



Shingles vaccine in preventing shingles and postherpetic neuralgia

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Introduction

Infection with the varicella-zoster virus (VZV) causes two distinct clinical manifestations, namely varicella (chickenpox) and herpes zoster (shingles).¹⁻⁴

Primary infection, which generally occurs during childhood, results in varicella (chickenpox).¹⁻⁸ Following the initial infection, the virus enters the nerves and travels along the nerves to infect dorsal root ganglia (nerve cells), where it remains dormant/latent for many years.^{2,3,5}

In the latent state the virus is inactive and may never cause symptoms again or the virus may be reactivated in the future (usually many years after the initial infection).^{2,5} Reactivation of the latent VZV results in shingles.²⁻⁸ VZV-specific host cell-mediated immune responses are essential for maintaining latency and limiting the likelihood for reactivation.^{3,6}

The risk of developing shingles is associated with age-related immune senescence and/or suppression of the immune system and seems to be causally related to a decrease in VZV-specific cell-mediated immunity.^{2,8} Although shingles can occur at any age, it is most common in persons over 50 years of age. The incidence of shingles increases with age.¹⁻⁸

The shingles rash is a painful, blistering skin rash that typically appears on one side of the body (unilateral) on the area/strip of the skin over the infected nerve fibres. The area/strip of the skin that is supplied with the nerve fibres from a single spinal nerve region is known as a dermatome. In some cases, the rash may also appear on the dermatomes next to the affected dermatome.^{3,5}

Reactivation of the VZV may occur earlier in life in immunocompromised people, for example those with human immunodeficiency virus (HIV) infection, malignancies or those on immunosuppressive therapy (such as chemotherapy, radiation). The severity of shingles is significantly higher amongst immunocompromised people and they are also at risk of developing disseminated disease with generalised skin lesions, pulmonary, hepatic and central nervous system involvement.^{1,3}

After the shingles rash has resolved, some people may experience persistent pain in the involved dermatome, known as postherpetic neuralgia (PHN).³ PHN is a common debilitating complication of shingles and occurs in 10–13% of shingles cases in persons over 50 years of age.^{4,7} PHN can last for months or even years and it often has a negative impact on the affected person's quality of life.¹⁻⁸ The incidence of PHN, among persons with shingles, also increases with age.⁴

Current treatment options for both shingles and PHN have limited effectiveness.^{3,7} The zoster vaccine protects against shingles and its complications by boosting VZV-specific immunity, making it an important intervention against shingles and PHN.^{3,8}

The role of the zoster vaccine

Zostavax[®] is the only zoster vaccine currently available in South Africa and it contains the live attenuated strain of the VZV.⁹

It is registered for use in immunocompetent adults aged ≥ 50 years of age to prevent or reduce the severity of:

- Shingles
- PHN
- Acute and chronic zoster-associated pain⁸

Dosage and directions for use

A single dose of the reconstituted vaccine should be administered by subcutaneous injection preferably into the deltoid region of the upper arm.⁸

In order to minimise loss of potency, the vaccine should be administered immediately after reconstitution.⁸ If more than 30 minutes has elapsed since reconstitution, the vaccine should be discarded.⁸

Efficacy and duration of protection

Efficacy

Results from the placebo-controlled, double blinded Shingles Prevention Study demonstrated that Zostavax[®] significantly

reduced zoster-associated pain and significantly reduced the risk of developing shingles and PHN, compared to placebo.⁸

In randomised controlled trials, the efficacy of the live zoster vaccine in preventing herpes zoster has been found to be:

- 70% (median follow-up time was 1.3 years) among persons aged 50–59 years⁴
- 64% in persons aged 60–69 years
- 38% in persons aged ≥ 70 years (median follow-up time was 3.1 years)^{4,8}

The efficacy against PHN has been found to be:

- 65.7% in persons aged 60–69 years⁴
- 66.8% in persons aged ≥ 70 years (median follow-up of 3.1 years)⁴

Tricco *et al.*¹⁰ compared the efficacy, effectiveness and safety of the herpes zoster live attenuated vaccine with the herpes zoster adjuvant recombinant subunit vaccine or placebo in adults aged 50 and older. They included 22 studies (2 044 504 patients) in their systematic review and network meta-analysis. Results from their study suggested that although the adjuvant recombinant subunit vaccine was superior to the live vaccine for the prevention of herpes zoster infection, it was associated with more injection site reactions.¹⁰

Duration of protection

According to the prescribing information the need for, or timing of, revaccination with Zostavax[®] has not yet been determined.⁸

Observational studies have found the effectiveness of the live zoster vaccine against PHN was longer lasting than the effectiveness against herpes zoster itself.⁴

Studies have shown that the vaccine effectiveness:⁴

- Decreases following the first year after receiving the live zoster vaccine
- Was < 35% by six years postvaccination
- Ranged from 21%–32% during years 7–8 postvaccination

A study has also shown that the estimates of effectiveness were no longer statistically significant nine to eleven years postvaccination.⁴

Precautions and contraindications

Vaccination should be delayed in persons who are acutely ill, until they have fully recovered.²

Zostavax[®] is not recommended for use in paediatric patients and is contraindicated in persons:

- With a history of anaphylactic reaction to any component in the vaccine, including gelatine or neomycin⁸
- With active untreated tuberculosis⁸

Due to the risk of developing disseminated VZV infections caused by the vaccine strain of the virus, Zostavax[®] is contraindicated in persons:

- With primary or acquired immunodeficiencies such as:
 - Acute or chronic leukaemia
 - Lymphoma
 - Other conditions affecting the bone marrow or lymphatic system
 - Immunosuppression due to HIV/acquired immune deficiency syndrome (AIDS)
 - Cellular immune deficiencies
- On immunosuppressive therapy, including high-dose corticosteroids (≥ 20 mg/kg/day of prednisone or equivalent for 14 days or longer)^{6,8}

Use in pregnancy is contraindicated, but also unlikely considering the target age group (it is not indicated for women of childbearing age).^{6,8} Nevertheless, pregnancy should be avoided for three months following vaccination.⁸ The Centers for Disease Control and Prevention (CDC) recommends that pregnancy should be deferred for four weeks after vaccination.^{1,11}

Safety

Several studies have investigated the safety of the live zoster vaccine. The most commonly reported side-effects in clinical trials were injection site reactions such as pain, swelling, erythema (redness), and pruritis (itching),^{2,6,8} 48% of vaccine recipients reported injection site reactions compared to 17% in placebo recipients.^{4,8}

Other common side-effects include headache, haematoma and pain in an arm or leg.^{2,8}

In rare cases, varicella-like rashes have been reported.^{2,8} Although transmission of the zoster vaccine virus has not been reported in clinical trials with Zostavax[®], a theoretical risk exists that the vaccine virus may be spread from a vaccinated person to a susceptible (chickenpox naïve) person, if the vaccinated person develops a rash.^{2,8}

As a precautionary measure, anyone who develops a rash following vaccination with the live zoster vaccine, should be instructed to cover the rash (until the rash has crusted over) when he/she is in contact with a susceptible person.²

Interactions

With other vaccines

Other vaccines that are routinely recommended for persons 60 years of age and older, such as influenza and 23-valent pneumococcal polysaccharide vaccine, may be administered on the same day, but at a different injection site to Zostavax[®].^{3,10-12}

With antiviral medication against herpesviruses

Antivirals against herpesvirus such as aciclovir, famciclovir, or valaciclovir may interfere with the replication of the vaccine virus.¹ As a result, it is recommended that these antivirals should:

- Be discontinued for at least 24 hours (to 48 hours) before the live zoster vaccine is administered.^{1,2,6}
- Not be taken for at least 14 days after vaccination.^{1,6}

The use of the live zoster vaccine in special groups

In patients with a history of herpes zoster

Vaccination is not a treatment for zoster or PHN.⁸ Owing to the recurring nature of shingles, vaccination may still be offered for a person with a history of shingles. However, vaccination should be delayed, until the acute stage of the illness is over, and symptoms have subsided.^{4,11}

The specific length of time to delay vaccination after a recent episode of zoster is uncertain.⁶ However, a recent case of shingles itself will boost VZV-specific immunity and it may therefore be prudent to delay vaccination for approximately one year after a case of shingles.⁶

In patients anticipating immunosuppressive therapy

The risk and severity of shingles is higher amongst immunocompromised persons. It is preferable to vaccinate eligible persons before immunosuppressive treatment is initiated, as the live zoster vaccine may be contraindicated after immunosuppressive treatment has started. If it is indicated, the live zoster vaccine should be given at least one month before such treatment is started.^{2,6}

In HIV-infected patients

HIV-infected persons have a 10-fold increase in the risk of developing shingles.⁷ In addition, the incidence of shingles in HIV-infected adults remains increased despite using effective antiretroviral therapy.¹³

According to the South African guidelines for the vaccination of HIV-infected adolescents and adults, the live zoster vaccine is not routinely recommended for HIV-infected patients. Vaccination should be based on clinical risk assessment and should only be considered in eligible HIV-infected patients with CD4+ counts above 200 cells/ μ L.^{2,13}

International guideline for the prevention of shingles and related complications

According to the Advisory Committee on Immunization Practices (ACIP) and the CDC, the recombinant zoster vaccine (which is not currently available in South Africa) is preferred over the live zoster vaccine for the prevention of shingles and related complications.¹¹

ACIP and CDC recommend the use of the live zoster vaccine in immunocompetent adults aged ≥ 60 years.^{4,11} However, they do not support the routine use of the live zoster vaccine in immunocompetent adults 50 through 59 years of age.^{4,11}

Protection from the zoster vaccine wanes over time. Consequently, a person who received a live zoster vaccine before 60 years of age, might not be protected when his/her risk for shingles and its complications is at the highest.¹¹

According to the CDC, the risks and benefits of vaccination should be considered before administering the ZVL to persons 50 through 59 years of age,¹¹ taking into consideration whether or not the person would be able to tolerate symptoms associated with shingles and/or PHN. Persons with anticipated poor tolerance to shingles and/or PHN include, but are not limited to, those:

- with severe depression, pre-existing chronic pain or other comorbidities,
- who may not tolerate treatment medication whether due to hypersensitivity or potential interactions, or
- with occupational/employment-related issues.¹¹

In a nutshell

- Anyone who has had chickenpox in the past, as well as those who have been infected with VZV without a clinical history of varicella, is at risk of developing shingles.⁸
- Vaccination is effective in reducing the incidence of both shingles and PHN.⁸
- Zostavax[®] contains the live attenuated strain of the VZV and is registered for persons 50 years of age and older.⁸
- ACIP and CDC recommends Zostavax[®] for immunocompetent persons 60 years of age and older.¹¹
- Other vaccines, such as influenza and pneumococcal vaccines, that are routinely recommended for persons 60 years of age and older, may be administered on the same day, but at a different injection site to Zostavax[®].¹¹

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