SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. NAME OF THE MEDICINAL PRODUCT

1.1 Product Name:

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2)

1.2 Strength:

50 doses

1.3 Pharmaceutical dosage form:

Oral Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

No.	Components	Quantity per dose	Function
1	live attenuated novel poliomyelitis virus type 2 (S2/cre5/S15domV/rec1/hifi3)	≥10 $^{5.0}$ $CCID_{50}$	Active ingredient
2	Sucrose	35 % (v/v)	Stabilizer
3	Acetic acid	q.s. to pH 6.5 – 7.2	pH adjuster
4	$NaHCO_3$	q.s. to pH 6.5 – 7.2	pH adjuster
5	Basal Medium Eagle (BME)	q.s. to bring to volume	Solvent

q.s.: quantity sufficient

3. PHARMACEUTICAL form

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) is a clear virus suspension, slightly yellow to light red color, containing live attenuated novel poliomyelitis virus type 2 of modified Sabin strain (S2/cre5/S15domV/rec1/hifi3) as an active stabilized with sucrose. It is formulated for oral drop administration as a sterile aqueous clear suspension of virus.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) is indicated for active immunization in all age groups for emergency use in response to outbreaks caused by Type 2 poliomyelitis virus when and where it is required by the Global Polio Eradication Initiative (GPEI) or WHO.

4.2 Posology and method of administration

Posology

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) is indicated for active immunization in all age groups and must only be administered orally. Two drops (0.1 mL containing $\geq 10^{5.0}$ $CCID_{50}$) are delivered directly into the mouth from the multi-dose vial by dropper or dispenser.

Method of administration

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) must only be administered orally. Two drops are delivered directly into the mouth from the multi-dose vial by dropper or dispenser. Care should be taken not to contaminate a multidose dropper of the vaccine with saliva. Should contact occur, vial should not be used for subsequent dosing.

Once opened, multi-dose vials should be kept between +2°C and +8°C.

4.3. Contraindication

Immune deficiency

The vaccine is contraindicated in those with primary immune deficiency disease or suppressed immune response from medication, leukemia, lymphoma or generalized malignancy.

Although no data are availble specific to the use of nOPV2 in individuals infected with human immunodeficiency virus (HIV), both asymptomatic and symptomatic,

given the derivation of this vaccine from the Sabin type 2 strain, health authorities may consider adopting an approach for nOPV2 similar to that accepted for Sabin-2 in this population.

In addition, vaccine should not be given to those with acute infection condition accompanied by fever.

4.4 Special warnings and precautions for use

Naive Infants

To date, the are no clinical data on the use of nOPV2 in infants who have not been previously immunized with poliovirus type 2.

Diarrhoea

In case of diarrhoea and/or vomiting (including gastrointestinal infection), the dose received will not be considered as adminstered, and it should be repeated after recovery.

Transmission

Like Sabin-2, nOPV2 is shed in stool, and possibly saliva of vaccine recipients. Transmission of vaccine virus to close contacts is possible and is likely to be no greater and possibly less than that of Sabin-2. This vaccine should be used with caution in close contacts of persons with immune deficiency disorder. If personal contact must occur, precautions should be taken to avoid contact with stool or saliva of the vaccinated individual.

Incompatibility

The vaccine should be given separately from any other live-vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Pregnancy and lactation

No studies have been performed, should not be administered to pregnant women.

4.7 Effect on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Although not observed in any study of nOPV2, in very rare cases (less than one case for every million children receiving their first dose, for whom rates are highest) Sabin-strain trivalent oral polio vaccines are associated with vaccine- associated paralytic poliomyelitis (VAPP) in vaccinees or susceptible contacts. The possibility of this occurrence or other unanticipated rare or very rare events following nOPV2 administration cannot be conclusively ruled out.

In the clinical development program to date, 132 adults, 49 children between 1 and 5 years of age, and 288 infants aged 18-22 weeks received either one or two doses of nOPV2 at either 10^5 or 10^6 $CCID_{50}$; 469 subjects in total.

The data gathered to-date indicate that nOPV2 is well-tolerated in adults, young children and infants, without safety concerns identified. As with mOPV2, immunization with nOPV2 is associated with generally mild or moderate solicited events (e.g., fever, vomiting and diarrhea) with data from clinical trials indicating no meaningful imbalance associated with vaccination between the nOPV2 and mOPV2 or placebo control groups.

Paediatric Population

Solicited events among infants (aged 18 – 22 wks) and children (aged 1- 5 years) receiving any nOPV2 vaccination were mostly mild or moderate in severity. These events included abnormal crying (15%), drowsiness (7%), fever (11%), irritability

(15%), loss of appetite (11%), and vomiting (13%). Such events were classified as severe for 4 (1.2%) subjects, including abnormal crying (1, 0.3%), loss of appetite (2, 0.6%), drowsiness (1, 0.3%) and vomiting (1, 0.3%). There were only 3 incidents of unsolicited adverse events considered related to vaccination: 1 infant and 1 child each with mild diarrhea (0.6%), and 1 infant (0.3%) with mild nasopharyngitis.

Adult Population

Most adult subjects reported mild or moderate solicited events composed predominantly of abdominal pain, diarrhea, fatigue, and headache, with severe events of headache (2.2%) and myalgia (0.8%). Common (>2%) unsolicited events considered related to vaccination were diarrhoea (5.3%) and upper respiratory tract infection (2.3%). Transient asymptomatic enzyme elevations (creatine kinase, aspartate aminotransferase, alanine transaminase, without changes in bilirubin and gamma-glutamyl transferase) were commonly observed in subjects in the phase 1 study. That level of frequency and severity was not reproduced in subsequent studies, supporting the initial assessment that the phase 1 observations were likely related to excessive exercise during the physical containment required in that initial uncontrolled study (profile of elevations consistent with that previously reported in association with excessive exercise).

4.9 Overdose

No available data

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, Viral Vaccine, ATC code: J07BF01

Mechanism of action

nOPV2 is a live, attenuated serotype-2 poliovirus derived from a modified Sabin type-2 infectious cDNA clone and is propagated in Vero cells. Immunization of subjects has been shown to engender a neutralizing antibody humoral immune response, which is universally considered to be the correlate of immune protection against disease.

· Clinical Immunogenicity

Paediatric Population

The seroprotection rate following administration of a single dose of nOPV2 has been demonstrated in a phase 2 study to be non-inferior to that of a prospectively generated historical control group administered Sabin-2 OPV (mOPV2) in an OPV2-naive infant population. Among infants previously immunized with 3 doses of bOPV and 1 dose of IPV, seroprotection rates following a single dose of vaccine were 93% and 94% for nOPV2 with the 10^5 and 10^6 $CCID_{50}$ doses, respectively, compared to 94% for mOPV2, with the lower confidence bound for rate differences exceeding the 10% non-inferiority boundary (lower bounds of -7.4% and -6.4% for 10^5 and 10^6 $CCID_{50}$, respectively). Rates of seroconversion (SCR) and fold-rise of neutralizing antibody support this conclusion, and a second dose further increased the level of neutralizing antibody (SCR >85% after 1 dose, > 97% after 2 doses).

Immunogenicity was further evident via observation of seroconversion (94%) and neutralizing antibody titer fold-rise among a small cohort of children aged 1 to 5 years administered 10^6 $CCID_{50}$ doses.

Adult Population

Phase 1 and 2 studies in previously OPV- and exclusively IPV-vaccinated adults support the immunogenicity conclusions from infants, with immunogenicity

observed via seroconversion (75-100%) and rises in absolute level of neutralizing antibody titer.

5.2 Pharmacokinetic properties

Not applicable

5.3 Preclinical safety data

Based on animal quality controls, non-clinical data reveal no special hazard for humans

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

No.	List of excipients	Quantity per dose	Function
1	Sucrose	35 % (v/v)	Stabilizer
2	Acetic acid	q.s. to pH 6.5 – 7.2	pH adjuster
3	$NaHCO_3$	q.s. to pH 6.5 – 7.2	pH adjuster
4	Basal Medium Eagle (BME)	q.s. to bring to volume	Solvent

q.s.: quantity sufficient

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

The stability data of nOPV2 provided to support use of nOPV2 stored for up to 19 months frozen at ≤ -20˚C, with up to 6 months at 2-8˚C allowed.

6.4 Special precautions for storage

Vaccine is potent if stored at not higher than -20°C until the expiry date indicated on the vial. It can be stored for up to six months between +2°C and +8˚C.

The vaccine may present a color varying from slightly yellow to light red color due to a slight variation of pH; however, this does not affect the quality of the vaccine.

6.5 Nature and contents of container <and special equipment for use, administration or implantation

· Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) comes in 50 doses in clear vials. Box of 10 vials @ 5 ml (50 doses) with 10 droppers blistered and packed in separate boxes.

6.6 Special precautions for disposal <and other handling>

Once opened, multi-dose vials should be kept between +2°C and +8°C.

After use, remaining vaccine and droppers should be disposed of safely following local procedures for monovalent OPV2 vaccines.

Multidose vials of nOPV2 from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 4 weeks, provided that all of the following conditions are met (as described in the WHO policy statement: Multidose Vial Policy (MDVP) WHO/IVB/14.07):

- The expiry date of the vaccine has not passed;
- The vaccine vial has been, and will continue to be, stored at WHO or manufacturer recommended temperatures; furthermore, the vaccine vial monitor (VVM) is attached and visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

After first opening, immediate use is recommended

7. APPLICANT/SUPPLIER

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8. WHO PREQUALIFICATION REFERENCE NUMBER

Not applicable

9. DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION

Not applicable

10. DATE OF REVISION OF THE TEXT

01/2022

"Harus Dengan Resep Dokter"

Reg. No :