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.**
Does, 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	Zoster vaccine is not on the Schedule.
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.
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.

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 disorders[6] 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.

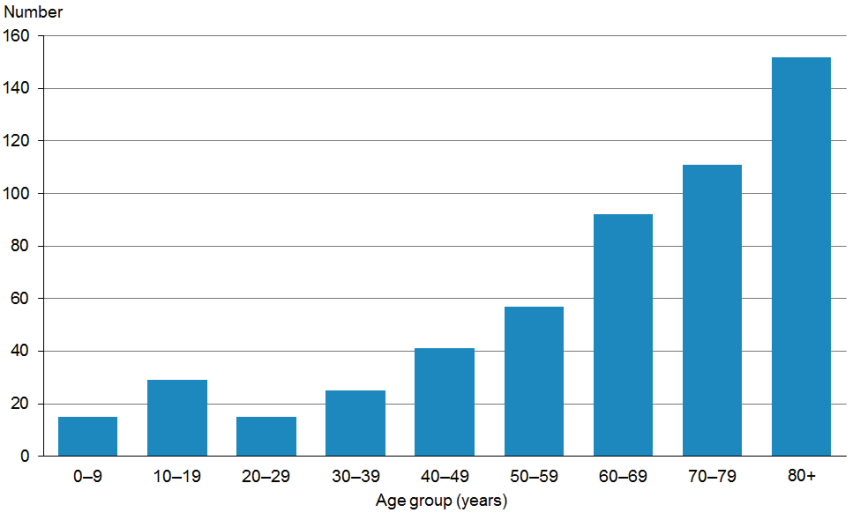
Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in HZ in older adults. However, studies that have investigated this issue have been unable to attribute any increase in

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

Herpes zoster vaccine (HZV) is not on the Schedule.

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.

Each 0.65 mL HZV dose 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.

22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[20] Store in the dark at +2°C to +8°C. The supplied diluent can be stored separately at +20°C to +25°C, or in the refrigerator 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.

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.

Evidence[21] 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.[21] 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.[22]

22.5 Recommended immunisation schedule

In New Zealand HZV (Zostavax) is licensed for adults age 50 years or older but is not on the New Zealand Schedule and is not funded. It must be prescribed and privately purchased. The vaccine is on the national schedules in the UK[23] and Australia[24] for individuals at age 70 years and in the US[25] for individuals aged 60 years and older.

HZV may be considered for adults aged 50 years and older to prevent shingles, particularly if they would have difficulty tolerating an episode of shingles and/or they are a household contact of an immunosuppressed individual. HZV may also be appropriate for some people on low-dose immunosuppression, and prior to commencing high-dose immunosuppressive therapy and/or solid organ transplantation.

22.6 Contraindications and precautions

Do not give to children.

Contraindications to HZV include:

- a history of hypersensitivity to any component of the vaccine, including gelatin and neomycin
- 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, cellular immune deficiencies

- 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 section 4.3.3
- active untreated TB
- pregnancy.

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

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.[26] 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.[27]

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[21, 22] (see section 22.4.4).

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