▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems

AUSTRALIAN PRODUCT INFORMATION

SHINGRIX (recombinant Varicella Zoster Virus glycoprotein E antigen) powder and suspension for suspension for injection

1 NAME OF THE MEDICINE

Recombinant Varicella Zoster Virus glycoprotein E antigen ($AS01_B$ adjuvanted vaccine)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 mL) contains 50 micrograms of gE antigen[1] adjuvanted with $AS01_B$[2].

[1] Varicella Zoster Virus (VZV) glycoprotein E (gE) produced by recombinant DNA technology in Chinese Hamster Ovarian (CHO) cells

[2] The GlaxoSmithKline proprietary $AS01_B$ Adjuvant System is composed of the plant extract *Quillaja saponaria* saponin (QS-21) (50 micrograms) and 3-O-desacyl-4'-monophosphoryl lipid A (MPL) from *Salmonella minnesota* (50 micrograms).

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Powder and suspension for suspension for injection

The powder is white.

The suspension is an opalescent, colourless to pale brownish liquid.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

SHINGRIX is indicated for the prevention of herpes zoster and post-herpetic neuralgia in adults 50 years of age or older.

4.2 DOSE AND METHOD OF ADMINISTRATION

The immunisation schedules for SHINGRIX should be based on official recommendations.

Further guidance regarding the use of vaccines can be found in the Australian Immunisation Handbook.

Dosage:

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.

The need for booster doses has not been established.

SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox) or for treatment of herpes zoster (HZ) or post-herpetic neuralgia (PHN).

Method of administration:

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

Instructions for Use and Handling:

The powder and suspension should be inspected visually for any particulate matter and/or variation to the expected appearance (i.e. white powder and opalescent, colourless to pale brownish liquid). 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 within 6 hours it should be discarded.

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.

SHINGRIX is for single use in one patient only.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substances or to any component of the vaccine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 vaccinees.

Precautions for use:

Do not administer the vaccine intravascularly or intradermally.

Subcutaneous administration is not recommended.

Maladministration via the subcutaneous route may lead to an increase in transient local reactions.

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 occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to prevent injury from faints and to manage syncopal reactions.

There are no safety, immunogenicity or efficacy data to support interchangeability of SHINGRIX with other HZ vaccines.

There are limited data to support the use of SHINGRIX in individuals with a history of HZ and in frail individuals including those with multiple comorbidities. Healthcare professionals therefore need to weigh the benefits and risks of HZ vaccination on an individual basis.

Systemic immunosuppressive medications and immunodeficiency:

Safety and immunogenicity data on a limited number of immunocompromised subjects with human immunodeficiency virus (HIV) or haematopoietic stem cell transplant (HCT) are available (see Section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials). The use of SHINGRIX in subjects with other confirmed or suspected immunosuppressive or immunodeficient conditions is under investigation.

As with other vaccines, an adequate immune response may not be elicited in these individuals. The administration of SHINGRIX to immunocompromised subjects should be based on careful consideration of potential benefits and risks.

Use in the elderly
There are no special precautions for use in the elderly

Paediatric use
The safety and efficacy of SHINGRIX have not been established in children and adolescents.

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Use with other vaccines

SHINGRIX can be given concomitantly with unadjuvanted seasonal influenza vaccine *(*see Section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials*)*.

The vaccines should always be administered at different injection sites.

No data are currently available regarding concomitant use with other vaccines.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Repeated exposure of male and female rats to SHINGRIX (0.1 and 0.2 mL respectively) by IM injection on 42, 28 and 14 days prior to mating (male) and 28 and 14 days prior to mating (female) had no effects on mating or fertility.

Use in pregnancy

(Pregnancy Category B2)

There are no data on the use of SHINGRIX in pregnant women.

In a reproductive and developmental toxicity study, female rats were administered SHINGRIX or the $AS01_B$ adjuvant alone by intramuscular injection 28 and 14 days prior to mating, on gestation Days 3, 8, 11, and 15, and on lactation Day 7. The total dose was 0.2 mL on each occasion (a single human dose of SHINGRIX is 0.5 mL). No adverse effects on preweaning development up to post-natal Day 25 were observed. There were no vaccine-related foetal malformations or variations.

Use in lactation
The effect on breast-fed infants of administration of SHINGRIX to their mothers has not been studied.

4.7 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.

However, some of the undesirable effects mentioned in Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) may temporarily influence the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The safety profile presented below is based on pooled data from 2 placebo-controlled clinical studies (ZOE-50 and ZOE-70) involving 29,305 subjects aged 50 years and older who received at least one dose of SHINGRIX (n = 14,645) or saline placebo (n = 14,660) administered according to a 0, 2-month schedule. These studies were conducted in Europe, North America, Latin America, Asia and Australia.

Solicited Adverse Events

In both studies, data on solicited local and general adverse events were collected using standardized diary cards for 7 days following each vaccine dose or placebo (i.e., day of vaccination and the next 6 days) in a subset of subjects (n = 4,886 receiving SHINGRIX, n = 4,881 receiving placebo with at least 1 documented dose). Across both studies, the percentages of subjects aged 50 years and older reporting each solicited local adverse reaction and each solicited general adverse event following administration of SHINGRIX (both doses combined) were pain (78.0%), redness (38.1%), and swelling (25.9%); and myalgia (44.7%), fatigue (44.5%), headache (37.7%), shivering (26.8%), fever (20.5%), and gastrointestinal symptoms (17.3%), respectively.

The reported frequencies of specific solicited local adverse reactions and general adverse events (overall per subject), by age group, from the 2 studies are presented in Table 1.

Table 1: Percentage of Subjects with Solicited Local Adverse Reactions and General Adverse Events within 7 Days[a] of Vaccination in Adults Aged 50 to 59 Years, 60 to 69 Years, and 70 Years and Older[b] (Total Vaccinated Cohort with 7-Day Diary Card)

	Aged 50 - 59 Years		Aged 60 - 69 Years		**Aged ≥70 Years**	
	SHINGRIX %	Placebo[c] %	SHINGRIX %	Placebo[c] %	SHINGRIX %	Placebo[c] %
Local Adverse Reactions	n = 1,315	n = 1,312	n = 1,311	n = 1,305	n = 2,258	n = 2,263
Pain	88.4	14.4	82.8	11.1	69.2	8.8
Pain, Grade 3[d]	10.3	0.5	6.9	0.5	4.0	0.2
Redness	38.7	1.2	38.4	1.6	37.7	1.2
Redness, >100 mm	2.8	0.0	2.6	0.0	3.1	0.0
Swelling	30.5	0.8	26.5	1.0	23.0	1.1
Swelling, >100 mm	1.1	0.0	0.5	0.0	1.3	0.0
General Adverse Events	n = 1,315	n = 1,312	n = 1,309	n = 1,305	n =2,252	n = 2,264
Myalgia	56.9	15.2	49.0	11.2	35.1	9.9

	Aged 50 - 59 Years		Aged 60 - 69 Years		**Aged ≥70 Years**	
	SHINGRIX %	Placebo[c] %	SHINGRIX %	Placebo[c] %	SHINGRIX %	Placebo[c] %
Myalgia, Grade 3[e]	8.9	0.9	5.3	0.8	2.8	0.4
Fatigue	57.0	19.8	45.7	16.8	36.6	14.4
Fatigue, Grade 3[e]	8.5	1.8	5.0	0.8	3.5	0.8
Headache	50.6	21.6	39.6	15.6	29.0	11.8
Headache, Grade 3[e]	6.0	1.7	3.7	0.2	1.5	0.4
Shivering	35.8	7.4	30.3	5.7	19.5	4.9
Shivering, Grade 3[e]	6.8	0.2	4.5	0.3	2.2	0.3
Fever	27.8	3.0	23.9	3.4	14.3	2.7
Fever, Grade 3[f]	0.4	0.2	0.5	0.2	0.1	0.1
GI[g]	24.3	10.7	16.7	8.7	13.5	7.6
GI, Grade 3[e]	2.1	0.7	0.9	0.6	1.2	0.4

Total vaccinated cohort for safety included all subjects with at least 1 documented dose (n).

[a] 7 days included day of vaccination and the subsequent 6 days.
[b] Data for subjects aged 50 to 59 years and 60 to 69 years are based on ZOE -50. Data for subjects 70 years and older are based on pooled data from ZOE-50 and ZOE-70.
[c] Placebo was a saline solution.
[d] Grade 3 pain: Defined as significant pain at rest; prevents normal everyday activities.
[e] Grade 3 myalgia, fatigue, headache, shivering, GI: Defined as preventing normal activity.
[f] Fever defined as ³ 37.5°C for oral, axillary, or tympanic route, or ³ 38°C for rectal route; Grade 3 fever defined as >39.0°C
[g] GI = Gastrointestinal symptoms including nausea, vomiting, diarrhea, and/or abdominal pain.

The incidence of solicited local and general symptoms was lower in subjects aged 70 years and older compared with those aged 50 to 69 years.

The majority of solicited local adverse reactions and general adverse events seen with SHINGRIX had a median duration of 2 to 3 days.

There were no differences in the proportions of subjects reporting any or grade 3 solicited local reactions between Dose 1 and Dose 2. Headache and shivering were reported more frequently by subjects after Dose 2 (28.2% and 21.4%, respectively) compared with Dose 1 (24.4% and 13.8%, respectively). Grade 3 solicited general adverse events (headache, shivering, myalgia, and fatigue) were reported more frequently by subjects after Dose 2 (2.3%, 3.1%, 3.6%, and 3.5%, respectively) compared with Dose 1 (1.4%, 1.4%, 2.3%, and 2.4%, respectively).

Unsolicited Adverse Events

In both studies, unsolicited adverse events occurring within 30 days of vaccination were reported in 50.5% and 32.0% of subjects who received SHINGRIX (n = 14,645) and placebo (n = 14,660), respectively (Total Vaccinated Cohort). Unsolicited adverse events that occurred in ≥1% of recipients of SHINGRIX and at a rate at least 1.5-fold higher than placebo included chills (3.5% versus 0.2%), injection site pruritus (2.2% versus 0.2%), and malaise (1.7% versus 0.3%), arthralgia (1.7% versus 1.2%), nausea (1.4% versus 0.5%), and dizziness (1.2% versus 0.8%).

Gout (including gouty arthritis) was reported by 0.18% (n = 27) versus 0.05% (n = 8) of subjects who received SHINGRIX and placebo, respectively, within 30 days of vaccination; available information is insufficient to determine a causal relationship with SHINGRIX.

In a clinical study where 119 subjects 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.

Potential Immune-Mediated Diseases

In the 2 studies, new onset potential immune-mediated diseases (pIMDs) or exacerbation of existing pIMDs were reported for 0.6% of subjects who received SHINGRIX and 0.7% of subjects who received placebo from the first administered dose up to 1 year post last vaccination. The most frequently reported pIMDs occurred with comparable frequencies in the group receiving SHINGRIX and the placebo group.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Insufficient data are available.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Varicella zoster vaccines, ATC code: J07BK03 zoster, purified antigen

Mechanism of action

By combining the VZV specific antigen (gE) with an adjuvant system ($AS01_B$), SHINGRIX induces antigen-specific cellular and humoral immune responses in individuals with pre-existing immunity against VZV.

Non-clinical data show that $AS01_B$ induces a local and transient activation of the innate

immune system. This facilitates the recruitment and activation of antigen presenting cells carrying gE-derived 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 $AS01_B$ is the result of interactions between MPL and QS-21 formulated in liposomes.

Clinical trials

Efficacy of SHINGRIX

Efficacy against Herpes Zoster (HZ) and Post-Herpetic Neuralgia (PHN)

In two phase III, placebo-controlled, observer-blind efficacy studies of SHINGRIX:

- ZOE-50 (Zoster-006): 15,405 subjects ≥ 50 years were randomised to receive two doses of either SHINGRIX (N=7,695) or placebo (N=7,710) administered 2 months apart

- ZOE-70 (Zoster-022): 13,900 subjects ≥ 70 years were randomised to receive two doses of either SHINGRIX (N=6,950) or placebo (N=6,950) administered 2 months apart.

Efficacy results against HZ and PHN observed in the modified Total Vaccinated Cohort (mTVC), i.e. excluding adults who did not receive the second dose of vaccine or who had a confirmed diagnosis of HZ within one month after the second dose, are presented in Table 2 and Table 3, respectively.

SHINGRIX significantly decreased the incidence of HZ compared with placebo in subjects ≥ 50 years (6 vs. 210 cases in ZOE-50) and in subjects ≥ 70 years (25 vs. 284 cases in the pooled analysis of ZOE-50 and ZOE-70).

Table 2: **SHINGRIX efficacy against HZ**

Age (years)	SHINGRIX			Placebo			Vaccine efficacy (%) [95% CI]
	Number of evaluable subjects	Number of HZ cases	Incidence rate per 1000 person years	Number of evaluable subjects	Number of HZ cases	Incidence rate per 1000 person years	
ZOE-50*							
≥ 50	7,344	6	0.3	7,415	210	9.1	97.2 [93.7; 99.0]
50-59	3,492	3	0.3	3,525	87	7.8	96.6 [89.6; 99.4]
≥ 60	3,852	3	0.2	3,890	123	10.2	97.6 [92.7; 99.6]
60-69	2,141	2	0.3	2,166	75	10.8	97.4

Age (years)	SHINGRIX			Placebo			Vaccine efficacy (%) [95% CI]
	Number of evaluable subjects	Number of HZ cases	Incidence rate per 1000 person years	Number of evaluable subjects	Number of HZ cases	Incidence rate per 1000 person years	
							[90.1; 99.7]
Pooled ZOE-50 and ZOE-70**							
≥ 70	8,250	25	0.8	8,346	284	9.3	91.3 [86.8 ; 94.5]
70-79	6,468	19	0.8	6,554	216	8.9	91.3 [86.0; 94.9]
≥ 80	1,782	6	1.0	1,792	68	11.1	91.4 [80.2; 97.0]

CI Confidence interval
* Over a median follow-up period of 3.1 years
** Over a median follow-up period of 4.0 years
Data in subjects ≥ 70 years of age are sourced from the pre-specified pooled analyses of ZOE-50 and ZOE-70 (mTVC) as these analyses provide the most robust estimates for vaccine efficacy in this age group.

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 and subjects ≥ 70 years, respectively.

The duration of protection beyond 4 years is currently under investigation.

SHINGRIX significantly decreased the incidence of PHN compared with placebo in subjects ≥50 years (0 vs. 18 cases in ZOE-50) and in subjects ≥ 70 years (4 vs. 36 cases in the pooled analysis of ZOE-50 and ZOE-70).

Table 3: SHINGRIX efficacy against PHN

Age (years)	SHINGRIX			Placebo			Vaccine efficacy (%) [95% CI]
	Number of evaluable subjects	Number of PHN* cases	Incidence rate per 1000 person years	Number of evaluable subjects	Number of PHN cases	Incidence rate per 1000 person years	
ZOE-50**							
≥ 50	7,340	0	0.0	7,413	18	0.6	100 [77.1; 100]
50-59	3,491	0	0.0	3,523	8	0.6	100

Age (years)	SHINGRIX			Placebo			Vaccine efficacy (%) [95% CI]
	Number of evaluable subjects	Number of PHN* cases	Incidence rate per 1000 person years	Number of evaluable subjects	Number of PHN cases	Incidence rate per 1000 person years	
							[40.8; 100]
≥ 60	3,849	0	0.0	3,890	10	0.7	100 [55.2; 100]
60-69	2,140	0	0.0	2,166	2	0.2	100§ [< 0; 100]
Pooled ZOE-50 and ZOE-70***							
≥ 70	8,250	4	0.1	8,346	36	1.2	88.8 [68.7; 97.1]
70-79	6,468	2	0.1	6,554	29	1.2	93.0 [72.4; 99.2]
≥ 80	1,782	2	0.3	1,792	7	1.1	71.2§ [< 0; 97.1]

* PHN was defined as zoster-associated pain rated as ≥3 (on a 0-10 scale), persisting or appearing more than 90 days after onset of zoster rash using Zoster Brief Pain Inventory (ZBPI)
CI Confidence interval
** Over a median follow-up period of 4.1 years
*** Over a median follow-up period of 4.0 years
Data in subjects ≥ 70 years of age are sourced from the pre-specified pooled analyses of ZOE-50 and ZOE-70 (mTVC) as these analyses provide the most robust estimates for vaccine efficacy in this age group.
§ Not statistically significant

The benefit of SHINGRIX in the prevention of PHN can be attributed to the effect of the vaccine on the prevention of HZ. Due to the very low numbers of shingles occurring in the Shingrix group, the efficacy of SHINGRIX in the prevention of PHN in subjects with confirmed HZ could not be demonstrated.

Other HZ-related complications

In a post-hoc analysis of the pooled data of ZOE-50 and ZOE-70, SHINGRIX reduced HZ-related complications (other than PHN) 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. The evaluated HZ-related complications were: HZ vasculitis, disseminated disease, ophthalmic disease, neurologic disease, visceral disease and stroke.

Reduction of use of pain medication

Among subjects ≥ 70 years with confirmed HZ, SHINGRIX reduced the use and the duration of HZ-related pain medication by 39.0% (95% CI: 11.9; 63.3) and 50.6% (95% CI: 8.8; 73.2), respectively.

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.

The immune responses to SHINGRIX were evaluated in a subset of subjects from the phase III efficacy studies ZOE-50 [humoral immunity and cell-mediated immunity (CMI)] and ZOE-70 (humoral immunity)]. SHINGRIX elicited higher gE-specific immune responses (humoral and CMI) at 1 month post-dose 2 when compared to pre-vaccination levels.

In ZOE-50 and ZOE-70, the immunogenicity of SHINGRIX was evaluated up to Month 38 (3 years post-dose 2).

The humoral immunogenicity and CMI results are presented in Tables 4 and 5, respectively.

Table 4: Humoral immunogenicity of SHINGRIX in adults ≥ 50 years (ATP cohort for immunogenicity)

Anti-gE immune response^							
Age group (years)	Month 3*				Month 38**		
	N	VRR§ (%) (95% CI)	GMC (95% CI)	Median fold increase of concentrations vs pre-vaccination	N	GMC (95% CI)	Median fold increase of concentrations vs pre-vaccination
ZOE-50							
≥ 50	1,070	98.5 (97.6; 99.1)	52,376.6 (50,264.1; 54,577.9)	41.9 (20.8; 86.9)	967	11,919.6 (11,345.6; 12,522.7)	9.3 (4.9; 19.5)
Pooled ZOE-50 and ZOE-70							
≥ 70	742	96.6 (95.1; 97.8)	49,691.5 (47,250.8; 52,258.2)	34.3 (16.7; 68.5)	648	10,507.7 (9,899.2; 11,153.6)	7.2 (3.5; 14.5)

ATP According-To-Protocol
^ Anti-gE immune response = anti-gE antibody levels, measured by anti-gE enzyme-linked immunosorbent assay (gE ELISA)
* Month 3 = 1 month post-dose 2
** Month 38 = 3 years post-dose 2
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

Table 5: Cell-mediated immunogenicity of SHINGRIX in adults ≥ 50 years (ATP cohort for immunogenicity)

gE-specific CD4[2+] T cell response^						
Age group (years)	Month 3*			Month 38**		
	N	Median frequency (Q1; Q3)	Median fold increase of frequency vs. pre-vaccination (Q1; Q3)	N	Median frequency (Q1; Q3)	Median fold increase of frequency vs. pre-vaccination (Q1; Q3)
ZOE-50						
≥ 50	164	1,844.1 (1,253.6; 2,932.3)	24.6 (9.9; 744.2)	152	738.9 (355.7; 1,206.5)	7.9 (2.7; 31.6)
≥ 70***	52	1,494.6 (922.9; 2,067.1)	33.2 (10.0; 1,052.0)	46	480.2 (196.1; 972.4)	7.3 (1.7; 31.6)

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)

* Month 3 = 1 month post-dose 2

** Month 38 = 3 years post-dose 2

N Number of evaluable subjects at the specified time point

Q1; Q3 First and third quartiles

*** The gE-specific CD4[2+] data in the ≥70 YOA group were generated in ZOE-50 because CD4+ T cell activity was not assessed in ZOE-70

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.

Immunogenicity following concomitant vaccination

In a phase III, controlled, open-label clinical study (Zoster-004), 828 adults ≥ 50 years of age were randomized to receive 2 doses of SHINGRIX 2 months apart administered either concomitantly at the first dose (N=413) or non-concomitantly (N=415) with unadjuvanted seasonal influenza vaccine. The vaccine response rate (in terms of anti-gE antibodies) following co-administration of SHINGRIX with the unadjuvanted influenza vaccine was 95.8% (95% CI: 93.3; 97.6). The antibody responses to both vaccines were similar, whether administered concomitantly or non-concomitantly.

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)].

Immunocompromised subjects

Two phase I/II clinical studies, Zoster-001 and Zoster-015, were conducted in subjects with autologous hematopoietic stem cell transplant or HIV infection. A total of 135 adults, of whom 73 were ≥50 years of age, received at least one dose of SHINGRIX, which was shown to be immunogenic and well-tolerated.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

SHINGRIX was not tested for genotoxicity.

Carcinogenicity

SHINGRIX was not tested for carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Powder (gE antigen):
Sucrose
Polysorbate 80
Monobasic sodium phosphate dihydrate
Dibasic potassium phosphate

Suspension ($AS01_B$ Adjuvant System):
Dioleoylphosphatidylcholine
Cholesterol
Sodium chloride
Dibasic sodium phosphate
Monobasic potassium phosphate
Water for injections

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

For shelf-life after reconstitution of the medicinal product, see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Instructions for Use and Handling.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in a refrigerator (2°C – 8°C).

Do not freeze.

Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Instructions for Use and Handling.

6.5 NATURE AND CONTENTS OF CONTAINER

SHINGRIX is presented as:

- 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 and container types may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

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

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Not relevant to vaccines.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

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