For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

SHINGRIX

1. GENERIC NAME

Herpes zoster vaccine (recombinant, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 mL) contains:
Varicella Zoster Virus[1] glycoprotein E antigen[2,3] 50 micrograms

[1] Varicella Zoster Virus = VZV
[2] adjuvanted with $AS01_B$ containing:
plant extract *Quillaja saponaria* Molina, fraction 21 (QS-21) 50 micrograms
3-O-desacyl-4'-monophosphoryl lipid A Ph. Eur. from *Salmonella minnesota*. 50 micrograms
[3] glycoprotein E (gE) produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology

List of Excipients

Powder (gE antigen):
Sucrose
Polysorbate 80
Sodium dihydrogen phosphate dihydrate
Dipotassium phosphate

Suspension ($AS01_B$ Adjuvant System):
Dioleoyl phosphatidylcholine
Cholesterol
Sodium chloride
Disodium phosphate anhydrous
Potassium dihydrogen phosphate
Water for injection

3. DOSAGE FORM AND STRENGTH

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 Indication

SHINGRIX is indicated for prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN), in adults 50 years of age or older (see section *5.2 Pharmacodynamic Properties*).

4.2 Posology and Method of Administration

Posology

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 (see section *5.2 Pharmacodynamic Properties*).

The need for booster doses following the primary vaccination schedule has not been established (see section *5.2 Pharmacodynamic Properties*).

SHINGRIX can be given with the same schedule in individuals previously vaccinated with live attenuated HZ vaccine (see section *5.2 Pharmacodynamic Properties*).

SHINGRIX is not indicated for prevention of primary varicella infection (chickenpox).

Paediatric Population:

The safety and efficacy of *SHINGRIX* in children and adolescents have not been established. No data are available.

Method of Administration

For intramuscular injection only, preferably in the deltoid muscle.

For instructions on reconstitution of the medicinal product before administration, see section *8.4 Storage and Handling Instructions*.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section *2. Qualitative and Quantitative Composition*.

4.4 Special Warnings and Precautions for Use

Prior to immunisation

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. However, 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.

The vaccine is for prophylactic use only and is not intended for treatment of established clinical disease.

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. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

In a post-marketing observational study in individuals aged 65 years or older, an increased risk of Guillain-Barré 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*.

There are no safety, immunogenicity or efficacy data to support replacing a dose of *SHINGRIX* with a dose of another HZ vaccine.

There are limited data to support the use of *SHINGRIX* in individuals with a history of HZ (see section *5.2 Pharmacodynamic Properties*). Healthcare professionals therefore need to weigh the benefits and risks of HZ vaccination on an individual basis.

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

This medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium-free'.

4.5 Drug Interactions

SHINGRIX can be given concomitantly with unadjuvanted inactivated seasonal influenza vaccine, 23-valent pneumococcal polysaccharide vaccine (PPV23), 13-valent pneumococcal conjugate vaccine (PCV13) or reduced antigen diphtheria-tetanus-acellular pertussis vaccine (dTpa). The vaccines should be administered at different injection sites.

In four phase III, controlled, open-label clinical studies, adults ≥ 50 years of age were randomised to receive 2 doses of *SHINGRIX* 2 months apart administered either concomitantly at the first dose or non-concomitantly with an unadjuvanted inactivated seasonal influenza vaccine (N=828; Zoster-004), a PPV23 vaccine (N=865; Zoster-035), a PCV13 vaccine

(N=912; Zoster-059) or a dTpa vaccine formulated with 0.3 milligrams Al^{3+} (N=830; Zoster-042). The immune responses of the co-administered vaccines were unaffected, with the exception of lower geometric mean concentrations (GMCs) for one of the pertussis antigens (pertactin) when *SHINGRIX* is co-administered with the dTpa vaccine. The clinical relevance of this data is not known.

The adverse reactions of fever and shivering were more frequent when PPV23 vaccine was co-administered with *SHINGRIX* (16% and 21%, respectively) compared to when *SHINGRIX* was given alone (7% for both adverse reactions).

Concomitant use with other vaccines is not recommended due to lack of data.

4.6 Use in Special Populations

Pregnancy

There are no data from the use of *SHINGRIX* in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post-natal development (see section *6. Nonclinical properties*).

As a precautionary measure, it is preferable to avoid the use of *SHINGRIX* during pregnancy.

Lactation

The effect on breast-fed infants of administration of *SHINGRIX* to their mothers has not been studied. It is unknown whether *SHINGRIX* is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect effects with respect to fertility in males or females (see section *6. Nonclinical properties*).

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.

SHINGRIX may have a minor influence on the ability to drive and use machines in the 2-3 days following vaccination. Fatigue and malaise may occur following administration (see section *4.8 Undesirable Effects*).

4.8 Undesirable Effects

Summary of the safety profile

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.

The incidence of some adverse reactions viz. myalgia, fatigue, headache, shivering, fever and gastrointestinal symptoms was higher in subjects aged 50-69 years compared to those aged 70 years and above.

Tabulated List of Adverse reactions

The safety profile presented below is based on a pooled analysis of data generated in placebo-controlled clinical studies on 5,887 adults 50-69 years of age and 8,758 adults ≥ 70 years of age.

Adverse reactions reported during post-marketing surveillance are also tabulated below.

Adverse reactions reported are listed according to the following frequency:

Very common	(≥1/10)
Common	(≥1/100 to <1/10)
Uncommon	(≥1/1,000 to <1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)

Within each frequency grouping the adverse reactions are reported in the order of decreasing seriousness.

System Organ Class[1]	Frequency	Adverse reactions
Blood and lymphatic system disorders	Uncommon	lymphadenopathy
Immune system disorders	Rare	hypersensitivity reactions including rash, urticaria, angioedema[2]
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 disorders and administration site conditions	Very common	injection site reactions (such as pain, redness, swelling), fatigue, chills, fever
	Common	injection site pruritus, malaise

[1] According to MedDRA (medical dictionary for regulatory activities) terminology
[2]Adverse reactions from spontaneous reporting

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

By combining the VZV specific antigen (gE) with an adjuvant system ($AS01_B$), *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 $AS01_B$ 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 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.

5.2 Pharmacodynamic Properties

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

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:

- ZOE-50 (Zoster-006): Total Vaccinated Cohort (TVC) of 15,405 adults ≥ 50 years were randomised to receive two doses of either *SHINGRIX* (N=7,695) or placebo (N=7,710)
- ZOE-70 (Zoster-022): TVC of 13,900 adults ≥ 70 years of either *SHINGRIX* (N=6,950) or placebo (N=6,950)

The studies were not designed to demonstrate efficacy in subgroups of frail individuals, including those with multiple comorbidities, although these subjects were not excluded from the studies.

Incidence of HZ and PHN cases as well as vaccine efficacy were evaluated 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.

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

Vaccine efficacy results against HZ are presented in Table 1.

Table 1: SHINGRIX efficacy against HZ (mTVC)

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** [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.

Approximately 13,000 subjects with underlying medical conditions, including conditions associated with a higher risk of HZ, were enrolled in ZOE-50 and ZOE-70. Post-hoc analysis of efficacy against confirmed HZ undertaken in patients with common conditions (chronic kidney disease, chronic obstructive pulmonary disease, coronary artery disease, depression or diabetes mellitus), indicates that the vaccine efficacy is aligned with the overall HZ efficacy.

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

Vaccine efficacy results against PHN are presented in Table 2.

Table 2: SHINGRIX efficacy against PHN (mTVC)

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** [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. A further reduction of PHN incidence in subjects with confirmed HZ could not be demonstrated due to the limited number of HZ cases in the vaccine 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 adults ≥ 50 years (ZOE-50) and adults ≥ 70 years(pooled ZOE-50 and ZOE-70), respectively.
The duration of protection beyond 4 years is currently under investigation.

Efficacy against HZ-related complications other than PHN

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 ZOE-50 and ZOE-70, *SHINGRIX* significantly reduced these HZ-related complications by 93.7% (95% CI: 59.5; 99.9) and 91.6% (95% CI: 43.3; 99.8) in adults ≥ 50 years (1 vs. 16 cases) and adults ≥ 70 years (1 vs. 12 cases), respectively. No cases of visceral disease or stroke were reported during these studies.

Effect of SHINGRIX on HZ-related pain

Overall in ZOE-50 and ZOE-70 there was a general trend towards less severe HZ-related pain in subjects vaccinated with *SHINGRIX* compared to placebo. As a consequence of the high vaccine efficacy against HZ, a low number of breakthrough cases were accrued, and it was therefore not possible to draw firm conclusions on these study objectives.

In subjects ≥ 70 years with at least one confirmed HZ episode (ZOE-50 and ZOE-70 pooled), *SHINGRIX* significantly 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. The median duration of pain medication use was 32.0 and 44.0 days in the *SHINGRIX* and placebo group, respectively.

In subjects with at least one confirmed HZ episode, *SHINGRIX* significantly reduced the maximum average pain score versus placebo over the entire HZ episode (mean = 3.9 vs. 5.5, P-value = 0.049 and mean = 4.5 vs. 5.6, P-value = 0.043, in subjects ≥ 50 years (ZOE-50) and ≥ 70 years (ZOE-50 and ZOE-70 pooled), respectively). In addition, in subjects ≥ 70 years

(ZOE-50 and ZOE-70 pooled), *SHINGRIX* significantly reduced the maximum worst pain score versus placebo over the entire HZ episode (mean = 5.7 vs. 7.0, P-value = 0.032).

The burden-of-illness (BOI) score incorporates the incidence of HZ with the severity and duration of acute and chronic HZ-related pain over a 6 month period following rash onset. The efficacy in reducing BOI was 98.4% (95% CI: 92.2; 100) in subjects ≥ 50 years (ZOE-50) and 92.1% (95% CI: 90.4; 93.8) in subjects ≥ 70 years (ZOE-50 and ZOE-70 pooled).

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,* given as 2 doses 2 months apart, 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). The gE-specific immune responses (humoral and CMI) elicited by *SHINGRIX* are presented in Tables 3 and 4, respectively.

Table 3: Humoral immunogenicity of SHINGRIX in adults ≥ 50 years (ATP cohort for immunogenicity)

Anti-gE immune response^						
Age group (years)	**Month 3***			**Month 38****		
	N	**GMC (mIU/mL) (95% CI)**	**Median fold increase of concentrations vs. pre-vaccination (Q1; Q3)**	**N**	**GMC (mIU/mL) (95% CI)**	**Median fold increase of concentrations vs. pre-vaccination (Q1; Q3)**
ZOE-50						
≥ 50	1,070	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	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)
CI Confidence interval
GMC Geometric Mean Concentration
Q1; Q3 First and third quartiles

Table 4: 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 for the median frequency

Q1; Q3 First and third quartiles

*** The gE-specific CD4[2+] data in the ≥70 years of age group were only 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 approximately 6 years 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 in subjects receiving 2 doses of SHINGRIX 6 months apart

Efficacy has not been assessed for the 0, 6-month schedule.

In a phase III, open-label clinical study (Zoster-026) where 238 adults ≥ 50 years of age were equally randomised to receive 2 doses of *SHINGRIX* 2 or 6 months apart, the humoral immune response following the 0, 6-month schedule was demonstrated to be non-inferior to the response with the 0, 2-month schedule. The anti-gE GMC at 1 month after the last vaccine dose was 38,153.7 mIU/ml (95% CI: 34,205.8; 42,557.3) and 44,376.3 mIU/ml (95% CI: 39,697.0; 49,607.2) following the 0, 6-month schedule and the 0, 2-month schedule, respectively.

Subjects with a history of HZ prior to vaccination

Subjects with a history of HZ were excluded from ZOE-50 and ZOE-70. In a phase III, uncontrolled, open-label clinical study (Zoster-033), 96 adults ≥ 50 years of age with a physician-documented history of HZ received 2 doses of *SHINGRIX* 2 months apart. Laboratory confirmation of HZ cases was not part of the study procedures. The anti-gE GMC at 1 month after the last vaccine dose was 47,758.7 mIU/ml (95% CI: 42,258.8; 53,974.4).

There were 9 reports of suspected HZ in 6 subjects over a one-year follow up period. This is a higher recurrence rate than generally reported in observational studies in unvaccinated individuals with a history of HZ. (See section *4.4 Special Warnings and Precautions for Use*)

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.

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

In a phase III, open-label, multi-centre clinical study (Zoster-048), a 2 dose schedule of *SHINGRIX* 2 months apart was assessed in 215 adults ≥ 65 years of age with a previous history of vaccination with live attenuated HZ vaccine ≥ 5 years earlier compared to 215 matched subjects who had never received live attenuated HZ vaccine. The immune response to *SHINGRIX* was unaffected by prior vaccination with live attenuated HZ vaccine.

5.3 Pharmacokinetic Properties

Not applicable.

6 NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

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

7. DESCRIPTION

See section *2. Qualitative and quantitative composition* and section *3. Dosage form and strength*.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

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

8.2 Shelf Life

36 months

The expiry date of the vaccine is indicated on the label and packaging.

After reconstitution:

Chemical and physical in-use stability has been demonstrated for 24 hours at 30°C.

From a microbiological point of view, the vaccine should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 6 hours at 2°C to 8°C.

8.3 Packaging Information

- 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.

All presentations may not be marketed in the country.

8.4 Storage and Handling Instructions

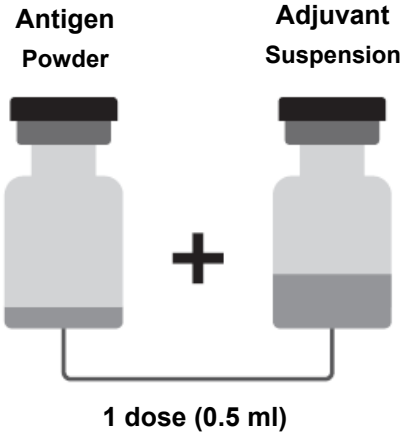
Store in a refrigerator (2°C – 8°C).
Do not freeze.
Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see *Section 8.2 Shelf Life*.

Keep out of reach of children.

SHINGRIX is presented as a vial with a brown flip-off cap containing the powder (antigen) and a vial with a blue-green flip-off cap containing the suspension (adjuvant).

The powder and the suspension must be reconstituted prior to administration.



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 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.

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

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) of the potential benefits and undesirable effects of vaccination with *SHINGRIX*. Patients (and/or patients' caregiver) may also be informed about posology (including vaccination schedule if applicable), method of administration and storage/handling information of *SHINGRIX* vaccine as applicable.

Registered Medical Practitioners may also choose to inform their patients (and/or patients' caregiver) about the special warnings and precautions for use, drug interactions, and any relevant contra-indications associated with *SHINGRIX* vaccine.

10. DETAILS OF MANUFACTURER

GlaxoSmithKline Biologicals S.A., Rue de I'Institut 89, B-1330, Rixensart, Belgium

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited
Registered Office
Dr. Annie Besant Road, Worli
Mumbai 400 030,
India

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Marketing Authorization Holder
GlaxoSmithKline Pharmaceuticals Limited
Registered Office

Dr. Annie Besant Road, Worli
Mumbai 400 030,
India

Marketing Authorization Details
Import Permission No.: IMP/BIO/22/000014 dated 21-Feb-2022

12. DATE OF REVISION

24-Jul-2024

Version SNX/PI/IN/2024/01

Adapted from EU SPC dated 20-Oct-2022 [GDS 07 dated 17-Feb-2022].