SKYZoster Inj.

Zoster Virus Vaccine (live) [Oka/SK] Subcutaneous Use Only

1. Composition

Each 0.5 mL of reconstituted vaccine contains:

Active ingredients:

Live, attenuated varicella-zoster virus (In-house) (Virus strain: Oka/SK, Cell line: MRC-5)	≥ 27,400 PFU

Excipients (Stabilizers):

Sucrose (Ph. Eur.)	25.00 mg
Hydrolyzed gelatin (NF)	12.50 mg
Urea (Ph. Eur.)	1.20 mg
Monosodium glutamate (NF)	0.55 mg
Disodium edetate (Ph. Eur.)	0.25 mg
L-cysteine (JP)	0.25 mg
Glycine (Ph. Eur.)	2.50 mg

Other Excipients:

Sodium dihydrogen phosphate dihydrate, Disodium phosphate dodecahydrate, Sodium chloride, Potassium chloride, Sodium hydroxide

Each diluent contains:

Sterilized water for injection (Ph. Eur.)	0.7 mL

2. Appearance

Lyophilized white crystalline pellet in a clear colorless vial. Colorless or pale yellow liquid in the vial when reconstituted to a suspension.

3. Indications

Prevention of herpes zoster (shingles) in individuals aged 50 years and older.

4. Dosage and administration

Administer total reconstituted vaccine volume (about 0.5 mL) as a single dose subcutaneously in the deltoid region of the upper arm. Do not inject intravascularly or intramuscularly.

5. Reconstitution and Administration instructions

Vial presentation

To reconstitute the vaccine, inject the entire content of the provided diluent into the vial of lyophilized vaccine using enclosed 23G needle and syringe.

Prefilled syringe presentation

To reconstitute the vaccine, inject the entire content of the provided diluent into the vial of lyophilized vaccine using enclosed 23G needle.

Gently agitate to dissolve completely. Withdraw the entire content (approximately 0.5 mL) of the reconstituted vaccine and inject the vaccine subcutaneously using enclosed 25G needle. The vaccine should be administered immediately after reconstitution, in order to minimize loss of potency. Discard reconstituted vaccine, if not used within 30 minutes.

6. Precautions for use

6.1 Contraindications

1) Individuals with a history of hypersensitivity reaction to gelatin or any other component in SKYZoster.

2) Individuals with a history of anaphylactic/anaphylactoid reaction to neomycin (trace amount of neomycin is present in the reconstituted vaccine).
3) Individuals with primary and acquired immunodeficiency states due to conditions such as acute and chronic leukemias; lymphoma; other conditions affecting the bone marrow or lymphatic system; immunosuppression due to HIV/AIDS; and cellular immune deficiencies.
4) Individuals on immunosuppressive therapy (including high-dose corticosteroids). However, SKYZoster is not contraindicated for use in individuals who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids or in patients who are receiving corticosteroids as replacement therapy for adrenal insufficiency. SKYZoster may cause disseminated diseases in individuals with immunodeficiency or on immunosuppressive therapy, as the vaccine is live, attenuated zoster virus vaccine.
5) Individuals with untreated active tuberculosis.
6) SKYZoster should not be administered to women who are or may be pregnant (refer to Section 6.5 Pregnancy and Lactation).

6.2 Adverse Reactions

1) Local (injection site) reaction: Pain, erythema/redness, and induration/swelling may occur.
2) Systemic reaction: Myalgia, fatigue/malaise, headache, diarrhea, vomiting and fever may occasionally occur after vaccination.
3) Safety of SKYZoster was evaluated in 842 subjects aged 50 years and older and 401 subjects (47.62%) experienced adverse drug reactions.

① Solicited adverse drug reactions† (local and systemic reactions) are summarized in below table.

		Total (N=842)	Phase I clinical trial (N=90)	Phase II/III clinical trial (N=340)	Phase III clinical trial (N=412)
Local reaction	Pain	22.92%	17.78%	27.94%	19.90%
	Erythema/redness	24.35%	30.00%	22.65%	24.51%
	Induration/swelling	9.98%	12.22%	12.06%	7.77%
Systemic reaction	Fever	0.59%	0.00%	1.18%	0.24%
	Vomiting	0.83%	0.00%	1.47%	0.49%
	Diarrhea	2.73%	3.33%	3.82%	1.94%
	Headache	8.31%	10.00%	9.12%	7.28%
	Fatigue/malaise	16.39%	20.00%	17.94%	14.32%
	Myalgia	16.75%	23.33%	14.41%	17.23%

†Adverse drug reactions were reported as per the clinical study protocols. The safety information of solicited adverse drug reactions was collected for 6 weeks post-vaccination in phase I clinical trial (N=90) and 5 days post-vaccination in phase II/III and III clinical trials (N=752).

② Unsolicited adverse drug reactions were reported in 19 (2.26%) out of 842 subjects during 6 weeks post-vaccination of SKYZoster. The most frequently reported unsolicited adverse drug reaction was skin and subcutaneous tissue disorders with 6 subjects (0.71%) reporting 7 cases. With regard to the outcomes of adverse drug reactions, all subjects were recovered without sequelae. Adverse drug reactions occasionally observed ($\geq$ 0.1 and < 5%) during the study period are shown below.

Disorders	Details
Respiratory, Thoracic and Mediastinal Disorders	Nasopharyngitis, upper respiratory tract infection
Skin and Subcutaneous Tissue Disorders	Pruritus, rash, erythematous rash, pruritus rash, rash vesicular, skin lesion, drug eruption
Psychiatric Disorders	Insomnia

Nervous System Disorders	Dreamy state, somnolence, dizziness, headache
Musculoskeletal and Connective Tissue Disorders	Musculoskeletal stiffness
Gastrointestinal Disorders	Nausea
Vascular Disorders	Vasculitis
General Disorder and Administration Site Conditions	Injection site pruritus
Ear and Labyrinth Disorders	Ear pain

③ 6 cases of serious adverse events were reported in 6 (0.71%) out of 842 subjects during 6 weeks post-vaccination reporting period (gastric cancer, bronchitis, contusion, lower limb fracture, pancreatitis, ligament sprain). All of these serious adverse events were determined to not have a causal relationship with SKYZoster.

④ Varicella-like and zoster-like rashes were diagnosed in 3 out of 842 subjects vaccinated with SKYZoster during 6 weeks post-vaccination reporting period and their causal relationship with SKYZoster could not be ruled out.

In phase I clinical trial, no subjects from the SKYZoster group and Zostavax® group reported varicella-like or zoster-like rash during 6 weeks post-vaccination reporting period.

In phase II/III clinical trial, 2 subjects reported varicella-like and zoster-like rash within 6 weeks post-vaccination. The specimen acquired from the subjects with zoster-like rash could not be determined as the specimen was inadequate for Polymerase Chain Reaction (PCR) testing. From the PCR testing result of the varicella-like rash specimen, varicella-zoster virus was detected, but not able to determine the virus strain (wild type or Oka/SK strain).

In phase III clinical trial, one subject from each SKYZoster and Zostavax® group reported varicella-like and zoster-like rashes. Of the reported cases, one case of varicella-like rash was reported in the SKYZoster group and while the PCR testing detected varicella-zoster virus, it could not determine virus strain (wild type or Oka/SK strain). The PCR testing on one case of zoster-like rash reported in Zostavax® group also detected varicella-zoster virus but the virus strain (wild type or Oka/Merck) could not be determined.

4) Post Marketing Experience in South Korea

During this 4-year post marketing surveillance (PMS) among 651 subjects for re-examination in South Korea, incidence rate of adverse events was reported by 11.67% (76/651 subjects, 121 cases) regardless of the causal relationship with the SKYZoster. No serious adverse drug reactions of which a causal relationship cannot be ruled out were reported. Unexpected adverse drug reactions of which causal relationship with the SKYZoster could not be ruled out are shown below according to its frequency.

	System Organ Class (SOC)	Unexpected adverse drug reactions were reported by 1.08% (7/651 subjects, 7 cases)
Uncommon (≥0.1% to <5%)	Musculoskeletal and Connective Tissue Disorders	Back pain
	General Disorders and Administration Site Conditions	Chills, Vaccination site discolouration
	Skin and Subcutaneous Tissue Disorders	Urticaria, Dermatitis contact

5) Analysis and assessment of post marketing adverse events in South Korea

Analysis and assessment of signal was conducted by comparing the adverse events from the post-marketing surveillance of SKYZoster with the post-marketing adverse events (Including adverse events from post-marketing surveillance) reported from all of licensed medicines in South Korea (1989-Dec 31, 2021), and the adverse event identified to occur more frequently in SKYZoster is as follows. However, this does not mean that the causal relationship between the component of this vaccine and the following adverse event has been proved.

- General disorders and administration site conditions: Chills

6.3 Precautions

1) The physicians should interview a recipient on post-vaccination experiences of live, attenuated varicella virus vaccine, before administrating SKYZoster.
2) SKYZoster should be administered only for prevention of herpes zoster (shingles) in individuals aged 50 years and older.
3) SKYZoster is not indicated for prevention of primary varicella infection (Chickenpox).
4) SKYZoster should be administered only to a recipient who can induce an adequate immune response.
5) SKYZoster is not indicated for treatment of zoster or post-herpetic neuralgia.
6) As with other vaccines, serious adverse reactions, including anaphylaxis, might occur with SKYZoster. Adequate treatment provisions, including epinephrine injection (1: 1,000), should be available for immediate use.
7) Deferral should be considered in acute illness (for example, in the presence of fever, > 38.0°C).
8) As with other vaccines, vaccination with SKYZoster does not result in protection of all vaccine recipients.
9) Effectiveness of the multiple-dose of SKYZoster has not been evaluated. The need for a boost dose is not defined.
10) Transmission of the vaccine virus has not been reported from SKYZoster clinical studies. However with live, attenuated varicella-zoster virus vaccines, transmission of vaccine virus may occur rarely between vaccinees with breakthrough infections and susceptible contacts.
11) No studies on the effects on the ability to drive or use machines have been performed.

6.4 Interaction

Concurrent administration of SKYZoster and anti-viral medications known to be effective against varicella-zoster virus has not been evaluated.

6.5 Pregnancy and Lactation

1) Safety of SKYZoster has not been evaluated in pregnant women. Direct and/or indirect adverse effect related to reproduction and developmental toxicity has not been observed in animal studies. However, SKYZoster should not be administered to pregnant women since naturally occurring varicella-zoster virus infection is known to sometimes cause fetal harm. Pregnancy should be avoided for 3 months following administration of SKYZoster (refer to Section 6.1 Contraindications).
2) It is not known whether varicella-zoster vaccine virus is excreted in human milk. However, since human milk transmission of maternal viral infection is established for some viruses, SKYZoster should not be administered to nursing mothers.

6.6 Pediatric Use

SKYZoster is not indicated for prevention of primary varicella infection (Chickenpox) and should not be used in children and adolescents.

6.7 Geriatric Use

The median age of subjects enrolled in the clinical studies (N=845), whom were administrated with SKYZoster, was 59 years (range 50-82 years). Of the subjects, 440 were 50-59 years of age, 298 were 60-69 years of age and 107 were 70 years and older. A total number of elderly subjects over 65 years of age was 229.

6.8 Special Precautions for Storage

1) Store SKYZoster refrigerated at 2°C to 8°C away from light.
2) SKYZoster should be reconstituted immediately upon removal from the refrigerator. After reconstitution, the vaccine should be used right away or up to 30 minutes when stored at room temperature. Do not freeze reconstituted vaccine.
3) To reconstitute and administer the vaccine in vial presentation, use the sterile syringe and needles provided. Dispose used needles appropriately to prevent being re-used to other individuals.

To reconstitute and administer the vaccine in prefilled syringe presentation, use the needles provided in the package. Dispose used needles appropriately to prevent being re-used to other individuals.

6.9 Others

Store in the original package and this medicinal product must not be mixed with other medicinal products in one syringe.

7. Storage

Keep refrigerated at 2°C to 8°C in a hermetic container away from light. Do not freeze.

8. Expiration date

As marked separately on the primary container.

9. Packaging units

Vial presentation

A package contains 1 single-dose vial of lyophilized vaccine, 1 vial of diluent (0.7 mL), 1 sterilized disposable syringe and 2 sterilized disposable needles (23G and 25G).

Prefilled syringe presentation

A package contains 1 single-dose vial of lyophilized vaccine and diluent (0.7 mL) in a prefilled syringe and 2 sterilized disposable needles (23G and 25G).

10. Manufacturer

SK bioscience Co., Ltd.
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11. Importer

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