For Egyptian health care Professionals Only

HERPES ZOSTER VACCINATION IN ADULTS

A PARADIGM SHIFT

SHINGRIX (ZOSTER VACCINE RECOMBINANT, ADJUVANTED)

Powder and suspension for suspension for IM Injection

Please see link to full Prescribing Information available at this presentation.

PM-EG-SGX-PPTX-230001 - Date of Preparation (January 2024)

PLACEHOLDER FOR CONFLICT OF INTEREST

AGENDA


What is the clinical impact of shingles on patients?
Why is it important to prevent shingles?
How was SHINGRIX designed?
What is the clinical profile of SHINGRIX?
How can you implement SHINGRIX in your practice?

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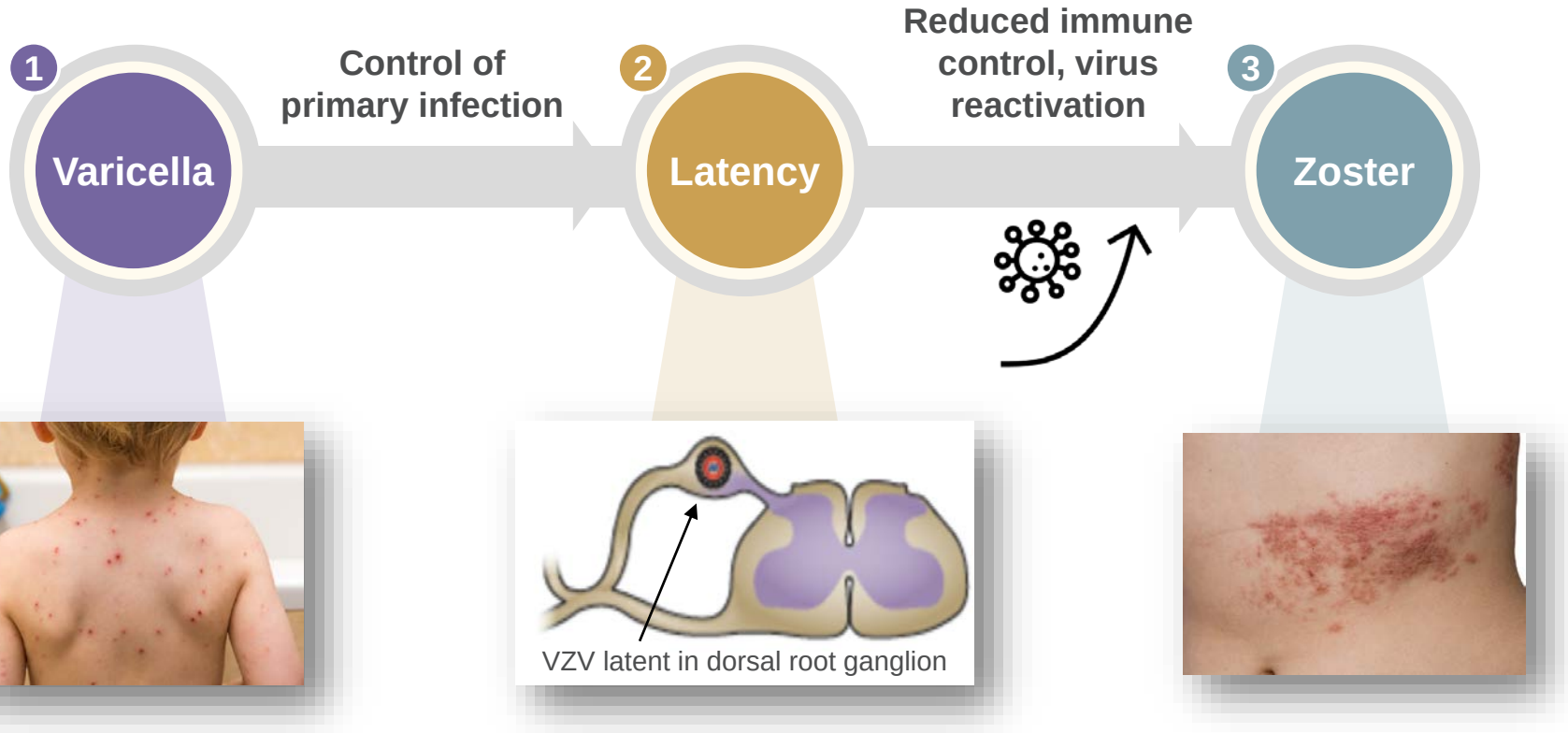
>90% OF ADULTS ≥50 YEARS OF AGE ARE INFECTED WITH VZV AND ARE AT RISK FOR SHINGLES[1]*



Up to 1 in 3 people will develop shingles in their lifetime due to VZV reactivation[2]

Incidence rates are similar between countries - **overall rate of ~6-8 per 1000 person years at age 60**[3]

Each year, there are an estimated **1 million** new cases of shingles in the United States,[2] **1.7 million** in Europe,[4] and **1.5 million** in China[5]

the image of VZV latent in dorsal root ganglion is adapted from Zerboni L, et al. 2014.
*US data; ~99.5% VZV seropositive. May not be representative of global population. SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox). [6]
VZV=varicella zoster virus.

1. Clinical Over view about Shingles Available at: https://www.cdc.gov/shingles/hcp/clinical-overview.html (Accessed: 04 February 2024). 2. Harpaz R, et al. MMWR Recomm Rep 2008;57:1-30. 3. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014 Jun 10;4(6):e004833. 4 Pinchinat S, Cebrián-Cuenca AM, Bricout H, Johnson RW. Similar herpes zoster incidence across Europe: results from a systematic literature review. BMC Infect Dis. 2013 Apr 10;13:170.. 5. Li Y, An Z, Yin D, Liu Y, Huang Z, Xu J, Ma Y, Tu Q, Li Q, Wang H. Disease Burden Due to Herpes Zoster among Population Aged ≥50 Years Old in China: A Community Based Retrospective Survey. PLoS One. 2016 Apr 7;11(4):e0152660. 6. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09\2023

SHINGLES CONSISTS OF PRODROMAL AND ACUTE PHASES WHICH CAN BE FOLLOWED BY CHRONIC COMPLICATIONS[1]

Prodromal phase[1]
4 days–2 weeks

Headache, photophobia, malaise, abnormal skin sensations, pain, fever (less common)[2]

Acute phase[2]
2–4 weeks

Unilateral, vesicular rash, associated aching, burning, stabbing, or shock-like pain[2]

Subacute Pain Phase[3]
Up to 3 months after rash healing.[3]

Up to 30% of patients[4]

Post-herpetic neuralgia[4]
More than 1 year

PHN is defined as neuropathic pain that persists ***for ≥90 days after the onset of HZ rash***[3]

New lesions appear (vesicles)[1]

Pustular lesions[1]

Lesions crust over and resolve[1]

Scarring and pigmentation can persist long after lesions have healed;[2] ~9.7% of patients with severe HZ have scarring 6 months after rash resolves (N=113)[5]

Week 1 | Week 2 | Week 3 | Week 4

Time after rash onset

HZ=herpes zoster; PHN=post-herpetic neuralgia

SHINGLES CONSISTS OF PRODROMAL AND ACUTE PHASES WHICH CAN BE FOLLOWED BY CHRONIC COMPLICATIONS[1]

Reference:

1 .Weinberg JM. Herpes zoster: epidemiology, natural history, and common complications. J Am Acad Dermatol. 2007 Dec;57(6 Suppl):S130-5

2. Harpaz R et al. MMWR Recommendations Rep 2008;57:1–30;

3. Johnson RW, Alvarez-Pasquin MJ, Herpes zoster epidemiology, management, and disease and economic burden in Europe: a multidisciplinary perspective. The Adv Vaccines. 2015 Jul;3(4):109-20.;

4. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014 Jun 10;4(6):e004833.

5. El Hayderi L, Nikkels-Tassoudji N, Nikkels AF. Incidence of and Risk Factors for Cutaneous Scarring after Herpes Zoster. Am J Clin Dermatol. 2018 Dec;19(6):893-897. doi: 10.1007/s40257-018-0385-2. PMID: 30151702.

SHINGLES CAN BE A PAINFUL DISEASE AND LEAD TO SERIOUS AND LONG-LASTING COMPLICATIONS[1]

Acute presentation

- Unilateral, vesicular rash[1]
- Pain can be “excruciating” – often described as aching, burning, stabbing or shock-like[1]
- Other symptoms of shingles include headache, photophobia, malaise and fever[1]

Complications

Post-Herpetic Neuralgia (PHN)
- Neuropathic pain that persists for >3 months[2]
- Affects up to 30% of patients with shingles[2]

Herpes Zoster Ophthalmicus (HZO)
- Affects up to 25% of patients with shingles[1]
- May lead to vision loss in rare cases[2]

Other complications
- Disseminated disease[1]
- Scarring[1]
- Neurological complications[3]
- Ramsay Hunt syndrome (incl. hearing loss)[1]
- Bell’s palsy[1]
- Cardiovascular and cerebrovascular events[4]

Recurrence

- ~5–10% of patients experience a recurrent episode[5]

HZ symptoms may be more severe and complications more frequent in immunocompromised patients[1]

HZ=herpes zoster; HZO=herpes zoster ophthalmicus; PHN=post-herpetic neuralgia.

SHINGLES CAN BE A PAINFUL DISEASE AND LEAD TO SERIOUS AND LONG-LASTING COMPLICATIONS[1]

References:.

1.Harpaz R, et al. MMWR Recommendation Rep 2008;57:1-30.

2. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014 Jun 10;4(6):e004833.

3. Kennedy PGE, Gershon AA. Clinical Features of Varicella-Zoster Virus Infection. Viruses. 2018 Nov 2;10(11):609.

4.Erskine N, Tran H, Levin L, Ulbricht C, Fingeroth J, Kiefe C, Goldberg RJ, Singh S. A systematic review and meta-analysis on herpes zoster and the risk of cardiac and cerebrovascular events. PLoS One. 2017 Jul 27;12(7):e0181565.

5. Batram M, Witte J, Schwarz M, Hain J, Ultsch B, Steinmann M, Bhavsar A, Wutzler P, Criée CP, Hermann C, Wahle K, Füchtenbusch M, Greiner W. Burden of Herpes Zoster in Adult Patients with Underlying Conditions: Analysis of German Claims Data, 2007-2018. Dermatol Ther (Heidelb). 2021 Jun;11(3):1009-1026

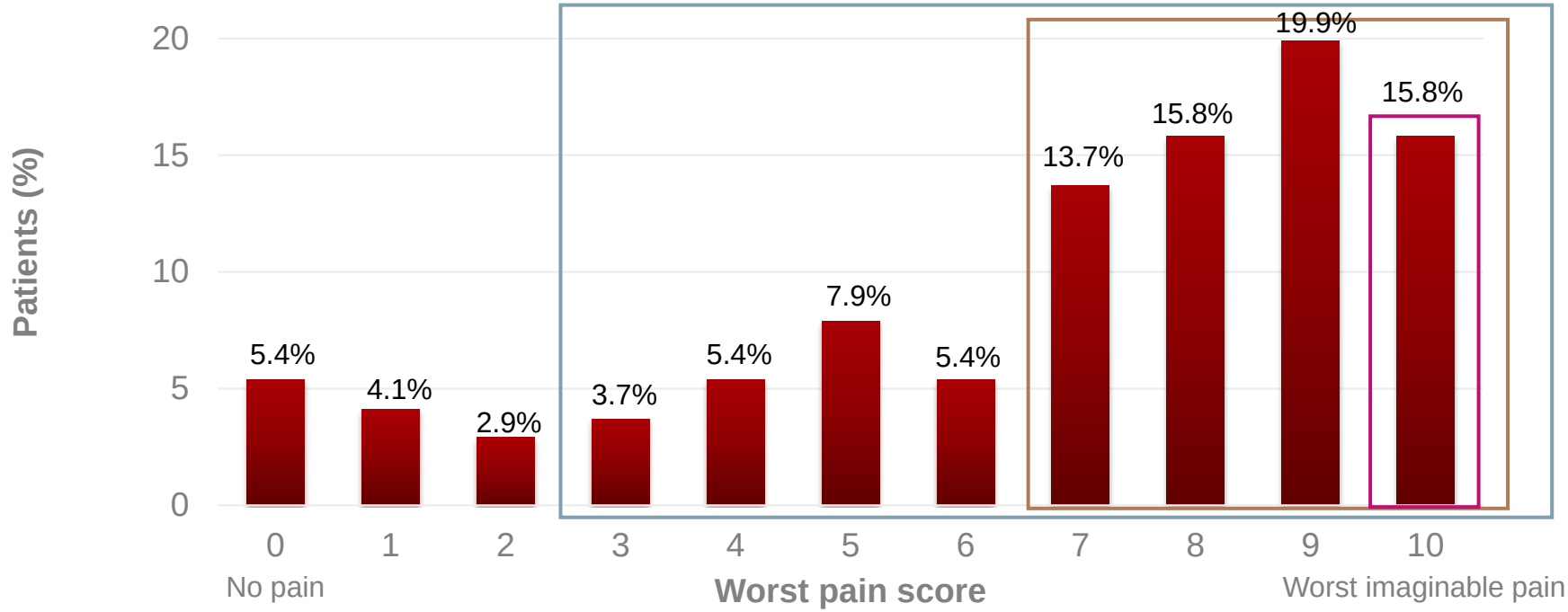
SHINGLES/PHN-RELATED PAIN CAN BE EXTREMELY DEBILITATING FOR PATIENTS[1]

87.6% of patients had clinically significant pain (n=211)

65% of patients had severe pain (n=157)

15.8% of patients had worst imaginable pain (n=38)

Maximum 'worst pain' scores for unvaccinated patients with HZ aged ≥50 years (N=241)[2]



- Patients with suspected HZ were asked to attend assessment visits and to complete the Zoster Brief Pain Inventory (ZBPI) daily for 28 days after rash onset and then weekly until either the patient had been pain free for four consecutive weeks or 90 days had elapsed after rash onset (whichever came last).
- The ZBPI asks the patients to rate four categories of pain (least, worst, average over the last 24 hours, and now) on 11-point Likert type scales (0–10, with 10 signifying the worst imaginable pain). The worst pain" over the last 24 hours category is considered the most reliable indicator of pain

HZ=herpes zoster; PHN=post-herpetic neuralgia.

1. Harpaz R, et al. MMWR Recomm Rep 2008;57:1-30; 2.Curran D, Oostvogels L, Heineman T, Matthews S, McElhaney J, McNeil S, Diez-Domingo J, Lal H, Andrews C, Athan E, Berglund J, Campora L, de Looze F, Korhonen T, Leung E, Levin M, Volpi A, Johnson RW; ZOE-50/70 Study Group. Quality of Life Impact of an Adjuvanted Recombinant Zoster Vaccine in Adults Aged 50 Years and Older. J Gerontol A Biol Sci Med Sci. 2019 Jul 12;74(8):1231-1238.

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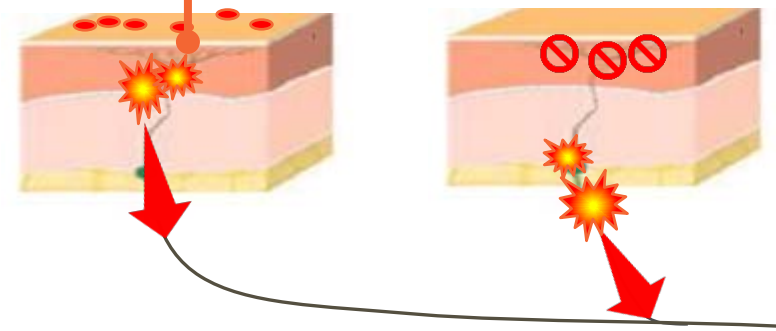
1. Harpaz R, et al. MMWR Recomm Rep 2008;57:1-30; 2. Cohen JI. Clinical practice: Herpes zoster. N Engl J Med. 2013 Jul 18;369(3):255-63.

SHINGLES PAIN MAY BE TRIGGERED BY INFLAMMATION OF NERVE ENDINGS AND DYING-BACK OF AXON ENDS[1]

1 **Inflammation** of and **damage** to **nociceptors**
➔ Light touch can cause pain (allodynia)



2 **Dying-back of axon ends**
Spontaneous signal firing at ectopic pacemaker sites even after the rash has healed

3 **Spontaneous signal firing from the dorsal root ganglion** even after the rash has healed[1]

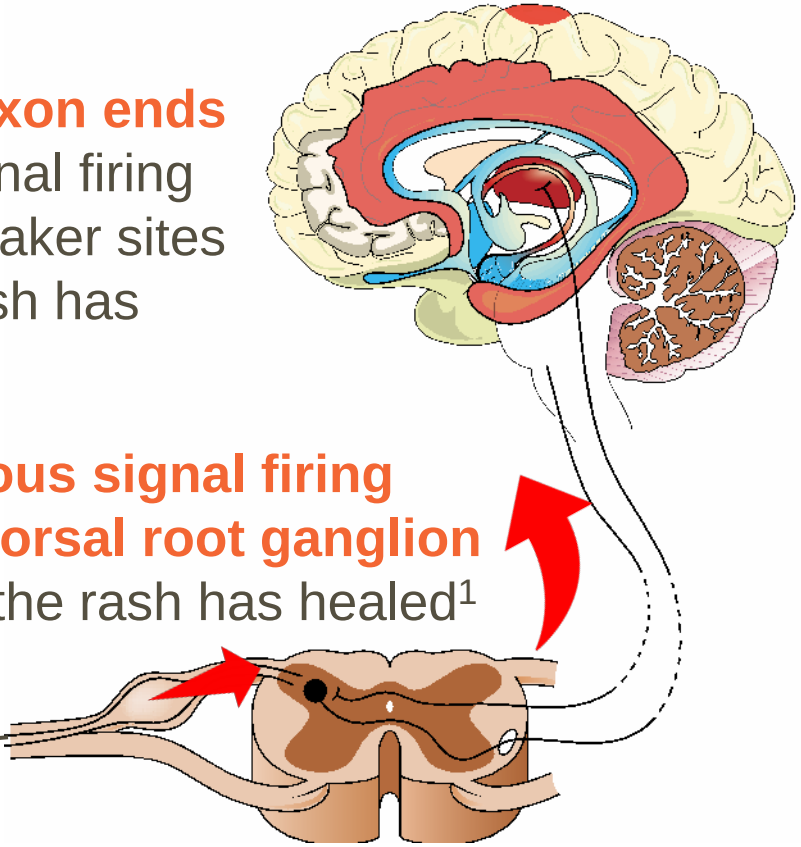
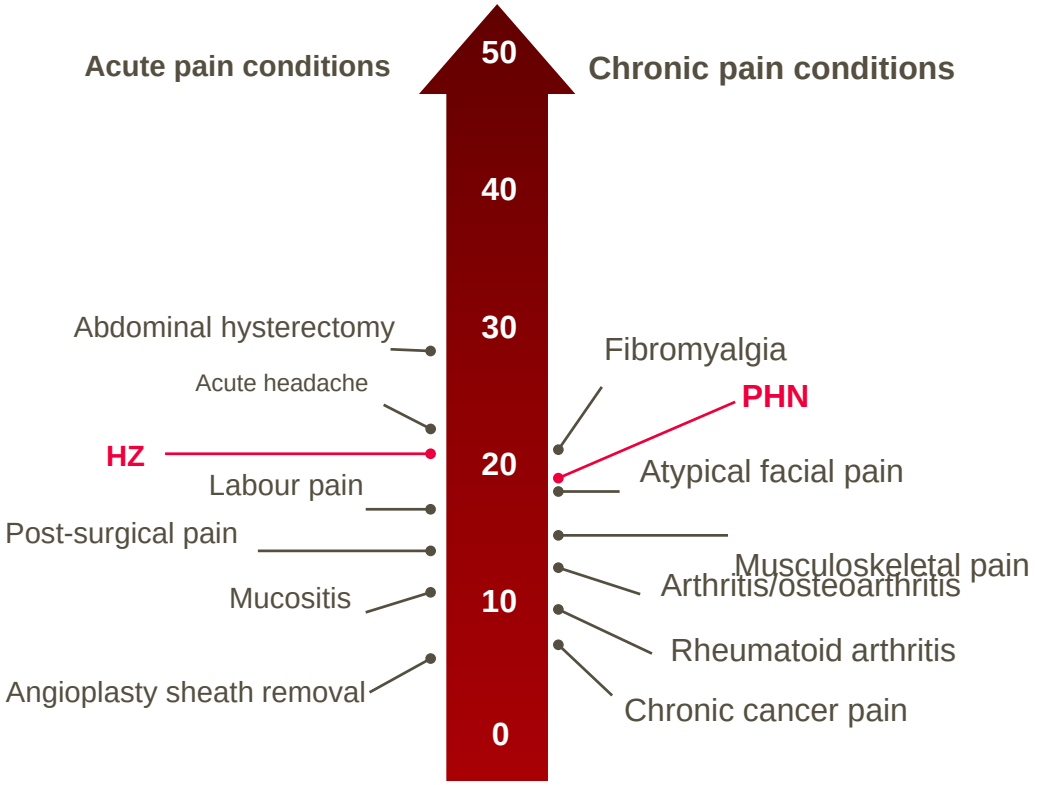


Figure created by GSK based on Devor M. Neural basis of pain in herpes zoster and postherpetic neuralgia. The ectopic pacemaker hypothesis in Watson et al. 2017. Herpes zoster: postherpetic neuralgia and other complications. Adis

1. Devor M. Rethinking the causes of pain in herpes zoster and postherpetic neuralgia: the ectopic pacemaker hypothesis. Pain Rep. 2018 Nov 7;3(6):e702.

MORE THAN JUST A RASH, IT IMPACTS DAILY LIFE[1]

Level of pain reported for different conditions using the short-form McGill Pain Questionnaire[3]



The same results were first published in Katz et al. 1999. The figure has been independently created by GSK from the original data

The same results were first published in Drolet, et al. 2010. The figure has been independently created by GSK from the original data

A total of 574 outpatients aged 50 years and older with a physician- confirmed diagnosis of herpes zoster were recruited at different times after rash onset. Of these patients, 266 were recruited within 14 days after rash onset and were considered to have incident herpes zoster. The outcome measures were herpes zoster pain and post -herpetic neuralgia, interference with activities of daily living and health-related quality of life. The median duration of interference with activities of daily living because of pain varied between 27.0 days (relations with others) and 29.8 days (sleep).[1]

HZ=herpes zoster; PHN=postherpetic neuralgia.

1. Drolet M, Brisson M, Schmader KE, Levin MJ, Johnson R, Oxman MN, Patrick D, Blanchette C, Mansi JA. The impact of herpes zoster and post herpetic neuralgia on health-related quality of life: a prospective study. CMAJ. 2010 Nov 9;182(16):1731-..2 Supplementry of : Drolet M, Brisson M, Schmader KE, Levin MJ, Johnson R, Oxman MN, Patrick D, Blanchette C, Mansi JA. The impact of herpes zoster and post herpetic neuralgia on health-related quality of life: a prospective study. CMAJ. 2010 Nov 9;182(16):1731-) **3.** Katz J, Melzack R. Measurement of pain. Surg Clin North Am. 1999 Apr;79(2):231-52.

13

AGENDA


What is the clinical impact of shingles on patients?
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THE IMMUNE SYSTEM CHANGES OVER AN INDIVIDUAL'S LIFE[1]

The immune system of newborns is immature, leaving them at risk of infection[1]

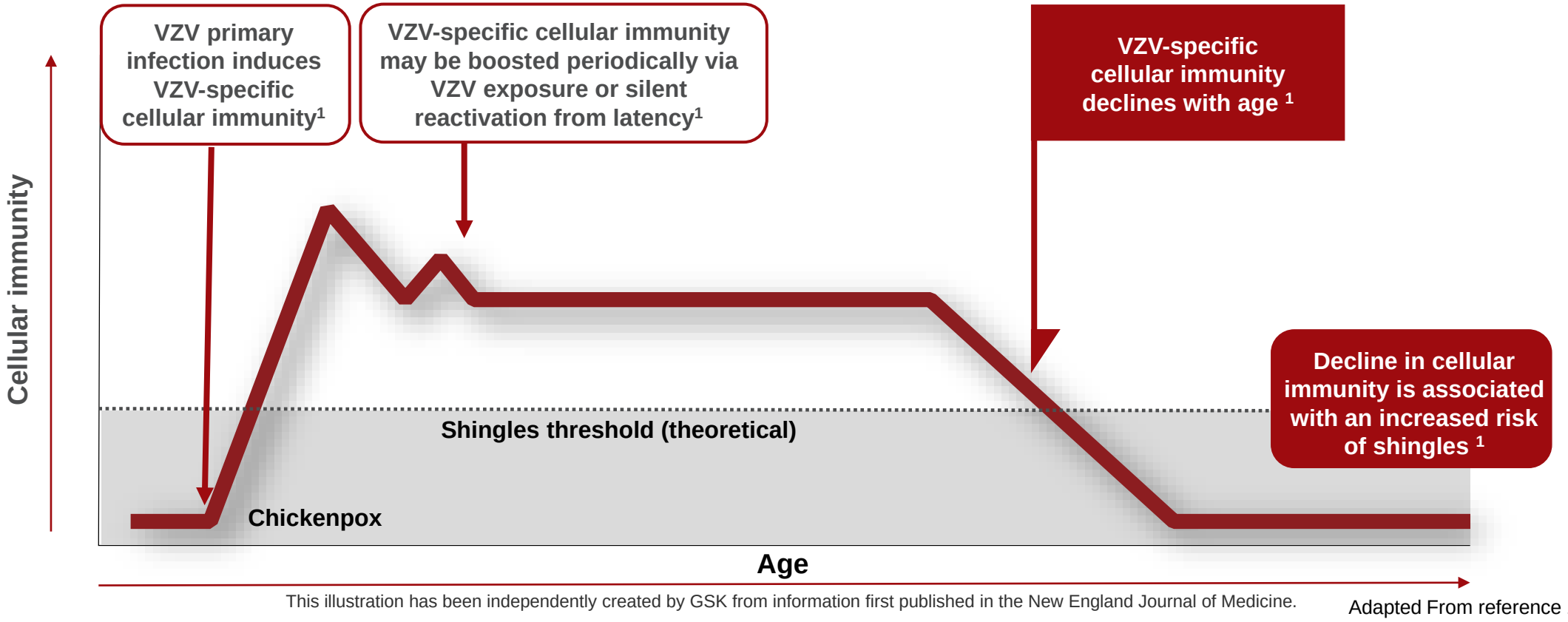
The immune system develops through childhood into adulthood[1]

It gradually weakens with age, a concept called 'immunosenescence'[2]

There is a need for vaccination programmed that protect individuals throughout all stages of their lives[3]

1. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. Proc Biol Sci. 2015 Dec 22;282(1821):20143085..; 2 Weiskopf D, Weinberger B, Grubeck-Loebenstein B. The aging of the immune system. Transpl Int. 2009 Nov;22(11):1041-50; 3. Global Coalition on Aging: life-course immunization, a driver of healthy aging. https://globalcoalitiononaging.com/wp-content/uploads/2018/07/life-course-immunization_gcoa-for-web-1.pdf (accessed February 2024)

AGE-RELATED DECLINE IN IMMUNITY IS THE DOMINANT DRIVER OF SHINGLES[1*]



This illustration has been independently created by GSK from information first published in the New England Journal of Medicine.

Adapted From reference 1

*Immunodeficiency caused by medical conditions or immunosuppressive medications may also increase the risk of shingles.[1]
VZV=varicella zoster virus.

1Kimberlin DW, Whitley RJ. Varicella-zoster vaccine for the prevention of herpes zoster. N Engl J Med. 2007 Mar 29;356(13):1338-43

THE BURDEN OF SHINGLES INCREASES WITH AGE, WITH A SHARP INCREASE FROM ≥50 YEARS ONWARDS[1]

The incidence of HZ increases with age[2]

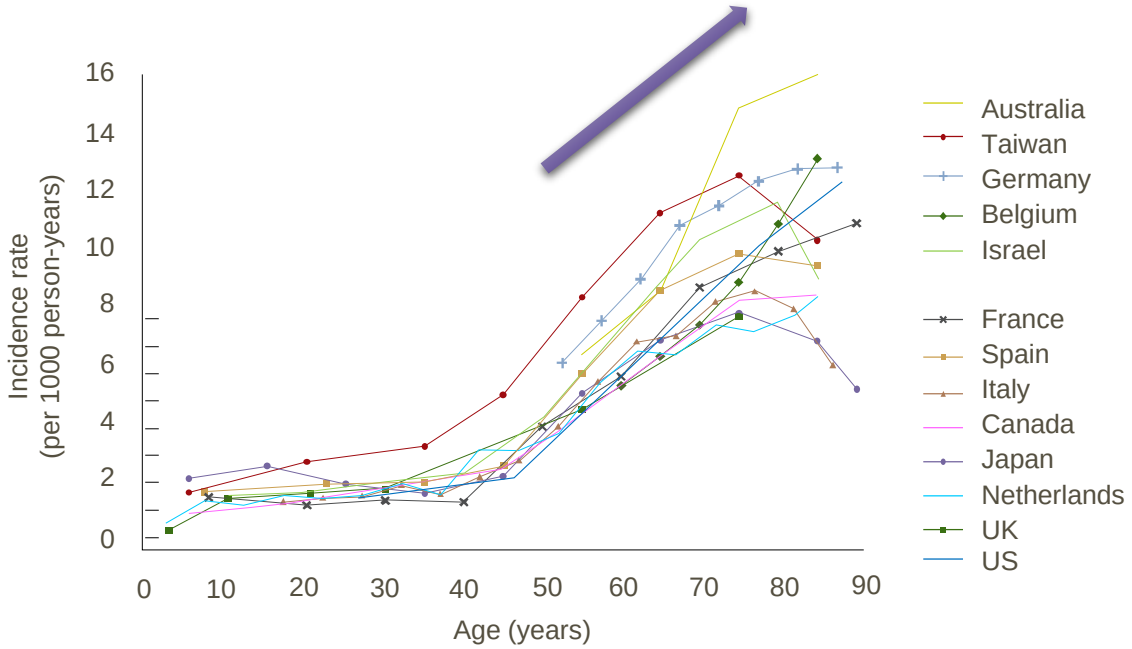
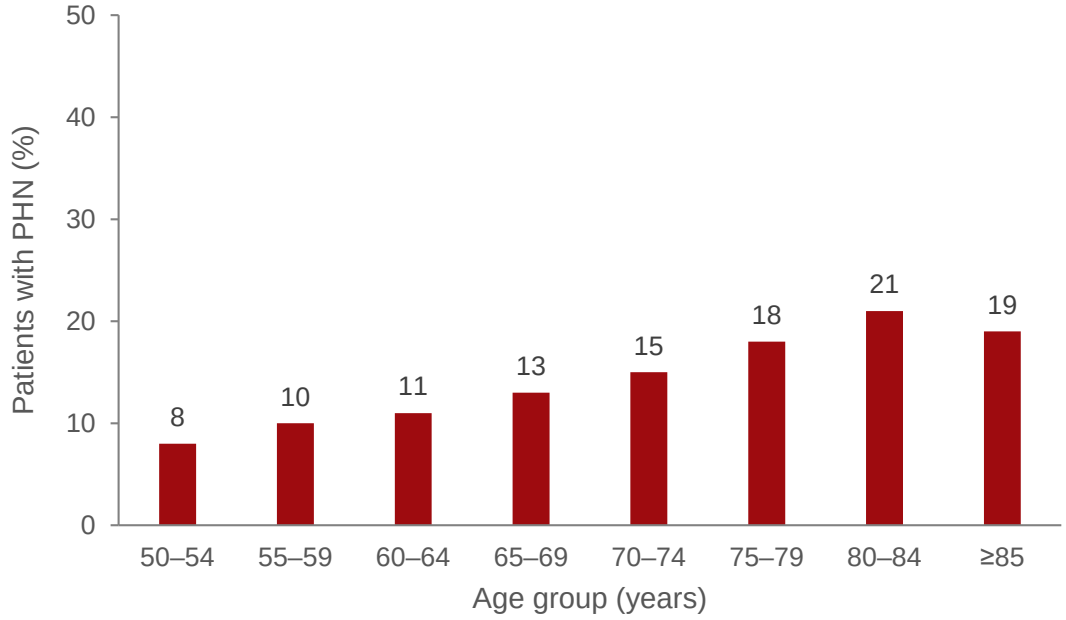


Figure reproduced from Kawai K et al. BMJ Open 2014;4:e004833 with permission from BMJ Publishing Group Ltd.

The incidence of PHN also increases with age[1]

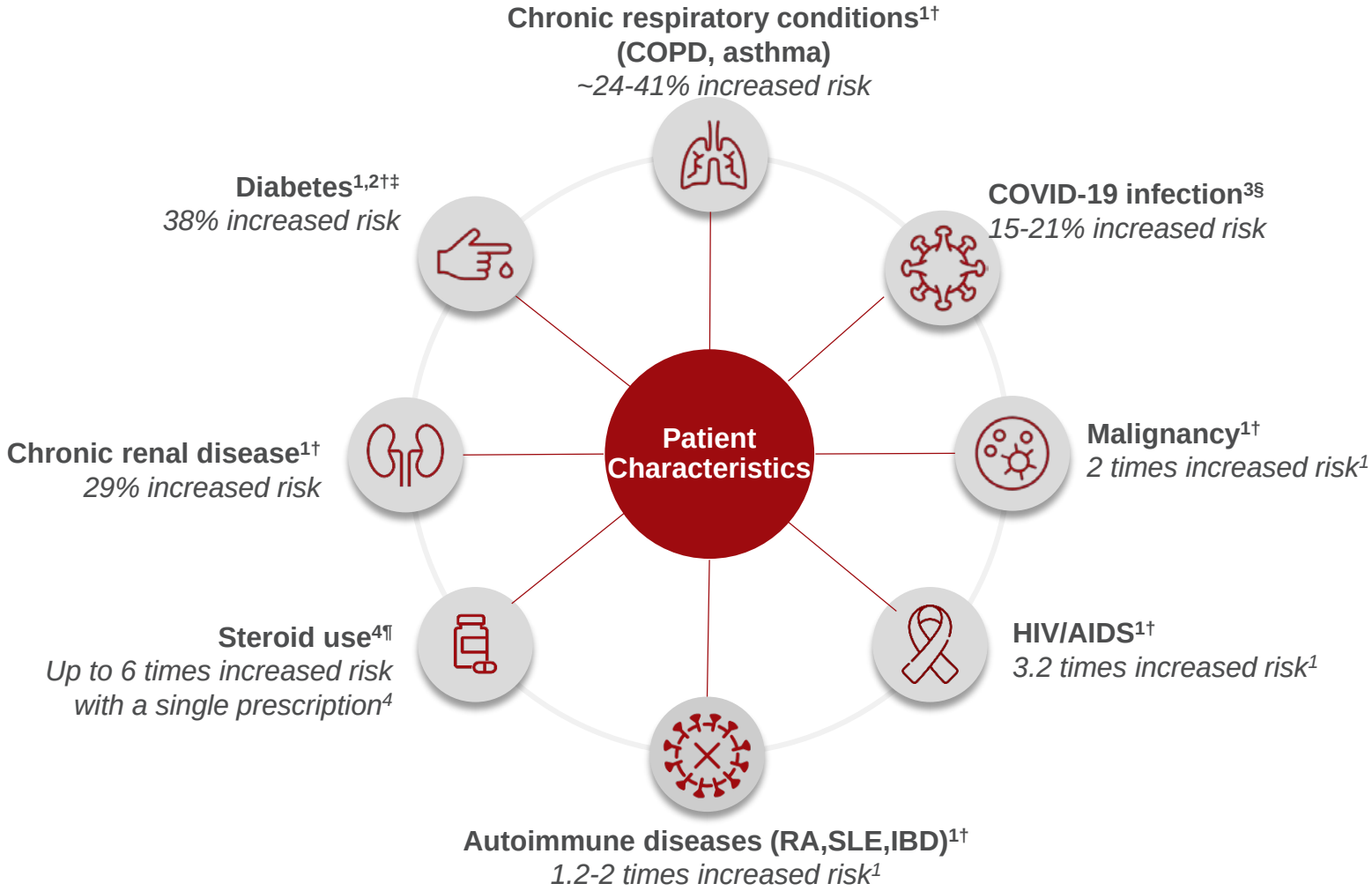


The graph is reproduced with the permission of Cambridge University Press. It was first published in Gauthier A et al. 2009

HZ=herpes zoster; PHN=postherpetic neuralgia.

1. Gauthier A, Breuer J, Carrington D, Martin M, Rémy V. Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. Epidemiol Infect. 2009 Jan;137(1):38-47 ,2Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open. 2014 Jun 10;4(6):e004833.

ON TOP OF AGE, A VARIETY OF OTHER FACTORS CAN FURTHER ELEVATE PATIENTS' RISK OF SHINGLES[1*]



*List of risk factors is not exhaustive and presented HZ risk may vary with age. †Meta-analysis of 88 studies (N=198,751,846); estimates based on risk ratio and age ranged from 3 months to 104 years.[1] ‡Meta-analysis of 16 studies (N=65,541,845); estimates based on risk ratio and age was ≥18 years.[2] §Retrospective cohort study of individuals ≥50 years of age (N=394,677); adjusted incidence rate ratios were estimated by Poisson regression.[3] ¶Prospective population-based study of adults ≥45 years of age (n=20,048) on new systemic corticosteroid users with a median equivalent systemic prednisolone dose of 300 mg[4]; ; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus .

ON TOP OF AGE, A VARIETY OF OTHER FACTORS CAN FURTHER ELEVATE PATIENTS' RISK OF SHINGLES[1*]

References:
1. Marra F, Parhar K, Huang B, Vadlamudi N. Risk Factors for Herpes Zoster Infection: A Meta-Analysis. Open Forum Infect Dis. 2020 Jan 9;7(1):ofaa005.
2. Huang CT, Lee CY, Sung HY, Liu SJ, Liang PC, Tsai MC. Association Between Diabetes Mellitus and the Risk of Herpes Zoster: A Systematic Review and Meta-analysis. J Clin Endocrinol Metab. 2022 Jan 18;107(2):586-59
3 .Bhavsar A, Lonnet G, Wang C, Chatzikonstantinidou K, Parikh R, Brabant Y, Servotte N, Shi M, Widenmaier R, Aris E. Increased Risk of Herpes Zoster in Adults ≥50 Years Old Diagnosed With COVID-19 in the United States. Open Forum Infect Dis. 2022 Mar 9;9(5):ofac118.
4 .Qian J, Banks E, Macartney K, Heywood AE, Lassere MN, Liu B. Corticosteroid Use and Risk of Herpes Zoster in a Population-Based Cohort. Mayo Clin Proc. 2021 Nov;96(11):2843-2853.

CHRONIC RESPIRATORY CONDITIONS ARE ASSOCIATED WITH AN INCREASED RISK OF SHINGLES PHN AND HOSPITALISATION[1*]

53%

increased risk of PHN in COPD patients

aOR 1.53 (99%CI 1.35–1.72)[2†]

21%

increased risk of PHN in asthma patients

aOR 1.21 (99%CI 1.06–1.37)[2†]

2.6x

increased risk of HZ-related hospitalisation in COPD patients

OR 2.66 (95%CI 2.17–3.24)[1‡]

CHRONIC RESPIRATORY CONDITIONS ARE ASSOCIATED WITH AN INCREASED RISK OF SHINGLES PHN AND HOSPITALISATION[1*]

*Presented risks may vary with age. †Compared to unaffected patients from a cohort study (N=119,413; age range 18–101 years). Multivariable logistic regression adjusted for age, sex, socioeconomic status, HIV, leukaemia, lymphoma, myeloma, haematopoietic stem cell transplantation, other unspecified cellular immune deficiencies, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, COPD, asthma, chronic kidney disease, depression, personality disorder, diabetes, recent cancer diagnosis, smoking, BMI category, site of zoster, antivirals and immunosuppressive therapies.[2] ‡Generalized linear models utilized to compare the COPD and the non-COPD populations from a cohort study of adults ≥50 years of age (N=2,289,485). Hospitalizations with a HZ CIE-9 code in any diagnostic position.[1]
aOR=adjusted odds ratio; COPD=chronic obstructive pulmonary disorder; HZ=herpes zoster; PHN=post-herpetic neuralgia

*Adjusted for age, sex, socioeconomic status, HIV, leukaemia, lymphoma, myeloma, haematopoietic stem cell transplantation, other unspecified cellular immune deficiencies, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, COPD, asthma, chronic kidney disease, depression,
personality disorder, diabetes, recent cancer diagnosis, smoking, BMI category, site of zoster, antivirals and immunosuppressive therapies.

Reference :
1. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J. Risk and impact of herpes zoster among COPD patients: a population-based study, 2009-2014. BMC Infect Dis. 2018 May 3;18(1):203
2.Forbes HJ, Bhaskaran K, Thomas SL, Smeeth L, Clayton T, Mansfield K, Minassian C, Langan SM. Quantification of risk factors for postherpetic neuralgia in herpes zoster patients: A cohort study. Neurology. 2016 Jul 5;87(1):94-102.

INDIVIDUALS WITH DIABETES HAVE AN INCREASED RISK OF DEVELOPING HZ AND USE MORE HEALTHCARE RESOURCES COMPARED TO PEOPLE WITHOUT DIABETES, WHICH MIGHT BE THE CONSEQUENCE OF A MORE SEVERE HZ[1]

In patients with diabetes mellitus, HZ is associated with:

Poor glycaemic control in

24%

patients[1†]

20%

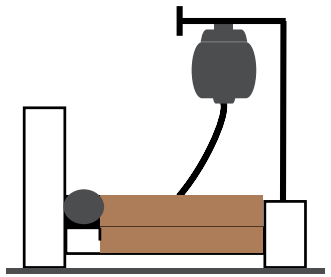
Increased risk of PHN

aOR 1.2 (99%CI 1.17–1.22)[1‡]

63%

Increased risk of HZ-related hospitalisation

OR 1.63 (95%CI 1.38–1.91)[1†]



18%

Increased risk of persistent post zoster pain for ≥6 months

aOR 1.18 (95%CI 1.13–1.24)[2§]

INDIVIDUALS WITH DIABETES HAVE AN INCREASED RISK OF DEVELOPING HZ AND USE MORE HEALTHCARE RESOURCES COMPARED TO PEOPLE WITHOUT DIABETES, WHICH MIGHT BE THE CONSEQUENCE OF A MORE SEVERE HZ[1]

†Retrospective cohort study in adults ≥50 years of age (N=2,289,485); poor glycaemic control in 24% of well controlled patients with diabetes (HbA1C levels ≤6.5%), HbA1C increased after HZ. Hospitalizations with a HZ CIE-9 code in any diagnostic position.[1] §Compared to individuals without diabetes from a retrospective observational study of adults ≥18 years of age (N=420,515). Multivariate regressions adjusted for age and sex as a function of immune competence.[2]

aOR=adjusted odds ratios; CI=confidence interval; HZ=herpes zoster; OR=odds ratio; PHN=post-herpetic neuralgia.

Reference :

1 Muñoz-Quiles C, López-Lacort M, Ampudia-Blasco FJ, Díez-Domingo J. Risk and impact of herpes zoster on patients with diabetes: A population-based study, 2009-2014. Hum Vaccin Immunother. 2017 Nov 2;13(11):2606-2611

2 Suaya JA, Chen SY, Li Q, Burstin SJ, Levin MJ. Incidence of herpes zoster and persistent post-zoster pain in adults with or without diabetes in the United States. Open Forum Infect Dis. 2014 Aug 2;1(2):ofu049.

TREATMENT OPTIONS FOR SHINGLES AND ITS COMPLICATIONS ARE LIMITED AND SUBOPTIMAL[1]

Rash onset[1]

Antiviral treatment of acute HZ

within 72 hours of the rash onset[2]

- Antivirals can reduce HZ severity and duration[1]

Oral acyclovir does not reduce PHN incidence; insufficient evidence for to determine if other antiviral agents prevent PHN.[3]

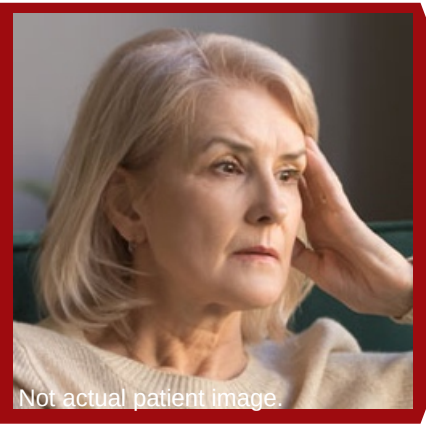
Rash lasts 7-10 days[1]

Additional pain control can be achieved in certain patients by supplementing antiviral agents with corticosteroids and with analgesics[2]

Caution is warranted when using corticosteroids without concomitant antiviral therapy, as this may promote viral replication and trigger acute retinal necrosis.[2]

Analgesics and corticosteroids agents.[2]

PHN months/years[1]



Not actual patient image.

Drugs for acute zoster pain

- Tricyclic antidepressants[2]
- Topical anesthetics[2]
- opiates [2]

Only 14% of patients with PHN are satisfied with their pain medication[4*]

HZ=herpes zoster; PHN=post-herpetic neuralgia.

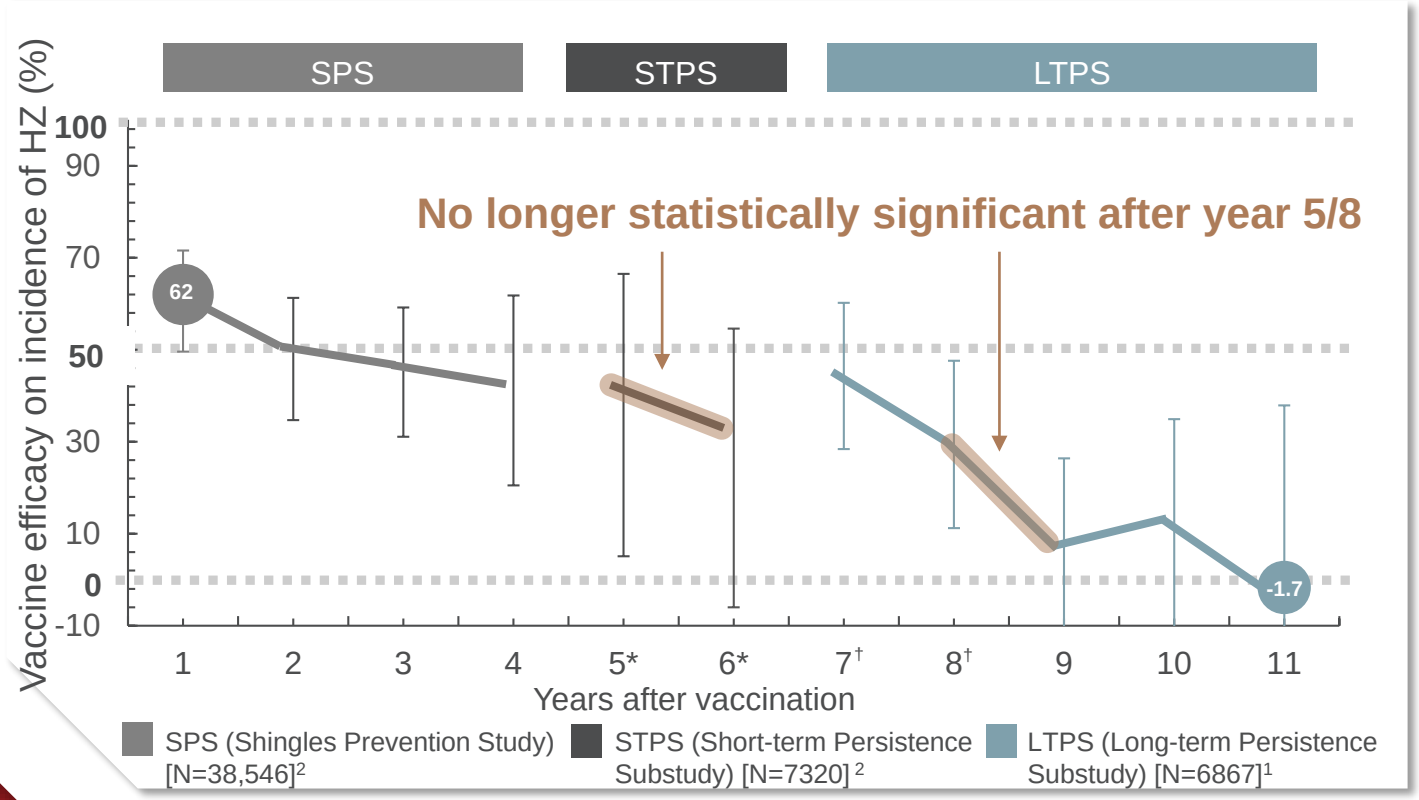
*Results from a single study. Patients with PHN (N=385) were asked how satisfied they were with their medication by using a 5-point Likert response scale (“a lot,” “quite a bit,” “some,” “a little,” “not at all”).

1. Harpaz R, et al. MMWR Recomm Rep. 2008 June;57(RR-5):1-30 **2.** Gross, G. E., Eisert, L., Doerr, H. W., Fickenscher, H., Knuf, M., Maier, P., Maschke, M., Müller, R., Pleyer, U., Schäfer, M., Sunderkötter, C., Werner, R. N., Wutzler, P., & Nast, A. (2020). S2k guidelines for the diagnosis and treatment of herpes zoster and postherpetic neuralgia. Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG, 18(1), 55–78. 3.Johnson RW, Bouhassira D, Kassianos G, Leplège A, Schmader KE, Weinke T. The impact of herpes zoster and post-herpetic neuralgia on quality-of-life. BMC Med. 2010 Jun 21;8:37.. **4**. Oster G, Harding G, Dukes E, Edelsberg J, Cleary PD. Pain, medication use, and health-related quality of life in older persons with postherpetic neuralgia: results from a population-based survey. J Pain. 2005 Jun;6(6):356-63survey. J Pain. 2005 Jun;6(6):356-63

AGENDA


What is the clinical impact of shingles on patients?
Why is it important to prevent shingles?
How was SHINGRIX designed?
What is the clinical profile of SHINGRIX?
How can you implement SHINGRIX in your practice?

LIVE ATTENUATED ZOSTER VACCINE (VZV) EFFICACY AGAINST HZ INCIDENCE WAS STATISTICALLY SIGNIFICANT FOR EACH YEAR THROUGH YEAR 5 AND REMAIN STATISTICALLY SIGNIFICANT THROUGH YEAR 8[1]



Age range (years)	Vaccine efficacy against HZ (95% CI)
50-59 (ZEST)*	**69.8%** (54.1-80.6)[3]
Overall (≥60) (SPS)	**51.3%** (44.2-57.6)[2]
60-69 (SPS)	**64%** (56-71)[3]
70-79 (SPS)	**41%** (28-52)[3]

ZVL is contraindicated in patients with immunosuppression or immunodeficiency[4]

Figures adapted from Morrison VA, et al. LTPS–subject mean age 74.5 years (standard deviation, 5.8 years). SPS–mean age 68.3 years (standard deviation, 5.7 years).[1] STPS–mean age 73.3 years.[2]

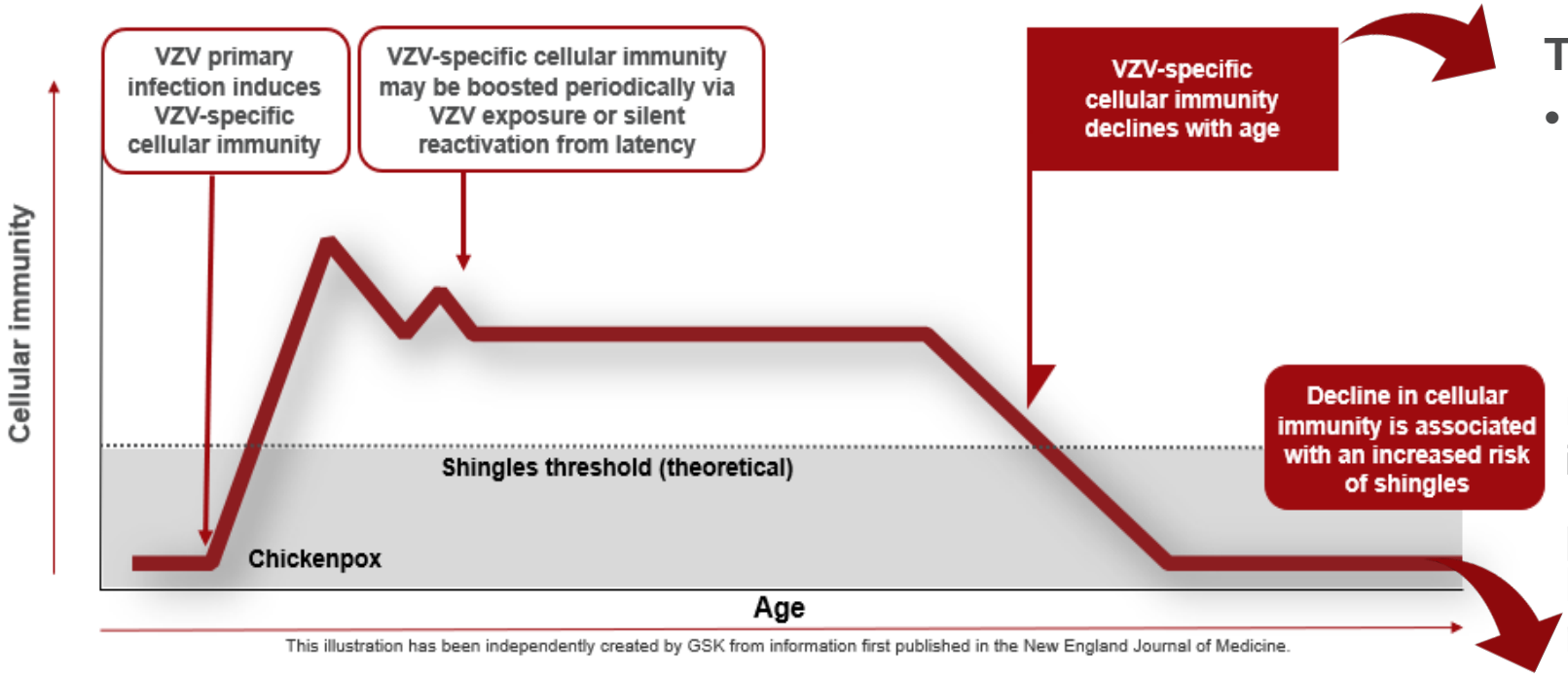
*Data for years 5–6 from the Long-term Persistence Substudy (LTPS) are excluded.[1] For years 7 and 8, both STPS and LTPS contributed to vaccine group data.[1]
CI=confidence interval; HZ=herpes zoster; LTPS=Long-term Persistence Substudy; SPS=Shingles Prevention Study; STPS=Short-term Persistence Substudy; ZEST=ZVL Efficacy and Safety Trial; ZVL=zoster vaccine live.

LIVE ATTENUATED ZOSTER VACCINE (VZV) EFFICACY AGAINST HZ INCIDENCE WAS STATISTICALLY SIGNIFICANT FOR EACH YEAR THROUGH YEAR 5 AND REMAIN STATISTICALLY SIGNIFICANT THROUGH YEAR 8[1]

References:

1. Morrison VA, et al. Clin Infect Dis. 2015 Mar;60(6):900-09.
2. .Schmader KE, Oxman MN, Levin MJ, Johnson G, P; Shingles Prevention Study Group. Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy. Clin Infect Dis. 2012 Nov 15;55(10):1320-8.
3. Schmader KE, Levin MJ, Gnann JW Jr, McNeil SA, Vesikari T, Betts RF, Keay S, Stek JE, Bundick ND, Su SC, Zhao Y, Li X, Chan IS, Annunziato PW, Parrino J. Efficacy, safety, and tolerability of herpes zoster vaccine in persons aged 50-59 years. Clin Infect Dis. 2012 Apr;54(7):922-8.
4. Zostavax (EU Summary of Product Characteristics). MSD; 2022; Accessed at :17 April 2024 .

RECOMBINANT SUBUNIT VACCINES ARE AN ALTERNATIVE APPROACH FOR HZ PREVENTION[1]



Adapted From Reference 2

Target population:

- Prevention of shingles in adults ≥50 years of age[3]

Formulation induce strong and sustained immune responses to VZV [1]**:**

promotes strong CD4+ T-cell and humoral immune responses against recombinant proteins.[3]

Exogenous exposure to VZV boosts the immune system and prevents reactivation [3]

VZV=varicella zoster virus.

RECOMBINANT SUBUNIT VACCINES ARE AN ALTERNATIVE APPROACH FOR HZ PREVENTION[1]

References:

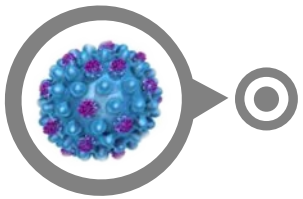
1. Chlibek R, Smetana J, Pauksens K, Rombo L, Van den Hoek JA, Richardus JH, Plassmann G, Schwarz TF, Ledent E, Heineman TC. Safety and immunogenicity of three different formulations of an adjuvanted varicella-zoster virus subunit candidate vaccine in older adults: a phase II, randomized, controlled study. Vaccine. 2014 Mar 26;32(15):1745-53.
2. Kimberlin DW, Whitley RJ. Varicella-zoster vaccine for the prevention of herpes zoster. N Engl J Med. 2007 Mar 29;356(13):1338-43
3. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09\2023

SHINGRIX IS SPECIFICALLY DESIGNED FOR PREVENTING HZ IN INDIVIDUALS AGED 50 YEARS AND ABOVE[1], WHO HAVE AGE-RELATED IMMUNITY DECLINE.[2]

Most abundant glycoprotein at the surface of VZV.[3]

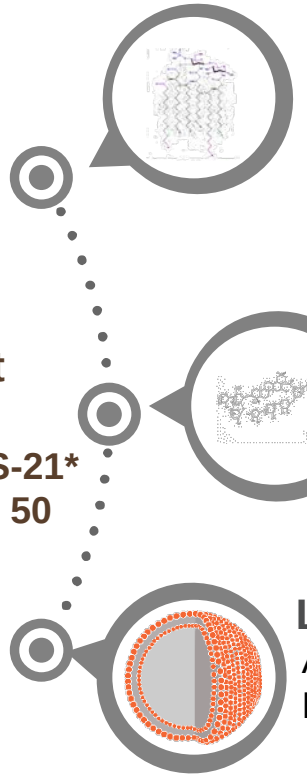
Essential for viral replication and cell-to-cell spread
It is a primary target of VZV-specific immune responses. [1]

Target of humoral and cellular response. [1]



Antigen
Glycoprotein E (gE) - 50 µg[4]

Adjuvant System
$AS01_B$: QS-21* and MPL - 50 µg.[3]



MPL
Detoxified *Salmonella Minnesota* LPS[4]

QS21
Purified natural saponin[4]

LIPOSOME
Artificial vesicles: MPL/QS21 vehicle[4]

RECOMBINANT SUBUNIT NON-LIVE VACCINE[4]

AS01B=Adjuvant System 01B; gE=glycoprotein E; HZ=herpes zoster; MPL=mono-phosphoryl lipid A; LPS=lipopolysaccharide; QS-21=Quillaja saponaria Molina fraction 21; VZV: varicella zoster virus

SHINGRIX IS SPECIFICALLY DESIGNED FOR PREVENTING HZ IN INDIVIDUALS AGED 50 YEARS AND ABOVE[1], WHO HAVE AGE-RELATED IMMUNITY DECLINE.[2]

References:

1.Lal H, Cunningham AL, Godeaux O, *et al*. N Engl J Med. 2015;372(22):2087-96.

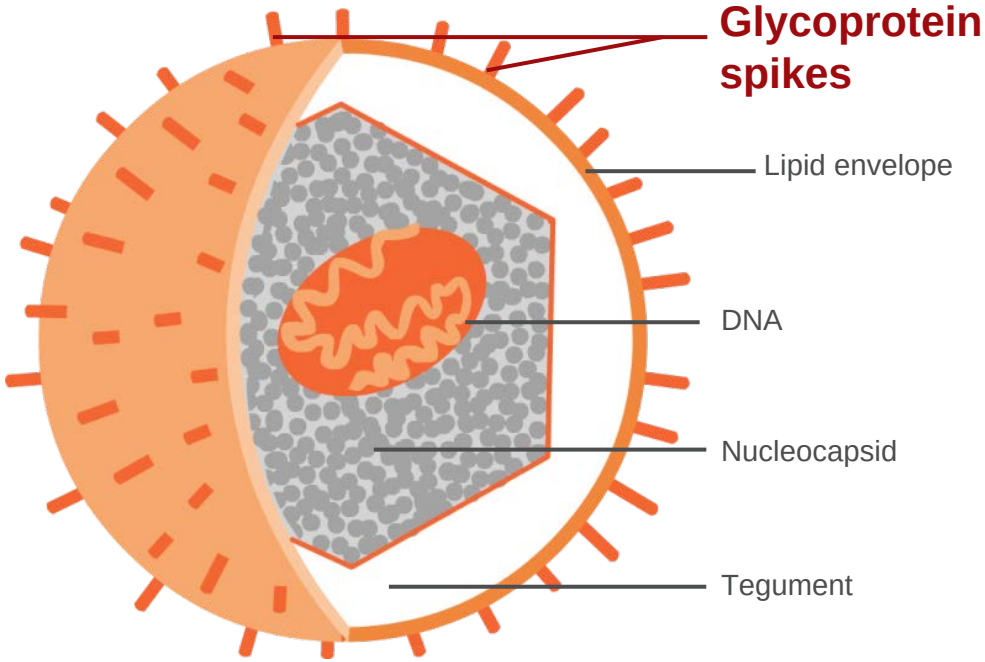
2. Oxman M. N. (1995). Immunization to reduce the frequency and severity of herpes zoster and its complications. Neurology, 45(12 Suppl 8), S41–S46.

3. Dendouga N, Fochesato M, Lockman L, et al. Vaccine. 2012;30(20):3126-35.

4. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09/2023

VZV GLYCOPROTEIN E (gE) IS PRIMARY TARGET FOR PROTECTIVE IMMUNE RESPONSE[1]

VZV STRUCTURE[4]



VZV gE

- **The most abundant VZV glycoprotein[2]**
- **Important role in viral infection**

  is a major target for VZV-specific antibody and T-cell responses and was selected as vaccine antigen based on its role in viral replication and cell-to-cell transfer[3]
- **Found in infected cells[3]**

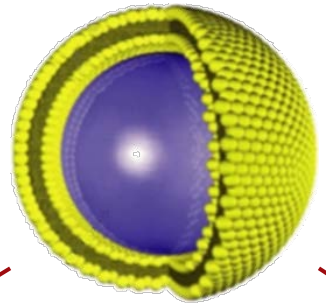
  promotes viral spread and the pathogenesis of skin lesions
- **Target of both humoral and cellular immune system[2]**

DNA=deoxyribonucleic acid; gE=glycoprotein E;VZV=varicella zoster virus

1.Lal H, Cunningham AL; ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015 May 28;372(22):2087-96
2.Dendouga N, Fochesato M. Cell-mediated immune responses to a varicella-zoster virus glycoprotein E vaccine using both a TLR agonist and QS21 in mice. Vaccine. 2012 Apr 26;30(20):3126 35.
3.Lecrenier N, Beukelaers P. Development of adjuvanted recombinant zoster vaccine and its implications for shingles prevention. Expert Rev Vaccines. 2018 Jul;17(7):619634 4. Zerboni L, Sen N, Oliver SL, Arvin AM. Molecular mechanisms of varicella zoster virus pathogenesis. Nat Rev Microbiol. 2014 Mar;12(3):197-210

RATIONALE FOR SELECTION OF THE ADJUVANT SYSTEM $AS01_B$

Liposome (carrier)[1]



MPL **Saponin QS-21**

Adjuvant system $AS01_B$

- Selected based on preclinical evaluation and previous clinical experience
- The combination of MPL and QS-21 enhances cellular response and antibody response to gE

During the preclinical development and early clinical trials, several adjuvant options were tested, and compared to the classical live-attenuated vaccine for the induction of CD4 Tcell.[1] The final selection was for the adjuvant system called AS01B, which is composed of two immunostimmulants incorporated into a liposomal carrier. It contains 50ug of each of mono-phosphoryl lipid A or MPL, and purified saponin fraction, QS-21 extracted from Quinalaja saponiaria tree bark. MPL is a detoxified derivative of Salmonella Minnesota LPS and stimulates activation of innate immunity via Toll-like receptor 4 (TLR4) . MPL acts in synergy with QS-21 to induce a stronger CD4 T cell response. However, the signaling pathways triggered by QS-21 are not fully understood. Also Co-localization of AS01 and antigen is necessary for adjuvant benefit.[2]

$AS01_B$=Adjuvant System 01_B; gE=glycoprotein E; MPL=monophosphoryl lipid A; QS-21=*Quillaja saponaria* Molina fraction 21

1.Garçon N, et al. Understanding Modern Vaccines. Amsterdam: Elsevier; 2011.
2. Didierlaurent, A.M. et al. (2016) 'Adjuvant system AS01: Helping to overcome the challenges of modern vaccines', Expert Review of Vaccines, 16(1), pp. 55–63. doi:10.1080/14760584.2016.1213632.

AGENDA


What is the clinical impact of shingles on patients?
Why is it important to prevent shingles?
How was SHINGRIX designed?
What is the clinical profile of SHINGRIX?
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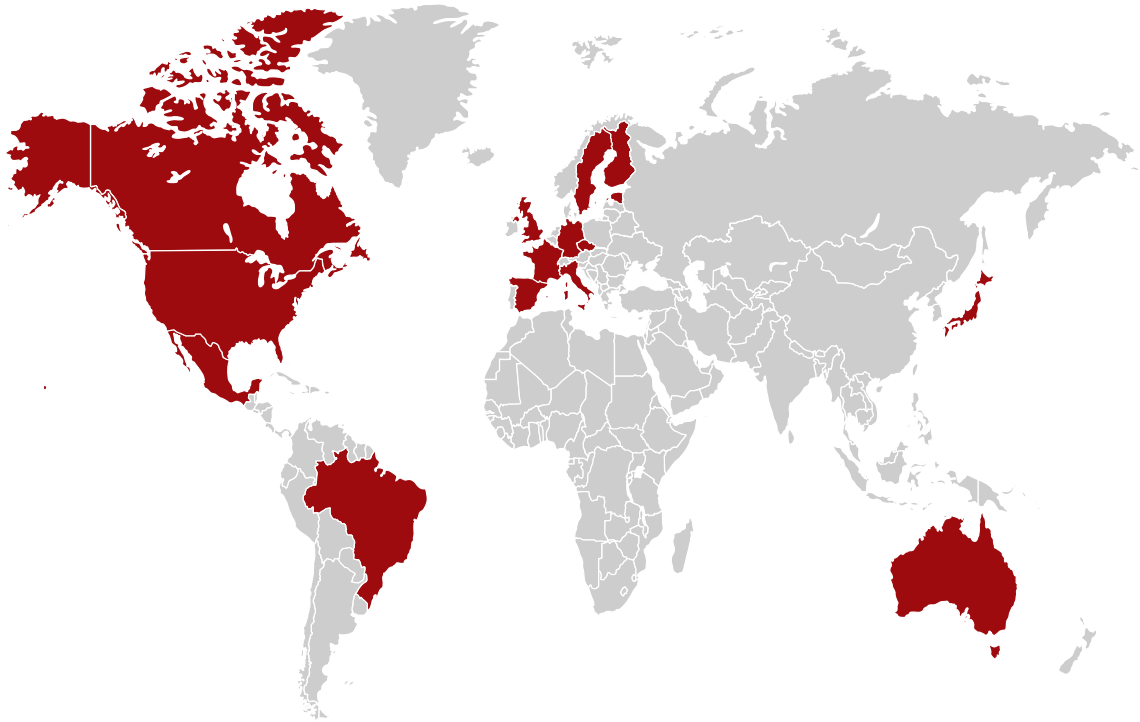
HZ/SU VACCINE SIGNIFICANTLY REDUCED THE RISK OF HERPES ZOSTER AMONG ADULTS WHO WERE 50 YEARS OF AGE OR OLDER, WELL PRESERVED AMONG 70 YEARS OF AGE OR OLDER.[1]

	ZOE-50[1]	ZOE-70[2]
AGE	50+	70+
Study design	randomized, placebo-controlled, phase 3 study in 18 countries.[1]	
Subject enrolled	16,160	14,816
Study endpoints	Efficacy against HZ*, PHN	
Pooled analysis	Pre-specified in subjects ≥70 YOA	



18 countries involved[2]

*Primary study objective. Mean follow-up 3.2 and 3.7 years for ZOE-50 and ZOE-70, respectively. ZOE-50/70 efficacy studies conducted at the same sites[2].

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The same results were first published in Lal H et al. 2015 and Cunningham AL et al. 2016. The graph has been independently created by GSK from the original data

HZ=herpes zoster; PHN=post-herpetic neuralgia; YOA=years of age.

1. Lal H, Cunningham AL, Godeaux O, Chlibek R; ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015 May 28;372(22):2087-96..2Cunningham AL, Lal H, Kovac MC; ZOE-70 Study Group. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med. 2016 Sep 15;375(11):1019-32

SHINGRIX DELIVERED 97% EFFICACY AGAINST SHINGLES IN PATIENTS ≥50 YOA[1*]

Age Group (years)	ZOE-50[2]
≥50	**97.2%** (93.7-99.0)
50-59	**96.6%** (89.6-99.3)
60-69	**97.4%** (90.1-99.7)
≥70	**97.9%** (87.9-100)

Age Group (years)	ZOE-50 and ZOE-70[1†] Pre-specified, pooled analyses
≥70	**91.3%** (86.8-94.5)
70-79	**91.3%** (86.0-94.9)
≥80	**91.4%** (80.2-97.0)

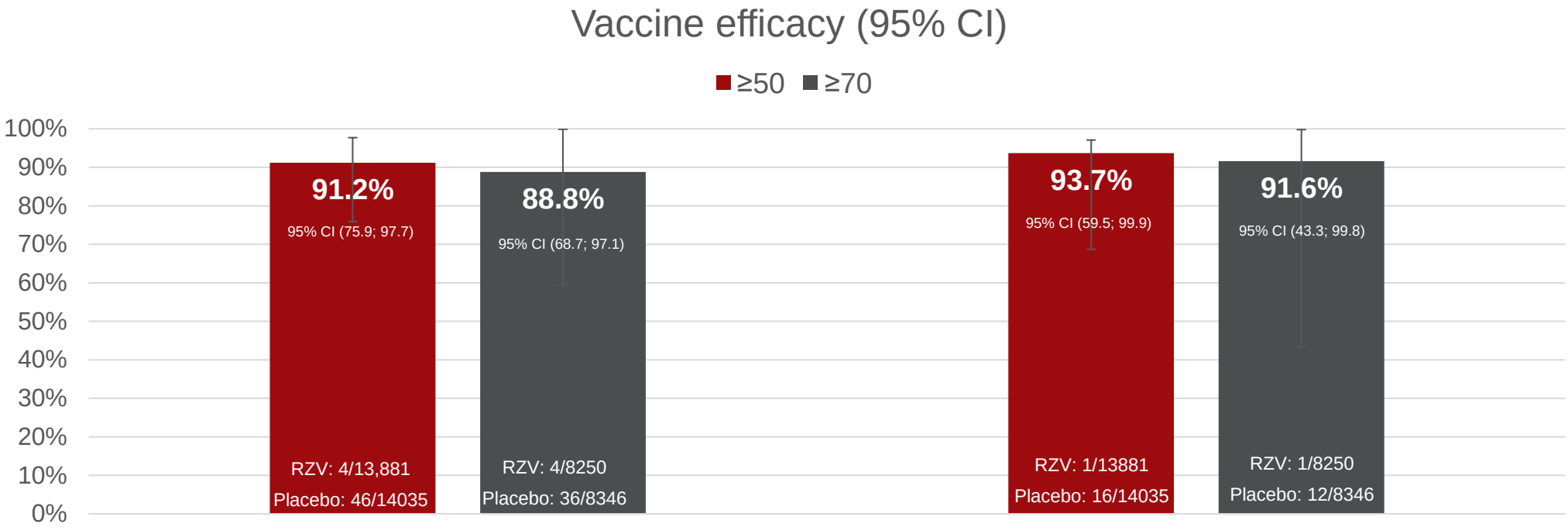
*In ZOE-50, RZV had a VE against HZ of 97.2% (95% CI: 93.7–99.0) in adults ≥50 years of age; n/N RZV (6/7344) vs. placebo (210/7415). In ZOE-70, RZV has a VE against HZ of 91.3% (95% CI: 86.8–94.5) in the pooled analysis of subjects ≥70 years old from ZOE-50/70; n/N RZV (25/8250) vs. placebo (284/8346).1 †Included 7344 randomized subjects ≥50 YOA who received second dose of the vaccine and did not develop shingles within 1 month after the second dose.[2]

. YOA=years of age

1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09\2023
2. Lal H, Cunningham AL, Godeaux O, Chlibek R; ZOE-50 Study Group. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015 May 28;372(22):2087-96

BY PREVENTING SHINGLES, SHINGRIX SIGNIFICANTLY REDUCED RISK OF PHN AND OTHER COMPLICATIONS[1]

SHINGRIX does not prevent 100% of shingles cases.



Figures independently created by GSK from the original data published in Cunningham et al. 2016 and Kovac et al. 2018.

PHN is defined as HZ-associated pain rated as ≥3 on a 0-10 scale, occurring or persisting for at least 90 days following the onset of rash using the Zoster Brief Pain Inventory questionnaire.[1]

Other complications included HZ vasculitis, disseminated disease, ophthalmic disease, neurological disease, visceral disease, and stroke.[2]

Pooled data from ZOE-50 (subjects ≥50 years old) and ZOE-70 (subjects ≥70 years old).[2]

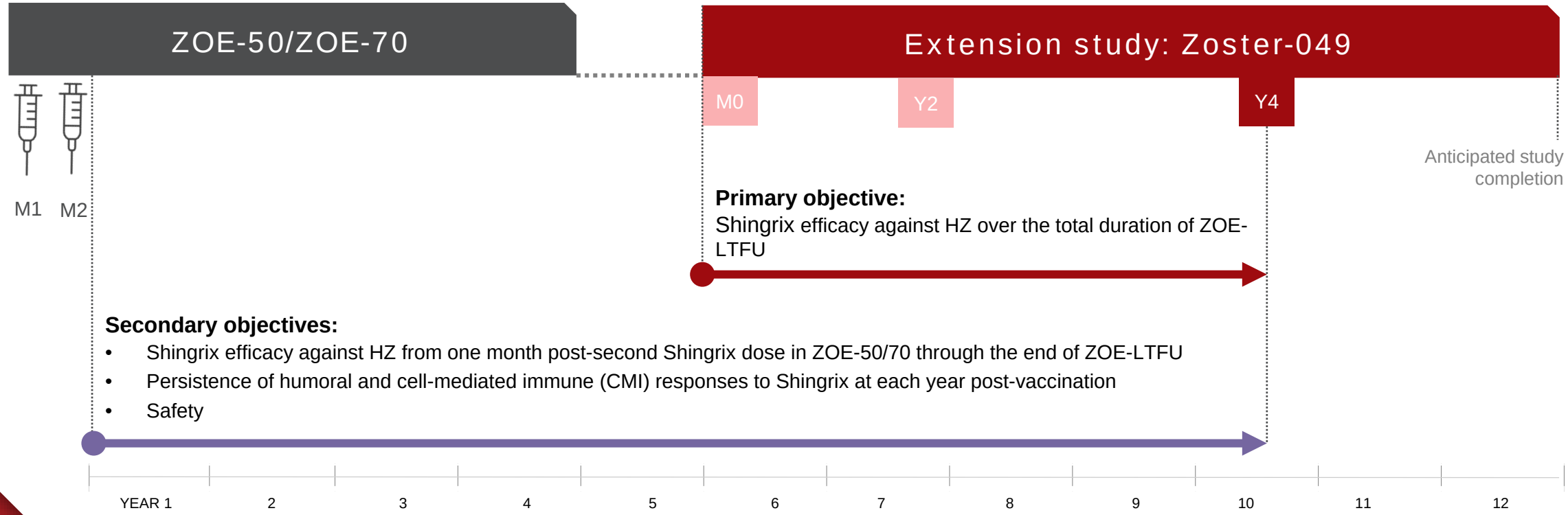
CI=confidence interval; HZ=herpes zoster; PHN=postherpetic neuralgia; RZV, recombinant zoster vaccine

1. Cunningham AL, Lal H, Kovac M, Chlibek R; ZOE-70 Study Group. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med. 2016 Sep 15;375(11):1019-32.. **2.** Kovac M, Lal H, Cunningham AL, Levin MJ, TC; ZOE-50/70 Study Group. Complications of herpes zoster in immunocompetent older adults: Incidence in vaccine and placebo groups in two large phase 3 trials. Vaccine. 2018 Mar 14;36(12):1537-1541.

LONG TERM FOLLOW UP STUDY (LTFU): ZOSTER-049 SECOND INTERIM ANALYSIS:[1]

Zoster-049:

- LTFU of ZOE-50/70 trials - ongoing
- 7277 participants. Conducted in 18 countries
- Second interim analysis: **≥4 years of follow-up,** from mean 5.6 (±0.3) to 9.6 (±0.3) years post vaccination

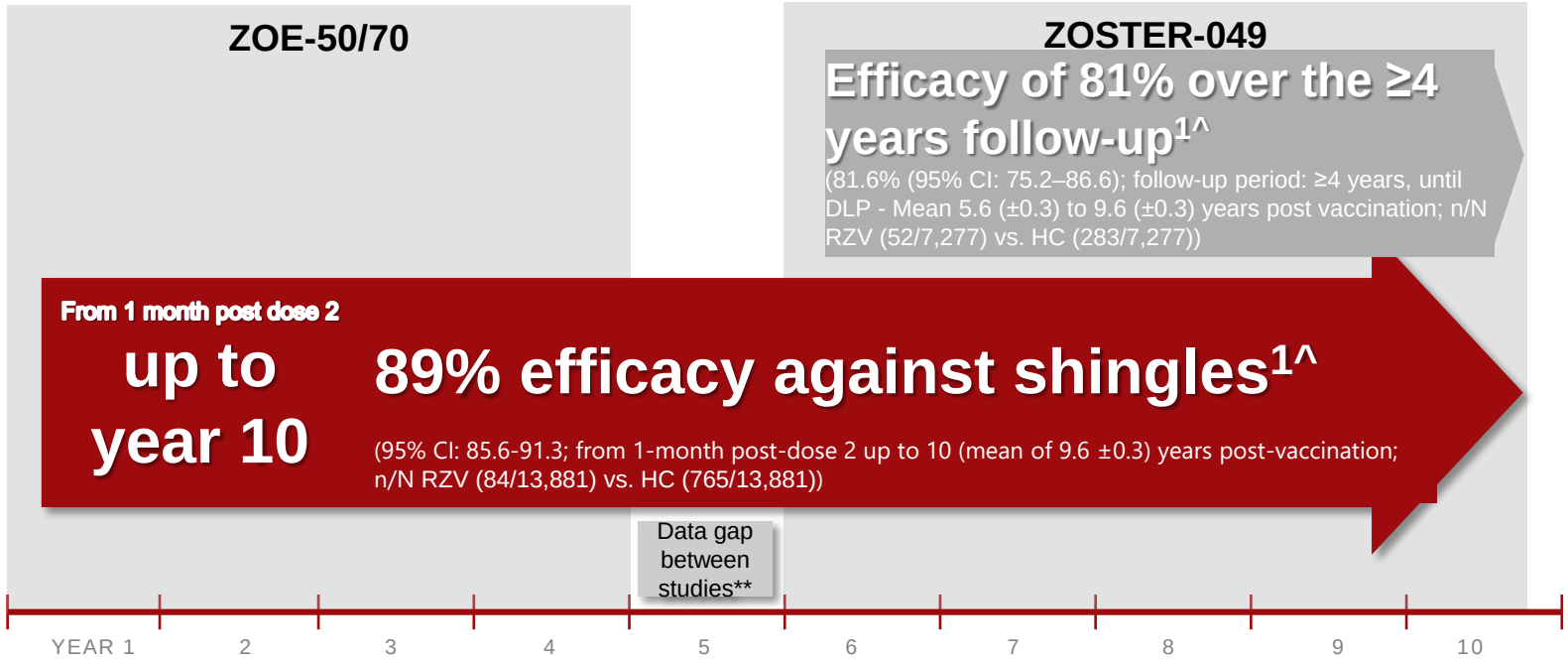


CMI=cell-mediated immune; HZ=herpes zoster; LTFU=long term follow-up; M=month; Y=year. The graph has been independently created by GSK from the original data published in Strezova A et al. 2022.

1. Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, Mwakingwe-Omari A; Zoster-049 Study Group. 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 Infect Dis. 2022 Oct 23;9(10):ofac485.

SHINGLES PROTECTION THAT LASTS UP TO YEAR 10[1]

ZOSTER-049 interim analysis:



The same results were first published in Strezova A, et al. Open Forum Infectious Diseases, 2022. The graph has been independently created by GSK from the original data.

**No data are available for year 5 because that period corresponds to the gap between ZOE-50/70 and the Zoster-049 follow-up study[1]

^ Of the 14,648 ZOE-50/70 participants who received at least 1 RZV dose, 7,413 (50.6%) were enrolled in ZOSTER-049. Of these, 7,277 had previously received both RZV doses and were included in the mTVC for the efficacy assessments. In the absence of an unvaccinated placebo group for the LTFU study, the efficacy analyses in ZOSTER-049 used historical control estimates from the ZOE-50/70 placebo groups recorded during the trials. At this DLP, data accrual was complete through year 9.[2]

Results for year 10 are also included although still incomplete, precision of estimates for this time point will increase at the final analysis.[1]

CI=confidence interval; DLP=data lock point, DLP set when the last participant had reached 4-years of follow-up; HC=historical controls; HZ=herpes zoster; mTVC, modified total vaccinated cohort; N, number of individuals included in each group; n, number of individuals having at least one confirmed herpes zoster episode; RZV, recombinant zoster vaccine.

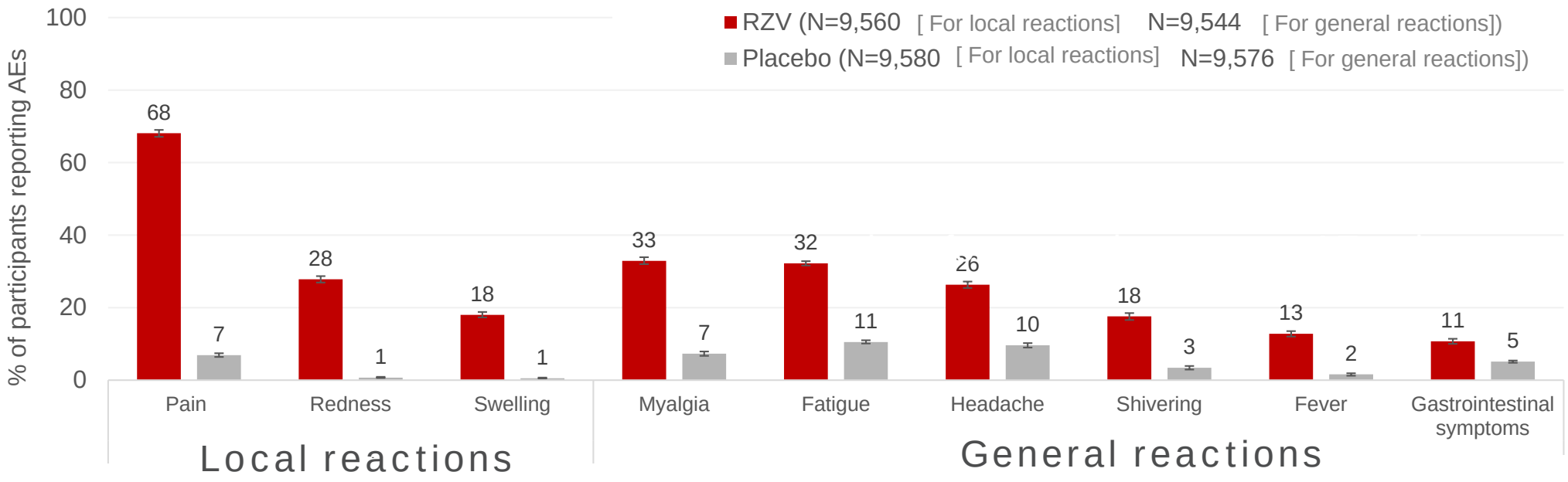
SHINGLES PROTECTION THAT LASTS UP TO YEAR 10[1]

References:

1. Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, Mwakingwe-Omari A; Zoster-049 Study Group. 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 Infect Dis. 2022 Oct 23;9(10):ofac485
2. Boutry C, Hastie A, Diez-Domingo J, A, Cunningham AL; Zoster-049 Study Group. The Adjuvanted Recombinant Zoster Vaccine Confers Long-Term Protection Against Herpes Zoster: Interim Results of an Extension Study of the Pivotal Phase 3 Clinical Trials ZOE-50 and ZOE-70. Clin Infect Dis. 2022 Apr 28;74(8):1459-1467

SHINGRIX HAS AN ESTABLISHED SAFETY PROFILE[1]

Most vaccination reactions were mild to moderate, with a median duration of 2-3 days[1^]



The figure is reproduced from López-Fauqued M et al. Vaccine 2019 (open access)

No increase in serious adverse events (SAEs) in ZOE-50/70 (median follow-up 4.4 years; 14,645 SHINGRIX and 14,660 placebo): Overall SAEs (SHINGRIX: 10.1%; placebo: 10.4%), fatal AEs (SHINGRIX: 4.3%; placebo: 4.6%), and pIMDs (SHINGRIX: 1.2%; placebo: 1.4%).[1]

Safety profile remained clinically acceptable up to year 10 post vaccination and no SAEs were considered causally related to vaccination in ZOSTER-049.[2]

^Median duration 3 days or less for local and 2 days or less for general symptoms.

.AE=adverse event; N=number of participants in the pooled total vaccinated cohort; pIMD=potential immune-mediated disease; RZV=recombinant zoster vaccine; SAE=serious adverse event

1López-Fauqued M, Campora L,; ZOE-50/70 Study Group. Safety profile of the adjuvanted recombinant zoster vaccine: Pooled analysis of two large randomised phase 3 trials. Vaccine. 2019 Apr 24;37(18):2482-2493.; 2. 1López-Fauqued M, Campora L(Appendix),; ZOE-50/70 Study Group. Safety profile of the adjuvanted recombinant zoster vaccine: Pooled analysis of two large randomised phase 3 trials. Vaccine. 2019 Apr 24;37(18):2482-24933. Strezova A, et al. Open Forum Infect Dis 2022;9:ofac485

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STORAGE AND ADMINISTRATION

SHINGRIX should be refrigerated. DO NOT FREEZE. Store in a refrigerator (2° C - 8° C).[1]
After reconstitution, the vaccine should be used promptly; if this is not possible, the vaccine should be stored in a refrigerator (2°C- 8°C). If not used within 6 hours it should be discarded.[1]

SHINGRIX is supplied in 2 vials for reconstitution: 1 vial of antigen should be reconstituted with 1 accompanying vial of adjuvant suspension.[1]

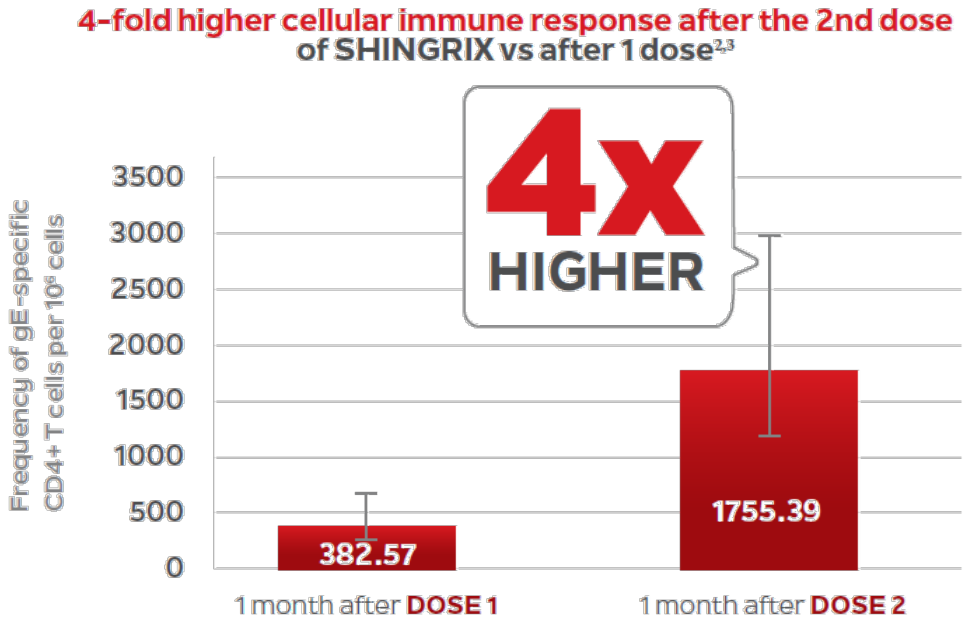
SHINGRIX is for intramuscular injection only.[1]

Shingrix is indicated for prevention of herpes zoster (HZ) and postherpetic neuralgia (PHN), in
• adults 50 years of age or older

Contraindications: Hypersensitivity to the active substances or to any of the excipients.
Limitations of Use: SHINGRIX is not indicated for the prevention of primary varicella infection (chickenpox).[1]

Note: The vial stoppers are made of butyl rubber.
HZ=herpes zoster; PHN=post-herpetic neuralgia
1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09\2023

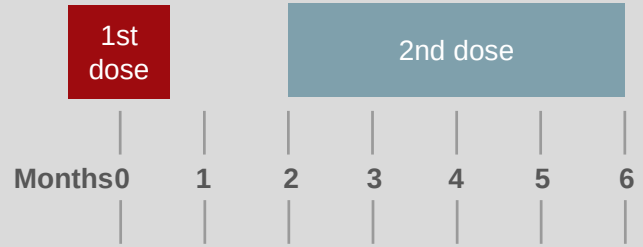
TWO DOSES OF SHINGRIX ARE REQUIRED TO INDUCE STRONG IMMUNE RESPONSE AGAINST VZV[1]



Vaccination schedule consists of initial dose followed by a second dose 2 months later[1]

If flexibility is necessary, the second dose can be administered between 2 and 6 months after the first dose[1]

For Adults 50 years of age or older



The figure is reproduced from López-Fauqued M et al. Vaccine 2019

Median gE-specific CD4+ T cell expressing at least two activation markers per 10 cells (Q1, Q3) was 122.18 (62.3-290.22) at baseline, 382.57 (236.79-615.51) at 1 month after dose 1, and 1755.39 (1210.8-2987.71) at 1 month after dose 2. *Data in subjects 60+. CD4=cluster of differentiation4, gE=glycoprotein E; HZ=herpes zoster; VZV=varicella zoster virus.

1. SHINGRIX Egyptian Drug Authority Approved Leaflet 11/9/2023 2. Chlibeck 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 Mar;32(15):1745-53. doi.org/10.1016/j.vaccine.2014.01.019 3. Chlibeck R, Smetana J, Pauksens K, et al. Safety and immunogenicity of three different formulations of an djuvanted varicella-zoster virus subunit candidate vaccine in older adults: a phase II, randomized, controlled study [webappendix]. Vaccine. 2014 Mar;32(15):1745-53. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0264410X14000516?via%3Dihub, Accessed September 3, 2023

DATA SUPPORT CO-ADMINISTRATION WITH THE FOLLOWING VACCINES

- ✓ **Influenza** (unadjuvanted inactivated seasonal)[1]
- ✓ **Pneumococcal** (PPV23)[1]
- ✓ **Diphtheria-Tetanus-Pertussis** (Tdap)[1]

Co-administration generally well tolerated[2]

No safety issue raised[2]

No immunologic interference observed[2]

PPV23=23-valent pneumococcal polysaccharide vaccine; Tdap=tetanus, diphtheria and acellular pertussis vaccine.

1 SHINGRIX Egyptian Drug Authority Approved Leaflet 11/9/2023. **2. Maréchal C, Lal H, Poder A, Ferguson M, Enweonye I, Heineman TC, Hervé C, Rheault P, Talli J, Wauters D, Oostvogels L. 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 Jul 5;36(29):4278-86.**.

CURRENT GUIDELINES AND RECOMMENDATIONS FOR SHINGRIX IN ADULTS 50+*

General Population (≥50 years of age)

- US Advisory Committee on Immunization Practices[1]
- Canadian National Advisory Committee on Immunization [2]

Common Comorbidities

Diabetes Mellitus

- American Diabetes Association (2024)[3]

Chronic Obstructive Pulmonary Disease (COPD)

- Global Initiative for Chronic Obstructive Lung Disease (GOLD) (2024) [4]

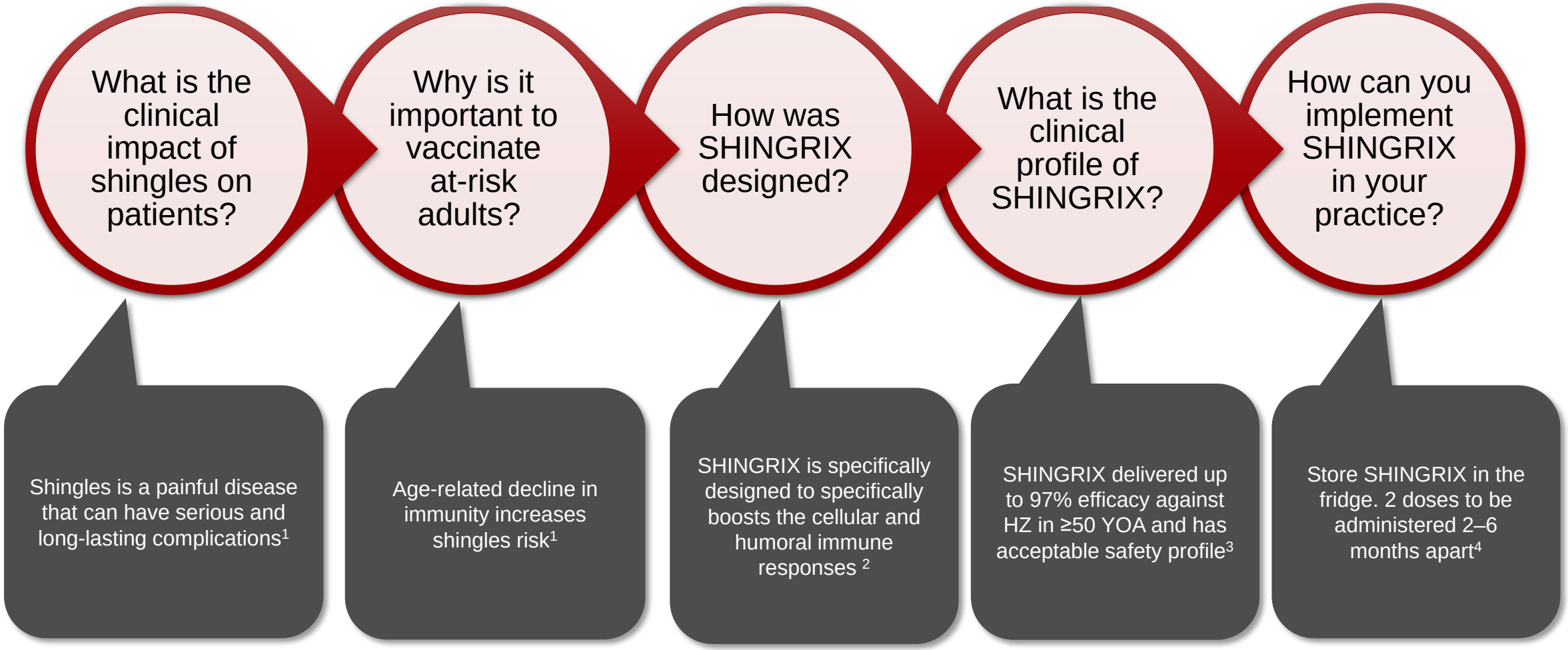
Asthma

- US Advisory Committee on Immunization Practices (2022)[1]

*Disclaimer: The following table is inclusive but not an exhaustive list or all society recommendations for recombinant zoster vaccine or protection against shingles
.

References :1. Anderson TC. Use of recombinant zoster vaccine in immunocompromised adults aged≥ 19 years: recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR. Morbidity and Mortality Weekly Report. 2022;71. 2. Public Health Agency of Canada. An advisory committee statement (ACS) National Advisory Committee On Immunization (NACI):updated recommendations of the Use of Herpes Zoster Vaccines. https://www.canada.ca/en/services/health/publications/healthy-living/updated-recommendations-use-herpes-zoster-vaccines.html Accessed December 17, 2023.
. 3. American Diabetes Association Professional Practice Committee. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S52-S76. doi: 10.2337/dc24-S004. PMID: 38078591; PMCID: PMC10725809. 4. 2024 Gold Report - Global Initiative for Chronic Obstructive Lung Disease. 2024. Available from: https://goldcopd.org/2023-gold-report-2/Accessed 7 April 2024 ..

SUMMARY



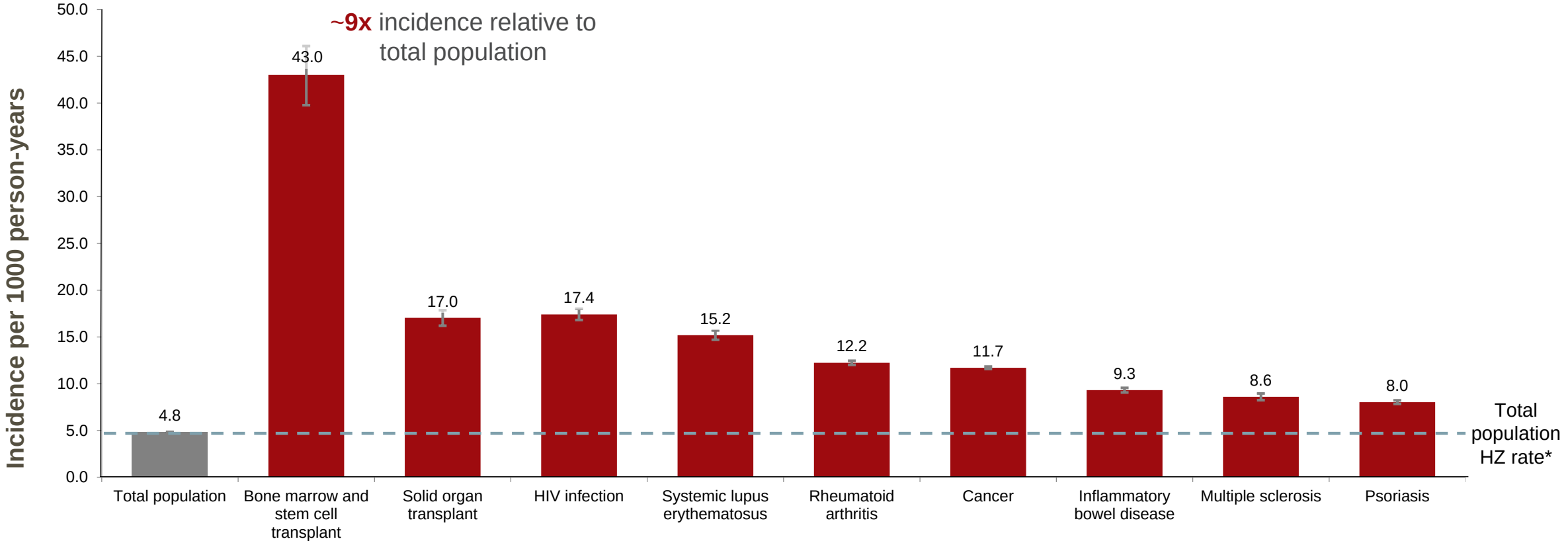
*US data. May not be representative of global population.
HZ=herpes zoster; YOA=years of age

1. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report: Recommendations and Reports. 2008 Jun 6;57(5):1-30. 2. Lecrenier N, Beukelaers P, Colindres R, Curran D, De Kesel C, De Saegher JP, Didierlaurent AM, Ledent EY, Mols JF, Mrkvan T, Normand-Bayle M. Development of adjuvanted recombinant zoster vaccine and its implications for shingles prevention. Expert review of vaccines. 2018 Jul 3;17(7):619-34. 3. Lal H, Cunningham AL, Heineman TC. Adjuvanted herpes zoster subunit vaccine in older adults. The New England journal of medicine. 2015 Oct 1;373(16):1576-7. 4. SHINGRIX Egyptian Drug Authority Approved Leaflet 11/9/2023

SHINGRIX Vaccination for Immunocompromised Patients

INCIDENCE OF SHINGLES IS HIGHER IN IC PATIENTS COMPARED WITH THE GENERAL POPULATION[1*]

Adults ≥18 YOA

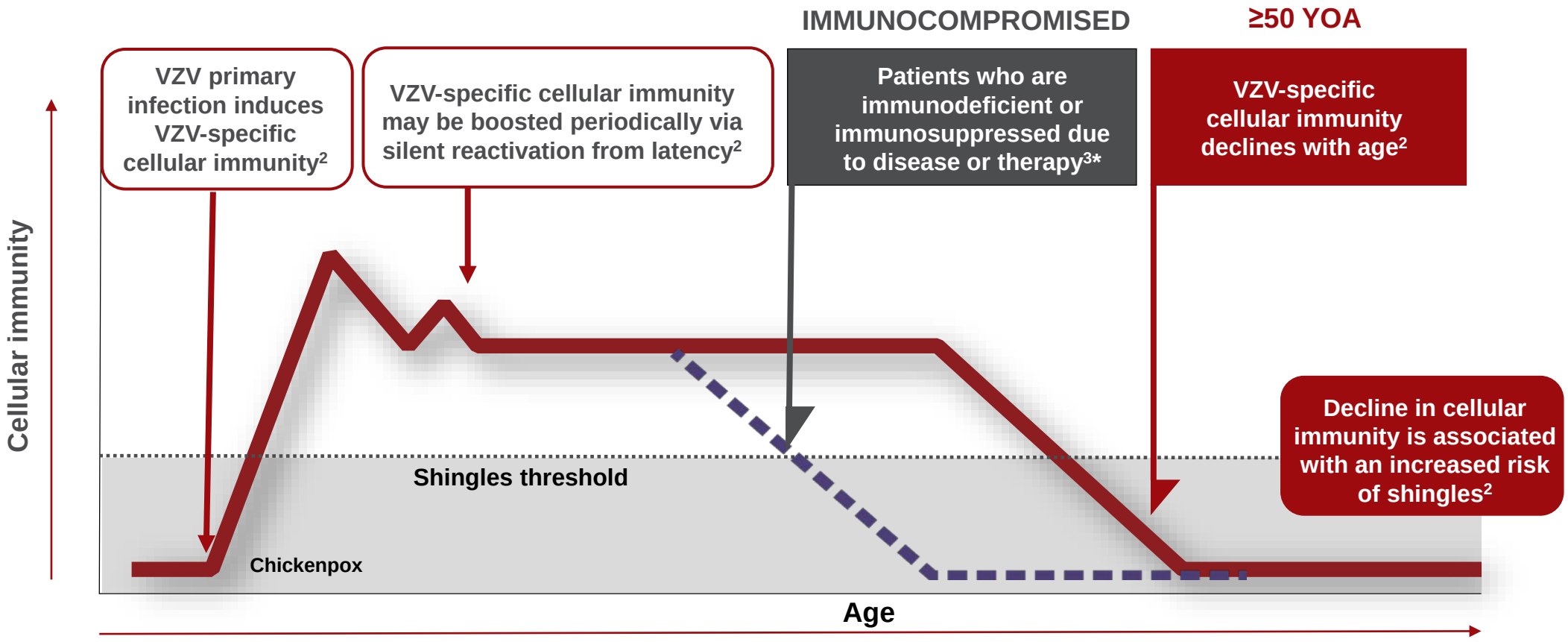


HIV=human immunodeficiency virus; HZ=herpes zoster; IC=immunocompromised; YOA=years of age.
*Total population from age 18. Mean age 43 YOA

This graph has been independently created by GSK from data first published in Infection.

1. Chen SY, Suaya JA, Li Q, Galindo CM, Misurski D, Burstin S, Levin MJ. Incidence of herpes zoster in patients with altered immune function. Infection. 2014 Apr;42:325-34..

AGE-RELATED DECLINE IN IMMUNITY AND IMMUNOSUPPRESSION INCREASES SHINGLES RISK[1]*



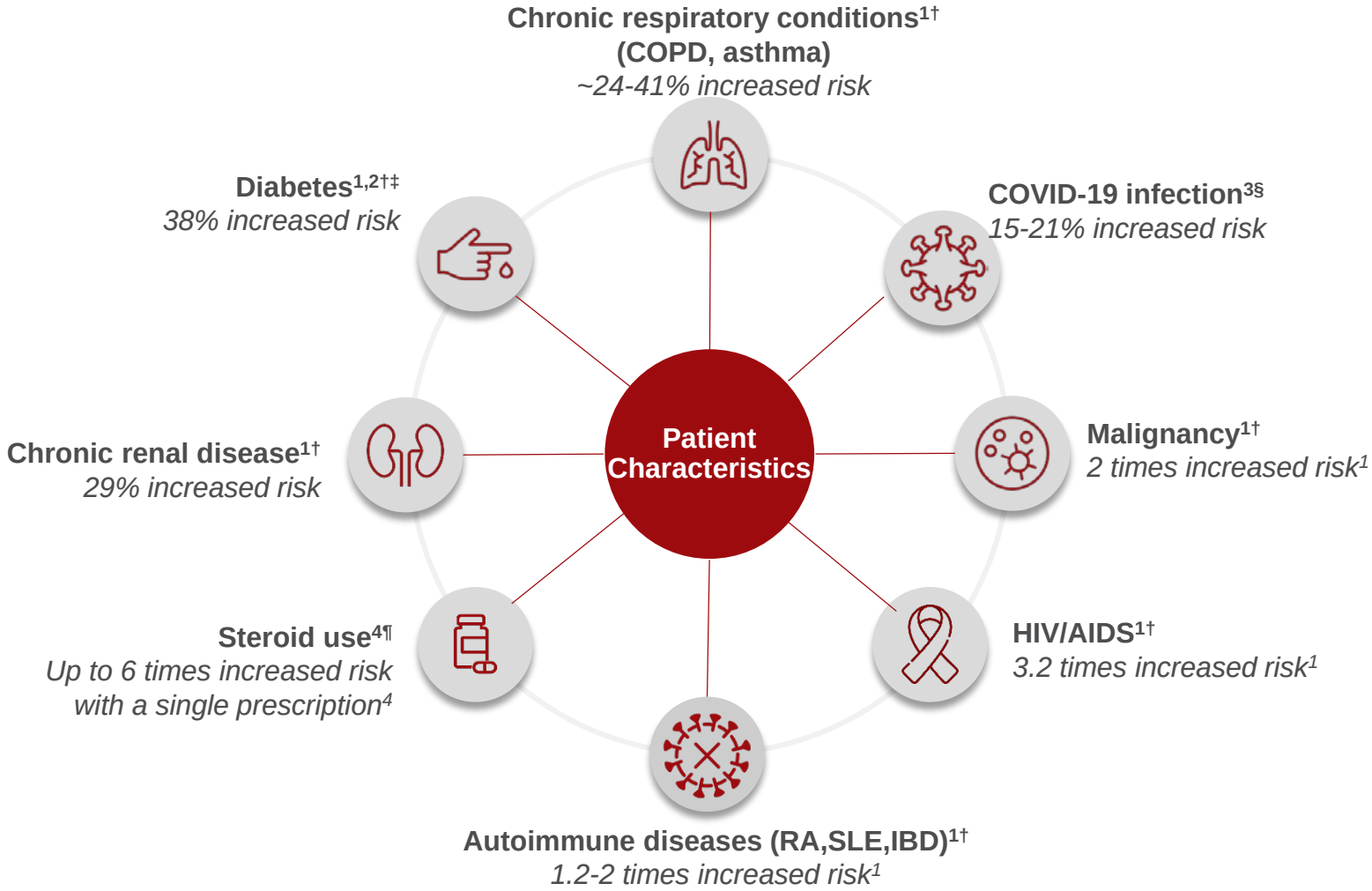
This illustration has been independently created by GSK from information first published in the New England Journal of Medicine.

Adapted From Reference 2

*Immunodeficiency caused by medical conditions or immunosuppressive medications may also increase the risk of shingles.[1]
VZV=varicella-zoster virus; YOA=years of age.

1 Anderson TC, Masters NB, Guo A, Shepersky L, Leidner AJ, Lee GM, Kotton CN, Dooling KL. Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022 Jan 21;71(3):80-84.2. Kimberlin DW, Whitley RJ. Varicella–zoster vaccine for the prevention of herpes zoster. New England Journal of Medicine. 2007 Mar 29;356(13):1338-43. 3. Dworkin RH, Johnson RW, Breuer J, Gnann JW, Levin MJ, Backonja M, Betts RF, Gershon AA, Haanpää ML, McKendrick MW, Nurmikko TJ. Recommendations for the management of herpes zoster. Clinical infectious diseases. 2007 Jan 1;44(Supplement_1):S1-26

ON TOP OF AGE, A VARIETY OF OTHER FACTORS CAN FURTHER ELEVATE PATIENTS' RISK OF SHINGLES[1*]



*List of risk factors is not exhaustive and presented HZ risk may vary with age. †Meta-analysis of 88 studies (N=198,751,846); estimates based on risk ratio and age ranged from 3 months to 104 years.[1] ‡Meta-analysis of 16 studies (N=65,541,845); estimates based on risk ratio and age was ≥18 years.[2] §Retrospective cohort study of individuals ≥50 years of age (N=394,677); adjusted incidence rate ratios were estimated by Poisson regression.[3] ¶Prospective population-based study of adults ≥45 years of age (n=20,048) on new systemic corticosteroid users with a median equivalent systemic prednisolone dose of 300 mg[4]; ; HIV, human immunodeficiency virus; IBD, inflammatory bowel disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus .

ON TOP OF AGE, A VARIETY OF OTHER FACTORS CAN FURTHER ELEVATE PATIENTS' RISK OF SHINGLES[1*]

References:
1. Marra F, Parhar K, Huang B, Vadlamudi N. Risk Factors for Herpes Zoster Infection: A Meta-Analysis. Open Forum Infect Dis. 2020 Jan 9;7(1):ofaa005.
2. Huang CT, Lee CY, Sung HY, Liu SJ, Liang PC, Tsai MC. Association Between Diabetes Mellitus and the Risk of Herpes Zoster: A Systematic Review and Meta-analysis. J Clin Endocrinol Metab. 2022 Jan 18;107(2):586-59
3 .Bhavsar A, Lonnet G, Wang C, Chatzikonstantinidou K, Parikh R, Brabant Y, Servotte N, Shi M, Widenmaier R, Aris E. Increased Risk of Herpes Zoster in Adults ≥50 Years Old Diagnosed With COVID-19 in the United States. Open Forum Infect Dis. 2022 Mar 9;9(5):ofac118.
4 .Qian J, Banks E, Macartney K, Heywood AE, Lassere MN, Liu B. Corticosteroid Use and Risk of Herpes Zoster in a Population-Based Cohort. Mayo Clin Proc. 2021 Nov;96(11):2843-2853.

IC PATIENTS INCLUDING THOSE WITH CANCER HAVE A HIGHER RISK OF HZ COMPLICATIONS[1]

Up to 40% of haematological malignancy and solid tumour patients with HZ develop PHN[2]*

Disseminated zoster was reported in 19.3% and 8.5% of hematological malignancy and solid tumor patients, respectively[3]†

Disseminated zoster can be life-threatening, with a mortality rate up to 50% in IC patients[4]‡

Image reproduced from Dworkin RH et al. Clin Infect Dis 2007;44:S1–26 with permission from Oxford University Press

*Systematic review of studies (N=32) examining risk of HZ and its complications in adult patients with hematopoietic stem cell transplants (HSCT), cancer (HM and ST), HIV, and SOT (kidney and other). PHN was reported in then range of 6–40% in HM and ST studies (n=4).[2] †Retrospective cohort study of members of Kaiser Permanente Northern California newly diagnosed with invasive cancer (N=14,670). Median follow-up of 22 months, 590 potential cases of HZ were identified. Disseminated zoster was defined as HZ rash ≥2 dermatomes.[3] ‡Disseminated VZV is observed more frequently in HSCT recipients compared with those patients undergoing conventional chemotherapy strategies .HIV=human immunodeficiency virus; HM=haematologic malignancies; HSCT=haematopoietic stem cell transplantation; HZ=herpes zoster; IC=immunocompromised; PHN=post-herpetic neuralgia; SOT=solid organ transplant; ST=solid tumour.

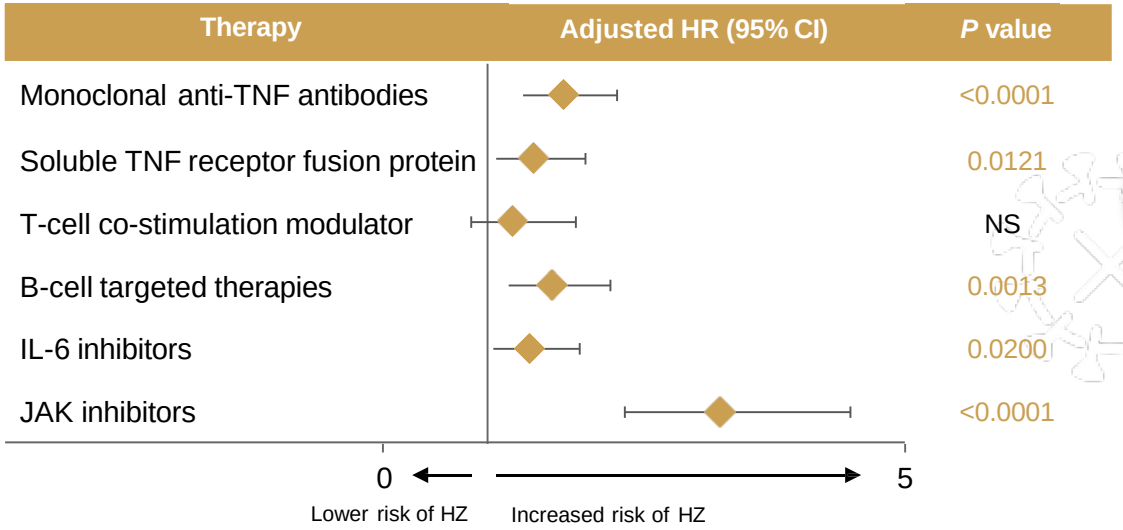
IC PATIENTS INCLUDING THOSE WITH CANCER HAVE A HIGHER RISK OF HZ COMPLICATIONS[1]

References

1. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, Orrico-Sánchez A. Herpes zoster risk and burden of disease in immunocompromised populations: a population-based study using health system integrated databases, 2009–2014. BMC infectious diseases. 2020 Dec;20:1-4. 2. McKay SL, Guo A, Pergam SA, Dooling K. Herpes zoster risk in immunocompromised adults in the United States: a systematic review. Clinical Infectious Diseases. 2020 Oct 1;71(7):e125-34. 3. Habel LA, Ray GT, Silverberg MJ, Horberg MA, Yawn BP, Castillo AL, Quesenberry Jr CP, Li Y, Sadier P, Tran TN. The epidemiology of herpes zoster in patients with newly diagnosed cancer. Cancer epidemiology, biomarkers & prevention. 2013 Jan 1;22(1):82-90. 4.Okuma HS, Kobayashi Y, Makita S, Kitahara H, Fukuhara S, Munakata W, Suzuki T, Maruyama D, Tobinai K. Disseminated herpes zoster infection initially presenting with abdominal pain in patients with lymphoma undergoing conventional chemotherapy: A report of three cases. Oncol Lett. 2016 Aug;12(2):809-814

RHEUMATOID ARTHRITIS TREATMENTS ARE ASSOCIATED WITH AN INCREASED RISK AND SEVERITY OF HERPES ZOSTER[1]

Rheumatoid arthritis medications differentially increase the risk of HZ[1*]



The same results were first published in Redeker I et al. 2022. The graph has been independently created by GSK from the original data published in Redeker I et al. 2022

Up to 40% of HZ cases in rheumatoid arthritis patients receiving biological treatment are severe[2†]

- Use of biological therapy is associated with an increased risk of severe HZ vs non-biologicals.
- The use of corticosteroids showed a strong dose-dependent association with HZ (p<0.001).
- Patients with RA taking specific non-biological medications (eg, methotrexate,) were similar or slightly less prone to develop HZ than patients taking anti-TNF biological medications
- Patients in biologicals medication groups had a shorter time period for HZ occurrence than those in the non-biologicals group (p<0.001).[2]

The risk of HZ complications and recurrence is also higher in patients with rheumatoid arthritis versus the general population[2]

*Prospective observational study (N=13,991) results of Anderson-Gill model without IPW. Adjusted regression analyses with csDMARD treatment used as reference. Weights were estimated using variables age, sex, disease duration, DAS28, FFbH, previous treatment with bDMARDs/tsDMARDs and osteoporosis. †Severe HZ defined as the need for IV antiviral treatment or HZ ophthalmicus (Anti-TNF=25.5%; non-anti-TNF=40.0%; non-biologicals=11%). bDMARD=biologic disease-modifying anti-rheumatic drug; CI=confidence interval; csDMARD=conventional synthetic disease-modifying anti-rheumatic drug; DAS28=Disease Activity Score of 28 joints; DMARD=disease-modifying anti-rheumatic drug; FFbH=Hannover Functional Status Questionnaire; HR=hazard ratio; HZ=herpes zoster; IL-6=interleukin 6; IPW=inverse probability weights; IV= intravenous; JAK=Janus kinase; NS=not significant; TNF=tumour necrosis factor; tsDMARD=targeted synthetic disease-modifying anti-rheumatic drug.

RHEUMATOID ARTHRITIS TREATMENTS ARE ASSOCIATED WITH AN INCREASED RISK AND SEVERITY OF HERPES ZOSTER[1]

References :
1. Redeker I, Albrecht K, Kekow J, Burmester GR, Braun J, Schäfer M, Zink A, Strangfeld A. Risk of herpes zoster (shingles) inpatients with rheumatoid arthritis under biologic, targeted synthetic and conventional synthetic DMARD treatment: data from the German RABBIT register. Annals of the Rheumatic Diseases. 2022 Jan 1;81(1):41-7.
2. Liao TL, Chen YM, Liu HJ, Chen DY. Risk and severity of herpes zoster in patients with rheumatoid arthritis receiving different immunosuppressive medications: a case–
control study in Asia. BMJ open. 2017 Jan 1;7(1):e014032.

SHINGRIX WAS ALSO INVESTIGATED IN 5 IMMUNOCOMPROMISED POPULATIONS (ADULTS ≥18 YEARS OF AGE)

HUMAN IMMUNODEFICIENCY VIRUS[1]

Living with HIV

AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANT[2]

Post transplant

HAEMATOLOGIC MALIGNANCIES[3]

Receiving immunosuppressive chemotherapy*

RENAL TRANSPLANTS[4]

Post-renal transplant

SOLID TUMOUR[5]

Receiving immunosuppressive chemotherapy

Trial	Zoster-015	Zoster-002	Zoster-039	Zoster-041	Zoster-028
Phases	Phase 1/2a (N=123)	Phase 3 (N=1846)	Phase 3 (N=562)	Phase 3 (N=264)	Phase 2/3 (N=232)
Trial Type	Placebo controlled, ≥18 years of age				
Endpoints	**Immuno/Safety**	**Efficacy/Immunogenicity/Safety**		**Immunogenicity/Safety**	
Dose Timeline	Month 0, 2, 6 (3 doses)	Month 0, 1-2	Month 0, 1-2	Month 0, 1-2	Month 0, 1-2

*Efficacy was measured in post-hoc analysis.[3] HIV=human immunodeficiency virus; HZ=herpes zoster :

SHINGRIX WAS ALSO INVESTIGATED IN 5 IMMUNOCOMPROMISED POPULATIONS (ADULTS ≥18 YEARS OF AGE)

References:

1. Berkowitz EM, Moyle G, Stellbrink HJ, Schürmann D, Kegg S, Stoll M, El Idrissi M, Oostvogels L, Heineman TC, Zoster-015 HZ/su Study Group, Brockmeyer N. 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 Apr 15;211(8):1279-87.
2. Bastidas A, De La Serna J, El Idrissi M, Oostvogels L, Quittet P, López-Jiménez J, Vural F, Pohlreich D, Zuckerman T, Issa NC, Gaidano G. Effect of recombinant zoster vaccine on incidence of herpes zoster after autologous stem cell transplantation: a randomized clinical trial. Jama. 2019 Jul 9;322(2):123-33.
3. Dagnew AF, Ilhan O, Lee WS, Woszczyk D, KwakJY, Bowcock S, Sohn SK, Macías GR, Chiou TJ, Quiel D, Aoun M. Immunogenicity and safety of the adjuvanted recombinantzoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. TheLancet infectious diseases. 2019 Sep 1;19(9):988-1000.
4. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, Kim SJ, Kim SI,Zaltzman J, Ortiz F, Campistol Plana JM, Fernandez Rodriguez AM, Rebollo Rodrigo H, Campins Marti M. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in chronically immunosuppressed adults following renal transplant: a phase 3, randomized clinical trial. Clinical Infectious Diseases. 2020 Jan 2;70(2):181-90.
5. Vink P, Zoster-028 Study Group. Immunogenicity and safety of a candidate subunit adjuvanted herpes zoster vaccine in adults with solid tumors vaccinated before or during immunosuppressive chemotherapy treatment: a phase II/III, randomized clinical trial. InOpen Forum Infectious Diseases 2017 (Vol. 4, No. suppl_1, pp. S417-S418). US: Oxford University Press

SHINGRIX DEMONSTRATED EFFICACY AMONG PATIENTS WITH au-HSCT AND HM[1]

AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANT (auHSCT)[1]

Post transplant

Vaccine efficacy against HZ by age (95% CI)[1]	
Aged ≥18 years (SHINGRIX n/N:49/870; placebo n/N;135/851)	68.2% (55.5-77.6)
Aged 18-49 years (SHINGRIX n/N:9/213; placebo n/N;29/212)	**71.8%** (38.7-88.3)
Aged ≥50 years (SHINGRIX n/N:40/657; placebo n/N;106/639)	**67.3%** (52.6-77.9)

HAEMATOLOGIC MALIGNANCIES[2]

Receiving immunosuppressive chemotherapy

Post hoc vaccine efficacy against Shingles (95% CI)[2]	
Aged ≥18 years (SHINGRIX n/N:2/259; placebo n/N;14/256)	**87.2%** (44.3-98.6)

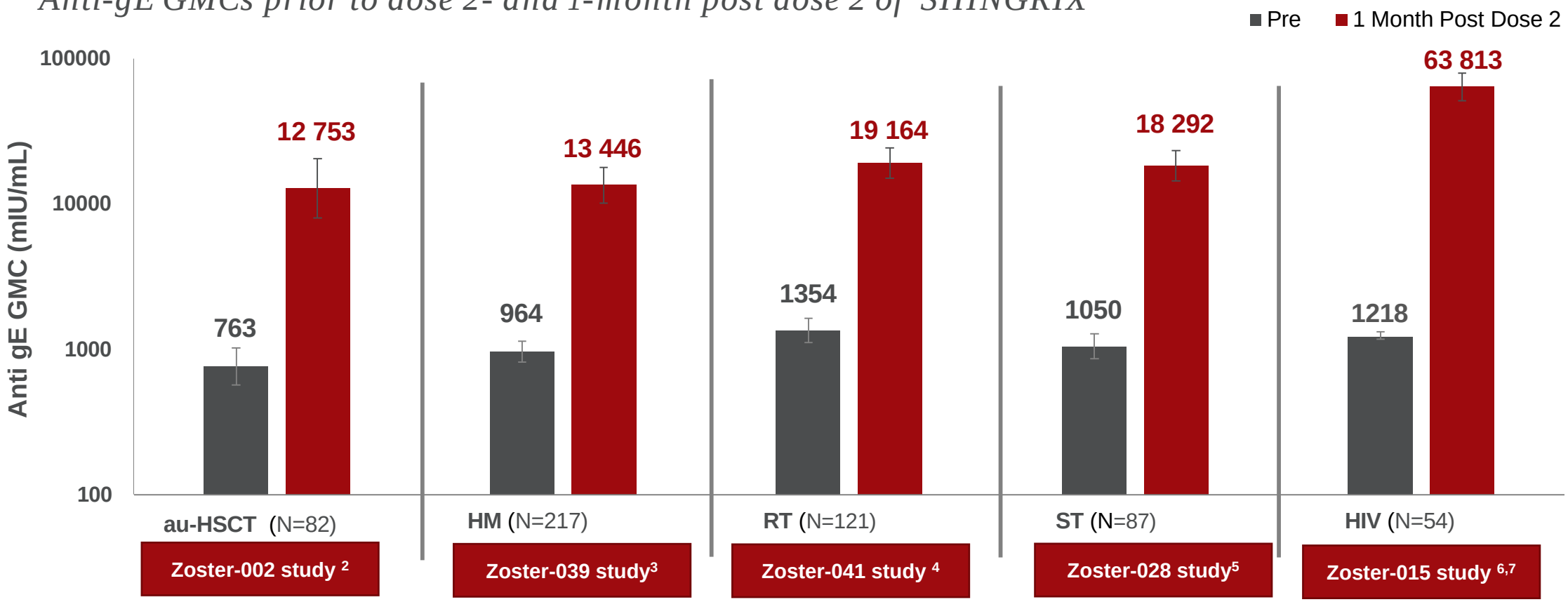
An immunological correlate of protection has not been established, therefore the level of immune response that provides protection against HZ is unknown.[2]

Au-HSCT= AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANT :HM = HAEMATOLOGIC MALIGNANCIES : HZ=HERPES ZOSTER

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09/2023

SHINGRIX ELICITED HUMORAL-MEDIATED IMMUNE RESPONSES ACROSS PHASE II/III TRIALS IN IMMUNOCOMPROMISED POPULATIONS[1,*]

Anti-gE GMCs prior to dose 2- and 1-month post dose 2 of SHINGRIX



*Each population was evaluated in a separate study.[1]

Figure independently created by GSK from the original data reported in: a) Dagnew AF, et al. Immunogenicity of the Adjuvanted Recombinant Zoster Vaccine in Immunocompromised Adults. IDWeek 2020; and b) GlaxoSmithKline.

Au-HSCT=autologous-haematopoietic stem cell transplant; gE=glycoprotein E; GMC=geometric mean concentration; HIV=human immunodeficiency virus; HM=haematologic malignancy; RT=renal transplant; ST=solid tumour.

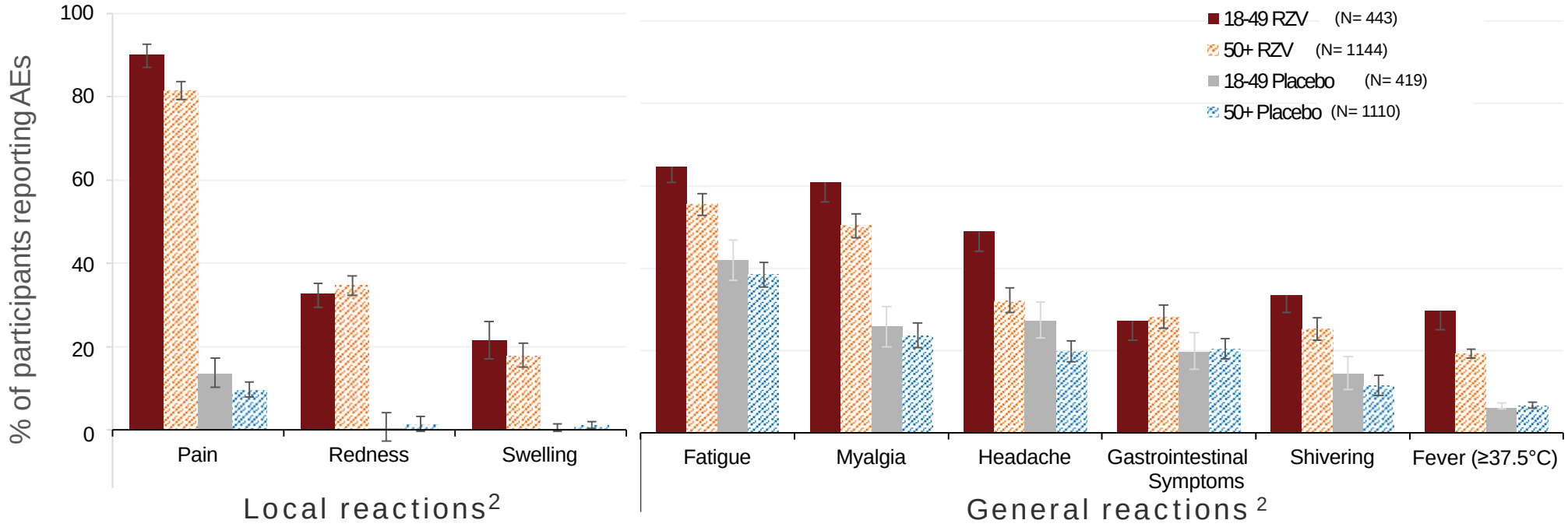
SHINGRIX ELICITED HUMORAL-MEDIATED IMMUNE RESPONSES ACROSS PHASE II/III TRIALS IN IMMUNOCOMPROMISED POPULATIONS[1,*]

References

1. SHINGRIX Egyptian Drug Authority Approved Prescribing information 11/9/2023.
2. Bastidas A, De La Serna J, El Idrissi M, Oostvogels L, Quittet P, López-Jiménez J, Vural F, Pohlreich D, Zuckerman T, Issa NC, Gaidano G. Effect of recombinant zoster vaccine on incidence of herpes zoster after autologous stem cell transplantation: a randomized clinical trial. Jama. 2019 Jul 9;322(2):123-33.
3. Dagnew AF, Ilhan O, Lee WS, Woszczyk D, Kwak JY, Bowcock S, Sohn SK, Macías GR, Chiou TJ, Quiel D, Aoun M. 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. The Lancet infectious diseases. 2019 Sep 1;19(9):988-1000.
4. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, Kim SJ, Kim SI,Zaltzman J, Ortiz F, Campistol Plana JM, Fernandez Rodriguez AM, Rebollo Rodrigo H, Campins Marti M. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in chronically immunosuppressed adults following renal transplant: a phase 3, randomized clinical trial. Clinical Infectious Diseases. 2020 Jan 2;70(2):181-90.
5. Vink P, Zoster-028 Study Group. Immunogenicity and safety of a candidate subunit adjuvanted herpes zoster vaccine in adults with solid tumors vaccinated before or during immunosuppressive chemotherapy treatment: a phase II/III, randomized clinical trial. InOpen Forum Infectious Diseases 2017 (Vol. 4, No. suppl_1, pp. S417-S418). US: Oxford University Press
6. Berkowitz EM, Moyle G, Stellbrink HJ, Schürmann D, Kegg S, Stoll M, El Idrissi M, Oostvogels L, Heineman TC, Zoster-015 HZ/su Study Group, Brockmeyer N. 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 Apr 15;211(8):1279-87
7. Supplementry of Berkowitz EM, Moyle G, Stellbrink HJ, Schürmann D, Kegg S, Stoll M, El Idrissi M, Oostvogels L, Heineman TC, Zoster-015 HZ/su Study Group, Brockmeyer N. 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 Apr 5;211(8):1279-87

SHINGRIX HAS CLINICALLY ACCEPTABLE SAFETY PROFILE IN IC PATIENTS[1]

In pooled analysis of six trials in IC patients[1^]
Most vaccination reactions were mild to moderate, with a median duration of 1-3 days[1*]



The incidence of unsolicited AEs, SAEs, fatal SAEs, and pIMDs showed no significant difference between RZV and placebo groups[1]

IC: Immunocompromised, RZV: Recombinant Zoster vaccine , AE: Adverse Events , SAEs: Seriuos Adverse Events ,pIMDs : potential immune-mediated diseases .

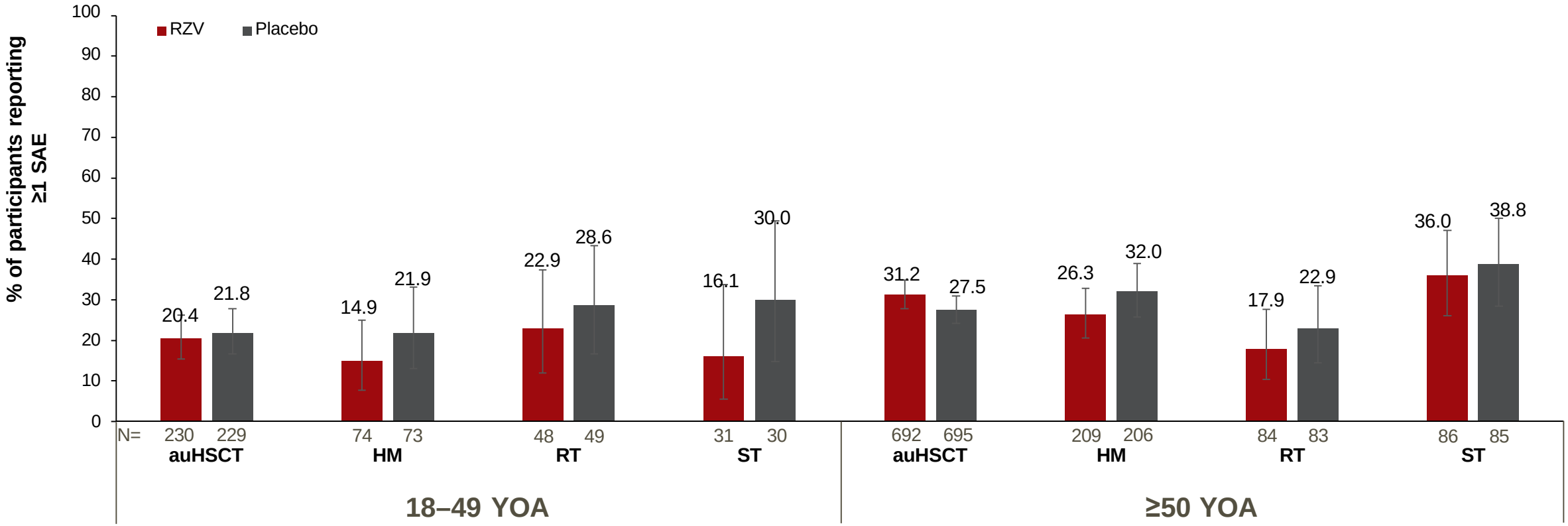
SHINGRIX HAS CLINICALLY ACCEPTABLE SAFETY PROFILE IN IC PATIENTS[1,2]

References

1. Lopez-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;37:2482-93.
2. Lopez-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 [supplement]. Vaccine. 2019;37:2482-93. Available from: https://www.sciencedirect.com/science/article/pii/S0264410X19303779?via%3Dihub#s0100, Accessed September 3, 2023.

SERIOUS ADVERSE EVENTS (SAES)

Percentage of participants reporting ≥1 SAE from dose 1 until 1-year post-last dose per study – TVC[1]



Percentage of adults with ≥1 SAE, causally related SAEs, fatal SAEs and pIMDs between RZV and placebo and between age groups

The same results were first published in López-Fauqued M et al. 2020. The figure has been independently created by GSK from the original data published in López-Fauqued M et al. 2020. Error bars represent 95% CI. Each population was evaluated in a separate study. **There are no head-to-head comparisons between immunocompromised populations.**
auHSCT=autologous hematopoietic stem cell transplant; CI=confidence interval; HM=hematological malignancies; pIMD=potential immune-mediated disease; RT=renal transplant; RZV=recombinant zoster vaccine; SAE=serious adverse event; ST=solid tumours; TVC=total vaccinated cohort; YOA=years of age.

SERIOUS ADVERSE EVENTS (SAES)

References

1. Lopez-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;37:2482-93.

Storage and Administration

SHINGRIX should be refrigerated. DO NOT FREEZE. Store in a refrigerator (2° C - 8° C). After reconstitution, SHINGRIX is stable for 6 hours when kept in a refrigerator (2° C - 8° C).[1]

SHINGRIX is supplied in 2 vials for reconstitution: 1 vial of antigen should be reconstituted with 1 accompanying vial of adjuvant suspension.[1]

SHINGRIX is for intramuscular injection only.[1]

Shingrix is indicated for prevention of herpes zoster HZ and PHN in
- adults 50 years of age or older;
- adults 18 years of age or older at increased risk of HZ[1]

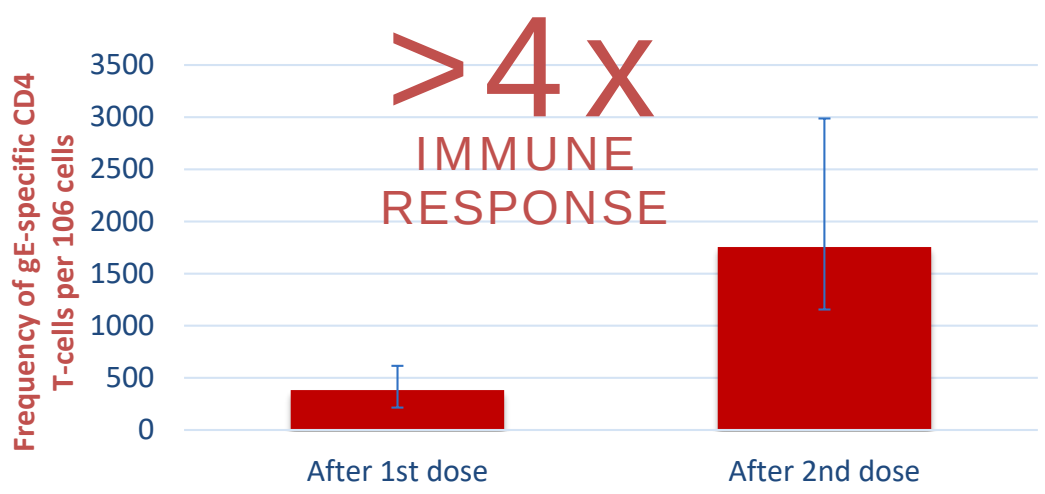
Contraindications: Hypersensitivity to the active substances or to any of the excipients.
Limitations of Use: SHINGRIX is not indicated for the prevention of primary varicella infection (chickenpox).[1]

Note: The vial stoppers are not made with natural rubber latex. HZ=herpes zoster, PHN=postherpetic neuralgia

Reference: 1 SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09/2023

Two doses of SHINGRIX are required to induce strong immune response against VZV[1]

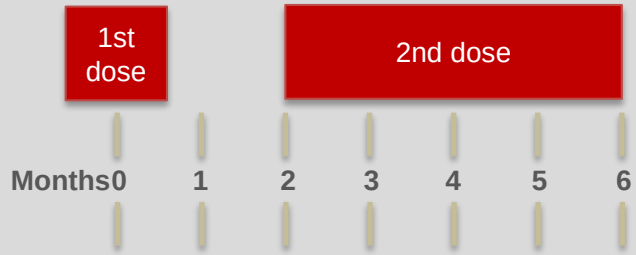
2 doses of SHINGRIX generated a >4x increase in cellular immune response vs to 1 dose[2*]



The same results were first published in Vaccine. Figure independently created by GSK from the original data published in Chlibek R, et al. 2014.[2]

Vaccination Schedule consistes of initial dose followed by a second dose 2 months later[1]
If flexibility is necessary, the second dose can be administered between 2 and 6 months after the first dose[1]

For Adults 50 years of age or older



For subjects who are or might become immunodeficient or immunosuppressed due to disease or therapy[1]

(1 – 2 months after 1st dose)

Shortter vaccination Schedule

An immunological correlate of protection has not been established; therefore, the level of immune response that provides protection against HZ is unknown.[1]
*Data in subjects 60+. CD4=cluster of differentiation 4; gE=glycoprotein E; HZ=herpes zoster; VZV=varicella zoster virus.

References: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date 11/09/2023]; **2**. Chlibek R, Smetana J, Pauksens K,. 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 Mar 26;32(15):1745-53.

CURRENT GUIDELINES AND RECOMMENDATIONS FOR SHINGRIX*

General Population (≥50 years of age)

- US Advisory Committee on Immunization Practices (2022)[1]
- Canadian National Advisory Committee on Immunization (2018)[2]

Common Comorbidities

Diabetes Mellitus
- American Diabetes Association (2024) [8]

Chronic Obstructive Pulmonary Disease (COPD)
- Global Initiative for Chronic Obstructive Lung Disease (GOLD) (2024)[9]

Asthma
- US Advisory Committee on Immunization Practices (2022)[1]

Autoimmune Diseases

Rheumatoid Arthritis
- European League Against Rheumatism (EULAR) 2019 [3]

Inflammatory Bowel Disease
- American College of Gastroenterology 2017 [4]
- Crohn's and Colitis Foundation 2017 [5]
- European Crohn's and Colitis Organization (ECCO) Guidelines 2021 [6]

Rheumatic and Musculoskeletal Diseases

American College of Rheumatology (2022) [7]

Immunocompromised (≥18/50 years of age)

Cancer
- US Advisory Committee on Immunization Practices (2022) [1]

Solid Organ/Renal Transplant
- US Advisory Committee on Immunization Practices (2022) [1]
- American Society of Transplantation (2019)[10]

Human Immunodeficiency Virus
- US Advisory Committee on Immunization Practices (2022) [1]
- European AIDS Clinical Society (2024)[11]

Multiple Myeloma
- European Myeloma Network (2020) [12]

*Disclaimer: The following table is inclusive but not an exhaustive list or all society recommendations for recombinant zoster vaccine or protection against shingles
AIDS=Acquired immune deficiency syndrome; NCCN=National Comprehensive Cancer Network

References

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SHINGRIX (ZOSTER VACCINE RECOMBINANT, ADJUVANTED) IMPORTANT SAFETY INFORMATION[1]

Dosage and Administration:

For intramuscular injection only, preferably in the deltoid muscle. The use of Shingrix should be in accordance with official recommendations:
• **Adults:** The primary vaccination schedule consists of two doses of 0.5 mL each: an initial dose followed by a second dose 2 months later. If flexibility in the vaccination schedule is necessary, the second dose can be administered between 2 and 6 months after the first dose.

• **Immunodeficient or Immunosuppressed Subjects**, and who would benefit from a shorter vaccination schedule, the second dose can be given 1 to 2 months after the initial dose.

The need for booster doses following the primary vaccination schedule has not been established.

Important Safety Information

• SHINGRIX is contraindicated in anyone with hypersensitivity to the active substances or to any of the excipients.
• As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.
• SHINGRIX should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration to these subjects.
• Syncope (fainting) can be associated with the administration of injectable vaccines, including SHINGRIX. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

• In a post-marketing observational study in individuals aged 65 years or older, an increased risk of Guillain-Barre syndrome (estimated 3 excess cases per million doses administered) was observed during the 42 days following vaccination with SHINGRIX. Available information is insufficient to determine a causal relationship with SHINGRIX.
• In adults aged 50 years and above, the most frequently reported adverse reactions were pain at the injection site (68.1% overall/dose; 3.8% severe/dose), myalgia (32.9% overall/dose; 2.9% severe/dose, fatigue (32.2% overall/dose; 3.0% severe/dose) and headache (26.3% overall/dose; 1.9% severe/dose). Most of these reactions were not long lasting (median duration of 2 to 3 days). Reactions reported as severe lasted 1 to 2 days.
• In adults ≥ 18 years of age who are immunodeficient or immunosuppressed due to disease or therapy (referred to as immunocompromised (IC)), the safety profile was consistent with that observed in adults ≥50 years of age. There are limited data in adults aged 18-49 years at increased risk of HZ who are not IC.

• Overall, there was a higher incidence of some adverse reactions in younger age groups:
- studies in IC adults ≥ 18 years of age (pooled analysis): the incidence of pain at the injection site, fatigue, myalgia, headache, shivering and fever
was higher in adults aged 18-49 years compared to those aged 50 years and above.
- studies in adults ≥ 50 years of age (pooled analysis): the incidence of myalgia, fatigue, headache, shivering, fever and gastrointestinal symptoms was higher in adults aged 50-69 years compared to those aged 70 years and above.
• There are no data from the use of SHINGRIX in pregnant women. As a precautionary measure, it is preferable to avoid the use of SHINGRIX during pregnancy. It is unknown whether SHINGRIX is excreted in human milk.
• As with any vaccine, a protective immune response may not be elicited in all vaccines.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

SHINGRIX PRESCRIBING INFORMATION SHINGRIX Herpes zoster (HZ, or shingles) vaccine (non-live recombinant, $AS01_B$ adjuvanted)

QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains 50 micrograms of gE antigen1 adjuvanted with $AS01_B$[2].
1 Varicella Zoster Virus (VZV) glycoprotein E (gE) produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cells
2 The GlaxoSmithKline proprietary AS0ls Adjuvant System is composed of the plant extract *Quillaja saponaria* Molina, fraction 21 (QS-21) (50 micrograms) and 3-0- desacyl-4'-monophosphoryl lipid A (MPL)from *Salmonella minnesota*(50micrograms)
The powder is white. The suspension is an opalescent, colourless to pale brownish liquid.

CLINICAL INFORMATION

Indications

Shingrix is indicated for the prevention of herpes zoster (HZ) and HZ-related complications, such as post-herpetic neuralgia (PHN), in:
• adults 50 years of age or older;
• adults 18 years of age or older at increased risk of HZ.
The use of Shingrix should be based on official recommendations.

Dosage and Administration

Pharmaceutical form: powder and suspension for suspension for injection.
The immunisation schedules for Shingrix should be based on official recommendations.

Posology

The primary vaccination schedule consists of two doses of 0.5 ml each; an initial dose followed by a second dose 2 to 6 months later.
For subjects who are immunodeficient, immunosuppressed or likely to become immunosuppressed due to known disease or the rapy, and whom would benefit from a shorter vaccination schedule, the second dose can be given 1 to 2 months after the initial dose (see *Pharmacodynamics Effects).*
The need for booster doses has not been established. Shingrix can be given with the same schedule in individuals previously vaccinated with live attenuated HZ vaccine (see *Pharmacodynamics Effects).* Shingrix is not indicated for prevention of primary varicella infection

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Method of administration

Shingrix is for intramuscular injection only, preferably in the deltoid muscle.

For instructions on reconstitution of the medicinal product before administration, see Use and Handling.

Contraindications

Hypersensitivity to the active substances or to any component of the vaccine (see *Qualitative and Quantitative Composition* and *List of Excipients).*

Warnings and Precautions

Prior to immunisation

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

As with other vaccines, vaccination with Shingrix should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

As with any vaccine, a protective immune response may not be elicited in all vaccines. In a post-marketing observational study in individuals aged 65 years or older, an increased risk of Guillain-Barre syndrome (estimated 3 excess cases per million doses administered) was observed during the 42 days following vaccination with Shingrix. Available information is to determine a causal relationship with Shingrix.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Precautions for use

Do not administer the vaccine intravascularly, intradermally or subcutaneously.
Maladministration via the subcutaneous route may lead to an increase in transient local reactions.
As with other vaccines administered in tramuscularly, Shingrix should be given with caution to individuals thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.
Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Interactions

Use with other vaccines
Shingrix can be given concomitantly with unadjuvanted seasonal influenza vaccine, 23- valent pneumococcal polysaccharide vaccine (PPV23), pneumococcal conjugate vaccine (PCV) or reduced antigen diphtheria-tetanusacellular pertussis vaccine (dTpa) (see Pharmacodynamics Effects).
The adverse reactions of fever and shivering were more frequent when PPV23 vaccine was co-administered with Shingrix compared to when Shingrix was given alone (see Adverse Reactions).
If Shingrix is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Pregnancy and Lactation

Fertility
Animal studies indicate no effects of Shingrix on male or female fertility.

Pregnancy
There are no data on the use of Shingrix in pregnant women. Animal studies performed with Shingrix administered to female rats do not indicate any harmful effects with respect to pregnancy (see *Non-clinical information).*

Lactation
The effect on breast-fed infants of administration of Shingrix to their mothers has not been studied.

Effects on Ability to Drive and Use Machines
No studies on the effects of Shingrix on the ability to drive and use machines have been performed.

Adverse Reactions
Clinical trial data
The safety profile presented below is based on a pooled analysis of more than 14,500 adults ≥ 50 years of age, who have received at least one dose of Shingrix. These data were generated in placebo-controlled clinical studies (conducted in Europe, North America, Latin America, Asia and Australia) where Shingrix was administered according to a 0, 2-month schedule.
Additionally, in clinical studies, 1,587 subjects ≥ 18 years of age who are immunodeficient or immunosuppressed due to disease or therapy (referred to as immunocompromised (IC)), were vaccinated with at least 1 dose of Shingrix. The reported adverse reactions were consistent with those presented in the Table below. Adverse reactions reported are listed according to the following frequency:
Very common ≥ 1/10);Common ≥ 1/100to<1/10);Uncommon ≥ 1/1,000to<1/100); Rare ≥ 1/10,000 to <1/1,000); Very rare(<1/10,000)

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

System Organ Class	Frequency	Adverse reactions
Nervous system disorders	Very common	headache
Gastrointestinal disorders	Very common	gastrointestinal symptoms (including nausea, vomiting, diarrhoea and/or abdominal pain)
Musculoskeletal and connective tissue disorders	Very common	myalgia
	Uncommon	arthralgia
General disorder s and administration site conditions	Very common	injection site reactions (such as pain, redness, swelling), fatigue, chills, fever
	Common	injection site pruritus, malaise

Overall, there was a higher incidence of some adverse reactions in younger age groups. However, the overall frequency and severity of these events did not indicate a clinically meaningful different reactogenicity profile in the younger age strata. In IC adult studies, there was a higher incidence of pain at the injection site, fatigue, myalgia, headache, shivering and fever in subjects aged 18 to 49 years compared with those aged 50 years and older. In older adult studies, there was a higher incidence of pain and swelling at the injection site, fatigue,myalgia,headache,shivering,fever and gastrointestinal symptoms in subjects aged 50 to 69 years compared with those aged 70 years and older.

In a clinical study where 119 subjects ≥ 50 years of age were vaccinated with Shingrix following a 0, 6-month schedule, the safety profile was similar to that observed in subjects vaccinated with Shingrix following a 0, 2-month schedule. In a clinical study including 865 adults ≥ 50 years of age, fever and shivering were reported more frequently when PPV23 vaccine was co-administered with Shingrix (16% and 21%, respectively) compared to when Shingrix was given alone (7% for both adverse reactions).

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Post-marketing data

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Rare	hypersensitivity reactions including rash, urticaria, angioedema

Overdose

Insufficient data are available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC Code

Pharmacotherapeutic group: Varicella zoster vaccines, ATC code: J07BK03.

Mechanism of Action

Shingrix is designed to induce antigen-specific cellular and humoral immune responses in individuals with pre-existing immunity against VZV.
Non-clinical data show that AS01B induces a local and transient activation of the innate immune system through specific molecular pathways. This facilitates the recruitment and activation of antigen presenting cells carrying gEderived antigens in the draining lymph node, which in turn leads to the generation of gE-specific CD4+ T cells and antibodies.
The adjuvant effect of AS01B Is is the result of interactions between MPL and QS-21 formulated in liposomes.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Pharmacodynamic Effects

1. Efficacy of Shingrix

Efficacy against Herpes Zoster (HZ) and Post-Herpetic Neuralgia (PHN) Two phase III, placebo-controlled, observer-blind efficacy studies of Shingrix were conducted in adults ≥ 50 years with 2 doses administered 2 months apart:

• Zoster-006 (ZOE-50): total vaccinated cohort (TVC) of 15,405 subjects 50 years who received at least one dose of either Shingrix (N=7,695) or placebo (N=7,710).

• Zoster-022(ZOE-70): TVC of 13,900 subjects 70 years who received at least one dose of either Shingrix (N=6,950) or placebo (N=6,950).

Two phase III, placebo-controlled, observer-blind studies evaluating Shingrix efficacy were conducted in IC adults ≥ 18 years with 2 doses administered 1-2 months apart:

• Zoster-002: TVC of 1,846 autologous hematopoietic stem cell transplants (aHSCT) recipients who received at least one dose of either Shingrix (N=922) or placebo (N=924)post-transplant.

• Zoster-039: TVC of 562 subjects with hematologic malignancies who received at least one dose of either Shingrix (N=283) or placebo (N=279) during a cancer therapy course or after the full cancer therapy course. Incidence of HZ and PHN cases as well as vaccine efficacy were evaluated in the modified Total Vaccinated Cohort (mTVC i. e. excluding subjects who did not receive the second dose of vaccine or who had a confirmed diagnosis of HZ within one month after the second dose).

Shingrix significantly decreased the incidence of HZ and PHN compared with placebo in:

• adults ≥ 50 years (Zoster-006): 6 vs. 210 HZ cases and 0 vs. 18 PHN cases;

• adults ≥ 70 years (pooled analysis of Zoster-006 and Zoster-022): 25 vs. 284 HZ cases and 4 vs. 36 PHN cases;

• adults ≥ 18 years with aHSCT (Zoster-002): 49 vs. 135 HZ cases and 1 vs. 9 PHN cases;

• adults ≥ 18 years with hematologic malignancies (Zoster-039): 2 vs. 14 HZ cases (PHN was not assessed as study endpoint). Vaccine efficacy was calculated post-hoc.

Vaccine efficacy results are presented in Table 1.

Table 1: Shingrix efficacy against HZ and PHN (mTVC)

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Age (Years)	HZ			7,340	100.0	PHN
	N	Efficacy (%)	95% CI	N	Efficacy (%)	95% CI
Zoster-006*						
≥ 50	7,344	97.2	93.7; 99.0	7,340	100.0	77.1; 100.0
50-59	3,492	96.6	89.6; 99.4	3,491	100.0	40.8; 100.0
≥ 60	3,852	97.6	92.7; 99.6	3,849	100.0	55.2; 100.0
60-69	2,141	97.4	90.1; 99.7	2,140	100.0§	< 0; 100.0
Pooled Zoster-006 and Zoster-022**						
≥ 70	8,250	91.3	86.8; 94.5	8,250	88.8	68.7; 97.1
70-79	6,468	91.3	86.0; 94.9	6,468	93.0	72.4; 99.2
≥ 80	1,782	91.4	80.2; 97.0	1,782	71.2§	< 0; 97.1
Zoster-002* (aHSCT recipients#)**						
≥ 18	870	68.2	55.5; 77.6	870	89.3	22.5; 99.8
18-49	213	71.8	38.7; 88.3	213	100.0§	< 0; 100.0
≥ 50	657	67.3	52.6; 77.9	657	88.0	10.4; 99.8
Zoster-039 (hematologic malignancy patients#)						
≥ 18	259	87.2****	44.2; 98.6	-	-	-

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

N Number of evaluable subjects
CI Confidence interval
* Over a median follow-up period of3.l and 4.1 years for reporting HZ and PHN cases, respectively
** Over a median follow-up period of 4.0 years for reporting HZ and PHN cases
*** Over a median follow-up period of21 months for reporting HZ and PHN cases
**** VE calculation was performed post-hoc; median follow-up period of 11.1 months
# antiviral prophylaxis in line with the local standard of care was permitted
§ Not statistically significant
Zoster-006 mTVC: N (Shingrix) = 7,344, N (Placebo) = 7,415
Pooled analysis of Zoster-006 and Zoster-022 mTVC: N (Shingrix) = 8,250, N (Placebo) = 8,346
Zoster-002 mTVC: N (Shingrix) = 870, N (Placebo) =851
Zoster-039 mTVC: N(Shingrix)=259,N(Placebo)=256

In the fourth year after vaccination, the efficacy against HZ was 93.1 % (95% CI: 81.2; 98.2) and 87.9% (95% CI: 73.3; 95.4) in subjects ≥ 50 years (Zoster-006) and subjects ≥ 70 years (pooled Zoster-006 and Zoster-022), respectively. In Zoster-002, during a follow-up period starting 1 month post-dose 2 (i.e. corresponding to approximately 6 months after aHSCT) until 1 year after aHSCT, when the risk for HZ is the highest, the efficacy against HZ was 76.2% (95% CI: 61.1;86.0).

Efficacy against other HZ-related complications
The evaluated HZ-related complications (other than PHN) were: HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease including stroke, and visceral disease. In the pooled analysis of Zoster-006 and Zoster-022, Shingrix significantly reduced HZ related
complications by 93.7% (95% CI: 59.5; 99.9) and 91.6% (95% CI: 43.3; 99.8) in subjects ≥ 50 years (1 vs. 16 cases) and subjects ≥ 70 years (1 vs. 12 cases), respectively.
In Zoster-002, Shingrix significantly reduced HZ-related complications by 77.8% (95% CI: 19.0; 96.0) in aHSCT recipients ≥ 18 years (3 vs 13 cases).
In addition, in Zoster-002, Shingrix significantly reduced HZ-related hospitalisations by 84.7% (95% CI: 32.1; 96.6) (2 vs. 13 cases).

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Effect of Shingrix on HZ-associated pain

In Zoster-022, Shingrix significantly reduced the use and the duration of HZ-associated pain medication by 39.6% (95% CI: 10.7; 64.8) and 49.3% (95% CI: 2.9; 73.5), respectively, in subjects ≥ 70 years with at least one confirmed HZ episode. The median duration of pain medication use was 30.0 and 38.0 days in the Shingrix and placebo group, respectively.

Overall there was a general trend towards less severe HZ-associated pain in subjects vaccinated with Shingrix compared to placebo.

In Zoster-002, Shingrix significantly reduced the duration of severe ‘ worst ‘ Hz associated pain by 38.5% (95% CI: 11.0; 57.6) in aHSCT recipients ≥ 18 years with at least one confirmed HZ episode.

2. Immunogenicity of Shingrix

An immunological correlate of protection has not been established; therefore the level of immune response that provides protection against HZ is unknown.

In adults ≥ 50 years, the immune responses to Shingrix were evaluated in a subset of subjects from the phase III efficacy studies Zoster-006 [humoral immunity and cell mediated immunity (CMI)] and Zoster-022 (humoral immunity). The gE-specific immune responses (humoral and CMI) elicited by Shingrix at 1 month post-dose 2 are presented in Tables 2 and
3, respectively.

Table 2: Humoral immunogenicity of Shingrix in adults ≥ 50 years at 1 month post-dose 2 (ATP cohort for immunogenicity)

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Anti-gE immune response^				
Age group (years)	N	VRR§ (%) (95%CI)	GMC (95% CI)	Median fold increase of concentrations vs pre-vaccination (Q1; Q3)
Zoster-006				
≥ 50	1,070	98·5 (97,9; 99.1)	52,376.6 (50,264.1; 54,577.9)	41.9 (20.8; 86.9)
Pooled Zoster-006 and Zoster-022				
≥ 70	742	96.6 (95,1; 97.8)	49,691.5 (47,250.8; 52,258.2)	34.3 (16.7; 68.5)

ATP According-To-Protocol
^ Anti-gE immune response = anti-gE antibody levels, measured by anti-gE enzyme-linked immunosorbent assay (gE ELISA)
N Number of evaluable subjects at the specified time point (for the GMC)
§ Vaccine response rate (VRR)for anti-gE is defined as the percentage of subjects who have at least a 4-fold increase in the post-dose 2 anti-gE antibodies concentration as compared to the pre- vaccination anti-gE antibodies (subjects seropositive at baseline), or as compared to the anti-gE antibodies cut-off value for seropositivity (subjects seronegative at baseline)
CI Confidence interval
GMC Geometric Mean Concentration
QI; Q3 First and third quartiles

At 3 years post-dose 2, the median fold increase over baseline was 9.3 (Q1: 4.9; Q3: 19.5) in adults ≥ 50 years (Zoster-006) and 7.2 (QI: 3.5; Q3: 14.5) in adults ≥ 70 years (pooled Zoster-006 and Zoster-022).

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Table 3: Cell-mediated immunogenicity of Shingrix in adults ≥ 50 years at 1 month post dose 2 (ATP cohort for immunogenicity)

gE-specific CD4[2+] T cell response^			
Age group (years)	N	Median frequency (Q1; Q3)	Median fold increase of frequency vs. pre-vaccination (Q1; Q3)
Zoster-006			
≥ 50	164	1,844.1 (1,253.6; 2,932.3)	24.6 (9.9; 744.2)
≥ 70	52	1,494.6 (922.9; 2,067.1)	33.2 (10.0; 1,052.0)

ATP According-To-Protocol
^ gE-specific CD4[2+] T cell response = gE-specific CD4+ T cell activity, measured by intracellular cytokine staining (ICS) assay (CD4[2+]T cells=CD4+Tcells expressing at least 2 of 4 selected immune markers)
N Number of evaluable subjects at the specified time point for the median frequency
QI; Q3 First and third quartiles
* The gE-specific CD4[2+] data in the ≥ 70 YOA group were only generated in Zoster-006 because CD4+ T cell activity was not assessed in Zoster-022

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

At 3 years post-dose 2, in Zoster-006, the median fold increase over baseline was 7.9 (Q1: 2.7; Q3: 31.6) in adults ≥ 50 years and 7.3 (QI: 1.7; Q3: 31.6) in adults ≥ 70 years.
Data from a phase II, open-label, single group, follow-up clinical study in adults ≥ 60 years (Zoster-024) indicate that the vaccine-induced immune response (humoral and CMI) persists up to Month 72 (approximately 6 years post-dose 1 i.e. 70 months post dose 2), following a 0, 2-month schedule (N= 119).

The median anti-gE antibody concentration was greater than 7-fold above the baseline pre-vaccination median concentration. The median frequency of gE-specific CD4[2+] T cells was greater than 3.7-fold above baseline pre-vaccination median frequency.

In IC adults ≥ 18 years, the humoral and CMI responses to Shingrix were evaluated in:
- one phase I/II study: Zoster-015 (HIV infected subjects);
- one phase II/III study: Zoster-028 (patients with solid tumours undergoing chemotherapy);
- three phase III studies: Zoster-002 (aHSCT recipients vaccinated post-transplant),Zoster-039 (patients with hematologic malignancies vaccinated during a cancer therapy course or after the full cancer therapy course) and Zoster-041 (renal transplant recipients on chronic immunosuppressive treatment at the time of vaccination).
The gE-specific immune responses (humoral and CMI) elicited by Shingrix at 1 month post-dose 2 in all IC populations studied are presented in Tables 4 and 5, respectively.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Table 4: Humoral immunogenicity of Shingrix in IC adults ≥ 18 years at 1 month postdose 2 (ATP cohort for immunogenicity)

Anti-gE immune response*			
N	VRR[1](%) (95%CI)	GMC (95%CI)	Median fold increase of concentrations vs pre- vaccination (Q1; Q3)
Zoster-002 (aHSCT recipients)			
82	67.1	12,753.2	14.1
	(55.8; 77.1)	(7,973.0; 20,399.4)	(1.7; 137.0)
Zoster-028 (solid tumor patients)			
87	86.2	18,291.7	21.5
	(77.1; 92.7)	(14,432.1; 23,183.5)	(7.0; 45.2)

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Zoster-039 (hematologic malignancy patients)			
217	65.4	13,445.6	17.2
	(58.7; 71.7)	(10,158.9; 17,795.6)	(1.4; 87.4)
Zoster-041 (renal transplant recipients)			
121	80.2	19,163.8	15.1
	(71.9; 86.9)	(15,041.5; 24,416.0)	(6.1; 35.0)
Zoster-015 (HIV infected subjects)			
53	98.1	42,723.6	40.9
	(89.9; 100)	(31,233.0; 58,441.6)	(18.8; 93.0)

ATP According-To-Protocol
^ Anti-gE immune response anti-gE antibody levels, measured by anti-gE enzyme-linked immunosorbent assay (gE ELISA)
N Number of evaluable subjects at the specified time point (for the GMC)
§ Vaccine response rate (VRR) for anti-gE is defined as the percentage of subjects who have at least a 4-fold increase in the post-dose 2 anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies (subjects seropositive at baseline), or as compared to the anti-gE antibodies cut-off value for seropositivity (subjects seronegative at baseline)
CI Confidence interval
GMC Geometric Mean Concentration
Q1; Q3 First and third quartiles

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Table 5: Cell-mediated immunogenicity of Shingrix in IC adults ≥ 18 years at 1 month post-dose 2 (ATP cohort for immunogen

gE-specific CD4[2+] T cell response"		
N	Median frequency (Q1; Q3)	Median fold increase of frequency vs. pre-vaccination (Q1; Q3)
Zoster-002 (aHSCT recipients)		
51	6,644.9	109.0
	(1,438.3; 13,298.6)	(34.4; 2,716.4)
Zoster-028* (solid tumor patients)		
22	778.8	4.9
	(393.1; 1,098.2)	(1.7; 33.0)
Zoster-039 (hematologic malignancy patients)		
53	3,081.9	45.9
	(1,766.2; 7,413.6)	(16.4; 2,221.9)
Zoster-041 (renal transplant recipients)		
32	2,149.0	47.7
	(569.4; 3,695.1)	(14.7; 439.6)
Zoster-015 (HIV infected subjects)		
41	2,809.7	23.4
	(1,554.5; 4,663.7)	(8.5; 604.1)

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

ATP According-To-Protocol
^ gE-specific CD4[2+] T cell response = gE-specific CD4+ T cell activity, measured by intracellular cytokine staining (ICS) assay (CD4[2 +] T cells = CD4+ T cells expressing at least 2 of 4 selected immune markers)
N Number of evaluable subjects at the specified time point for the median frequency
Q1; Q3 First and third quartiles SHINGRIX

*Blood for CMI was only collected from the group of subjects that received the first dose of Shingrix 8-30 days before the start of a chemotherapy cycle (i.e. largest group of the study)

At 1 year post-dose 2, the median fold increase over baseline ranged from 2.7 to 6.5 in terms of anti-gE antibody concentration and from 2.0 to 43.6 in terms of gE-specific CD4[2+] T-cell frequencies (studies Zoster-002, Zoster-028, Zoster-039 and Zoster-041).

At 2 years post-dose 2, in Zoster-002, the median fold increase over baseline was 1.3 in terms of anti-gE antibody concentration and 50.9 in terms of gE-specific CD4[2+] T-cell frequencies.

Immunogenicity following concomitant vaccination
In four phase III, controlled, open-label clinical studies, adults ≥ 50 years of age were randomized to receive 2 doses of Shingrix 2 months apart administered either
concomitantly at the first dose or non-concomitantly with unadjuvanted seasonal influenza vaccine (N=828; Zoster-004), PPV23 vaccine (N=865; Zoster 035), PCV13 vaccine(N=912;Zoster-059)or dTap vaccine formulated with 0.3 milligrams Al3+ (N=830; Zoster-042). The vaccine response rate (in terms of anti-gE antibodies) was 95.8% (95% CI: 93.3; 97.6), 98.3% (95% CI: 96.4; 99.3), 99.1% (95% CI: 97.6; 99.7) and 97.8% (95% CI: 95.8; 99.1) following co administration of Shingrix with the in fluenza, PPV2 3, PCV13 and dTap vaccine respectively. The immune responses of the co-administered vaccines were un affected, with the exception of lower geometric mean concentrations (GMCs) for one of the pertussis antigens (pertactin) when Shingrix is coa-dministered with the dTpa vaccine. However, these data do not suggest clinically relevant interference.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Immunogenicity in subjects with a history of HZ prior to vaccination

In a phase III, uncontrolled, open-label clinical study (Zoster-033), 96 adults ≥ 50 years of age, with a history of HZ, received 2 doses of Shingrix 2 months apart. The vaccine response rate (anti-gE antibodies) at 1 month post-vaccination was 90.2% (95% CI:81.7; 95.7).

Immunogenicity in subjects receiving 2 doses of Shingrix 6 months apart

In a phase III, open-label clinical study (Zoster-026) where 238 subjects ≥ 50 years of age were equally randomised to receive 2 doses of Shingrix 2 or 6 months apart, the vaccine response rate (anti-gE antibodies) at 1 month post-vaccination following the 0, 6-month schedule was 96.5% (95% CI: 90.4; 99.2).
The humoral immune response (anti-gE antibodies concentration) following the 0, 6- month schedule was not inferior to the humoral immune response following the 0, 2- month schedule, as the 97.5% CI upper limit of the antibodies concentration ratio was below 1.50 [1.16 (97.5% CI: 0.98; 1.39)].

Immunogenicity in individuals previously vaccinated with live attenuated herpes zoster (HZ) vaccine

In a phase III, open-label, multicentre clinical study (Zoster-048), 430 adults ≥ 65 years of age with or without a previous history of vaccination with live attenuated HZ vaccine ≥ 5 years earlier were group-matched at a 1:1 ratio to receive 2 doses of Shingrix 2 months apart. The immune response to Shingrix was unaffected by prior vaccination with live attenuated HZ vaccine.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Pharmacokinetics

Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical Studies

See *Pharmacodynamics Effects.*

Non-Clinical Information

Reproductive Toxicology

Administration of VZV gE ASO1B to female rats did not indicate any harmful effects with respect to fertility, pregnancy, embryo-foetal development, parturition or postnatal development.
Treatment of male rats did not affect mating performance, fertility or early embryonic development.

Animal toxicology and/or pharmacology

Non-clinical data reveal no special hazard for humans based on conventional studies of acute and repeated dose toxicity, local tolerance and cardiovascular/respiratory safety pharmacology.

PHARMACEUTICAL INFORMATION

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

List of Excipients

Powder (gE antigen):
Sucrose, polysorbate 80, sodium dihydrogen phosphate dihydrate, dipotassium phosphate
Suspension (ASO1B Adjuvant System):
Dioleoyl phosphatidylcholine, cholesterol, sodium chloride, disodium phosphate anhydrous, potassium dihydrogen phosphate, water for injections

Shelf Life

The expiry date is indicated on the packaging.
For shelf-life after reconstitution of the medicinal product, see *Use and Handling.*

Storage

Store in a refrigerator (2°C - 8°C). Do not freeze. Store in the original package in order to protect from light. The storage conditions are detailed on the packaging.
For storage conditions after reconstitution of the medicinal product, see *Use and Handling.*

Nature and Contents of Container

• Powder for 1 dose in a vial (type I glass) with a stopper (butyl rubber)
• Suspension for 1 dose in a vial (type I glass) with a stopper (butyl rubber).
Shingrix is available in a pack size of 1 vial of powder plus 1 vial of suspension or in a pack size of 10 vials of powder plus 10 vials of suspension.
Not all pack sizes may be marketed.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Use and Handling

The powder and suspension should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, do not reconstitute the vaccine.

How to prepare Shingrix:

Shingrix must be reconstituted prior to administration.

1. Withdraw the entire contents of the vial containing the suspension into the syringe.
2. Add the entire contents of the syringe into the vial containing the powder.
3. Shake gently until the powder is completely dissolved.

The reconstituted vaccine is an opalescent, colourless to pale brownish liquid.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and /or variation of appearance. If either is observed, do not administer the vaccine.

After reconstitution, the vaccine should be used promptly; if this is not possible, the vaccine should be stored in a refrigerator(2°C-8°C).If not used with in 6 hours it should be discarded.

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023

Before administration:

1. Withdraw the entire contents of the vial containing the reconstituted vaccine into the syringe.
2. Change the needle so that you are using a new needle to administer the vaccine.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Version number: GDS07/IPI02

Date of issue: 14 June 2022

Always read the full prescribing information.
Healthcare professionals are asked to report any suspected adverse reactions to Egyptian Pharmacovigilance Centre e-mail: pv.followup@edaegypt.gov.eg or Egyptian Drug Authority (EDA) website: https://www.edaegypt.gov.eg or (EPVC) [hotline 15301].
Egyptian Drug Authority Shingrix Approved Leaflet approval date: 11/9/2023

For full prescribing information, see data sheet or contact:
GlaxoSmithKline S.A.E. Building no. 46, Block (J), Fifth District, Boomerang,New Cairo, Egypt.Tel.: +202 26185000

Adverse events should be reported to GlaxoSmithKline on +202 26185150 or by e-mail at: ae.egypt@gsk.com.
For any medical information requests, please reach us at: mi.egypt@gsk.com

Reference: 1. SHINGRIX Egyptian Drug Authority Approved leaflet approval date11/9/2023