

GCFLU Quadrivalent Pre-filled Syringe inj.

2024-2025 Season

Split Virion, Influenza Vaccine

[Description]

GCFLU Quadrivalent Pre-filled Syringe inj. is a vaccine containing colorless or slightly whitish liquid made by splitting and inactivating influenza virus cultured by inoculating the allantoic cavity of embryonated egg in order to maintain antigenicity.

[Composition]

1 Pre-filled Syringe 0.5ml contains,

| | |
|--|--------|
| Active Ingredient: Purified inactivated influenza virus antigen (In-house) | 60 µg |
| A/Victoria/4897/2022 IVR-238 (H1N1) | 15 µg |
| A/Thailand/8/2022 IVR-237(H3N2) | 15µg |
| B/Austria/1359417/2021 BVR-26 | 15µg |
| B/Phuket/3073/2013 | 15 µg |
| Buffer: Sodium chloride (EP) | 4 mg |
| Potassium chloride (EP) | 0.1 mg |
| Disodium hydrogen phosphate dihydrate (EP).... | 0.6 mg |
| Potassium dihydrogen phosphate (EP) | 0.1 mg |
| Diluent: Water for Injection (EP) | q.s. |
| Needle (Sterilized disposable needle (25G x 5/8 (0.5 x 16 mm)..... | ea |

This vaccine complies with the WHO recommendations (Northern Hemisphere) for 2024-2025 season.

[Indications]

Prophylaxis against influenza caused by influenza A subtype viruses and type B viruses in persons aged 6 months and older.

[Dosage & Administration]

An intramuscular injection of the following dose and immunization of one dose is necessary in every year at same volume. Aged 6 months and older: A single dose of 0.5 ml

The children younger than 9 years of age who have not been vaccinated should be vaccinated two doses at an interval of at least 4 weeks.

The preferred sites for intramuscular injection are the anterolateral aspect of the thigh (or the deltoid muscle of the upper arm if muscle mass is adequate) in children 6 through 35 months of age, or the deltoid muscle of the upper arm in children from 36 months of age and adults.

The safety and efficacy of the vaccine was not established in children younger than 6 months.

[Precautions for use]

1. Contraindications

Examine subjects by history taking and visual inspection and if necessary, by auscultation and percussion. Vaccination is prohibited when subject is diagnosed as one of the following cases. However, if there is a possibility of influenza infection and it is determined that there is no concern for significant disorder due to vaccination, subject may be vaccinated.

- 1) Febrile patient or person with malnutrition.
- 2) Patients with cardiovascular disorders, kidney disorders, or liver disease in which the disease is in acute phase, stadium incrementi, or in active phase.
- 3) Patients with acute respiratory disease or other active infectious disease.
- 4) Patients in latent and convalescence period.
- 5) Person who showed anaphylaxis by the components of the product.
- 6) Person with hypersensitivity to egg, chicken, any other chicken component, and the product component.
- 7) Person who had fever within 2 days or a symptom of allergy such as generalized rash after the injection at previous vaccination.
- 8) Person who showed the symptom of convulsion within 1 year before vaccination.
- 9) Person who showed Guillain-Barre syndrome within 6 weeks from the previous influenza vaccination or person with neurological disorders.
- 10) Person diagnosed with immunodeficiency disease.
- 11) Person in inappropriate condition to be vaccinated.

2. Adverse Reactions

1) There is possibility of local reactions such as redness, swelling and pain, or systemic reactions such as fever, chills, headache, fatigue and vomiting. But they usually disappear within 2-3 days.

2) In rare cases, acute disseminated encephalomyelitis (ADEM) may occur.

Fever, headache, convulsions, dyskinesia and consciousness disorder usually occur within 2 weeks following the administration of the vaccine. When these symptoms are suspected, appropriate medical treatment should be available by diagnosis with MRI and so on.

3) Allergic reaction or anaphylactic shock may occur in very rare cases.

4) Transient disorders of systemic and local nervous system may rarely occur. Palsy, neuralgia, cerebral hemorrhage or inflammation of the nervous system (ex: Guillain-Barre syndrome) have been reported.

5) Safety of the vaccine was evaluated for the 4 clinical studies performed with healthy children, adults, and elderly. In children aged 6 through 35 months who received the vaccine, 115 subjects (67.6%) out of 170 subjects showed adverse events. Adverse drug reactions were 82 subjects (48.2%) and no serious adverse drug reactions were reported. In children aged 3 through 18 years who received the vaccine, 218 subjects (68.3%) out of 319 subjects showed adverse events. Adverse drug reactions were 204 subjects (63.9%) and no serious adverse drug reactions were reported. In adults aged 19 through 64 years who received the vaccine, 415 subjects (71.2%) out of 583 subjects showed adverse events. Adverse drug reactions were 399 subjects (68.4%) and no serious adverse drug reactions were reported.

In elderly over 65 years of age who received the vaccine, 148 subjects (43.8%) out of 338 subjects showed adverse events.

Adverse drug reactions were 140 subjects (41.4%) and no serious adverse drug reactions were reported.

(1) Solicited adverse drug reactions within 7 days of vaccination are listed in the table below.

| | | Children aged 6 through 35 months (n=170) | Children aged 3 through 18 years (n=319) | Adults aged 19 through 64 years (n=583) | Elderly over 65 years of age (n=338) |
|----------|--------------------------|---|--|---|--|
| Local | Pain | 27.6% | 52.7% | 48.9% | 21.0% |
| | Tenderness | | 54.5% | 56.8% | 27.5% |
| | Erythema/Redness | 11.8% | 6.6% | 7.9% | 3.8% |
| | Induration/ Swelling | 5.9% | 8.2% | 5.8% | 3.6% |
| Systemic | Drowsiness ¹⁾ | 15.9% | - | - | - |
| | Fever | 6.5% | 3.1% | 0.9% | 0.3% |
| | Sweating | 2.4% | 2.2% | 4.3% | 2.7% |
| | Chills | 2.4% | 5.0% | 7.7% | 4.4% |
| | Nausea/ vomiting | 2.4% | 0.6% | 2.2% | 0.9% |
| | Diarrhea | 5.9% | 0.3% | 1.5% | 1.2% |
| | Fatigue | - | 15.4% | 25.6% | 10.7% |
| | Malaise | - | 11.0% | 7.5% | 8.3% |
| | Headache | 0.6% | 6.9% | 13.4% | 7.1% |
| | Muscle aches | 7.6% | 8.2% | 26.4% | 6.5% |
| | Arthralgia | - | 1.6% | 5.8% | 3.6% |

1) Drowsiness only applies for children aged 6 months through 35 months

(2) Unsolicited adverse drug reactions occurring within 28 days or 21 days of vaccination were reported in 4 subjects (2.4%) from children aged 6 through 35 months (Infections and infestations: 3 subjects, Skin and subcutaneous tissue disorders: 1 subject), 3 subjects (0.9%) from children aged 3 through 18 years (General disorders and administration site conditions: 2 subjects, Infections and infestations: 1 subject), 13 subjects (2.2%) from adults (Infections and infestations: 5 subjects, investigations: 2 subjects, Respiratory thoracic and mediastinal disorders: 2 subjects, Musculoskeletal and connective tissue disorders: 1 subject, Nervous system disorders: 1 subject, Skin and subcutaneous tissue disorders: 1 subject, General disorders and administration site conditions: 2 subjects), and 4 subjects (1.2%) from elderly (Infections and infestations: 1 subject, General disorders and administration site conditions: 1 subject, investigations: 1 subject, Nervous system disorders: 1 subject)

(3) Serious adverse events occurring within 6 months of vaccination were reported in 13 subjects (7.6%) from children aged 6 through 35 months (Pneumonia: 4 cases, Influenza: 3 cases, Bronchitis: 2 cases, Pneumonia respiratory syncytial viral: 1 case, Bronchiolitis: 1 case, Croup infectious: 1 case, Gastroenteritis norovirus: 1 case, Gastroenteritis rotavirus: 1 case, Urinary tract infection: 1 case, Gastrointestinal infection: 1 case, Impaired healing: 1 case, Foreign body in gastrointestinal tract: 1 case, Febrile convulsion: 1 case), 5 subjects (1.6%) from children aged 3 through 18 years (Pharyngitis: 1 case, Headache: 1 case, Mesenteric lymphadenitis: 1 case, Acute gastroenteritis: 1 case, Peritonsillar Abscess: 1 case, Acute appendicitis: 1 case), 5 subjects (0.9%) from adults (Cystitis: 1 case, Pulmonary Tuberculosis: 1 case, Breast mass: 1 case, ileus: 1 case, Gastric cancer: 1 case), and 4 subjects (1.2%) from elderly (Pain: 1 case, Arthralgia: 1 case, Herpes zoster: 1 case, Gastric cancer: 1 case), but they were evaluated as 'not related' to the product.

6) Results of post-marketing surveillance in South Korea

(1) The results of post-marketing surveillance conducted domestically for 4 years on 2,060 adult subjects aged 19 years and older in order to go through a re-examination showed that the incidence of adverse events was 10.49% (216 out of 2,060 subjects, 578 cases in total, regardless of causal relationship. Among these, no serious adverse events and serious adverse drug reactions have been reported. In addition, unexpected adverse events and unexpected adverse drug reactions are listed in the following table according to their frequency of onset.

| | | Unexpected Adverse Events Regardless of Causal Relationship 2.33% (48 out of 2,060 subjects, 72 cases) | Unexpected Adverse Drug Reactions of Which Causal Relationship Cannot Be Ruled Out 0.29% (6 out of 2,060 subjects, 7 cases) |
|---|---|--|---|
| Rarely ($\geq 0.01\%$ and $< 0.1\%$) | Respiratory, thoracic, and mediastinal disorders | Asthma | Cough |

| | | | |
|---|---|---|-----------------------------|
| | Gastrointestinal disorders | Dyspepsia, benign gastrointestinal neoplasm, gastrointestinal disorder NOS, hemorrhoids | - |
| | General disorders and administration site condition | Injection site inflammation | Injection site inflammation |
| | Nervous system disorder | Apathy, insomnia, dizziness, cerebral ischemia. | Apathy, dizziness |
| | Eye disorders | Blepharitis, conjunctivitis | - |
| | General disorders and administration site condition | Back pain | - |
| | Vascular disorders | Hypertension | - |
| | Cardiac disorders | Palpitation | Palpitation |
| | Metabolism and nutrition disorders | Hyperlipidemia | - |
| | Infections and infestations | Fungal dermatitis, moniliasis | - |
| Uncommonly ($\geq 0.1\%$ and $< 1\%$) | Respiratory, thoracic, and mediastinal disorders | Rhinitis, sinusitis, cough, upper respiratory tract infection | - |
| | Gastrointestinal disorders | Gastritis, gastroesophageal reflux, abdominal pain, irritable bowel syndrome | - |
| | Skin and subcutaneous tissue disorders | Dermatitis, pustular rash, contact dermatitis, urticaria | - |
| | General disorders and administration site condition | Cellulitis, injection site pruritus | Injection site pruritus |

(2) The results of post-marketing surveillance conducted domestically for 4 years on 2,033



pediatric subjects aged \geq postnatal 6 months and < 19 years showed that the incidence of adverse events was 30.74% (625 out of 2,033 subjects, 1,221 cases in total), regardless of causal relationship. Among these, serious adverse events and serious adverse drug reactions are listed in the following table according to their frequency of onset.

| | | | |
|--|---|---|---|
| | | Serious adverse Events 0.10% (2 out of 2,033 subjects; 2 cases) | Serious adverse Drug Reactions 0.00% (0 out of 2,033 subjects; 0 cases) |
| Rarely ($\geq 0.01\%$ and $< 0.1\%$) | White cell and reticuloendothelial system disorders | Kawasaki disease* | - |
| | Respiratory system disorders | Bronchitis | - |

* Unexpected serious adverse event

In addition, unexpected adverse events and unexpected adverse drug reactions are listed in the following table according to their frequency of onset.

| | | | |
|--|---|--|---|
| | | Unexpected Adverse Events Regardless of Causal Relationship 7.82% (159 out of 2,033 subjects; 178 cases) | Unexpected Adverse Drug Reactions of which Causal Relationship Cannot Be Ruled Out 0.49% (10 out of 2,033 subjects; 10 cases) |
| Rarely ($\geq 0.01\%$ and $< 0.1\%$) | Application site disorders | Cellulitis, Injection site bruising | Injection site bruising |
| | Body as a whole-general disorders | Leg pain, Influenza-like symptoms, Hypothermia, Temperature changed sensation | Leg pain, Hypothermia, Temperature changed sensation |
| | Gastrointestinal system disorders | Constipation, Gastroesophageal reflux | - |
| | Skin and appendages disorders | Acne, dermatitis contact, Dermatitis fungal, Skin disorder | Rash pustular |
| | Resistance mechanism disorders | Moniliasis | Otitis media |
| | White cell and reticuloendothelial system disorders | Kawasaki disease, Lymphadenopathy | |
| | Secondary terms-events | Varicella | |

الإدارة المركزية للمستحضرات الحيوية والمبتكرة
 إدارة تسجيل المستحضرات الصيدلانية
 وزارة الصحة
 تاريخ: ١٠/١٠/٢٠١٩
 ملاحظة: يرجى إكمال الملف

2) The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

3) Following influenza vaccination, false positive results in serologic tests using the ELISA method to detect antibodies against HIV-1, Hepatitis C, and especially HTLV-1 have been observed (The Western Blot technique disproves the false-positive ELISA test results). These transient false-positive results could be due to the IgM response by the vaccine.

5. Use in Pregnancy and Nursing Mothers

1) Pregnancy

Inactivated Influenza vaccine (egg-derived) is known that it can be used in all pregnancy cycles regardless of the pregnancy stage. There are more safety data for second trimester and third trimester compared with the first trimester. In addition, according to data on the usage of inactivated influenza vaccine collected globally, no adverse effects of the vaccine on the fetus and maternity were reported.

In addition, no direct or indirect adverse effects related to reproductive toxicity and developmental toxicity were observed in animal studies conducted using this vaccine. However, clinical trials have not evaluated the safety of the pregnant women when administered this vaccine.

2) Nursing Mothers

- Inactivated Influenza vaccine (egg-derived) is known that it can be used to lactating women. Restricted data indicate that the vaccine is not known whether the product is excreted in human milk. However, there is no adequate study of vaccination in animals during lactation, and clinical trials have not evaluated the safety of nursing mothers when administered this vaccine.

6. Precautions in Administration

1) Before use check this product visually for particles or discoloration. If either is present, do not use.

2) The injection site is usually lateral upper arm and disinfected with ethanol or tincture of iodine. Repeated injections at the same site should be avoided.

3) Intravenous administration is prohibited.

4) The tip of needle should not penetrate blood vessel.

5) Do not mix with other vaccines in same syringe.

6) Pre-filled syringes are disposable and should not be reused.

7. Precautions for Handling

1) Store at 2-8°C without freezing.

2) The vaccine should be shaken well and mixed homogeneously before use.

Store at 2-8°C without freezing in hermetic container and protect from light. The shelf life is 42 months from the date of manufacture.

0.5 mL/ Pre-filled Syringe x In-house packing unit.

June 2024.

