PUBLIC ASSESSMENT SUMMARY REPORT

SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK]

SK bioscience Co., Ltd., Republic of Korea

What is SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK]?

SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK] is the SK bioscience Co., Ltd., trade name for live, attenuated varicella-zoster virus vaccine. The vaccine is prepared in MRC-5 cell line.

The SKYVaricella Inj. Vaccine is a lyophilized (Freeze-dried) white crystalline pellet and the vaccine is accompanied with a clear glass vial of 0.7 mL diluent (water for injections) for reconstitution as a single dose.

The SKYVaricella Inj. Vaccine single-dose vial presentation consists of the following composition per 0.5mL dose:

Components	Quantity (per 0.5 mL)
Active ingredient	
Live, attenuated varicella-zoster virus (Virus strain: Oka/SK)	≥ 2,400 PFU
Diluent	
Water for injections	0.7 mL
Excipients	
Sodium dihydrogen phosphate dihydrate, Disodium phosphate dodecahydrate, Sodium chloride, Potassium chloride, Sucrose, Hydrolyzed gelatin, Urea, Monosodium glutamate, Disodium edetate, L-cysteine, Glycine, Sodium hydroxide	

The vaccine and diluent are presented in a Type I borosilicate glass vial with 3 mL of capacity, with a pharmaceutical grade rubber stopper made out of Chlorobutyl rubber, with an 13mm flip off aluminum seals.

The shelf-life of SKYVaricella Inj. Vaccine is 24 months at storage conditions 2 – 8°C.

The SKYVaricella Inj. Vaccine vial bears a Vaccine Vial Monitor (VVM) type 7 as part of the label.

The manufacture of bulks, formulation and filling occur in the facilities of SK bioscience Co., Ltd. at L HOUSE, GMP facility in Andong, Korea

What is SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK] used for?

The SKYVaricella Inj. Vaccine is indicated for prevention of varicella in children 12 months to 12 years of age.

How is SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK] used?

The SKYVaricella Inj. Vaccine is colorless or pale yellow liquid when reconstituted to a suspension. The total volume (approximately 0.5 mL) of reconstituted vaccine is administered as a single dose subcutaneously into the outer aspect of the upper arm (deltoid region), immediately after reconstitution.

What is SKYVaricella Inj. Varicella Virus Vaccine (live) [Oka/SK] characteristic?

The SKYVaricella Inj. Vaccine must be stored between 2 to 8°C. Under the recommended storage conditions, the vaccine is stable for 24 months from the date of manufacture.

Cold chain volume per dose is 14.7 cm^3 in the secondary carton of single-dose vial presentation

Who is the regulatory authority responsible for its oversight vis a vis WHO?

The SKYVaricella Inj. Vaccine is manufactured and licensed in Republic of Korea by SK bioscience Co., Ltd. The Republic of Korea is the country of manufacturing. The Korea Ministry of Food and Drug Safety (MFDS) is the authority responsible for the continuing oversight of this WHO prequalified vaccine.

How has SKYVaricella Inj. Varicella Virus Vaccine been studied from the clinical point of view?

Clinical data presented in this application were from three clinical trials:
- A phase 1 trial entitled "An open label, active controlled, parallel group Phase I clinical trial to assess the safety, tolerability and immunogenicity of NBP608 in healthy adult volunteers", Clinicaltrials.gov: NCT03121638.
- A phase 2 study entitled "Randomized, double-blinded, parallel-group, exploratory study to assess the immunogenicity and safety of NBP608 and Varivax™ in healthy children", Clinicaltrials.gov: NCT03114982
- A phase 3 study "A multi-national, multi-center, randomized, double blinded, parallel-group study to assess the immunogenicity and safety of NBP608 compared to Varivax™ in healthy children 12 months to 12 years of age", Clinicaltrials.gov: NCT03114943

Overall, a total of 455 individuals received SKYVaricella vaccine, including 365 children aged 12 months to 12 years (the target population). The clinical trials included in the clinical development of SKYVaricella were conducted between 2012 and 2017 in Korea, Mexico and Philippines. SK bioscience selected Varivax as reference vaccine in the clinical development of SKYVaricella. Varivax is prepared from the OKA strain, has consistently proven efficacy and effectiveness, has been licensed and used worldwide since 2002 and has been pre-qualified by WHO in 2018. Demonstrating non-inferior immunogenicity to Varivax using the FAMA assay inferred that SKYVaricella vaccine protective efficacy would be non–inferior.

Both the phase 2 and 3 studies which were conducted in the targeted age indication have consistently demonstrated that one 0.5mL dose of NBP608 vaccine containing 12,933 PFU is immunogenic FAMA seroconversions which was considered the primary endpoint of immunogenicity was achieved in more than 99% of children. In the phase 2 study there were no difference in vaccine induced antibody response across three dose levels, 4,867, 12,933 and 19,733 PFU. Mid dose level was selected for non-inferiority assessment compared to Varivax™ in the phase 3 study. The primary endpoint for non-inferiority, FAMA seroconversion, was largely met. The analysis of secondary endpoints related to both the FAMA and ELISA antibody responses consistently showed superior immunogenicity of mid dose level NBP608 compared to Varivax™. Altogether, the safety data from the phase 2 and 3 clinical trials indicate that SKYVaricella vaccine has an acceptable safety and reactogenicity profile that is similar to Varivax™. Applicant provided the data of SKYZoster vaccine and Periodic Benefit-Risk Evaluation report (PBRER) of SKYVaricella. This showed that an estimated one hundred and fifteen thousand patients have received the vaccine with no safety concern.

Other information about evaluation of SKYVaricella Inj. Varicella Virus Vaccine:

As part of the prequalification process for SKYVaricella Inj. Vaccine, the Common Technical Document and the responses provided by the manufacturer to observations made by WHO have been reviewed for quality, safety and efficacy by a team of WHO experts, and found to meet WHO requirements of WHO Technical Report Series TRS 848 Annex 1, Varicella vaccine, 1994 (Requirements for varicella vaccine (live).

The manufacturing facility was audited by a WHO team of experts and found to be in compliance with the WHO GMP requirements (WHO TRS 996, Annex 3 2016; TRS 961, Annexes 2, 3 and 6).

WHO has conducted independent testing of batches of the SKYVaricella Inj. Vaccine for critical release parameters in contracted laboratories qualified by WHO for the purpose, and results obtained were in compliance with the quality specifications of the product as specified in the WHO TRS 848 Annex 1, Varicella vaccine, 1994.

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