National Immunisation Advisory Committee

HERPES ZOSTER VACCINE RECOMMENDATIONS

NIAC | 12.02.2024

About NIAC

NIAC membership includes nominees from the Royal College of Physicians in Ireland, its Faculties and Institutes, the Royal College of Surgeons in Ireland, the Irish College of General Practitioners, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are attended by representatives from the Department of Health and the HSE. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

NIAC considers the evidence about vaccines and provides advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the Health Service Executive.

HERPES ZOSTER VACCINE RECOMMENDATIONS

1. IMMUNOCOMPETENT ADULTS

   NIAC recommends the immunisation of all adults aged 65 years and older with recombinant zoster vaccine (RZV).

2. IMMUNOCOMPROMISED ADULTS

   (a) NIAC recommends the immunisation of adults with immunocompromising conditions (Table 1) aged 50 years and older with RZV.

   (b) NIAC recommends the immunisation of HSCT recipients, aged 18 years and older, with RZV.

   (c) NIAC recommends that immunisation with RZV is considered for patients aged 18-49 years and older with immunocompromising conditions (Table 1) in particular solid organ transplant recipients, those with haematological malignancies and those with advanced or untreated HIV (CD4 count <200 cells/µl), in consultation with their treating hospital specialist.

3. For both immunocompetent and immunocompromised adults, RZV should be given as two doses (0.5ml) with a 2–6-month interval between doses.*

* For subjects who are or might become immunodeficient or immunosuppressed due to disease or therapy, and who would benefit from a shorter vaccination schedule, the second dose can be given 1 to 2 months after the initial dose.

Recommendations may be updated if more information becomes available.

Table 1: Immunocompromising conditions that increase the risk of HZ†
Hematopoietic Stem Cell Transplant Recipients
Solid Organ Transplant Recipients
Patients with cancer *Includes solid tumours and haematological malignancy e.g., leukaemia*
Patients with primary or acquired cellular and combined immune deficiencies resulting in lymphopenia (<1000 lymphocytes/µl) or functional lymphocyte disorder. *Includes people living with HIV who are severely immunosuppressed (CD4 count <200 cells/µl)*
Patients with immune mediated inflammatory disorders who are receiving, have received, or are planned to receive immunosuppressive therapy e.g., rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease. Immunosuppressive therapy includes but is not limited to: • Corticosteroids: Either high doses‡ intermittently or long-term use of more than 5mg of prednisolone or equivalent per day. • Non-biologic immunosuppressive therapy e.g., methotrexate, systemic calcineurin inhibitors, cyclosporin, cyclophosphamide, azathioprine, JAK inhibitors. • Biologic agents e.g., B-cell monoclonal antibodies, TNF alfa blockers.
† Optimal age and precise timing of vaccination should be determined by treating hospital specialist taking patient specific factors into account (see Appendix 1). ‡ High dose steroids: Adults and children ≥10kg: ≥40 mg/day for more than one week, or ≥20 mg/day for two weeks or longer and Children <10kg: 2mg/kg/day for two weeks or longer. See Chapter 3 Immunisation Guidelines of Ireland.

LIST OF ABBREVIATIONS

AE	Adverse event
ART	Antiretroviral therapy
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CRF	Chronic renal failure
DM	Diabetes mellitus
ESRD	End stage renal disease
GSK	GlaxoSmithKline
HIPE	Hospital In-Patient Enquiry
HIV	Human immunodeficiency virus
HSCT	Hematopoietic stem cell transplant
HZ	Herpes Zoster
IBD	Inflammatory Bowel Disease
JAKi	Janus kinase inhibitors
LTFU	Long term follow up
MS	Multiple sclerosis
nbDMARDS	non-biologic disease-modifying antirheumatic drugs
NIAC	National Immunisation Advisory Committee
NNV	Number needed to vaccinate
PCV	Pneumococcal conjugate vaccine
PHN	Postherpetic neuralgia
PPSV	Pneumococcal polysaccharide vaccine
PS	Psoriasis
RA	Rheumatoid arthritis
RCT	Randomised controlled trial
RSV	Respiratory syncytial virus
RZV	Recombinant zoster vaccine
SGPN	Sentinel General Practitioner Network
SLE	Systemic lupus erythematosus
SOM	Solid organ malignancy
SOT	Solid organ transplant
Tdap	Tetanus, Diphtheria, and Pertussis
TNF	Tumour necrosis factor
VE	Vaccine efficacy
VZV	Varicella zoster virus
ZVL	Zoster live vaccine

1. EXECUTIVE SUMMARY

- Herpes zoster (shingles) and its complications impact the health of older adults and immunocompromised patients in Ireland and is linked to a considerable number of hospital admissions annually (approximately 100 admissions per 100,000 population in those aged ≥65 years). Incidence starts to increase in the population from 50 years of age and continues to increase with advancing age.
- Rates of complications of herpes zoster (HZ) increase with age and immunocompromise. These complications can be severe and long-lasting, significantly impacting the quality of life of those affected. The most common complication of HZ, post herpetic neuralgia (PHN), occurs in approximately 8% of cases and almost 20% in those over 70 years of age.
- Within the immunocompromised cohort, those at the highest risk of HZ are patients receiving hematopoietic stem cell transplant (HSCT) and their risk is high regardless of their age. Solid organ transplant (SOT) patients and patients with hematologic malignancy (HM), solid organ malignancy (SOM) and human immunodeficiency virus (HIV) are also at significantly increased risk.
- Other groups at increased risk of HZ and its complications include those with chronic immune mediated inflammatory disease, those with primary or acquired immunodeficiency states, and those on immunosuppressive therapies.
- A non-live, recombinant vaccine to protect against HZ (recombinant zoster vaccine RZV), Shingrix, was approved for use by the European Medicines Agency in March 2018. Shingrix is more effective than the previously available live vaccine Zostavax (ZVL) and can be safely administered to immunocompromised patients. RZV has replaced ZVL as the preferred vaccine against HZ internationally.
- Clinical trials have demonstrated that RZV is safe and efficacious in preventing HZ and post herpetic neuralgia (PHN) for at least 10 years in immunocompetent older adults. Vaccine efficacy is comparable across age groups. Ongoing data collection from trials aims to assess if efficacy is sustained over a longer period.
- Immunogenicity studies have demonstrated sustained antibody responses (12-24 months) in HSCT recipients, renal transplant recipients, patients with haematological and solid organ malignancies and HIV.
- Duration of immunity in immunocompromised patients has not been studied past 24 months.
- It is not yet known if booster vaccines will be required in immunocompromised or immunocompetent populations.
- Efficacy data in immunocompromised patients is available only for HSCT recipients where RZV has been shown to be safe and efficacious in preventing HZ in clinical trials.
- The optimal timing for RZV administration in immunocompromised patients will vary according to condition, associated risk of HZ, and intensity of planned immunosuppression.
- Many countries have national recommendations for RZV vaccination for older adults and immunocompromised adults and several countries including Belgium, Spain, Germany, the United Kingdom (UK), and Australia have funded national programmes.
- Age cut-off for RZV vaccine recommendations and funded programmes vary internationally.
- Population health modelling studies from Germany, the UK and Belgium predicted national vaccination programmes at age 60 years old to have the greatest clinical impact on the burden of

HZ, with Germany and the UK both predicting similar results by vaccinating at age 60 or 65 years old.

- The optimum age of a national vaccination programme for the reduction of PHN was 65 years old in the UK model and 70 years old in the German model.
- RZV has been shown to be comparably safe and efficacious when administered concomitantly with several other adult vaccinations including unadjuvanted inactivated seasonal influenza, Tdap, PCV13, PPSV23 and COVID-19 mRNA-1273 vaccines.

2. INTRODUCTION

Herpes zoster (shingles) is caused by the reactivation of latent varicella zoster virus (VZV) and usually occurs decades after primary infection. Vesicles appear in a dermatomal distribution where the virus has been dormant. In immunocompromised individuals, a rash involving multiple dermatomes may occur. Headache, photophobia, malaise and less commonly fever may occur as part of the prodromal phase. The affected area may be intensely painful with associated paraesthesia. The incidence and severity of HZ increases with age and approximately one in four adults will experience an attack in their lifetime.

Complications associated with HZ infection include PHN, ocular complications, meningitis and herpes zoster oticus.[1] Pain associated with HZ, persisting or appearing more than 90 days after the onset of rash is a commonly accepted definition of PHN.[2] The risk of PHN increases with age, as does the severity and duration of related pain. Immunosuppression due to disease or treatment also increases the risk of HZ and HZ-related complications.

A non-live recombinant vaccine (RZV, Shingrix) is licensed for prevention of HZ and PHN in adults aged 50 years and above and in adults aged 18 years and above at increased risk of HZ. Shingrix (RZV) is more effective than the previously available live vaccine Zostavax (ZVL) and can be safely administered to immunocompromised patients. In these recommendations only RZV is considered as RZV has replaced ZVL as the preferred vaccine against HZ internationally and production of ZVL will cease in the coming months.

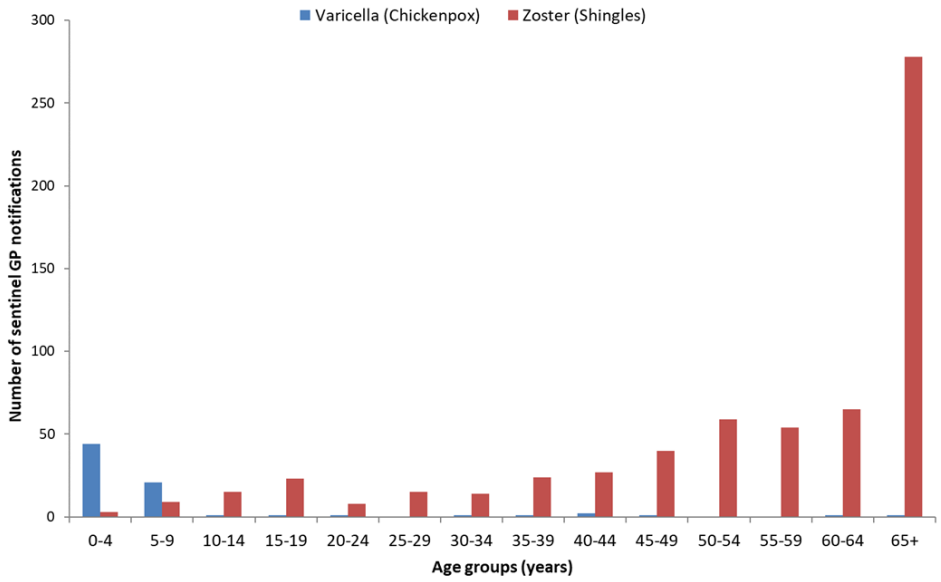
These recommendations take into consideration the burden of HZ infection and its complications in Ireland, and the safety, immunogenicity, efficacy and effectiveness of RZV in different at-risk populations.

3. EPIDEMIOLOGY

On average from 2009 to 2022 there has been approximately 680 cases of HZ reported by the Sentinel General Practitioner Network (SGPN) annually in Ireland. This number was 826 in 2019 and, with the exception of 2020 and 2021 throughout the COVID-19 pandemic, there has been an upward trend in cases reported by the SGPN year on year. The reasons for this increase in HZ cases, also observed internationally, remain unclear but may, in part, be related to the trend of aging populations in high

income countries. In 2022, 52% of cases reported by SGPN occurred in those over the age of 60 years old. (Figure 1)[3]

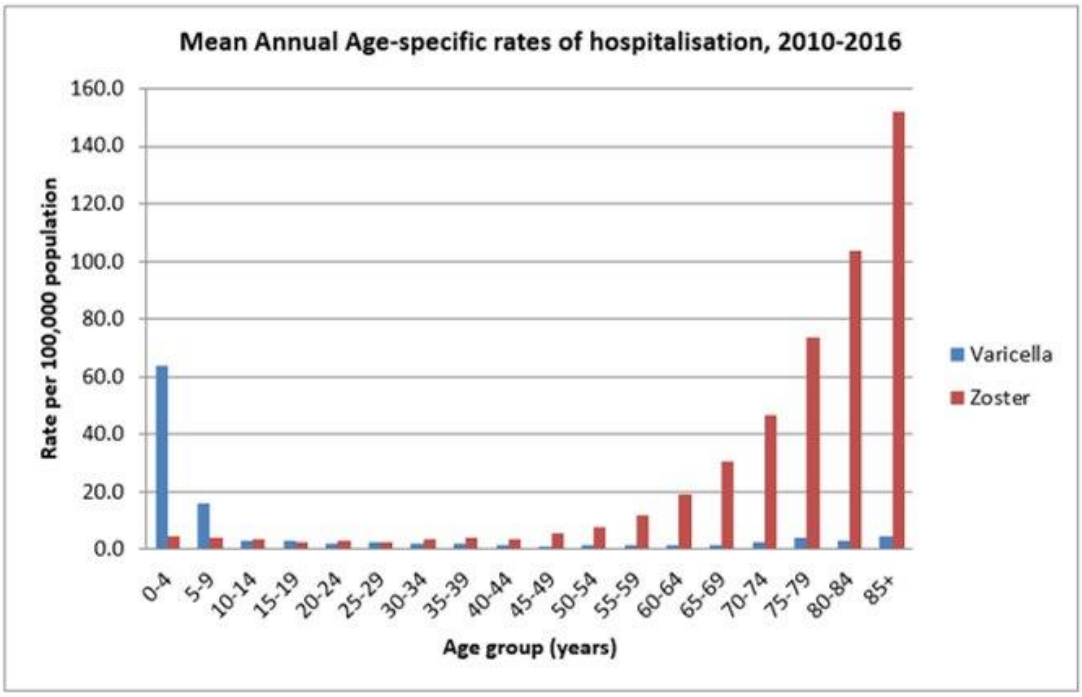
Figure 1. Age distribution of varicella and zoster clinical cases reported by Sentinel GP Network, Ireland, 2022. Source: HPSC.[3]



Between 2010 and 2016 the rate of HZ related hospitalisations was approximately 20 per 100,000 population in those aged 60-65 years, increasing with advancing age up to 150 per 100,000 population in those aged 85 years and above. (Figure 2) Over the same time frame the total number of zoster related complications, including PHN and zoster ocular disease, recorded in Hospital In-Patient Enquiry (HIPE) was 246[a]. While HZ related mortality is relatively low, HZ was registered as the cause of 48 deaths with the Central Statistics Office between 2007 and 2020. There were no HZ related deaths in those aged under 70 years, the majority of deaths were in those aged 85 years and over, and in women.[3]

[a] This is not directly equal to the number of patients affected by HZ complications as some episodes of care had more than one zoster related diagnosis. It is a crude estimate of complications experienced by HZ patients in Ireland.

Figure 2. Mean annual age-specific rates of hospitalisation in Ireland, 2010-2016. Source: HIPE data.[3]



While a specific incidence rate of PHN is not available for Ireland, internationally, the incidence among those who experience HZ has been estimated to be between 5 and 30% depending on age and definition of PHN.[4] The risk of PHN increases with age being less than 10% in individuals aged 50-59 years and between 10 and 20% in individuals aged 70-79 years.[5] Prospective cohort studies demonstrated that approximately 30-50% of patients with PHN experienced pain lasting more than one year and, in some cases, up to 10 years.

Immunocompromised individuals of any age are at increased risk of HZ. Risk varies depending on the underlying condition and immunocompromising treatment. Data on incidence of HZ and its complications in immunocompromised individuals in Ireland is limited. Systematic reviews of the incidence of HZ in adult patients with immunocompromise published in 2020 and 2023 report the highest incidence of HZ in haematologic stem cell transplant (HSCT) patients, followed in order of incidence by haematological malignancies (HM), solid organ transplant (SOT), solid organ malignancies (SOM) and human immunodeficiency virus (HIV). (Table 2)[6 7]

Table 2. Incidence rate of HZ by immune altering condition. Adapted from Sullivan et al, 2023.[7]

Author, year, study region and timeframe	Age	Total cohort (n)	IC cohort (n)	Incidence rate per 1,000 person years										
				HSCT	SOT	HM	SOM	HIV	ESRD	SLE	RA	IBD	MS	PS
Yanni et al. 2018.[8] England. 2000-2012	≥18 years	621,588	621,588	41.7	12.1	15.2	8.8	11.8	12.3	10.9	10.6	7.0	5.7	5.3
Munoz-Quillez et al. 2020.[9] Valencia. 2009-2014	≥18 years	4.3 million	578,873	56.1	12.7	11.9	10.9	12.9		13.4	11.1	8.3	6.3	6.1
Imafuku et al. 2019.[10] Japan. 2005-2014	18-74 years	2.7 million	51,818	151.7		28.2	9.4			15.9	9.2	7.4		5.6
Chen et al. 2014.[11] US. 2005-2009	18-64 years	51 million	3.4 million	43.0	17.0	11.7	11.7	17.4		15.2	12.2	9.3	8.6	8.0

ESRD: end stage renal disease SLE: systemic lupus erythematosus RA: rheumatoid arthritis
IBD: inflammatory bowel disease MS: multiple sclerosis PS: psoriasis

The risk of HZ associated with these conditions is greater than the risk associated with older age in the immunocompetent. However, within patients with these conditions the risk of HZ increases with increasing age except in the case of HSCT and in those living with HIV prior to the introduction of antiretroviral therapy. For HSCT patients the risk is comparably high across age groups from 18 years old and above. (Table 3)[11]

Table 3. Incidence of HZ by immune altering condition by age group. Source: Chen et al, 2014.[11]

Characteristics of study population	Incidence[a] (cases per 1000 person years) (95% Confidence interval)				Incidence rate ratio (95% Confidence interval)		
	18-49 years	50-59 years	60-64 years	≥65 years	50-59 vs. 18-49	60-64 vs. 18-49	≥65 vs. 18-49
Total study population	3.37 (3.35–3.38)	6.43 (6.40–6.47)	7.71 (7.64–7.79)	8.43 (8.37–8.49)	1.91 (1.90–1.92)	2.29 (2.27–2.31)	2.50 (2.48–2.52)
Bone marrow or stem cell transplant	40.20 (35.6–45.12)	43.22 (38.2–48.65)	50.71 (41.8–60.92)	44.73 (33.2–58.97)	1.08 (0.91–1.27)	1.26 (1.01–1.57)	1.11 (0.81–1.51)
Solid organ transplant	13.30 (12.2–14.43)	19.41 (17.9–20.91)	19.76 (17.2–22.56)	23.15 (19.9–26.76)	1.46 (1.30–1.63)	1.49 (1.27–1.74)	1.74 (1.46–2.06)
Human immunodeficiency virus infection	17.83 (17.1–18.55)	16.42 (15.1–17.75)	16.02 (12.8–19.78)	10.70 (6.62–16.35)	0.92 (0.84–1.01)	0.90 (0.72–1.11)	0.60 (0.37–0.92)
Systemic lupus erythematosus	13.39 (12.7–14.04)	15.40 (14.5–16.35)	20.01 (18.0–22.18)	23.39 (21.0–25.91)	1.15 (1.07–1.24)	1.49 (1.33–1.67)	1.75 (1.56–1.96)
Rheumatoid arthritis	8.32 (8.02–8.63)	12.75 (12.3–13.15)	15.31 (14.5–16.08)	18.34 (17.6–19.04)	1.53 (1.46–1.61)	1.84 (1.73–1.96)	2.20 (2.09–2.32)
Cancer	8.39 (8.15–8.64)	10.94 (10.7–11.17)	13.05 (12.6–13.42)	14.14 (13.8–14.40)	1.30 (1.26–1.35)	1.55 (1.49–1.62)	1.68 (1.63–1.74)
Inflammatory bowel disease	6.89 (6.59–7.19)	11.02 (10.5–11.55)	11.67 (10.7–12.69)	15.48 (14.4–16.53)	1.60 (1.50–1.71)	1.69 (1.54–1.86)	2.25 (2.08–2.43)
Multiple sclerosis	6.83 (6.42-7.27)	10.75 (10.0–11.52)	11.91 (10.2–13.75)	12.35 (10.4–14.50)	1.57 (1.43–1.73)	1.74 (1.48–2.04)	1.81 (1.51–2.15)
Psoriasis	5.28 (5.08–5.49)	9.46 (9.08–9.86)	13.11 (12.2–13.99)	15.39 (14.5–16.27)	1.79 (1.69–1.90)	2.48 (2.30–2.68)	2.91 (2.72–3.12)

[a] Linear trend of incidence rate was significant at P < 0.01 except for bone marrow or stem cell transplant (p = 0.08)

With respect to HZ risk in HIV patients, cohort studies included in Table 2 were conducted between 2000 and 2014 at a time when HIV treatment was evolving. The condition was not as well controlled as it currently is in Ireland. It has been shown that the risk of HZ among HIV patients receiving antiretroviral therapy (ART) is substantially lower than those not receiving ART and that the risk of HZ is higher in those with CD4 counts <200 cells/µl.[12 13]

Although HSCT, HM, SOT, SOM and HIV patients are at the highest risk of HZ and its complications, patients with autoinflammatory and immunocompromising conditions such as rheumatoid arthritis and systemic lupus erythematosus have also been shown to be at increased risk.[7] An increased risk has been observed among patients receiving therapy with biologics especially those treated with TNF-α antagonists and patients who received high-dosage non-biologic disease-modifying antirheumatic drugs (nbDMARDS), Janus kinase inhibitors (JaKi) or high-dose corticosteroids.[14 15]

4. VACCINATION

Recombinant zoster vaccine, RZV (Shingrix), is an inactivated vaccine which contains varicella zoster virus glycoprotein E antigen produced by recombinant DNA technology, adjuvanted with $AS01_B$. It was approved by the European Medicines Agency in 2018 and is licensed for use in the prevention of HZ and PHN in adults aged ≥50 years and those aged ≥18 years who are at increased risk of HZ. Two doses are required 2-6 months apart. The need for booster doses following the primary vaccination schedule has not been determined.

The majority of evidence related to the efficacy and safety of RZV is derived from clinical trials conducted by the manufacturer GlaxoSmithKline (GSK). Trial data in immunocompetent populations was gathered primarily in two phase 3 trials, the ZOE-50 study and ZOE-70 study which were double blind, placebo-controlled multicentre studies focused on efficacy and safety of RZV in adults aged ≥50 years old and ≥70 years old respectively, and from which a number of extension studies and sub analyses have been conducted.[16 17] Trial data in immunocompromised populations are derived from a phase 3 study of efficacy and safety of RZV in HSCT patients (ZOE-HSCT) and a number of phase 2 and 3 randomised controlled trials (RCTs) of immunogenicity and safety in patients with haematological malignancies, solid organ tumours, HIV or postrenal transplant all funded by industry.[18-22]

Safety

Immunocompetent

The safety of RZV in immunocompetent populations was evaluated using data pooled from the ZOE-50 and ZOE-70 clinical trials.[23] RZV was found to be a reactogenic vaccine with more solicited adverse events (AE) reported in the RZV group (n=14,645) vs the placebo group (n=14,660). Injection site pain was the most common solicited AE (RZV: 78.0%; placebo: 10.9%). Grade-3 pain occurred in 6.4% of RZV and 0.3% of placebo recipients. Myalgia, fatigue, and headache were the most commonly reported general solicited AEs (RZV: 44.7%, 44.5%, and 37.7%, respectively; placebo: 11.7%, 16.5%, and 15.5%, respectively). However, most symptoms were mild to moderate and resolved within 2-3 days and there were no clinically relevant differences between RZV and placebo groups for serious AE, fatal AE or potential immune-mediated diseases, irrespective of age, gender, or race.[23] With respect to immunocompetent adults with underlying medical conditions, no safety concern was identified by the type or number of medical conditions present at trial enrolment. Results of post-licensure safety surveillance studies were consistent with safety profile of the vaccine reported in clinical trials.[24-27]

Immunocompromised

López-Fauqued et al. reported on the safety of RZV in the immunocompromised in a study that pooled the results of six trials.[18-23 28] Recipients had one of the following: HSCT, haematological malignancy, solid tumour malignancy, renal transplant, or HIV. A total of 1,587 recipients received at least one dose of RZV, and 1,529 recipients received at least one dose of placebo. As in the immunocompetent trials, solicited adverse events (AE) were more common after RZV than placebo. They were generally more common in those aged 18-49 years compared to those aged ≥50 years. Solicited AEs (such as injection site pain, myalgia, fatigue and headache) were mostly mild to moderate and resolved within three days (median duration). There were no clinically relevant differences between RZV and placebo

groups for serious AE, fatal AE or potential immune-mediated diseases irrespective of age. No safety concerns were identified.

Vaccine performance

Immunocompetent

Immunogenicity

RZV induces a robust humoral and cell mediated immune response to HZ. A phase 1/2 open label, randomised, parallel group study to determine the immunogenicity of two candidate HZ vaccines, one of which was RZV, in those aged between 50 and 70 years, reported that humoral and cell mediated responses were higher in those vaccinated with RZV than in the other candidate vaccine. These responses persisted for up to at least 42 months. A phase 2 randomised controlled trial to determine the immunogenicity of three different formulations of RZV, in those aged ≥60 years, reported that humoral and cell mediated responses were higher in all vaccinated groups than in placebo groups. These immune responses persisted for up to at least 36 months.[29 30]

Efficacy

RZV has been shown to be an efficacious vaccine in immunocompetent older adults in clinical trials conducted between 2010 and 2011. In ZOE-50, a phase 3 randomised placebo controlled clinical trial of immunocompetent adults aged ≥50 years, 7,344 of whom received two doses of RZV two months apart, vaccine efficacy (VE) against HZ was estimated at 97.2% (95% CI 93.7-99.0) at a mean follow up of 3.2 years.[16] In ZOE-70 in an older population (≥70 years), 6,541 of whom received two doses of RZV, VE against HZ was estimated at 89.8% (95% CI 84.2-93.7) at a mean follow up of 3.7 years.[17] In pooled analysis of participants aged ≥70 years (ZOE-50 and ZOE-70) who had received two doses of RZV (n=8,250), VE against HZ was estimated at 91.3% (95% CI 86.8-94.5).

VE against PHN was estimated at 88.8% (95% CI 68.7-97.1) in a pooled analysis of those aged ≥70 years. No case of PHN developed in vaccinated participants aged <70 years.[17 31]

Post hoc analysis of participants aged ≥50 years in ZOE-50/70 with at least one of fifteen medical conditions including hypertension, dyslipidaemia, coronary artery disease and diabetes mellitus (type 1 predominantly) was conducted to determine vaccine efficacy. The efficacy of RZV against HZ ranged from 84-97% for fourteen out of fifteen conditions. There was no significant difference in HZ in those with renal disorders who received RZV, however this was potentially related to the low number of participants in this cohort which limited the statistical power to assess VE.[31]

Effectiveness

RZV has been shown to be effective in a real-world retrospective cohort study of 173,745 immunocompetent adults aged ≥50 years, using a de-identified administrative claims database in the US. The estimated overall effectiveness of RZV against HZ was 85.5% (95% CI 83.5-87.3) with a median follow up of seven months. This ranged from 85.6% (95% CI 53.3-95.6) in those aged 50-59 years to 80.3% (95% CI 75.1-84.3) in those aged ≥80 years.[32]

Duration of protection

RZV protects against HZ for at least ten years in immunocompetent recipients (Long Term Follow-up (LTFU) of ZOE-50 and ZOE-70).[33] In a pooled analysis of participants from the ZOE-50 and ZOE-70

clinical trials, after the second dose of RZV, vaccine efficacy against HZ was estimated at 88.5% (95% CI 74.9-95.6) at year six and at 73.3% (95% CI 46.9-87.6) at year 10. The duration of protection against PHN is unknown beyond four years.[33]

Immunocompromised

RZV has been shown to be efficacious in clinical trials in the prevention of HZ in HSCT patients and immunogenic against HZ in patients with haematological malignancies, HSCT, renal transplant and solid organ transplant patients and HIV patients. Vaccine efficacy in the presence of other immunosuppressive conditions is not well known as only immunogenicity studies are available, and the threshold of cell-mediated immunity ensuring protection is unknown.

Immunogenicity

In phase 2 and 3 randomised, controlled trials conducted between 2010 and 2017 in patients aged 18 years and over with haematological malignancies, renal transplants, solid organ tumours and patients with HIV, humoral and cell mediated responses were higher in the vaccinated group than in the placebo group.[19] Immune responses persisted up to 12 months after the second or third dose of RZV. In a separate post hoc efficacy analysis of the clinical trial data collected in patients with haematologic malignancies, a vaccine efficacy against HZ of 87.2% (95% CI 44.3-98.6) at month 13 was estimated.[19] [34]

Efficacy

In a phase 3 clinical trial in autologous haemopoietic stem cell transplant recipients (ZOE-HSCT) aged ≥18 years who received two doses of RZV, robust humoral and cellular responses persisted at one year after vaccination.[18] Vaccine efficacy against HZ overall was estimated at 68.2% (95% CI 55.6-77.5), with a median follow up period of 21 months. A separate post-hoc subgroup analysis of the ZOE-HSCT trial data by age reported efficacy against HZ in those aged 18-49 years reported a VE of 72% (95% CI 39-88). Post hoc efficacy analysis of patients aged 18-49 years with haematological malignancies reported VE against HZ of 87.2% (95% CI 44.3-98.6) at 13 months.[34]

Effectiveness

One and two dose real world vaccine effectiveness of RZV was estimated at 56.9% and 70.1% respectively in a US study of adults aged ≥65 years, including those with autoimmune conditions or immunocompromising conditions.[35] Two-dose vaccine effectiveness against PHN was estimated at 76.0% (95% CI, 68.4-81.8). The two-dose vaccine effectiveness was not significantly lower for adults ≥80 years, for second doses received at ≥180 days, or for individuals with autoimmune conditions. The VE of two doses of RZV in participants who received Zostavax in the previous five years was 63.0% (95% CI 58.3-67.2) compared to 71.1% (95% CI 69.5-72.6) in those who had not.

Duration of immunity

Seven studies on the duration of immunogenicity following RZV, in HSCT recipients and in those with haematological malignancies, solid organ tumours, renal transplant and HIV ranged from 12 to 24 months. The duration of immunity in these conditions is not known beyond this time range. A recent overview concluded that RZV induced robust and persistent humoral, and cell mediated responses in these five immunocompromised populations.[36]

Co-administration of RZV with other vaccinations

As RZV is a non-live subunit vaccine it is generally considered safe to administer concomitantly with other vaccines at different injection sites. In five RCTs non-inferiority was demonstrated with respect to humoral immunogenicity for the co-administration of RZV with other vaccines, including the reduced-antigen-content diphtheria-tetanus-acellular pertussis vaccine (Tdap), unadjuvanted inactivated seasonal influenza vaccine, 13-valent pneumococcal conjugate vaccine (PCV13), 23-valent pneumococcal polysaccharide vaccine (PPSV23) and COVID-19 (mRNA-1273) vaccine in adults aged 50 years or older.[37-42] Effect on cell-mediated immune response was not reported. The safety profile was acceptable in all studies. The adverse reactions of fever and shivering were more frequent when PPV23 vaccine was co-administered with RZV (16% and 21%, respectively) compared to when RZV was given alone (7% for both adverse reactions). Systemic adverse reactions that are very commonly reported, such as myalgia 32.9%, fatigue 32.2%, and headache 26.3%, and uncommonly reported arthralgia, following administration of RZV alone, were reported with increased frequency when RZV was co-administered with a COVID-19 mRNA vaccine (myalgia 64%, fatigue 51.7%, headache 39%, arthralgia 30.3%). Interim data from the Centers for Disease Control and Prevention on co-administration with adjuvant influenza vaccine is reassuring.[43] The concomitant administration of other vaccines than those listed above with RZV has not yet been studied.

International modelling of national RZV vaccination strategies

Since 2018, a number of countries have modelled the clinical impact and cost-effectiveness of various RZV vaccination strategies. A 2019 UK economic analysis model was designed to estimate the impact of the introduction of a national RZV vaccination programme in adults aged 50, 60, 65, 70 and 80 years. In this model, the number needed to vaccinate (NNV) to prevent one case of HZ was lowest at age 60 years (NNV=9) and to prevent one case of PHN was lowest at age 65 years (NNV=54). NNV increased in the 70-year-old cohort and more so in the 80-year-old cohort, where a proportion of the simulated cohort died due to natural causes before any health benefit of vaccination occurred. The number of GP visits avoided per 100,000 was greatest for the 65-year-old cohort and the number of hospitalisations avoided per 100,000 increased linearly with age from 50 years and was greatest for the 80-year-old cohort.[44]

In Germany, a modelling study of the epidemiological effects of HZ vaccination in a cohort of one million 50-year-olds, followed to the end of life, reported that vaccination at age 60 years would prevent the most HZ cases and vaccination at age 70 years would prevent the most PHN cases. The health economic model showed that vaccination at age 65 years was the most cost-effective and was only slightly more cost-effective than vaccination at 60 years of age. The NNV to prevent one case of HZ was lowest (n=15) for vaccination at both 60 and 65 years of age.[45]

Modelling based on Belgian data, showed duration of protection to be a key factor in model outcome. By assuming a slow waning of protection in their model, vaccination at age ≥50 years yielded the greatest reduction in burden of HZ. While if a shorter duration of protection was assumed, the greatest burden of illness was avoided at ≥70 years of age. The conclusion of the modelling exercise was that a cut-off of 60 years of age was deemed to yield the best clinical return in the Belgian immunocompetent population.[5]

5. INTERNATIONAL RECOMMENDATIONS

Many countries have national HZ vaccination recommendations that are not funded. The UK, Germany, Switzerland and Australia have funded national HZ vaccination programmes. (Table 4)

Table 4. International recommendations regarding RZV as of 10 January 2024.

Country	Immunocompetent adults	Immunocompromised adults
UK[46]	60-80 years (phased implementation over 10 years)	≥50 years - immunocompromise ≥18 years - stem cell transplant
USA[47]	≥50 years	≥19 - have or will have weakened immune systems because of disease or therapy chronic medical conditions (e.g., CRF, DM, RA, and COPD)
Australia[48]	≥50 years	≥18 - immunocompromised with medical conditions including HSCT, SOT, haematological malignancy, advanced or untreated HIV
New Zealand[49]	≥65 years (started with aged 65 exactly in 2023)	≥18 years - prior to planned, receiving or post immunosuppressive therapy, HIV infection, CKD stages 4–5), prior to or post SOT, prior to or post HSCT, with immune-mediated inflammatory disease receiving immunomodulatory agents
Austria[50]	≥50 years	≥18 years - serious underlying disease, severe immunosuppression. Individual case basis
Belgium[51]	≥60 years	≥16 years - immunocompromised, including those under immunosuppressive therapy and those under treatment with anti-JAK therapy
Germany[52]	≥60 years	≥50 years - congenital or acquired immunodeficiency, immunosuppression, HIV, RA, SLE, IBD, COPD, bronchial asthma, CRF, DM
Netherlands[53]	≥60 years	≥18 years - immunocompromise, based on individual case basis or guidelines on off-label use in certain patient groups
Sweden[54] (Under consideration)	(≥65 years with oldest prioritised first)	≥18 years with disease or treatment that induce immunosuppression (to be prioritised)

Switzerland[55]	≥65 years	≥18 years - current severe immunodeficiency or immunosuppressive treatment in foreseeable future including haematological malignancies, HSCT, solid organ transplant, JAK inhibitors or intensive immunosuppression (e.g., combination of immunosuppressant, high dose corticosteroids) dues to an immune mediated disease such as e.g., RA or IBD and HIV positive patients with CD4 <200cells/mm3 or < 15% of lymphocytes

6. DISCUSSION

Herpes Zoster (HZ) and its complications have a significant impact on the health of older adults and adults of all ages who are immunocompromised. The risk of HZ increases with age, increasing more steeply from approximately aged 60 years old. The risk of post herpetic neuralgia is increased in those aged over 70 years. The purpose of vaccination is to prevent HZ and its complications. A new recombinant herpes zoster vaccine (RZV) is now available, with good safety and effectiveness data in older adults (aged ≥50 years). There is evidence of very good protection out to 10 years in immunocompetent adults aged 50 years and over who receive the vaccine with only moderate waning. While duration of protection may be longer, as yet there is no data available past 10 years and thus the requirement for booster doses is unknown. Considering both the age associated risk of HZ, and available information around duration of protection NIAC recommends vaccination of all adults aged 65 years and above. The precise cut-off of age 65 years was chosen to align with other current adult vaccination recommendations such as pneumococcal vaccines. NIAC believes this will facilitate implementation and uptake. Additionally, vaccinating at 65 years of age will optimise protection into older adulthood and international modelling studies have found little difference in clinical impact in vaccinating at 60 or 65 years of age. NIAC recommends that all people aged 65 years and above receive RZV. To achieve this, a catch-up programme will be necessary.

There are important ethical considerations surrounding herpes zoster vaccination. In Ireland RZV is available to buy privately, but only to those who are informed and can afford it, perpetuating health care disparities. The vaccine's high cost further exacerbates this issue. The introduction of a targeted, national HZ vaccination programme has the potential to address these inequities by making the vaccine accessible to all those most at risk of HZ and its complications.

People who are immunocompromised due to disease or treatment are also at increased risk of HZ. The degree of risk depends on the underlying condition and immunosuppressive treatment. Optimal timing of vaccination will vary according to underlying condition and planned immunosuppression. Effectiveness data in this population are more limited, and there is no available data on duration of protection past two years. Thus, it is important that the decision to vaccinate at younger ages is done in conjunction with the treating specialist, who can consider individual patient and treatment factors to determine the optimal timing for RZV vaccination.

For those with immunocompromising conditions, due to a cumulative age and condition-related risk, NIAC recommends RZV vaccination from aged 50 years. Among immunocompromised patients, HSCT

recipients are at highest risk of HZ. RZV has been shown to be safe and efficacious in this population. NIAC recommends RZV vaccination for all HSCT recipients aged 18 years and above. There are other immunocompromising conditions where the risk of HZ has been shown to be high across age groups including those ≤50 years old but in whom there is no available vaccine efficacy data, in particular patients with haematological malignancies, solid organ transplant patients and those with advanced or untreated HIV. NIAC recommends that RZV vaccination be considered in these groups and in other high risk immunocompromised patients aged 18-49 years following discussion between the patient and their treating hospital specialist. NIAC will continue to review new scientific data on HZ and RZV on an ongoing basis and provide updated guidance where appropriate.

ACKNOWLEDGEMENTS

NIAC would like to thank all the individuals and organisations who provided data, time, advice and information in support of this work.

REFERENCES

1. Galil K, Choo PW, Donahue JG, et al. The Sequelae of Herpes Zoster. *Archives of Internal Medicine* 1997;157(11):1209-13. doi: 10.1001/archinte.1997.00440320105010

2. Oxman MN, Levin MJ, Johnson GR, et al. A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. *New England Journal of Medicine* 2005;352(22):2271-84. doi: 10.1056/NEJMoa051016

3. HPSC. Epidemiology of Varicella Zoster Virus Ireland. Provided directly to NIAC by HPSC., 2023.

4. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open* 2014;4(6):e004833. doi: 10.1136/bmjopen-2014-004833 [published Online First: 2014/06/12]

5. Roberfroid D, Zeevaert R, Maertens de N.C., et al. Evaluation of shingrix vaccine against herpes zoster. Health Technology Assessment (HTA). Brussels. : Belgian Health Care Knowledge Centre (KCE); 2022 [Available from: https://kce.fgov.be/en/evaluation-of-shingrix-vaccine-against-herpes-zoster.

6. McKay SL, Guo A, Pergam SA, et al. Herpes Zoster Risk in Immunocompromised Adults in the United States: A Systematic Review. *Clin Infect Dis* 2020;71(7):e125-e34. doi: 10.1093/cid/ciz1090 [published Online First: 2019/11/05]

7. Sullivan KM, Farraye FA, Winthrop KL, et al. Safety and efficacy of recombinant and live herpes zoster vaccines for prevention in at-risk adults with chronic diseases and immunocompromising conditions. *Vaccine* 2023;41(1):36-48. doi: https://doi.org/10.1016/j.vaccine.2022.10.063

8. Yanni EA, Ferreira G, Guennec M, et al. Burden of herpes zoster in 16 selected immunocompromised populations in England: a cohort study in the Clinical Practice Research Datalink 2000-2012. *BMJ Open* 2018;8(6):e020528. doi: 10.1136/bmjopen-2017-020528 [published Online First: 2018/06/09]

9. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, et al. Herpes zoster risk and burden of disease in immunocompromised populations: a population-based study using health system integrated databases, 2009-2014. *BMC Infect Dis* 2020;20(1):905. doi: 10.1186/s12879-020-05648-6 [published Online First: 2020/12/02]

10. Imafuku S, Matsuki T, Mizukami A, et al. Burden of Herpes Zoster in the Japanese Population with Immunocompromised/Chronic Disease Conditions: Results from a Cohort Study Claims Database from 2005-2014. *Dermatol Ther (Heidelb)* 2019;9(1):117-33. doi: 10.1007/s13555-018-0268-8 [published Online First: 2018/11/21]

11. Chen SY, Suaya JA, Li Q, et al. Incidence of herpes zoster in patients with altered immune function. *Infection* 2014;42(2):325-34. doi: 10.1007/s15010-013-0550-8 [published Online First: 2013/11/12]

12. Ku HC, Tsai YT, Konara-Mudiyanselage SP, et al. Incidence of Herpes Zoster in HIV-Infected Patients Undergoing Antiretroviral Therapy: A Systematic Review and Meta-analysis. *J Clin Med* 2021;10(11) doi: 10.3390/jcm10112300 [published Online First: 2021/06/03]

13. Kawai K, Hawkins CA, Hertzmark E, et al. Impact of Antiretroviral Therapy on the Risk of Herpes Zoster among Human Immunodeficiency Virus-Infected Individuals in Tanzania. *The American Journal of Tropical Medicine and Hygiene* 2018;98(2):396-401. doi: 10.4269/ajtmh.17-0568

14. Marra F, Lo E, Kalashnikov V, et al. Risk of Herpes Zoster in Individuals on Biologics, Disease-Modifying Antirheumatic Drugs, and/or Corticosteroids for Autoimmune Diseases: A

Systematic Review and Meta-Analysis. *Open Forum Infectious Diseases* 2016;3(4) doi: 10.1093/ofid/ofw205

15. Atzeni F, Gozza F, Riva A, et al. Conventional, biological disease-modifying anti-rheumatic drugs and Janus kinase inhibitors and varicella zoster virus. *Expert Opinion on Pharmacotherapy* 2023;24(6):679-89. doi: 10.1080/14656566.2023.2195050

16. Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults. *New England Journal of Medicine* 2015;372(22):2087-96. doi: 10.1056/NEJMoa1501184

17. Cunningham AL, Lal H, Kovac M, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. *New England Journal of Medicine* 2016;375(11):1019-32. doi: 10.1056/NEJMoa1603800

18. Bastidas A, de la Serna J, El Idrissi M, et al. Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation: A Randomized Clinical Trial. *JAMA* 2019;322(2):123-33. doi: 10.1001/jama.2019.9053

19. Dagnew AF, Ilhan O, Lee WS, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. *Lancet Infect Dis* 2019;19(9):988-1000. doi: 10.1016/s1473-3099(19)30163-x [published Online First: 2019/08/11]

20. Vink P, Delgado Mingorance I, Maximiano Alonso C, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in patients with solid tumors, vaccinated before or during chemotherapy: A randomized trial. *Cancer* 2019;125(8):1301-12. doi: 10.1002/cncr.31909 [published Online First: 2019/02/02]

21. Berkowitz EM, Moyle G, Stellbrink H-J, et al. Safety and Immunogenicity of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in HIV-Infected Adults: A Phase 1/2a Randomized, Placebo-Controlled Study. *The Journal of Infectious Diseases* 2015;211(8):1279-87. doi: 10.1093/infdis/jiu606

22. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, et al. Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: A Phase 3, Randomized Clinical Trial. *Clin Infect Dis* 2020;70(2):181-90. doi: 10.1093/cid/ciz177 [published Online First: 2019/03/08]

23. López-Fauqued M, Campora L, Delannois F, et al. Safety profile of the adjuvanted recombinant zoster vaccine: Pooled analysis of two large randomised phase 3 trials. *Vaccine* 2019;37(18):2482-93. doi: https://doi.org/10.1016/j.vaccine.2019.03.043

24. Fiore J, Co-van der Mee MM, Maldonado A, et al. Safety and reactogenicity of the adjuvanted recombinant zoster vaccine: experience from clinical trials and post-marketing surveillance. *Ther Adv Vaccines Immunother* 2021;9:25151355211057479. doi: 10.1177/25151355211057479 [published Online First: 2022/01/11]

25. Hesse E.M, Tom T. Shimabukuro, John R. Su, et al. Postlicensure Safety Surveillance of Recombinant Zoster Vaccine (Shingrix) — United States, October 2017–June 2018. MMWR Morb Mortal Wkly Rep 2019;68:91–94. 2019 [

26. Pirrotta P, Tavares-Da-Silva F, Co M, et al. An Analysis of Spontaneously Reported Data of Vesicular and Bullous Cutaneous Eruptions Occurring Following Vaccination with the Adjuvanted Recombinant Zoster Vaccine. *Drug Saf* 2021;44(12):1341-53. doi: 10.1007/s40264-021-01118-3 [published Online First: 2021/10/09]

27. Tavares-Da-Silva F, Co MM, Dessart C, et al. Review of the initial post-marketing safety surveillance for the recombinant zoster vaccine. *Vaccine* 2020;38(18):3489-500. doi: 10.1016/j.vaccine.2019.11.058 [published Online First: 2019/12/11]

28. Stadtmauer EA, Sullivan KM, Marty FM, et al. A phase 1/2 study of an adjuvanted varicella-zoster virus subunit vaccine in autologous hematopoietic cell transplant recipients. *Blood* 2014;124(19):2921-29. doi: 10.1182/blood-2014-04-573048

29. Chlibek R, Smetana J, Pauksens K, et al. Safety and immunogenicity of three different formulations of an adjuvanted varicella-zoster virus subunit candidate vaccine in older adults: A phase II, randomized, controlled study. *Vaccine* 2014;32(15):1745-53. doi: https://doi.org/10.1016/j.vaccine.2014.01.019

30. Leroux-Roels I, Leroux-Roels G, Clement F, et al. A Phase 1/2 Clinical Trial Evaluating Safety and Immunogenicity of a Varicella Zoster Glycoprotein E Subunit Vaccine Candidate in Young and Older Adults. *The Journal of Infectious Diseases* 2012;206(8):1280-90. doi: 10.1093/infdis/jis497

31. Oostvogels L, Heineman TC, Johnson RW, et al. Medical conditions at enrollment do not impact efficacy and safety of the adjuvanted recombinant zoster vaccine: a pooled post-hoc analysis of two parallel randomized trials. *Hum Vaccin Immunother* 2019;15(12):2865-72. doi: 10.1080/21645515.2019.1627818 [published Online First: 2019/06/20]

32. Sun Y, Kim E, Kong CL, et al. Effectiveness of the Recombinant Zoster Vaccine in Adults Aged 50 and Older in the United States: A Claims-Based Cohort Study. *Clinical Infectious Diseases* 2021;73(6):949-56. doi: 10.1093/cid/ciab121

33. Strezova A, Diez-Domingo J, Al Shawafi K, et al. Long-term Protection Against Herpes Zoster by the Adjuvanted Recombinant Zoster Vaccine: Interim Efficacy, Immunogenicity, and Safety Results up to 10 Years After Initial Vaccination. *Open Forum Infectious Diseases* 2022;9(10):ofac485. doi: 10.1093/ofid/ofac485

34. Racine É, Gilca V, Amini R, et al. A systematic literature review of the recombinant subunit herpes zoster vaccine use in immunocompromised 18–49 year old patients. *Vaccine* 2020;38(40):6205-14. doi: https://doi.org/10.1016/j.vaccine.2020.07.049

35. Izurieta HS, Wu X, Forshee R, et al. Recombinant Zoster Vaccine (Shingrix): Real-World Effectiveness in the First 2 Years Post-Licensure. *Clinical Infectious Diseases* 2021;73(6):941-48. doi: 10.1093/cid/ciab125

36. López-Fauqued M, Co-van der Mee M, Bastidas A, et al. Safety Profile of the Adjuvanted Recombinant Zoster Vaccine in Immunocompromised Populations: An Overview of Six Trials. *Drug Safety* 2021;44(7):811-23. doi: 10.1007/s40264-021-01076-w

37. Naficy A, Kuxhausen A, Pirrotta P, et al. No Immunological Interference or Safety Concerns When Adjuvanted Recombinant Zoster Vaccine Is Coadministered With a Coronavirus Disease 2019 mRNA-1273 Booster Vaccine in Adults Aged 50 Years and Older: A Randomized Trial. *Clinical Infectious Diseases* 2023;77(9):1238-46. doi: 10.1093/cid/ciad361

38. Maréchal C, Lal H, Poder A, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine co-administered with the 23-valent pneumococcal polysaccharide vaccine in adults ≥50 years of age: A randomized trial. *Vaccine* 2018;36(29):4278-86. doi: 10.1016/j.vaccine.2018.05.110 [published Online First: 2018/06/16]

39. Strezova A, Lal H, Enweonye I, et al. The adjuvanted recombinant zoster vaccine co-administered with a tetanus, diphtheria and pertussis vaccine in adults aged ≥50 years: A randomized trial. *Vaccine* 2019;37(39):5877-85. doi: 10.1016/j.vaccine.2019.08.001 [published Online First: 2019/08/25]

40. Levin MJ, Buchwald UK, Gardner J, et al. Immunogenicity and safety of zoster vaccine live administered with quadrivalent influenza virus vaccine. *Vaccine* 2018;36(1):179-85. doi: https://doi.org/10.1016/j.vaccine.2017.08.029

41. Schwarz TF, Aggarwal N, Moeckesch B, et al. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine Coadministered With Seasonal Influenza Vaccine in Adults Aged 50 Years or Older. *J Infect Dis* 2017;216(11):1352-61. doi: 10.1093/infdis/jix481 [published Online First: 2017/10/14]

42. Min JY, Mwakingwe-Omari A, Riley M, et al. The adjuvanted recombinant zoster vaccine co-administered with the 13-valent pneumococcal conjugate vaccine in adults aged ≥50 years: A randomized trial. *J Infect* 2022;84(4):490-98. doi: 10.1016/j.jinf.2021.12.033 [published Online First: 2021/12/30]

43. Grohskopf LA BL, Ferdinands JM, Chung JR, Broder KR, Talbot HK. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season. MMWR Recomm Rep 2023;72(No. RR-2):1–25. 2023 [

44. Oorschot DAMv, Hunjan M, Bracke B, et al. Public health impact model estimating the impact of introducing an adjuvanted recombinant zoster vaccine into the UK universal mass vaccination programme. *BMJ Open* 2019;9(5):e025553. doi: 10.1136/bmjopen-2018-025553

45. Siedler A, Koch J, Garbe E, et al. Background paper to the decision to recommend the vaccination with the inactivated herpes zoster subunit vaccine. *Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz* 2019;62(3):352-76. doi: 10.1007/s00103-019-02882-5

46. Agency UHS. Shingles (herpes zoster): the green book, chapter 28a. Shinlges immunisation information for public health professionals. Published 2013 Last Updated 2023 [Available from: https://www.gov.uk/government/publications/shingles-herpes-zoster-the-green-book-chapter-28a accessed 20th November 2023.

47. Prevention CfDCa. Shingles (Herpes Zoster) Vaccination [Available from: https://www.cdc.gov/shingles/vaccination.html#:~:text=CDC%20recommends%20two%20doses%20of,because%20of%20disease%20or%20therapy. accessed January 2024.

48. Care AGDoHaA. Autralian Immunisation Handbook - Zoster (herpes zoster) [Available from: https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/zoster-herpes-zoster accessed January 2024.

49. Health NZMo. Immunisation Handbook 2020 Chapter 23. Zoster (herpes zoster/shingles) [Available from: https://www.health.govt.nz/our-work/immunisation-handbook-2020/23-zoster-herpes-zoster-shingles accessed January 2024.

50. Bundesministerium Soziales G, Pflege, und Konsumentenschutz. Vaccination Plan Austria 2023/2024 [Available from: https://www.sozialministerium.at/Themen/Gesundheit/Impfen/Impfplan-%C3%96sterreich.html accessed January 2024.

51. Belgium SHC. Report 9684 Vaccination against Herpes Zoster [Available from: https://www.health.belgium.be/en/report-9684-vaccination-against-herpes-zoster accessed January 2024.

52. Institute SCoVSRK. STIKO Recommendations 2023 [Available from: https://www.rki.de/EN/Content/infections/Vaccination/recommandations/recommendations_node.html accessed January 2024.

53. Netherlands ZNHIT. GVS Advice Shingrix [Available from: https://english.zorginstituutnederland.nl/publications/reports/2021/06/14/gvs-advice-shingrix accessed January 2024.

54. Sweden PHAo. Changing national vaccine programmes [Available from: https://www.folkhalsomyndigheten.se/the-public-health-agency-of-sweden/communicable-disease-control/vaccinations/changing-national-vaccination-programmes/ accessed January 2024.

55. Switzerland FOoPH. Chickenpox / Shingles [Available from: https://www.bag.admin.ch/bag/en/home/krankheiten/krankheiten-im-ueberblick/windpocken.html#:~:text=Immunisation%20against%20herpes%20zoster%20(shingles,immunodeficiency%20aged%2018%20and%20over. accessed January 2024.

APPENDIX 1. CLINICAL CONSIDERATIONS FOR DETERMINING THE OPTIMAL AGE AND PRECISE TIMING FOR RZ VACCINATION IN PATIENTS WITH IMMUNOCOMPRIMISING CONDITIONS.

The optimal age and timing of vaccination for immunocompromised individuals depends on patient and treatment specific factors. The age and precise timing of vaccination should be determined by the treating specialist physician. The following guidance is provided to support treating specialist physicians in determining when to vaccinate their patients with RZV.

Hematopoietic Stem Cell Transplant Recipients

NIAC recommends that HSCT patients should be vaccinated for HZ if they are aged 18 years old or over. Most HSCT patients should be vaccinated by 6 months but no sooner than 3 months post-transplant. Where feasible, patients should be vaccinated before stopping antiviral prophylaxis. Certain patient specific factors may warrant deferral of vaccination past 6 months, for example, patients with moderate or severe GVHD receiving intense immunosuppression or patients planned to receive donor lymphocyte infusions.

Solid Organ Transplant Recipients

SOT patients should be considered for HZ vaccination if they are aged 18 years old or older. Where feasible, vaccination should be completed pre-transplant. If vaccination prior to transplantation is not possible, administration at a time of stable graft function, when on maintenance immunosuppression is recommended. If receiving antiviral prophylaxis, vaccination should ideally occur prior to stopping prophylaxis.

Patients with cancer

Patients with cancer should be considered for HZ vaccination if they are aged 18 years old or older. Risk of HZ for this patient group is related to degree of immunosuppression. Patients receiving regimes that include B-cell depleting therapy, CAR-T cell therapy, high dose steroids or other therapies that significantly impair lymphocyte function are likely at higher risk and would benefit from HZ vaccination regardless of age. When feasible, (e.g., some solid tumours), vaccination prior to initiation of chemotherapy is preferable in order to maximise response to the vaccine.

Patients ≥18 years of age with primary or acquired cellular and combined immune deficiencies resulting in lymphopenia (<1000 lymphocytes/µl) or functional lymphocyte disorder, i*ncluding people living with HIV who are severely immunosuppressed (CD4 count <200 cells/µl).*

It is recommended that this patient group should be vaccinated for HZ if they are aged 50 years old or older. Age independent risk will depend on degree and anticipated duration of lymphopenia/impaired lymphocyte function. Some patients may benefit from RZV between 18 and 49 years of age depending on degree of immunosuppression, for example patients living with HIV with a CD4 count of <200 cells/µl.

Patients ≥18 years of age with immune mediated inflammatory disorders who are receiving, have received, or are planned to receive immunosuppressive therapy *e.g., rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease (see Table 1 for further detail).*

For this patient group the age at which RZV is given will depend on the degree of prior and anticipated immunosuppression. Guiding principles are that patients should be protected during times of greatest anticipated risk. For patients on minimal immunosuppression their risk is driven by age, and they are unlikely to benefit from HZ vaccination before the age of 50 years. For others, earlier vaccination (between 18 and 49 years of age) may be appropriate. Where feasible, patients should be vaccinated during periods of relatively low immunosuppression to maximise response to the vaccine.