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Live Attenuated Varicella Virus Vaccine

BARYCELA inj.

BARYCELA inj. is a lyophilized formulation containing live Attenuated Varicella Virus Vaccine

[Composition]

Each 0.5 ml of reconstituted vaccine contains,

Active ingredient: Live attenuated varicella virus (Virus strain: MAV/06, cell line: MRC-5)....≥ 3,800 PFU

Above Buffering agent insert Excipients: Potassium dihydrogen phosphate.....0.06 mg

Dibasic sodium phosphate hydrate.....1.14 mg

Sodium L-glutamate hydrate.....0.40 mg

Sucrose..... 18.21 mg

L-cysteine..... 0.18 mg

Glycine..... 1.82 mg

Disodium edetate hydrate.....0.18 mg

Urea..... 0.87 mg

Gelatin (Animal-derived ingredient: derived from porcine skin).. 8.74 mg

Enclosed solvent: Sterile Water for injection (diluent)..... 0.7 mL

[Description]

This vaccine is a white lyophilized formulation for injection contained in a colorless and transparent vial, and appears colorless or light yellow when reconstituted with the enclosed solvent.

[Indication and usage]

This vaccine is indicated for active immunization for the prevention of varicella in children from 12 months to 12 years of age.

[Dosage & Administration]

1. Recommended Dose

the entire quantity of this vaccine (approximately 0.5ml) shall be subcutaneously injected into the outer aspect of the upper arm (deltoid region). **Do not administer this product intravascularly or intramuscularly.**

2. Reconstitution Instructions

To reconstitute this vaccine, fill a syringe with the entire quantity of the enclosed diluent, and inject it into the vial containing the lyophilized vaccine. Then, agitate the vial to mix completely. Fill a syringe with the entire quantity of this solution, and then inject the entire quantity (approximately 0.5 ml) subcutaneously into the outer aspect of the upper arm (deltoid region). To minimize the loss of potency,

this drug must be administered immediately after preparation, and it must be discarded if it is not used within 30 minutes after preparation.

[Precautions for use]

1. This vaccine is contraindicated to the following patients:

1) Patients who have had hypersensitivity reactions (especially anaphylactic reactions) to the component of this vaccine, such as gelatin;

2) Patients who are in a state of primary and acquired immunodeficiency due to the following conditions: Acute and chronic leukemia, lymphoma or other conditions affecting the bone marrow/lymphatic system, immunosuppression due to HIV/AIDS, cell-mediated immunodeficiency;

3) Patients receiving immunosuppressive therapy (Since BARYCELA inj. is a live attenuated varicella vaccine, rash or disseminated disease may manifest more severely if it is administered to patients with immunodeficiency, patients receiving immunosuppressive therapy, and patients being administered immunosuppressive doses of corticosteroids.);

4) Patients with untreated active tuberculosis;

5) Pregnant women and women of childbearing potential (see section "5. Administration in Pregnant women and nursing mothers");

6) Patients with febrile respiratory disease or other febrile infections.

2. Adverse reactions (Adverse Reactions)

1) The information on adverse reactions obtained from the safety evaluation of this vaccine in 484 pediatric subjects from 12 months to 12 years of age is shown below. After vaccination, adverse reactions occurred in 275 subjects (56.8%).

2) Local reactions: Reactions such as pain, tenderness, and erythema/redness may occur.

3) Systemic reactions: Systemic reactions such as cough, fever, and anorexia/loss of appetite may occur after vaccination.

① Solicited local site/systemic adverse reaction that were observed for 7 days after vaccinationwith this vaccine are as follows:

		Phase 2/3 (N = 484)
Local Reaction	Pain	21.7%
	Tenderness	21.1%
	Erythema/Redness	23.1%
	Induration	9.5%
	Pruritus	3.9%
	Urticaria	1.4%
	Swelling	3.1%
Systemic Reactions	Cough	13.6%
	Fever	9.9%
	Anorexia/loss of appetite	8.5%
	Vomiting/nausea	5.2%
	Rash	4.8%
	Constipation	3.9%
	Headache	3.9%
	Abdominal pain	2.9%
	Dyspnea	2.5%
	Fatigue	2.1%
	Allergy	1.9%
	Hypersensitivity	1.0%
	General mucositis	0.2%

② Unsolicited adverse drug reactions observed for 42 days after this vaccination were reported in 70 subjects (14.5%) out of 484 pediatric subjects from ≥ 12 months to ≤ 12 years of age. Adverse reactions related to infections and infestations were the most prevalent with 48 cases in 46 subjects (9.5%). Adverse reactions related to general disorders and administration site conditions, Adverse reactions related to gastrointestinal system disorders, and Adverse reactions related to skin and subcutaneous tissue disorders were shown in 11 cases in 11 subjects (2.3%), 10 cases in 9 subjects (1.9%), and 11 cases in 10 subjects (2.1%), respectively. The adverse reactions occurred as shown below. (rarely: 0.1 to < 5%)

- Infections and infestations

Occasionally: Adenoviral conjunctivitis, bronchitis, infectious diarrhea, viral gastritis, gastroenteritis, viral gastroenteritis, herpangina, impetigo, nasopharyngitis, pharyngitis, bacterial tonsillitis, upper respiratory tract infection, varicella, viral infection, viral pharyngitis

- Systemic disorders and administration site conditions

Occasionally: Fever, injection site reaction

- Skin and subcutaneous tissue disorders

Occasionally: Dermatitis, atopic dermatitis, rash, papular rash, vesicular rash- Gastrointestinal system

Occasionally: Diarrhea, food poisoning, gastrointestinal inflammation, vomiting

- Respiratory system

Occasionally: Epistaxis

- Vascular disorders

Occasionally: Hypertension

③ Forty (40) Serious Adverse Events (1 case each of diarrhea, gastrointestinal inflammation, influenza-like illness, and fever; 8 cases of bronchitis; 1 case of infectious croup; 1 case of infectious diarrhea; 4 cases of gastroenteritis; 1 case of rotaviral gastroenteritis; 1 case of viral gastroenteritis; 1 case of hand-foot-mouth disease; 1 case of flu; 1 case of pharyngitis; 4 cases of pneumonia; 1 case of bacterial pneumonia; 1 case of respiratory syncytial virus pneumonia; 4 cases of viral pneumonia;and 1 case each of tonsillitis, bacterial tonsillitis, viral pharyngitis, accidental exposure to drugs, accidental exposure to drug packaging materials, and laceration) occurred in 36 subjects (7.4%) out of 484 subjects during a period of 6 months following vaccination. Of these serious adverse events ,4 cases (1 case each of (1 case of gastrointestinal inflammation, infectious diarrhea, viral gastroenteritis, and viral pharyngitis) were related to use of this vaccine.

④ During a period of 42 days after this vaccination, one or more varicella-like rash occurred in a total of 9 (1.9%) of 484 subjects. Samples were taken from the subjects' lesion sites and VZV genotyping was performed. The results were "VZV not detectable" for 7 subjects. One subject was confirmed as having wild type. VZV genotyping was not performed for the remaining 1 subject since only a phone call visit was made anda blister swab could not be collected.

To report any side effect(s):

• **Egypt:**

- **Egyptian Pharmacovigilance Centre (EPVC):**

- e-mail for reporting: **pv.followup@edaegypt.gov.eg**
- Website for reporting: **https://vigiflow-eforms.who-umc.org/eg/med**
- Hotline: 15301
- Scan QR code:

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3. General precautions

1) The duration of prophylaxis of this vaccine against varicella infection is unknown.
2) Efficacy has not been established for multiple injections of this vaccine. The necessity for a second vaccination is unclear.

3) As with other vaccines, this vaccine does not have prophylactic effects in every vaccinated individual.
4) As with other vaccines, appropriate emergency measures, including epinephrine injections (1:1000), shall be available for immediate use since anaphylaxis/anaphylactoid reactions may occur after vaccination.
5) If acute conditions such as fever exceeding 38°C are shown, postponement of vaccination should be considered.
6) If blood or plasma was transfused, or if immunoglobulins or varicella-zoster immunoglobulins were administered, this vaccine should be administered after a minimum vaccination interval (3 to 11 months) has passed, depending on the type and dose of the blood or immunoglobulin formulation.
7) This vaccine must not be administered concomitantly with immunoglobulins, including varicella-zoster immunoglobulins. In addition, immunoglobulins must not be administered for 2 months after this vaccination, unless the benefits of administration of all immunoglobulins including varicella-zoster immunoglobulins outweigh the benefits of the vaccination.
8) As Reye's syndrome has been reported after the use of salicylate for natural varicella infection, the vaccinated individual should avoid using salicylate for 6 weeks after vaccination.
9) Transmission of the vaccine virus was not observed in the clinical trials of this vaccine. However, in the case of a similar vaccine, a post-marketing study verified that the virus can be transmitted through contact between healthy vaccinated individuals showing a varicella-LIKE rash and healthy but susceptible individuals in rare cases. In addition, transmission of the virus from vaccinated individuals who do not manifest a varicella-LIKE rash has been reported. Thus,if possible, vaccinated individuals should avoid close contact with highly susceptible individuals for 6 weeks. If contact with individuals having high-risk susceptibility cannot be avoided, the potential risks of viral transmission due to the vaccine and the risks of acquisition and transmission of natural varicella virus should be compared. Individuals with high-risk susceptibility are as follows:

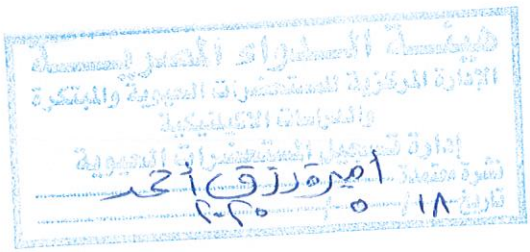
   • Immunocompromised persons;
   • Pregnant women without medical history of varicella or evidence of infection based on clinical test results;
   • Newborns of pregnant women without medical history of varicella or evidence of infection based on clinical test results.

4. Interactions

Refer to section "3. General precautions" for matters regarding immunoglobulins, salicylate, and transfusions.

5. Administration in pregnant women and nursing mothers

1) The safety of this vaccine when administered to pregnant women has not been evaluated. However, pregnant women should not be given this vaccine since naturally occurring varicella-zoster virus infection is sometimes known to have harmful effects on the fetus. In addition, pregnancy should be avoided for 3 months after vaccination (see section "1. This vaccine must not be administered to the following patients").
2) It is unknown whether live attenuated varicella virus is secreted in human milk. However, since some viruses are secreted in human milk, caution should be taken when administering this vaccine to nursing mothers.



6. Administration in children

This vaccine should not be administered to children aged < 12 months since its safety and efficacy have not been established for children of this age.

7. Administration in the elderly

This vaccine should not be used in adults including the elderly for the purpose of prophylaxis against varicella.

8. Precautions for administration

1) This vaccine should be stored under refrigeration. It should be taken from the refrigerator and prepared immediately prior to vaccination, and once dissolved, it should be used within 30 minutes. The prepared vaccine must not be frozen.
2) Separate sterile needles and syringes should be used for each individual to prevent transmission of infectious diseases. Once used, the needles must not be reused and must be appropriately discarded.
3) When preparing this vaccine, it must be dissolved with its own enclosed solvent since there are concerns of virus inactivation if preservatives or antiviral substances are present in the solvent.

9. Precautions for storage and handling

1) Storage of the vaccine in any container other than the original packaging may cause accidents and is undesirable in terms of maintaining quality.
2) This vaccine must not be used by being dissolved together or mixed with other drugs, including other virus vaccines.

10. Information for specialists

1) Information on pharmacological action

As a live attenuated varicella vaccine made of varicella-zoster virus (attenuated MAV/06 Strain), this vaccine includes immune response to varicella infection.

2) Information on clinical trial

The immunogenicity of this vaccine was evaluated in a randomized, double-blind, multicenter, multinational, active-controlled, non-inferiority study in healthy children aged from 12 months and to 12 years, 515 children were randomized and received either BARYCELA (N=258) or active control (N=257). The results of performing an evaluation of the primary immunogenicity in 478 subjects included in the per control set (PPS) showed that the seroconversion rate assessed by the fluorescent-antibody-to-membrane-antigen (FAMA) assay for antibody titer satisfied the non-inferiority criterion. The non-inferiority outcome was to be achieved if the lower limit of 2-sided 95% CI of the Seroconversion rate (SCR) difference between the 2 groups was greater than -15%. The following table shows the statistical analysis of non-inferiority in seroconversion rate at 42 days post-vaccination in a phase 3 clinical trial.

		BARYCELA (N=239)	Active Control (Varicella Virus Vaccine Live) (N=239)
Seroconversion rate	% (n/N)	97.91 (234/239)	99.16 (237/239)
	95% CI of Seroconversion rate	(95.19, 99.32)	(97.01, 99.90)
	Difference between two vaccines	-1.3	
	95% CI of the difference between two vaccines	[-4.03, 1.22]	
*Definition of Seroconversion rate: the appearance of antibody titer of 1:4 or higher from seronegative status by fluorescent antibody to membrane antigen (FAMA) assay is considered seroconversion at 42 days after administration			

3) Information on non-clinical studies
No significant findings that may be of particular importance to use in humans were identified in the results of repeat-dose toxicity and local tolerance studies performed on this vaccine.

[Storage Method and Shelf Life]

Store under refrigeration at 2–8°C (Do not freeze) and protected from light. Shelf-life is 24 months from the date of manufacture.

[Packing Unit]

A box of 1 vaccine vial (≥3800 PFU per 0.5 ml vial) and 1 diluent vial (0.7 ml).

A box of 10 vaccine vials (≥3800 PFU per 0.5 ml vial) and 10 diluent vials (0.7 ml).

[Revision date]

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GC Biopharma

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