

22 Zoster (herpes zoster/shingles)

Key information

Mode of transmission	<p>Zoster is a reactivation of the varicella-zoster virus in someone who has previously had varicella disease (most often as chickenpox).</p> <p>Direct contact with zoster vesicles has a low risk of causing varicella in non-immune individuals – can be prevented by covering rash.</p> <p>There is potential for aerosol transmission from some immunocompromised cases with viraemia.</p>
Period of communicability	Until lesions have crusted.
Incidence and burden of disease	Increasing incidence with age; lifetime risk about 1 in 3. For those aged over 85 years, the risk is 1 in 2. Complications include post-herpetic neuralgia and herpes zoster ophthalmicus.
Funded vaccine	<p>Zoster vaccine (Zostavax), a higher titre formulation of the live attenuated varicella vaccine.</p> <p>Zoster vaccine is registered for use from age 50 years.</p> <p>Do not give to children.</p>
Dose, presentation, route	<p>0.65 mL per reconstituted dose.</p> <p>Vial of vaccine, plus diluent in a pre-filled syringe. The vaccine must be reconstituted prior to injection.</p> <p>Intramuscular or subcutaneous injection.</p>
Funded vaccine indications and recommended schedule	<p>One dose of ZV is funded for:</p> <ul style="list-style-type: none">• individuals at age 65 years, on or after 1 April 2018, or• catch-up of individuals aged 66–80 years, inclusive (the catch-up programme ceases on 31 December 2020). <p>ZV 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.</p>
Recommended	<p>May be considered for individuals aged 50–64 years with increased risk of zoster due to comorbidities (unfunded).</p> <p>Household contacts (age from 50 years) of immunocompromised individuals who are non-immune to varicella (unfunded unless within eligible age groups).</p>
Vaccine efficacy/ effectiveness	<p>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.</p> <p>The role of revaccination is currently unknown.</p>

Contraindications	See section 22.6.1 Risk of disseminated vaccine-derived disease including certain primary and secondary immune deficiencies and 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. The virus is usually acquired in childhood and primary infection with VZV causes varicella disease (chickenpox). Herpes zoster (zoster), or 'shingles', is a clinical syndrome caused reactivation of latent VZV, which resides in the dorsal root or trigeminal nerve ganglia after primary infection. VZV is usually acquired in childhood, but it is often many decades before the virus reactivates, at times when cellular immunity is compromised and is unable to maintain suppression of the virus.

22.2 Clinical features

Herpes zoster (shingles) occurs when the cell-mediated immune response is impaired and unable to maintain suppression of latent varicella-zoster virus reactivation (see chapter 21). Zoster occurs only by loss of suppression and reactivation of the patient's own virus – which is often acquired in childhood; it is not acquired from other patients with zoster or varicella.¹ But the zoster rash vesicles contain low levels of VZV that are able, through direct contact, to potentially cause varicella in VZV-naïve individuals.

Zoster presents clinically as a unilateral vesicular rash in a dermatomal distribution in most cases. The dermatomal distribution of the rash is the key diagnostic feature. In 70–80 percent of zoster 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, zoster is an acute and self-limiting disease, with the rash lasting 10–15 days. However, complications can occur, especially with increasing age.

Although most zoster cases occur in adults aged 40 years or older, it may be seen less commonly in infants and children. In those aged under 2 years may reflect *in utero* chickenpox, with the greatest risk arising following exposure between 25 and 36 weeks' gestation, and reactivation in early life. Infants who get varicella at a young age have a higher chance of having zoster before the age 20 years.

A common complication of zoster is post-herpetic neuralgia (PHN), a chronic, often debilitating pain condition that can last several 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 The risk rises with age, and it is uncommon in healthy children and young people.

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, if that dermatome is affected, and the risk is similar across all age groups.³

Zoster occurs more commonly in immunocompromised individuals, such as due to immunosuppression (eg, organ transplant patients, treatments for cancer and immune-mediated inflammatory diseases) and those with HIV. Up to 10 percent of children treated for a malignant neoplasm may develop zoster. In immunocompromised patients, extensive viraemia in the absence of a vigorous immune response can result in a disseminated form of zoster that includes severe multi-organ disease.^{2, 4} There is an increased risk of airborne transmission of VZV for immunocompromised individuals with viraemia. Other risk factors for developing zoster include rheumatoid arthritis,⁵ sleep disorders⁶ and type 2 diabetes.⁷

22.3 Epidemiology

22.3.1 Global burden of disease

Zoster 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 50 percent of those aged 85 years or over will 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.

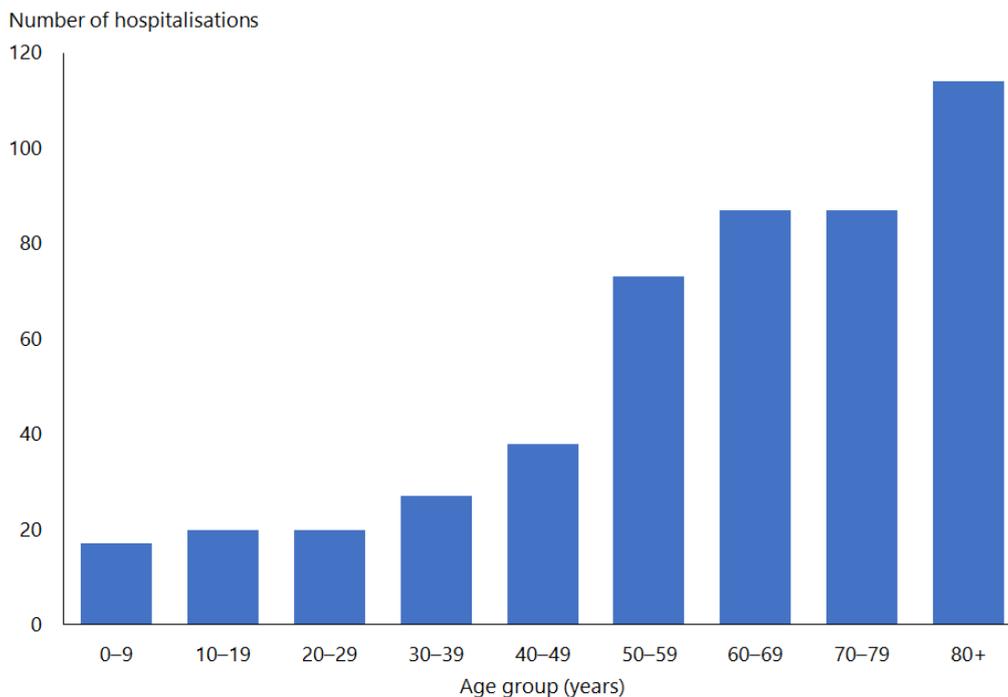
VZV is present in lesions of zoster and is transmissible via direct contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immunocompromised individuals with disseminated zoster. Episodes of zoster in older individuals provide a constant 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 zoster in older adults. However, several studies that have investigated this issue, observed an increase in zoster prior to VV programme introductions and have been unable to attribute any increase in incidence of zoster to childhood VV programmes.^{11, 12, 13, 14} Such increases have been observed in countries both with and without childhood varicella immunisation.

22.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2018/2019 are shown in Figure 22.1, with around 60 percent occurring in adults aged 60 years and older. Hospitalisations are predicted to account for only a very small proportion of the overall zoster cases as most are managed in primary care. Interrogation of general practice electronic records found the incidence of zoster in New Zealand to be similar (approximately 5 per 100,000 patient-years rising to 12.8 per 100,000 in those aged 80-90 years) to the global incidence estimates described in section 22.3.1.¹¹ In 2018/2019, there were 483 hospitalisations associated with herpes zoster.

Figure 22.1: Hospitalisations with herpes zoster as primary diagnosis by age group, 2018/2019



Source: Ministry of Health.

22.4 Vaccine

22.4.1 Available vaccine

ZV (Zostavax, MSD) is a live attenuated varicella-zoster virus vaccine. It is a higher titre formulation of the varicella vaccine and is designed to protect against zoster in those already immune to varicella.¹² By mimicking the immune response seen following a case of zoster and boosting cell-mediated immunity in older adults, the incidence and severity of zoster is reduced by the high-titre vaccine.

Funded vaccine

Each 0.65 mL dose of ZV (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.

Other vaccine

An adjuvanted recombinant subunit zoster vaccine (Shingrix, GSK), containing recombinant VZV glycoprotein E and AS01_B adjuvant system, is designed to specifically boost T-cell immunity against VZV. It has shown good efficacy in older adult age groups and immunocompromised groups against zoster and associated complications.^{13, 14} This vaccine is not available currently in New Zealand.

22.4.2 Efficacy and effectiveness

A pivotal clinical trial, the Shingles Prevention Study (SPS), recruited 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, in which, the participants received the high-dose live 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.¹² 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) incident zoster and 62 percent (95% CI: 32–77) reduction in PHN.¹⁵

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

Following the introduction of zoster vaccination programme to adults aged 70 years (with catch up for those aged 71–79 years) in the UK, vaccine effectiveness was estimated to be 64 percent (95% CI: 60–80) against zoster and 81 percent (95% CI: 61–91) against PHN. Vaccine effectiveness was lower in those who had a previous history of zoster (47 percent; 95% CI: 31–58).¹⁶

Duration of protection

The persistence of ZV 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 zoster until eight years post-vaccination.¹⁷ Clinical efficacy of ZV was shown to be increasingly limited with time beyond five years post-vaccination.

In older adults in the UK, effectiveness of ZV against zoster waned with time by the third year post-vaccination to an estimated 45 percent (95% CI: 29–57).¹⁶ In adults aged 60 years or older in the US, the effectiveness of ZV against zoster was shown to decrease from 69 percent in the first year to 4 percent eight years after vaccination; however, after an initial decline in the first year, effectiveness remained at around 30–40 percent up to five years after vaccination.¹⁸ Duration of protection is therefore variable. A compromise is required around the timing of the vaccination –vaccine effectiveness against zoster is highest when a person is vaccinated at a younger age but protection from a single dose may not last to an age where the risk of incidence of PHN is greatest.

Studies have shown that booster doses in adults are immunogenic, but there are no reports on efficacy of giving further doses. The immune response to a second dose declines with advancing age but is similar to the response seen following first doses of individuals of the same age: a prior dose neither enhances nor impairs the response to a booster dose.¹⁹ There do not appear to be any safety concerns with administering a second dose of ZV.²⁰ Although it is not currently recommended, individuals who previously received an unfunded ZV dose may choose to receive a funded ZV dose, if eligible. At the time of writing, there were no current international guidelines on giving further doses of ZV.

22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017).

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

22.4.4 Dosage and administration

ZV is registered for adults aged 50 years and older. **Do not give to children.** If a patient age is less than 50 years, consider giving VV if the patient is not immune to varicella.

The dose of reconstituted ZV is 0.65 mL, to be administered intramuscularly or subcutaneously if indicated, in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

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

Historically, there were concerns that VZV antibody titres were lower in individuals who received ZV and 23PPV at the same visit, compared with those given the vaccines four weeks apart. However, VZV antibodies are not considered a measure of protection against zoster, and all recent evidence suggests that ZV can be given concurrently with 23PPV.²¹ The US Centers for Disease Control and Prevention continues to recommend that ZV and 23PPV be administered at the same visit if the individual is eligible for both vaccines.²²

22.5 Recommended immunisation schedule

Table 22.1: Herpes zoster vaccine (ZV) recommendations

Note: Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of ZV (except for certain immunocompromised persons, refer below). **Funded individuals are shown in the shaded rows.**

Recommended and funded
1 dose of ZV is recommended and funded for: <ul style="list-style-type: none">• individuals aged 65 years, on or after 1 April 2018• catch-up of individuals aged 66–80 years, inclusive (until 31 December 2020).
For consideration, but not funded
1 dose of ZV may be considered, but is not funded, for individuals aged 50–64 years: <ul style="list-style-type: none">• who are at increased risk of zoster^{23, 24, 25, 26} and who may benefit from being vaccinated earlier than the routine schedule:<ul style="list-style-type: none">– with asymptomatic HIV^a (if CD4+ lymphocyte count is ≥ 200 cells/mm³)– with end-stage kidney disease^a (CKD stages 4–5)– at least 4 weeks prior to commencing high-dose immunosuppressive therapy^{a,b} and/or solid organ transplantation^{a,b}– after ceasing high-dose immunosuppressive therapy^{a,b}– at least 2 years post-HSCT^{a,b}– with autoimmune disease^{a,b} (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. Seek specialist advice. Serological confirmation of previous VZV infection is recommended before administering ZV. If an individual is VZV-seronegative, give VV. If VZV-seropositive, give ZV. See also section 4.3.
b. See Table 4.1 and Table 4.2.

22.5.1 Recommended and funded

Recommendations for ZV (Zostavax) are in Table 22.1 above. One dose of ZV is funded for individuals at age 65 years (on or after 1 April 2018), with a catch-up programme until 31 December 2020, with one dose of ZV funded for individuals aged 66–80 years, inclusively.

22.5.2 Other considerations

Vaccination of individuals aged 50–64 years (unfunded)

ZV (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 due to comorbidities^{23, 24, 25, 26} 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 probable that protection following a single vaccine dose wanes with time.²³ The need for revaccination is not yet determined.²³ Dosing with ZV is often strategic and based on clinical consideration (see below).

Individuals with a history of zoster (shingles)

Individuals with a history of a previous episode of zoster can be given ZV. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis.²³ In addition, the risk of a repeat episode of zoster has been estimated at approximately 5 percent in immunocompetent individuals.²³

There are no recognised safety concerns in giving the vaccine to people with prior history of zoster.²⁷ The length of time following an episode of zoster after which it may be beneficial to vaccinate has not been established.²³ It is suggested that the vaccine could be given at least one year after the episode of zoster has resolved.²³

Household contacts of immunocompromised individuals

ZV 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 ZV 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 ZV (funded at age 65 years with a catch-up, until 31 December 2020, for those aged 66–80 years inclusive; unfunded for those 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, at least until it crusts.²³

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

Serological testing

Generally, neither a history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the zoster vaccine.²³ 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 ZV to individuals with HIV, and in those who are anticipating significant future immunosuppression or who have ceased immunosuppressive therapy (see section 22.6.2).²³ Individuals in these categories who have negative VZV IgG should generally not be given ZV. Upon specialist advice, VV may be given instead of ZV to seronegative individuals.

Laboratory testing to check for an immune response after ZV is not recommended.²³

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. Seek specialist advice for primary and secondary immunodeficiency conditions (see section 22.6.2).

22.6.1 Contraindications

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

Do not give to children.

Contraindications to ZV include:

- a history of anaphylaxis to neomycin and gelatin (refer to chapter 2)
- 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); and cellular immune deficiencies – see sections 4.3.2 and 4.3.3

- during immunosuppressive therapy (including high-dose corticosteroids and biologics). Note: ZV 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 section 4.3.3)
- active untreated TB
- pregnancy.

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 ZV was generally safe and immunogenic in those with CD4+ lymphocyte count ≥ 200 cells/mm³, with no cases of vaccine strain infection.^{28, 29}

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

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

Immunocompromised individuals

ZV 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 ZV upon specialist advice.²⁷ This includes individuals due to receive solid organ transplant, chemotherapy or systemic radiotherapy, and individuals with IMIDs (autoimmune disease). Vaccination at least four 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 in these immunocompromised groups. If a person is seronegative, give VV (funded if an eligible condition); if seropositive give ZV (one dose is funded at age 65 years with a catch-up for those aged 66–80 years inclusive, until 31 December 2020; unfunded for those aged 50–64 years).

Individuals who are only receiving localised radiotherapy to treat a tumour or lesion can be vaccinated with live vaccines, such as ZV, at any time prior to, during or after radiotherapy.³⁰

See Table 4.1 and Table 4.2 in sections 4.3.5 and 4.3.6 for recommendations for the use of ZV in individuals on immunosuppressive therapy.

22.7 Potential responses and AEFIs

22.7.1 Potential responses

ZV is generally well tolerated. In clinical trials, injection-site reactions occurred more commonly in ZV 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 ZV in 193,083 individuals aged 50 years and older supports the pre-licensure clinical trial data.³¹ The ZV 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 ZV vaccine.³²

22.8 Variations from the vaccine data sheet

The ZV (Zostavax) data sheet states that the ZV vaccine and 23PPV (Pneumovax 23) should not be given concurrently. The Ministry of Health recommends that ZV vaccine and 23PPV may be given concurrently^{21, 22} (see section 22.4.4).

The ZV data sheet states that ZV 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).^{21, 22}

References

1. Gilden D. 2011. Efficacy of live zoster vaccine in preventing zoster and postherpetic neuralgia. *Journal of Internal Medicine* 269(5): 496–506.
2. Gershon A, Marin M, Seward JF. 2018. Varicella vaccines. In Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th edition)*. Elsevier: Philadelphia, US.
3. Kawai K, Gebremeskel BG, Acosta CJ. 2014. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open* 4(6): e004833.
4. Gnann JW Jr, Whitley RJ. 2002. Clinical practice: herpes zoster. *New England Journal of Medicine* 347(5): 340–6.
5. Che H, Lukas C, Morel J, et al. 2014. Risk of herpes/herpes zoster during anti-tumor necrosis factor therapy in patients with rheumatoid arthritis. Systematic review and meta-analysis. *Joint, Bone, Spine: Revue du Rhumatisme* 81(3): 215–21.
6. Chung WS, Lin HH, Cheng NC. 2016. The incidence and risk of herpes zoster in patients with sleep disorders: a population-based cohort study. *Medicine (Baltimore)* 95(11): e2195.
7. Guignard AP, Greenberg M, Lu C, et al. 2014. Risk of herpes zoster among diabetics: a matched cohort study in a US insurance claim database before introduction of vaccination, 1997–2006. *Infection* 42(4): 729–35.
8. Wehrhahn M, Dwyer D. 2012. Herpes zoster: epidemiology, clinical features, treatment and prevention. *Australian Prescriber* 35(5): 143–7.
9. Brisson M, Edmunds WJ, Law B, et al. 2001. Epidemiology of varicella zoster virus infection in Canada and the United Kingdom. *Epidemiology and Infection* 127(2): 305–14.
10. Schmader K. 2001. Herpes zoster in older adults. *Clinical Infectious Diseases* 32(10): 1481–6.
11. Turner NM, MacRae J, Nowlan ML, et al. 2018. Quantifying the incidence and burden of herpes zoster in New Zealand general practice: a retrospective cohort study using a natural language processing software inference algorithm. *BMJ Open* 8(5): e021241.
12. Oxman MN, Levin MJ, Johnson GR, et al. 2005. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *New England Journal of Medicine* 352(22): 2271–84.
13. Syed YY. 2018. Recombinant zoster vaccine (Shingrix®): a review in herpes zoster. *Drugs and Aging* 35(12): 1031–40.
14. Levin MJ, Weinberg A. 2020. Adjuvanted recombinant glycoprotein E herpes zoster vaccine. *Clinical Infectious Diseases* 70(7): 1509–15.
15. Langan SM, Smeeth L, Margolis DJ, et al. 2013. Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study. *PLoS Medicine* 10(4): e1001420.
16. Walker JL, Andrews NJ, Amirthalingam G, et al. 2018. Effectiveness of herpes zoster vaccination in an older United Kingdom population. *Vaccine* 36(17): 2371–7.
17. Morrison VA, Johnson GR, Schmader KE, et al. 2015. Long-term persistence of zoster vaccine efficacy. *Clinical Infectious Diseases* 60(6): 900–9.
18. Tseng HF, Harpaz R, Luo Y, et al. 2016. Declining effectiveness of herpes zoster vaccine in adults aged ≥ 60 years. *Journal of Infectious Diseases* 213(12): 1872–5.
19. Levin MJ, Schmader KE, Pang L, et al. 2016. Cellular and humoral responses to a second dose of herpes zoster vaccine administered 10 years after the first dose among older adults. *Journal of Infectious Diseases* 213(1): 14–22.
20. Vesikari T, Hardt R, Rümke HC, et al. 2013. Immunogenicity and safety of a live attenuated shingles (herpes zoster) vaccine (Zostavax(R)) in individuals aged ≥ 70 years: a randomized study of a single dose vs two different two-dose schedules. *Human Vaccines & Immunotherapeutics* 9(4): 858–64.

21. Tseng HF, Smith N, Sy LS, et al. 2011. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine* 29(20): 3628–32.
22. Centers for Disease Control and Prevention. 2015. *Herpes Zoster Vaccination*. 31 July. URL: <https://www.cdc.gov/vaccines/vpd/shingles/hcp/hcp-vax-recs.html> (accessed 15 April 2020).
23. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Zoster (herpes zoster). In *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/zoster-herpes-zoster> (accessed 21 April 2020).
24. Gershon AA, Mervish N, LaRussa P, et al. 1997. Varicella-zoster virus infection in children with underlying human immunodeficiency virus infection. *Journal of Infectious Diseases* 176(6): 1496–500.
25. Kawai K, Yawn BP. 2017. Risk factors for herpes zoster: a systematic review and meta-analysis. *Mayo Clinic Proceedings* 92(12): 1806–21.
26. Yenikomshian MA, Guignard AP, Haguinet F, et al. 2015. The epidemiology of herpes zoster and its complications in Medicare cancer patients. *BMC Infectious Diseases* 15: 106.
27. Centers for Disease Control and Prevention. 2018. *Zostavax Recommendations*. URL: <https://www.cdc.gov/vaccines/vpd/shingles/hcp/zostavax/recommendations.html> (accessed 20 May 2020).
28. Benson CA, Andersen JW, Macatangay BJC, et al. 2018. Safety and immunogenicity of zoster vaccine live in human immunodeficiency virus-infected adults with CD4+ cell counts >200 cells/mL virologically suppressed on antiretroviral therapy. *Clinical Infectious Diseases* 67(11): 1712–19.
29. Shafran SD. 2016. Live attenuated herpes zoster vaccine for HIV-infected adults. *HIV Medicine* 17(4): 305–10.
30. Belka C, Ottinger H, Kreuzfelder E, et al. 1999. Impact of localized radiotherapy on blood immune cells counts and function in humans. *Radiotherapy and Oncology* 50(2): 199–204.
31. Tseng HF, Liu A, Sy L, et al. 2012. Safety of zoster vaccine in adults from a large managed-care cohort: a Vaccine Safety Datalink study. *Journal of Internal Medicine* 271(5): 510–20.
32. Baxter R, Tran TN, Hansen J, et al. 2012. Safety of Zostavax – a cohort study in a managed care organization. *Vaccine* 30(47): 6636–41.