Summary of Product Characteristics

1. Name of the Medicinal Product

Brand Name: NEXIPOX PLUS®

Generic Name or International Non-Proprietary Name (INN):
Live Attenuated Varicella Vaccine

2. Qualitative and Quantitative Composition
2.1 Qualitative Declaration
Oka virus strain

2.2 Quantitative Declaration
Each 0.5 ml contains:
Oka Virus Strain…..... ≥3.31g PFU (2000 PFU)

3. Pharmaceutical Form
White fluey pellet in the glass vial.
The reconstituted vaccine after dissolution with diluent is a clear solution without visually detectable presence of foreign particles.

4. Clinical Particulars
4.1 Therapeutic indications
The vaccine is indicated for active immunisation against varicella in healthy adults and adolescents (≥ 13 years) who have been found to be seronegative with respect to the varicella-zoster virus and are, therefore, at risk of developing chickenpox.

4.2 Posology and method of administration
Children 1-12 years, adolescents (≥ 13 years) and adults

Two doses (each of 0.5 ml of reconstituted vaccine) should be given, with an interval between doses of at least 6 weeks but in no circumstances less than 4 weeks.

One dose may be administered after a first dose of another varicella containing vaccine.

There are insufficient data to determine the long-term protective efficacy of the vaccine. However, there is currently no evidence that further doses are routinely required following completion of a two-dose regimen in healthy adolescents and adults.

If it is to be administered to seronegative subjects before a period of planned or possible future immunosuppression (such as those awaiting organ transplantation and those in remission from malignant disease), the timing of the vaccinations should take into account the delay after the second dose before maximal protection might be expected.
Varicella Vaccine should not be administered to children aged less than one year.

Elderly
There are no data on immune responses to Varicella Vaccine in the elderly.

Method of administration
Varicella Vaccine is for subcutaneous administration only. The upper arm (deltoid region) is the preferred site of injection.

Varicella Vaccine should not be administered intradermally.

Varicella Vaccine must under no circumstances be administered intravascularly.
Varicella Vaccine must not be mixed with any other medicinal product in the same syringe.

4.3 Contraindications
Varicella Vaccine is contra-indicated in subjects who have a history of hypersensitivity to neomycin, or to any of the excipients in the vaccine, or to any other varicella vaccine.

A second dose of Varicella Vaccine is contra-indicated in subjects who have had a hypersensitivity reaction following the first dose.

Varicella Vaccine is contra-indicated during pregnancy and breast-feeding.

Furthermore, pregnancy should be avoided for 1 month following vaccination.

Varicella Vaccine must not be administered to subjects with primary or acquired immunodeficiency states with a total lymphocyte count less than 1,200 per mm^3 or presenting other evidence of lack of cellular immune competence, such as subjects with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infection, or patients receiving immunosuppressive therapy (including high dose corticosteroids).

Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia and AIDS or symptomatic HIV infection or an age-specific CD4+ T-lymphocyte percentage in children below 12 months: CD4+ <25%; children between 12-35 months: CD4+ < 20%; children between 36-59 months: CD4+ < 15%.

Administration of Varicella Vaccine must be postponed in subjects suffering from acute, severe febrile illness. In healthy subjects the presence of a minor infection, however, is not a contraindication.

4.4 Special warnings and precautions for use
As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic reaction following the administration of the vaccine.

Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents 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.

Serological studies of efficacy and post-marketing experience indicate that the vaccine does not completely protect all individuals from naturally-acquired varicella and cannot be expected to provide maximal protection against infection with varicella-zoster virus until about six weeks after the second dose.
Administration of Varicella Vaccine to subjects who are in the incubation period of the infection cannot be expected to protect against clinically manifest varicella or to modify the course of the disease.

The rash produced during naturally-acquired primary infection with varicella-zoster may be more severe in those with existing severe skin damage, including severe eczematous conditions. It is not known if there is an increased risk of vaccine-associated skin lesions in such persons, but this possibility should be taken into consideration before vaccination.

Transmission of the vaccine viral strain

Transmission of vaccine viral strain has been shown to occur from healthy vaccinees to healthy contacts, to pregnant contacts and to immunosuppressed contacts. However, transmission to any of these groups occurs rarely or very rarely and has not been confirmed to occur in the absence of vaccine-associated cutaneous lesions in the vaccine.

In healthy contacts of vaccinees, seroconversion has sometimes occurred in the absence of any clinical manifestations of infection. Clinically apparent infections due to transmission of the vaccine viral strain have been associated with few skin lesions and minimal systemic upset.

However, contact with the following groups must be avoided if the vaccine develops a cutaneous rash thought likely to be vaccine-related (especially vesicular or papulovesicular) within four to six weeks of the first or second dose and until this rash has completely disappeared.

- varicella-susceptible pregnant women and

- individuals at high risk of severe varicella, such as those with primary and acquired immunodeficiency states. These include individuals with leukaemias, lymphomas, blood dyscrasias, clinically manifest HIV infections, and patients who are receiving immunosuppressive therapy, including high dose corticosteroids.

In the absence of a rash in the vaccine, the risk of transmission of the vaccine viral strain to contacts in the above groups appears to be extremely small. Nevertheless, vaccinees (*e.g.* healthcare workers) who are very likely to come into contact with persons in the above groups should preferably avoid any such contact during the period between vaccinations and for 4-6 weeks after the second dose. If this is not feasible, then vaccinees should be vigilant regarding the reporting of any skin rash during this period, and should take steps as above if a rash is discovered.

Healthy seronegative children may be vaccinated if they are close contacts of persons who are at high risk of severe varicella infection. In these circumstances, continued contact between the vaccine and the person at risk may be unavoidable. Therefore, the risk of transmission of the attenuated vaccine viral strain from the vaccine should be weighed against the potential for acquisition of wild-type varicella-zoster by the at-risk person.
The Oka vaccine viral strain has recently been shown to be sensitive to acyclovir. Vaccination may be considered in patients with selected immune deficiencies where the benefits outweigh the risks (e.g. asymptomatic HIV subjects, IgG subclass deficiencies, congenital neutropenia, chronic granulomatous disease, and complement deficiency diseases).

Immunocompromised patients who have no contraindication for this vaccination may not respond as well as immunocompetent subjects, therefore some of these patients may acquire varicella in case of contact, despite appropriate vaccine administration. These patients should be monitored carefully for signs of varicella.

4.5 Interaction with other medicinal products and other forms of interaction
In subjects who have received immune globulins or a blood transfusion, vaccination should be delayed for at least three months because of the likelihood of vaccine failure due to passively acquired antibody to the varicella-zoster virus.

Aspirin and systemic salicylates should not be given to children under the age of 16, except under medical supervision, because of the risk of Reye's syndrome. Reye's syndrome has been reported in children treated with aspirin during natural varicella infection. However, there is no evidence to suggest that vaccination with Varicella Vaccine should be contraindicated for older age-groups who need to take aspirin.
In a study in which Varicella Vaccine was administered to toddlers at the same time as, but at a different site to, a combined measles, mumps and rubella vaccine, there was no evidence of significant immune interference between the live viral antigens.

If a measles containing vaccine is not given at the same time as Varicella Vaccine, it is recommended that an interval of at least one month between vaccinations is respected, since it is recognized that measles vaccination may cause short-term suppression of the cell-mediated response.

If it is considered necessary to administer another live vaccine at the same time as Varicella Vaccine, the vaccines must be given as separate injections and at different body sites.

4.6 Pregnancy and lactation
Pregnancy
Pregnant women should not be vaccinated with Varicella Vaccine. However, fetal damage has not been documented when varicella vaccines have been given to pregnant women.

Pregnancy should be avoided for 1 month following vaccination. Women who intend to become pregnant should be advised to delay.

Lactation
The infants of seronegative women would not have acquired transplacental antibody to varicella-zoster virus. Therefore, due to the theoretical risk of transmission of the vaccine viral strain from mother to infant, women should not be vaccinated while breastfeeding.

Fertility
No fertility data are available

4.7 Effects on ability to drive and use machines
It would not be expected that vaccination would affect the ability to drive or operate machinery.

4.8 Undesirable effects
Clinical trials in healthy subjects

Total sample size in Phase III clinical trials should be 600, 400 in test group and 200 in control group, respectively. Subjects aged range 1-12 years old would be assigned to two sub-groups, Infant Sub-group (age 1 to 5) and Child Sub-group (age 6 to 12), and 300 subjects for each sub-group. Every subject should receive single dose of test vaccine or control vaccine randomly. Compliances for immunogenicity and safety observation were 88.00% and 100.00%, respectively, which both met protocol requirements.

Total incidences of local adverse reactions in test group and control group were 5.25% and 6.00%, respectively, for which difference had no statistical significance ($X^2 = 0.1443$, $p = 0.7035$). Except for 1 local (0.25%) Grade 2 reactions in test group recorded, no other reactions were observed higher than Grade 2; therefore, difference between two groups had no statistical significance. Difference of incidences of local reaction between Infant sub-group and Child sub-group in test group had no statistical significance. No serious local adverse reactions were observed.

Frequencies are reported as:

Very common:	≥10%
Common:	≥1% and <10%
Uncommon:	≥0.1% and <1%
Rare:	≥0.01% and <0.1%
Very rare:	<0.01%

Blood and lymphatic system disorders
Uncommon: lymphadenopathy

Nervous system disorders
Uncommon: headache, somnolence
Very rare: dizziness

Eye disorders
Rare: conjunctivitis

Respiratory, thoracic and mediastinal disorders
Uncommon: cough, rhinitis

Gastrointestinal disorders
Uncommon: nausea, vomiting
Rare: abdominal pain, diarrhoea

Skin and subcutaneous tissue disorders
Common: rash

Uncommon: varicella-like rash, pruritus
Rare: urticaria

Musculoskeletal and connective tissue disorders
Uncommon: arthralgia, myalgia
Infections and infestations
Uncommon: upper respiratory tract infection, pharyngitis

General disorders and administration site conditions
Very common: pain, redness and swelling at the injection site*, fever (oral/axillary temperature ≥ 37.5°C or rectal temperature ≥ 38.0°C)*
Uncommon: fever (oral/axillary temperature > 39.0°C or rectal temperature > 39.5°C), fatigue, malaise

Very rare: face oedema

Psychiatric disorders
Uncommon: irritability

* Swelling at the injection site and fever were commonly reported in studies conducted in children ≤ 12 years.

In general, the reactogenicity profile after the second dose was comparable to that after the first dose. However, the rates of injection site reactions (primarily redness and swelling) were higher after the second dose in children aged ≤12 years.

No differences were seen in the reactogenicity profile between initially seropositive and initially seronegative subjects.

4.9 Overdose and special antidotes
Cases of accidental administration of more than the recommended dose of Varicella Vaccine have been reported. Amongst these cases, the following adverse events were reported: lethargy and convulsions. In other cases, no associated adverse events were reported.

5. Pharmacological properties

5.1 Pharmacodynamic properties
The Oka strain virus contained in Varicella Vaccine was initially obtained from a child with natural varicella; the virus was then attenuated through sequential passage in tissue culture.

Natural infection induces a cellular and humoral immune response to the varicella-zoster virus, which can be rapidly detected following infection. IgG, IgM and IgA directed against viral proteins usually appear at the same time that a cellular immune response can be demonstrated, making the relative contribution of humoral and cellular immunity to disease progression difficult to ascertain. Vaccination has been shown to induce both humoral and cell-mediated types of immunity.

Varicella is an acute infectious and highly contagious disease especially for children caused by varicella-zoster virus (VZV). Almost all people aged about 20 are easy to be infected. Varicella may be accompanied by severe complications, including pneumonia, encephalitis, acute cerebellar ataxia, Reye syndrome and hepatitis, in particular in immunosuppression patients and old people. Reactivation of latent virus may result in herpes zoster (shingles).

5.2 Pharmacokinetic properties
Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data
There is no other relevant information that has not already been stated above.

6. Pharmaceutical particulars
6.1 List of excipients
Sucrose
Trehalose
Sodium Glutamate
Urea
Arginine
Glucose
Human Albumin
Sterile Water for Injection (as diluent)

6.2 Incompatibilities
Varicella Vaccine should not be mixed with other vaccines in the same syringe.

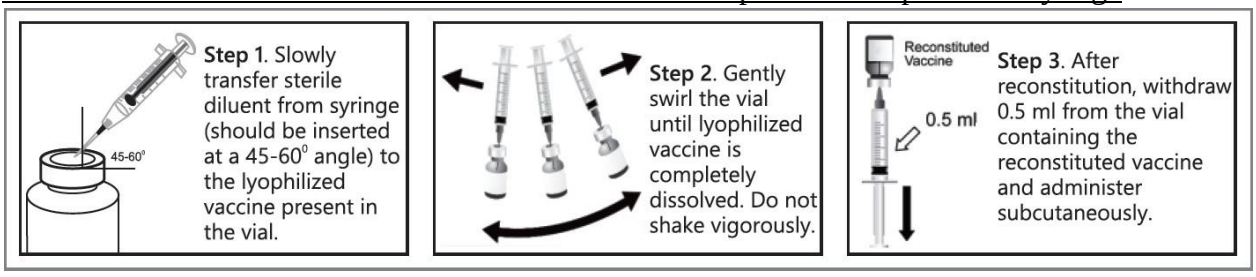
6.3 Shelf life
36 months
The vaccine should be used immediately after reconstitution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should normally not be longer than 1 hour at +2°C to +8°C (in a refrigerator). Do not freeze

6.4 Special precaution for storage
Store at +2°C to +8°C (in a refrigerator). Do not freeze.
Protect from light.

6.5 Nature and contents of container
1 dose vial with freeze-dried vaccine & 0.5 ml sterile diluent in pre filled syringe

6.6 Instructions for use and handling

Instructions for reconstitution of the vaccine with diluent presented in pre-filled syringe



Alcohol and other disinfecting agents must be allowed to evaporate from the skin before injection of the vaccine since they may inactivate the virus.

6.7 Special precautions for disposal of unused medicinal products
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder
NOVO MEDI SCIENCES PVT. LTD.
40-B/1, Shankar Smruti, Sir Bhalchandra Road,
Dadar (East), Mumbai - 400014, Maharashtra, INDIA.

8. Marketing Authorization Number (s)
Not Applicable

9. Date of first authorization/renewal of the authorization
Not Applicable