
22 Zoster (herpes zoster/ shingles)

Key information

Mode of transmission	Zoster is a reactivation of the varicella zoster virus in someone who has previously had varicella disease. Contact with zoster vesicles can cause varicella in non-immune individuals. Some airborne spread may be possible from immunocompromised patients.
Period of communicability	Until lesions have crusted.
Burden of disease	Increasing incidence with age; lifetime risk about 1 in 3. For those who live to 85 years, the risk is 1 in 2.
Vaccine	Zoster vaccine (Zostavax), a higher titre formulation of the live attenuated varicella vaccine. Zoster vaccine is registered for use from age 50 years. Do not give to children.
Dose, presentation, route	0.65 mL per reconstituted dose. Vial of vaccine, plus diluent in a pre-filled syringe. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Recommended immunisation schedule	From 1 April 2018, 1 dose of HZV is funded for: <ul style="list-style-type: none">• individuals at age 65 years, or• catch-up of individuals aged 66–80 years, inclusive (the catch-up programme ceases on 31 December 2020). HZV may be given to individuals with a prior history of zoster. After the zoster episode has resolved the vaccination benefit is unclear – wait at least 1 year before administering the vaccine.
Vaccine efficacy/ effectiveness	Reduces the burden of zoster illness by 61 percent in all adults aged over 60 years, by 66 percent in those aged 60–69 years and by 55 percent in those aged 70 years and older. The role of revaccination is currently unknown.

Continued overleaf

Contraindications	Certain primary and secondary immune deficiencies – consult the individual's specialist for advice. Immunosuppressive therapy, including high-dose steroids. Known systemic hypersensitivity to neomycin. Active untreated TB. Pregnancy.
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22.1 Virology

Varicella-zoster virus (VZV) is a DNA virus from the herpesvirus family. Primary infection with VZV causes varicella zoster disease (chickenpox). Herpes zoster (HZ), or 'shingles', is a clinical syndrome caused by reactivation of latent VZV, which resides in the dorsal root or trigeminal nerve ganglia following primary infection.

22.2 Clinical features

HZ (shingles) occurs when the cell-mediated immune response is impaired and unable to prevent latent VZV reactivation (see chapter 21). Zoster occurs only by reactivation of the patient's own virus; it is not acquired from other patients with zoster or varicella.¹

HZ presents clinically as a unilateral vesicular rash in a dermatomal distribution in the majority of cases. The dermatomal distribution of the rash is the key diagnostic feature. In 70–80 percent of HZ cases in older adults, prodromal pain and/or itching occurs three to four days before the appearance of the rash.² 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.

The majority of zoster cases occur in adults aged 40 years or older. HZ does occur in infants and children, but it is uncommon. When it occurs in those aged under 2 years it may reflect *in utero* chickenpox, with the greatest risk arising following exposure between 25 and 36 weeks' gestation, with reactivation in early life.

A common complication of zoster is post-herpetic neuralgia, a chronic, often debilitating pain condition that can last months or even years. A systematic review of the incidence and complications of zoster found that the risk of developing post-herpetic neuralgia ranges between 5 and about 30 percent (depending on the type of study design, age distribution of the study populations and definition),³ although it is uncommon in healthy children and young people and the risk rises with age.

Herpes zoster ophthalmicus (HZO) is another complication of zoster, which occurs when VZV reactivation affects the ophthalmic branch of the trigeminal nerve. HZO can occur with or without eye involvement, and can result in prolonged or permanent pain, facial scarring and loss of vision. About 10 percent of zoster patients develop HZO, and the risk is similar across all age groups.³

HZ occurs more commonly in immunosuppressed individuals (eg, cancer treatment or organ transplant patients) and those with HIV. Up to 10 percent of children treated for a malignant neoplasm may develop HZ. In immunocompromised patients,⁴ extensive viraemia in the absence of a vigorous immune response can result in a disseminated form of HZ that includes severe multi-organ disease.² Other risk factors for developing HZ include rheumatoid arthritis,⁵ sleep disorders⁶ and type 2 diabetes.⁷

22.3 Epidemiology

22.3.1 Global burden of disease

HZ is a sporadic disease occurring as a reactivation of the VZV in individuals who have previously had chickenpox. Approximately one in three people will develop zoster during their lifetime with the incidence rising as cell-mediated immunity to VZV declines with age.⁸ Fifty percent of those who live to 85 years suffer zoster.^{9, 10} A systematic review documented an incidence rate between 3 and 5 per 1,000 person-years in North America, Europe and Asia-Pacific.³ The incidence rate was about 6–8 per 1,000 person-years at age 60 years and 8–12 per 1,000 person-years at age 80 years.

Recurrence is greater in females than males (about 7 percent after eight years compared with 4 percent for males). Third episodes are rare.

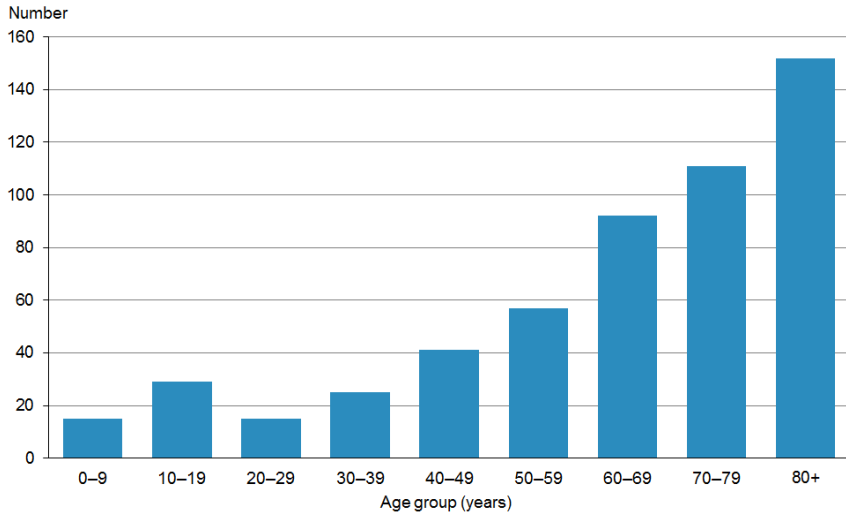
VZV is present in lesions of HZ and is transmissible via contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immunocompromised individuals with disseminated HZ. Episodes of HZ in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals.

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in HZ in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to childhood varicella vaccination programmes.^{11, 12} Studies from the UK and Canada reported increases in HZ not associated with a vaccination programme, and some US data showed HZ rates were increasing prior to the initiation of their varicella vaccination programme.^{13, 14}

22.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2015 are shown in Figure 22.1 below, with more than 65 percent occurring in adults aged 60 years and older. Hospitalisations are predicted to account for only a very small proportion of the overall HZ cases as most are managed in primary care. A retrospective review of cases at a large New Zealand general practice suggests an incidence similar to the global incidence estimates described in section 22.3.1 above.¹⁵

Figure 22.1: Herpes zoster hospitalisations by age group, 2015



Source: Ministry of Health

22.4 Vaccine

22.4.1 Available vaccine

HZV (Zostavax, MSD) is a live attenuated virus vaccine. It is a higher titre formulation of the varicella vaccine and has been tested as a vaccine to protect against HZ.¹⁶ By mimicking the immune response seen following a dose of shingles and boosting cell-mediated immunity in older adults, the incidence and severity of HZ is reduced by the high-titre vaccine.

Funded vaccine

Each 0.65 mL HZV dose of HZV (Zostavax, MSD) contains a minimum of 19,400 PFU of the Oka/Merck strain of VZV. Other components include sucrose, hydrolysed porcine gelatin, urea, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, residual components of MRC-5 cells (including DNA and protein), and trace quantities of neomycin and bovine calf serum. The vaccine contains no preservative.

22.4.2 Efficacy and effectiveness

In a large clinical trial (the Shingles Prevention Study) of 38,546 adults aged 60 years and older, with either a history of chickenpox or of having lived in the US for more than 30 years, the participants received the high-dose zoster vaccine or a placebo. The results showed that the zoster vaccine reduced the burden of illness of zoster by 61 percent (95% CI: 51–69) in all age groups, by 66 percent (95% CI: 52–76) in the age group 60–69 years, and by 55 percent (95% CI: 40–67) in those aged 70 years and older. There was also a 67 percent reduction (95% CI: 48–79) in post-herpetic neuralgia in all age groups.¹⁶ A cohort study of individuals in the US aged 65 years and older found zoster vaccine was associated with a 48 percent reduction (95% CI: 39–56) in incident zoster, including a 37 percent reduction (95% CI: 6–58) in those with immunosuppression.¹⁷

A review of the efficacy of HZV in preventing zoster and post-herpetic neuralgia concluded that zoster vaccine is safe, effective and highly recommended for the immunisation of immune-competent individuals over the age of 60 years.¹

Duration of protection

The persistence of HZV efficacy was measured for 11 years using a subgroup of individuals from the Shingles Prevention Study discussed above. Vaccine efficacy was statistically significant for the incidence of HZ until eight years post-vaccination.¹⁸ Compared to the original study, estimates for vaccine efficacy decreased from 61.1 percent to 37.3 percent for the HZ burden of illness, from 66.5 percent to 35.4 percent for incidence of postherpetic neuralgia, and from 51.3 percent to 21.1 percent for incidence of HZ. Studies have shown that booster doses in adults are immunogenic, but there are no reports on efficacy of booster doses. The immune response following a booster dose declines with advancing age but is similar to the response seen following first doses of individuals of the same age; ie, a prior dose neither enhances nor impairs the response to a booster dose.¹⁹ At the time of writing, there were no current international guidelines on booster doses.

There do not appear to be any safety concerns with administering a second dose of HZV.²⁰ Although not currently recommended, individuals who previously received an unfunded HZV dose may choose to receive a funded HZV dose, if eligible.

22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.²¹ Store in the dark at +2°C to +8°C.

The vaccine must be reconstituted with the supplied diluent. Once reconstituted, HZV must be used within 30 minutes.

22.4.4 Dosage and administration

HZV is registered for adults aged 50 years and older. **Do not give to children.**

The dose of reconstituted HZV is 0.65 mL, to be administered subcutaneously in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

HZV can be concurrently administered with influenza vaccine using separate syringes and sites.

Evidence²² suggests that HZV can be concurrently delivered with 23PPV, despite earlier research to the contrary. The earlier research showed the average antibody titre against VZV was lower in individuals who received HZV and 23PPV at the same visit, compared to those who received these vaccines four weeks apart.

However, there is no evidence to suggest that antibodies against VZV are a measure of protection against HZ.²² The US Centers for Disease Control and Prevention has not changed its recommendation for either vaccine and continues to recommend that HZV and 23PPV be administered at the same visit if the individual is eligible for both vaccines.²³

22.5 Recommended immunisation schedule

Table 22.1: Herpes zoster vaccine (HZV) recommendations

Note: Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of HZV (with the exception of certain immunocompromised persons, refer below).

Recommended and funded

1 dose of HZV is recommended and funded for:

- individuals at age 65 years, or
- catch-up^a of individuals aged 66–80 years, inclusive.

For consideration, but not funded

1 dose of HZV may be considered, but is not funded, for individuals aged 50–64 years:

- who are at increased risk of zoster^{24, 25, 26, 27} and who may benefit from being vaccinated earlier than the routine schedule:
 - with asymptomatic HIV^b (if CD4+ lymphocyte count is ≥ 200 cells/mm³)
 - with end-stage kidney disease^b (CKD stages 4–5)
 - at least 4 weeks prior to commencing high-dose immunosuppressive therapy^{b,c} and/or solid organ transplantation^{b,c}
 - after ceasing high-dose immunosuppressive therapy^{b,c}
 - at least 2 years post-HSCT^{b,c}
 - with autoimmune disease^{b,c} (eg, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis)
 - with a first generation family history of zoster
 - with depression
 - with diabetes
 - with psychiatric disorders
 - with chronic obstructive pulmonary disease.
- who are household contacts of immunocompromised individuals.

a The catch-up programme ceases on 31 December 2020.

b Seek specialist advice. Serological confirmation of previous VZV infection is recommended before administering HZV. If VZV-seronegative, give VV. If VZV-seropositive, give HZV. See also section 4.3.3.

c See Table 22.2: Recommendations for individuals on immunosuppressive therapy.

22.5.1 Recommended and funded

Recommendations for HZV (Zostavax) are in Table 22.1 above. From 1 April 2018, one dose of HZV will be funded for individuals at age 65 years. There will be a catch-up programme from 1 April 2018 until 31 March 2020, with one dose of HZV funded for individuals aged 66 to 80 years, inclusive.

22.5.2 Other considerations

Vaccination of individuals aged 50–64 years (unfunded)

HZV (Zostavax) is registered in New Zealand for individuals aged 50 years or older. It may be considered, but is not funded, for individuals aged 50–64 years who are at increased risk of zoster^{24, 25, 26, 27} and who may benefit from being vaccinated earlier than the routine schedule and/or they are a household contact of an immunocompromised individual (see Table 22.1). However, the exact duration of vaccine efficacy is not known, and it is possible that protection following a single vaccine dose wanes with time.²⁷ The need for revaccination is not yet determined.²⁷ Dosing with HZV is often strategic and based on clinical consideration (see below).

Individuals with a history of HZ (shingles)

Individuals with a history of a previous episode of HZ can be given HZV. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis.²⁷ In addition, the risk of a repeat episode of zoster has been estimated at approximately 5 percent in immunocompetent individuals.²⁷

There are no recognised safety concerns in giving the vaccine to people with prior history of HZ.²⁸ The length of time following an episode of HZ after which it may be beneficial to vaccinate has not been established.²⁷ It is suggested that the vaccine could be given at least one year after the episode of HZ has resolved.²⁷

Household contacts of immunocompromised individuals

HZV is contraindicated in individuals with current or recent severe immunocompromise due to primary and secondary immune-deficiency states, or due to immunosuppressive therapy (see section 22.6). However, VV or age-appropriate HZV can be given safely to their household contacts. VV is funded for non-immune household contacts of patients who are immunocompromised or undergoing a procedure or treatment leading to immunocompromise. If the household contact is immune to varicella and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

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.²⁷

See also ‘Household contacts’ in section 4.3.1 for general recommendations for vaccination of household contacts of immunocompromised individuals.

Serological testing

Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the herpes zoster vaccine.²⁷ Most older people in New Zealand are seropositive to VZV due to previous primary varicella infection.

Serological confirmation of previous VZV infection is recommended before administering HZV to individuals with HIV, and in those who are anticipating significant future immunocompromise or who have ceased immunosuppressive therapy (see section 22.6.2).²⁷ Individuals in these categories who have negative VZV IgG should generally not be given HZV. Upon specialist advice, VV may be given instead of HZV to seronegative individuals.

Laboratory testing to check for an immune response after HZV is not recommended.²⁷

22.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

22.6.1 Contraindications

HZV is a live attenuated varicella-zoster vaccine and administration to individuals who are immunosuppressed or immunodeficient may result in disseminated varicella-zoster virus disease, including fatal outcomes. If HZV is inadvertently administered to these individuals, seek specialist advice immediately and notify CARM.

Contraindications to HZV include:

- a history of anaphylactic reaction to neomycin. A history of hypersensitivity to any other component of the vaccine, including gelatin
- primary and secondary immune-deficiency states due to conditions such as acute and chronic leukaemias, lymphoma, other conditions affecting the bone marrow or lymphatic system, immunosuppression due to HIV/AIDS (see section 22.6.2 for asymptomatic HIV infection), cellular immune deficiencies – see sections 4.3.2 and 4.3.3
- immunosuppressive therapy (including high-dose corticosteroids and biologics). Note: HZV is *not* contraindicated for use in individuals who are receiving low-level immunosuppressive therapy, for example: topical/inhaled corticosteroids or low-dose systemic corticosteroids; who are receiving corticosteroids as replacement therapy (eg, for adrenal insufficiency); low-dose weekly methotrexate or azathioprine – see Table 22.2 below and section 4.3.3
- active untreated TB
- pregnancy.

Do not give to children.

22.6.2 Precautions

HIV

Asymptomatic HIV-positive individuals with a CD4+ lymphocyte count ≥ 200 cells/mm³ may be vaccinated upon specialist advice. Results of a phase II trial in HIV-infected adults indicated that HZV was generally safe and immunogenic in those with CD4+ lymphocyte count ≥ 200 cells/mm³, with no cases of vaccine strain infection.^{29, 30}

Serological confirmation of previous VZV infection is recommended prior to vaccination.²⁷ If seronegative, give VV (funded); if seropositive give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Individuals with symptomatic HIV infection or AIDS should not be vaccinated.

Immunocompromised individuals

HZV is contraindicated in individuals with current or recent severe immunocompromise due to primary and secondary immune-deficiency states, or due to immunosuppressive therapy. However, individuals receiving low-level immunosuppressive therapy may be considered for vaccination upon specialist advice.

Individuals who anticipate significant future immunocompromise because of an existing illness and/or its treatment may be given HZV upon specialist advice.²⁷ This includes prior to solid organ transplant, chemotherapy or radiation therapy, and individuals with autoimmune disease. Vaccination at least 4 weeks prior to the onset of immunocompromise may be appropriate, upon specialist advice.²⁷ Individuals whose treatment with high-dose systemic immunosuppressive therapy has ceased may be vaccinated upon specialist advice if an appropriate time interval has passed.²⁷ Serological confirmation of previous VZV infection is recommended prior to vaccination. If seronegative, give VV (funded if an eligible condition); if seropositive give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Table 22.2 below provides recommendations for the use of HZV in persons on immunosuppressive therapy.

See also section 4.3.3.

Table 22.2: Recommendations for use of herpes zoster vaccine for individuals on immunosuppressive therapy

Immunosuppressive therapy	Treatment regimen	Potential timing of vaccination
High-dose corticosteroid monotherapy (≥ 20 mg per day of prednisone or equivalent)	<14 days	Immunise 4 weeks before treatment starts OR any time after treatment stops ^a
	≥ 14 days	Immunise 4 weeks before treatment starts OR at least 4 weeks after treatment stops
DMARDs:		
• Azathioprine	>3.0 mg/kg per day	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
• Methotrexate	>0.4 mg/kg per week	
• All other DMARDs ^{b,c}	All regimens	
T-cell inhibitors (eg, tacrolimus, cyclosporin)	All regimens	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
Other unspecified immunosuppressants (eg, chemotherapy ^d) ^e	All regimens	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
Targeted biological therapies (eg, monoclonal antibodies) ^f	All regimens	Immunise 4 weeks before treatment starts OR at least 12 months after treatment stops ^g

a Can be given immediately on discontinuation, but delay 2 weeks if possible.

b See Table 4.3 for a list of other DMARDs.

c Does not include sulfasalazine which is considered safe at any dose.

d For patients who have recently received chemotherapy and/or radiotherapy waiting at least 6 months rather than 3 months may be appropriate.

e This does not include individuals who have received HSCT, who should not receive HZV until at least 2 years post-HSCT. (See also the 'Vaccination after haematopoietic stem cell transplant (HSCT)/bone marrow transplant' discussion in section 4.3.3.)

f See Table 4.3 for a list of targeted biological therapies.

Continued overleaf

- g 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 specialist after evaluation of the delay since last treatment and in some cases an assessment of immunological recovery.

Source: Adapted from: Australian Technical Advisory Group on Immunisation (ATAGI). 2017. *The Australian Immunisation Handbook* 10th edition (2017 update), Table 4.24.1. Canberra: Australian Government Department of Health. URL: <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home> © Commonwealth of Australia 2016.

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22.7 Expected responses and AEFIs

22.7.1 Expected responses

HZV is generally well tolerated. In clinical trials, injection site reactions occurred more commonly in HZV recipients than in placebo recipients. PCR testing of VZV from zoster-like rashes occurring in the 42-day period following vaccination are much more likely to be due to wild VZV than to the vaccine virus.²

22.7.2 AEFIs

A large safety review of HZV in 193,083 individuals aged 50 years and older supports the pre-licensure clinical trial data.³¹ The HZV was found to be safe and well tolerated with no increased risk for the adverse event groupings of cerebrovascular events, cardiovascular events, meningitis, encephalitis, encephalopathy, Ramsay–Hunt syndrome or Bell’s palsy. A small increased risk of allergic reactions one to seven days after vaccination was reported.

A post-marketing observational study of 29,000 individuals aged 60 years and older did not identify any safety concerns within 42 days of receiving HZV vaccine.³²

22.8 Variations from the vaccine data sheet

The HZV (Zostavax) data sheet states that the HZV vaccine and 23PPV (Pneumovax 23) should not be given concurrently. The Ministry of Health recommends that HZV vaccine and 23PPV may be given concurrently^{22, 23} (see section 22.4.4).

The HZV data sheet states that HZV should not be given to individuals with HIV/AIDS. The Ministry of Health recommends that asymptomatic HIV-positive individuals with a CD4+ lymphocyte count ≥ 200 cells/mm³ may be vaccinated upon specialist advice (see section 22.6.2).²²²²²²²²²²²²²²²²²²

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