Recombinant varicella zoster virus glycoprotein E antigen vaccine

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Approved indication: prevention of herpes zoster and postherpetic neuralgia

Shingrix (GlaxoSmithKline)
single-dose vials containing powder for reconstitution

Herpes zoster (shingles) is a painful condition characterised by a unilateral vesicular rash with a dermatomal distribution. The number of blisters and the area of affected skin vary, as does the severity of associated symptoms and complications, such as muscle weakness and postherpetic neuralgia. Herpes zoster may occur in anyone who has previously had varicella zoster infection (chickenpox) as it is caused by reactivation of the latent varicella zoster virus from a dorsal nerve root ganglion. Such reactivation is more likely in older age or during immunosuppression which results in lowered zoster-specific cell-mediated immunity. While herpes zoster resolves in most people without sequelae, some have persistent and significant discomfort. Postherpetic neuralgia, which is more common in people over 50 years old, is characterised by debilitating pain and dysaesthesia for more than three months.

The first vaccine against herpes zoster became available in Australia in 2006. Ten years later, this live attenuated vaccine was offered through the National Immunisation Program to people aged 70–79 years. It has a moderate protective efficacy of 51% in adults 60 years of age or older. However, as a live vaccine, it cannot be administered to immunocompromised patients.[1]

This new vaccine is a recombinant form of the herpes zoster glycoprotein E antigen, also known as Hz/su. It does not contain live virus and therefore may be suitable for immunocompromised patients pending the results of further studies. The US Centers for Disease Control and Prevention advises that the vaccine can be administered to people on low-dose immunosuppressive therapy.[2] Glycoprotein E has a central role in herpes zoster infection and is an important target for immune responses. The vaccine is designed to induce antigen-specific cellular and humoral immune responses in persons with pre-existing immunity against herpes zoster virus. However, it is not necessary to have a documented history or serological evidence of prior varicella infection.[2] Vaccination involves two 0.5 mL intramuscular injections, preferably in the deltoid muscle, with a two-to-six-month interval between doses.

A placebo-controlled phase III trial, ZOE-50, involved 15,411 participants, aged 50 years or older with no history of zoster infection or vaccination. There were 7698 people who were randomised to receive the vaccine and 7713 who received injections of placebo. The second dose was given two months after the first. After a mean follow-up of 3.2 years, herpes zoster was diagnosed in six people in the vaccine group and 210 in the placebo group.[3]

A parallel trial, ZOE-70, randomised 14,816 adults 70 years of age or older. Among the people who could be evaluated after 3.7 years of follow-up, herpes zoster occurred in 23 of the 6541 vaccine recipients and in 223 out of the 6622 placebo recipients.[4]

In pooled data from both trials for participants age 70 years and older, the vaccine efficacy was 91.3%.[4] Pooled data from all participants 50 years and older showed that the incidence of postherpetic neuralgia was 0.1 per 1000 person-years in the vaccine group and 0.9 in the placebo group, indicating a vaccine efficacy of 91.2%.[4] The efficacy in preventing postherpetic neuralgia is most likely due to the vaccine reducing the rate of herpes zoster, because there was no reduction in the incidence of postherpetic neuralgia in the small number of vaccinated people who did develop herpes zoster.

In ZOE-70 a randomly selected subgroup of 1025 participants recorded adverse events within seven days of vaccination. Injection-site reactions were reported in 74.1% of vaccine recipients and 9.9% of those who received placebo. The most common local reactions to the vaccine were pain (68.7%), redness (39.2%) and swelling (22.6%). These symptoms typically lasted less than four days. General symptoms included myalgia (31.2%) and fatigue (32.9%). In the mean follow-up period of four years, the incidence of serious adverse events was similar in the vaccine (16.6%) and placebo (17.5%) groups. Potential immune-mediated diseases occurred in 1.3% and 1.4%.[4]

The vaccine may be given at the same time as seasonal influenza vaccine, but at a different site. There are no data in relation to concomitant injection with other vaccines.

The recombinant herpes zoster glycoprotein E vaccine appears to be of higher efficacy than the live vaccine.[1] However, the incidence of injection-site reactions is higher than with live vaccine (74.1%[4] vs 48%[5]). The live vaccine protects for about five years, but its efficacy declines from 63.9% in the 60–69-year-old group to 37.6% in those aged 70 years or over with respect to protecting against herpes zoster. In contrast, in

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ZOE-50 and ZOE-70, the efficacy of the recombinant vaccine did not appear to decline with increasing age. It was similar in all age groups (50–59, 60–69, and 70 years and over).[4] However, if herpes zoster does occur after vaccination with the live vaccine, its efficacy against postherpetic neuralgia (66.5%) does not decline with age.[6] The recombinant vaccine has evidence of maintaining its effectiveness for four years, but studies are required to explore its longer term efficacy.

Since 2020, when the live vaccine was discontinued in the USA, the recombinant vaccine has been the only vaccine available.[2] The Australian approval is for people aged 50 years or older.

[X] manufacturer did not respond to request for data

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.