise in the future due to their disease and/or treatment. Since these persons are at high risk of developing zoster in the future, vaccination at least 1 month prior to the onset of immunocompromise may be appropriate (after seeking specialist advice). Serological confirmation of previous VZV infection is recommended prior to vaccination (refer to 4.24.7 Recommendations, ‘Serological testing before and after zoster vaccination’ above).

Vaccination before or after immunoglobulin or blood product administration

Zoster vaccine can be given at any time before or after administration of immunoglobulin or any antibody-containing blood product. This is because zoster vaccine is indicated in persons who, because of their age, are assumed to have had a previous VZV infection and, therefore, already have serum antibody levels comparable to those found in blood products. (Refer also to 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other blood products.)

Persons receiving long-term aspirin or salicylate therapy

Persons receiving long-term salicylate therapy (aspirin) can be vaccinated if indicated. There have been no reports of an association between Reye syndrome and varicella vaccination, and it is unlikely that vaccination of a previously VZV-infected older person with zoster vaccine carries any risk of Reye syndrome.

Persons receiving antiviral medication

It is possible that the use of antivirals with anti-VZV activity, such as acyclovir, foscavir or valaciclovir, may interfere with the replication of the Zostavax live attenuated virus. Persons on such antiviral medication should cease treatment no less than 24 hours prior to vaccination and for at least 14 days after vaccination.
4.24.11 Adverse events

Injection site reactions (including erythema, pain, swelling and/or itch at the injection site) occurred in approximately half of clinical trial participants given Zostavax, irrespective of a previous history of HZ (refer also to 4.24.4 Vaccine above).

Varicella-like rashes at the injection site occurred rarely, in 0.1% of recipients; however, they were more common than in placebo recipients. Varicella-like rashes that were not localised to the injection site were also rare, and did not occur more often in vaccine compared with placebo recipients (0.1% in both groups). In the clinical trials in which rashes were analysed by PCR for VZV, the majority were due to wild-type virus; only 2 subjects were found to have rashes due to the Oka/Merck VZV vaccine strain (refer also to 4.24.4 Vaccine above).

Fever >38.3°C was not seen more commonly in vaccine recipients, and occurred in <0.1% of subjects overall.

Systemic symptoms were reported in vaccine recipients more commonly than in placebo recipients (Zostavax 6.3% versus placebo 4.9%), with the most frequently reported systemic symptoms being headache and fatigue.

Post-marketing surveillance in the United States in a cohort of almost 200,000 adults who received the zoster vaccine found no increased risk for a number of potential adverse events occurring after vaccination (such as cerebrovascular events, encephalitis, etc.), but did find a 2-fold increased risk in the 1st week after vaccination for events coded as ‘allergic reactions’, of which the majority were injection site reactions.

Zostavax is contraindicated in severely immunocompromised persons. Administration to persons with severe immunocompromise has been documented to result in disseminated disease due to unchecked replication of the Oka vaccine virus. This includes two people with chronic lymphocytic leukaemia who were not on treatment at the time of vaccination who died from disseminated Oka vaccine virus disease.

4.24.12 Variations from product information

The product information for Zostavax states that the vaccine can be administered concurrently with inactivated influenza vaccine but not with 23vPPV. The ATAGI instead recommends that Zostavax may be administered concurrently with other vaccines (including 23vPPV).

The product information for Zostavax states that the safety and efficacy of Zostavax have not been established in adults with known HIV infection, with or without evidence of immunocompromise. The ATAGI recommends instead that Zostavax may be administered to HIV-infected persons without immunocompromise and following confirmation of pre-existing immunity to VZV.

References

A full reference list is available on the electronic Handbook or website www.immunise.health.gov.au.


20. 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 and Infection* 2003;131:675-82.


