SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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)	$\geq 10^{5.0}$ $CCID_{50}$	Active ingredient
2	Sucrose	35 % (w/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 substance and 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 Contraindications

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, there 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

This 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 Effects 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-naïve 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 % (w/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 program for nOPV2 has been designed to support use of nOPV2 stored for up to 12 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 colour varying from slightly yellow to light red colour 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: Multi-dose 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/MANUFACTURE

PT. Bio Farma (Persero)

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Website : www.biofarma.co.id

8. WHO PREQUALIFICATION REFERENCE NUMBER

Not applicable

9. DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION

Not applicable

10. DATE OF REVISION OF THE TEXT

10/2020

Reference list

II/VPD/nOPV2/Aug/2020

"Harus Dengan Resep Dokter"

Reg. No. :

NOVEL ORAL POLIOMYELITIS VACCINE (nOPV2) **Type 2**

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DROPS

DESKRIPSI

Novel Oral Poliomyelitis Vaccine Type 2 adalah vaksin polio yang berisi virus poliomyelitis 2 yang dilemahkan (strain Sabin yang dimodifikasi) yang disiapkan dalam sel Vero. Setiap dosis (2 tetes = 0,1 mL) mengandung tidak kurang dari $10^{5.0}$ $CCID_{50}$ unit infektif tipe 2. Sukrosa digunakan sebagai penstabil.

POSOLOGI DAN METODE ADMINISTRASI

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) hanya boleh diberikan secara oral (lewat mulut). Dua tetes vaksin ini diteteskan langsung ke mulut melalui penetes.
Setelah dibuka, vial *multidose* harus disimpan pada suhu antara +2 °C dan +8 °C.
Vial *multidose* dari vaksin nOPV2 dimana satu dosis atau lebih sudah diambil pada suatu rangkaian imunisasi dapat digunakan untuk rangkaian imunisasi selanjutnya sampai maksimal 4 minggu, asalkan semua kondisi berikut terpenuhi:

- Belum melewati tanggal kedaluwarsa vaksin;
- Vial vaksin telah, dan akan terus disimpan, pada suhu yang direkomendasikan oleh WHO atau pabrik; Selanjutnya, *Vaccine Vial Monitor* (VVM) terpasang dan terlihat pada label vaksin serta belum melewati titik akhir, dan vaksin belum rusak karena pembekuan.

Setelah pembukaan pertama, disarankan untuk segera digunakan.

INDIKASI

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2) diindikasikan untuk imunisasi aktif pada semua kelompok umur dan hanya boleh diberikan secara oral.

EFEK SAMPING

Data terbatas yang dikumpulkan hingga saat ini menunjukkan bahwa nOPV2 dapat ditoleransi dengan baik pada orang dewasa, anak kecil (usia 1 hingga 5 tahun) dan bayi (usia 18 hingga 22 minggu), tanpa adanya masalah keamanan yang teridentifikasi. Dalam uji klinis, kejadian yang diperkirakan pada bayi dan anak-anak yang menerima vaksinasi nOPV2 mencakup tangisan abnormal yang dominan ringan atau sedang (15%), mengantuk (7%), demam (11%), lekas marah (15%), kehilangan nafsu makan (11%), dan muntah (13%), dengan tingkat yang sama di antara penerima vaksin kontrol mOPV2. Di antara orang dewasa, sebagian besar subjek melaporkan kejadian yang diperkirakan dengan tingkat ringan atau sedang yang didominasi oleh nyeri perut, diare, kelelahan, dan sakit kepala dengan kejadian serius sakit kepala (2,2%) dan nyeri otot (0,8%). Kejadian serius yang tidak diharapkan berdasarkan penilaian peneliti yang terkait dengan vaksinasi terjadi pada> 2% penerima vaksin mencakup diare (5,3%) dan infeksi saluran pernapasan atas (2,3%). Data dari uji klinis mengindikasikan tidak ada perbedaan bermakna terkait dengan vaksinasi antara nOPV2 dan mOPV2 atau kelompok kontrol plasebo. Meskipun tidak muncul dalam penelitian yang lain tentang nOPV2, dalam kasus yang sangat jarang (kurang dari satu kasus untuk setiap juta anak yang menerima dosis pertama mereka, dengan angka tertinggi) vaksin oral polio trivalen jenis Sabin dikaitkan dengan *Vaccine-Associated Paralytic Poliomyelitis* (VAPP) atau kelumpuhan yang berhubungan dengan vaksin polio pada penerima vaksin (*vaccinees*) atau subjek yang rentan.
Kemungkinan kejadian ini atau kejadian langka atau sangat jarang tak terduga lainnya setelah pemberian nOPV2 tidak dapat secara tegas dikesampingkan.

PERINGATAN KHUSUS DAN TINDAKAN PENCEGAHAN UNTUK PENGGUNAAN

nOPV2 tidak boleh diberikan pada wanita hamil.
Sampai saat ini, belum ada data klinis penggunaan nOPV2 pada bayi yang belum pernah diimunisasi dengan virus polio tipe 2.
Dalam kasus diare dan / atau muntah (termasuk infeksi saluran cerna), dosis yang diterima tidak akan dianggap sebagai pemberian, dan harus diulang setelah sembuh.
Penularan:
Seperti Sabin-2, nOPV2 keluar melalui tinja, dan kemungkinan terkandung dalam air liur penerima vaksin. Penularan virus vaksin memungkinkan dalam jarak dekat dan kemungkinan besar tidak melebihi dan mungkin kurang dari Sabin-2. Vaksin ini harus digunakan dengan hati-hati dalam penggunaan jarak dekat dengan orang yang mengalami gangguan defisiensi imun. Jika kontak personal harus terjadi, tindakan pencegahan harus dilakukan untuk menghindari kontak dengan tinja atau air liur individu yang divaksinasi.

KONTRAINDIKASI

Immune defisiensi
Vaksin tidak boleh digunakan pada orang dengan gangguan sistem kekebalan tubuh. Jika anda menderita / dicurigai HIV, konsultasikan dengan dokter/apoteker/tenaga kesehatan.

Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2)
GTIN : **8994957001956**

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NOVEL ORAL POLIOMYELITIS VACCINE (nOPV2) **Type 2**

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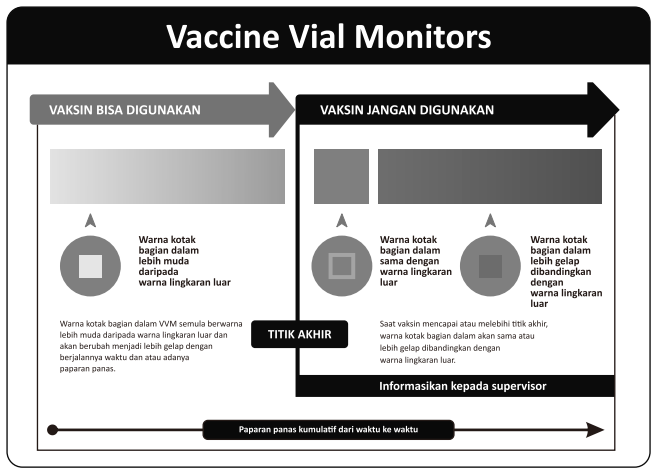
CARA PENYIMPANAN

Potensi vaksin akan terjaga sampai dengan waktu kadaluarsa yang terdapat pada vial jika disimpan pada suhu tidak lebih dari -20 °C. Dan hanya dapat disimpan selama 6 bulan pada suhu antara +2 °C dan +8 °C.
Vaksin memiliki warna bervariasi dari kuning muda hingga merah muda karena adanya variasi pH, namun hal ini tidak mempengaruhi kualitas vaksin.

KEMASAN

Vaksin ini tersedia dalam kemasan vial 50 dosis.

Reg. No: xxxxxxxxxxxxxx



Vaccine Vial Monitor (VVM) merupakan bagian dari etiket nOPV2 yang di produksi oleh TempTime. Noktah berwarna yang muncul pada etiket vial adalah VVM. Ini adalah noktah yang sensitif terhadap suhu-waktu (time temperature sensitive) dan berfungsi sebagai indikator adanya akumulasi paparan panas yang dialami oleh vial (vaksin). Hal tersebut merupakan petunjuk bagi pemakai apakah vaksin masih dapat digunakan atau tidak.

Interpretasi VVM sederhana. Fokus pada kotak di tengah. Warnanya akan berubah secara bertahap. Selama warna kotak ini lebih terang dari warna cincinnya, maka vaksin dapat digunakan. Segera setelah kotak pusat berwarna sama dengan warna cincin atau lebih gelap dari warna cincin, maka vial harus dibuang.

Harus Dengan Resep Dokter

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Novel Oral Poliomyelitis Vaccine Type 2 (nOPV2)
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01102020-INA

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Produsen	: PT Bio Farma (Persero)	The final dimension of folding : 100 x 35 mm
Address	: Jl. Pasteur No 28 Bandung 40161	Folding amount : 3x fold
Product Name	: Leaflet nOPV2 50 Dosis (1 Bahasa Indonesia)	Color : 2 Color
Material	: HVS 60 gsm	PMS Black U PMS Red 223 U
Dimension	: 100 x 280 mm, ± 2 mm	
Scale	: 100 %	
Edition	: 01102020-INA	
Note	: -	

DISETUJUI OLEH BPOM 27 OKTOBER 2020

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