English

# Influenza Vaccine, Live Attenuated (Human)

## NASOVAC-S

Seasonal, Trivalent

2020-21 Formula Northern Hemisphere Freeze dried

**DESCRIPTION**

NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), freeze dried is a live trivalent vaccine for administration by intranasal spray. NASOVAC-S contains three vaccine virus strains of A/H1N1, A/H3N2 and Type B influenza virus cultivated on embryonated hen eggs. The three strains are antigenically similar to the strains recommended by the World Health Organization (W.H.O.) for 2020-21.

**COMPOSITION**

[Propagated in Embryonated hen eggs]
Each vial of single dose (0.5 ml) contains:

| | |
|---|---|
| A(H1N1) Strain- A/17/Guangdong-Maonan/2019/211 (H1N1)* | Not less than $10^{7}$ $EID_{50}$ |
| A(H3N2) Strain-A/17/Hong Kong/2019/2573 (H3N2)* | Not less than $10^{7}$ $EID_{50}$ |
| B Strain - B/60 / Washington / 2019 / 3676* | Not less than $10^{6.5}$ $EID_{50}$ |

* Antigenic specificity of Hemagglutinin and Neuraminidase identical to wild type virus as recommended by W.H.O. for influenza vaccine for the year 2020-21 Northern hemisphere influenza season:

- A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09 - like virus
- A/Hong Kong/2671/2019 (H3N2) - like virus
- B/Washington / 02 / 2019 - like virus (B/Victoria lineage)

Partially hydrolyzed gelatin 2.5%, Sorbitol 5.0%, L-Alanine 0.1%, L-Histidine 0.21%, Tricine 0.3%, L-Arginine hydrochloride 1.6%, Lactalbumin hydrolysate 0.35%, Phosphate buffer saline Base. Reconstitute with Sterile Water for Inhalation IP. The vaccine contains no preservatives.
Dose: 0.5 ml intranasal (spray 0.25 ml per nostril). The tip attached to the sprayer is equipped with a nozzle that produces a fine mist that is primarily deposited in the nose and nasopharynx.
The vaccine complies with the W.H.O. recommendations.

**INDICATIONS**

NASOVAC-S is indicated in individuals above 2 years of age for the active immunization for the prevention of influenza disease caused by two influenza A subtype viruses and one influenza Type B virus which are expected to circulate in the 2020-21 season. NASOVAC-S should be used in accordance with official guidance.

**POSOLOGY AND METHOD OF ADMINISTRATION**

Each freeze-dried vaccine vial is reconstituted using the entire contents of sterile water for inhalation that is supplied along with the vaccine, using the supplied syringe and vial adapter.
A dose of 0.5 ml is administered as 0.25 ml per nostril using a 1.0 ml syringe and a spray device. Withdraw the entire reconstituted vaccine for administration. The spray device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx. A single intranasal dose is recommended for people above 2 years of age.
For further information, see (Pharmacodynamic properties).
Use immediately after reconstitution. If the vaccine is not used immediately then it should be stored in the dark at 2-8°C for no longer than 6 hours.
Any opened container remaining at the end of a session (within six hours of reconstitution) should be discarded. The vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.
The diluent supplied is specially designed for use with the vaccine. Only this diluent must be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or from other manufacturers. Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen, but should be kept cool.
The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

**CONTRAINDICATIONS**

**Hypersensitivity**

NASOVAC-S is contraindicated in individuals with a history of hypersensitivity, especially anaphylactic reactions to eggs, egg proteins, gelatin, or Lactalbumin or with other vaccine components.

**Concomitant Pediatric and Adolescent Aspirin Therapy and Reye's syndrome**

NASOVAC-S is contraindicated in children and adolescents (2-17 years of age) receiving aspirin therapy or aspirin-containing therapy, because of the association of Reye's syndrome with aspirin and wild-type influenza infection.

**WARNINGS AND PRECAUTIONS**

NASOVAC-S should under no circumstances be injected.
As with all vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.
NASOVAC-S should not be administered to any individuals with active wheezing.
If the individual has a history of Guillain-Barré syndrome the decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.
Immunization should be postponed in patients with severe febrile illness or acute infection. The vaccine can be given to people with minor illnesses (e.g., diarrhea or mild upper respiratory tract infection without fever). However, if nasal congestion is present that might limit delivery of the vaccine to the nasal lining, then delaying of vaccination until the nasal congestion is reduced should be considered.
People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.
Administration of NASOVAC-S, to immune-compromised persons should be based on careful consideration of potential benefits and risks. There is no clinical data available on the use of this vaccine in immune-compromised persons. Antibody response in such patients may be insufficient.
The safety of NASOVAC-S in individuals with underlying medical conditions that may predispose them to complications following wild-type influenza infection has not been established. The decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.

**Pregnancy and lactation**

A developmental and reproductive toxicity study has been performed in female rats administered Nasovac (Live attenuated pandemic H1N1 vaccine) either once, twice or thrice (during the period of organogenesis), at approximately 2 human dose equivalents per occasion, by intranasal instillation and has revealed no evidence of maternal toxicity, fetotoxicity or teratogenicity due to Nasovac. There are however, no studies in pregnant women. Because animal studies are not always predictive of human response, Nasovac-S should be administered during pregnancy only if clearly needed.
It is not known whether NASOVAC-S is excreted in human milk. Therefore, as some viruses are excreted in human milk and additionally, because of the possibility of shedding of vaccine virus and the close proximity of a nursing infant and mother, caution should be exercised if NASOVAC-S is administered to nursing mothers.

**DRUG INTERACTIONS**

Do not administer NASOVAC-S to children or adolescents who are receiving aspirin therapy or aspirin-containing therapy (see Contraindications).
The concurrent use of NASOVAC-S with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for antiviral agents to reduce the effectiveness of NASOVAC-S, do not administer this vaccine until 48 hours after the cessation of antiviral therapy and antiviral agents should not be administered until two weeks after administration of this vaccine unless medically indicated. If antiviral agents and NASOVAC-S are administered concomitantly, revaccination should be considered when appropriate.
There are no data on co-administration of NASOVAC-S with other vaccines. However, if co-administration with another vaccine is indicated, immunisation may be carried. It should be noted that the adverse reactions may be intensified.
There are no data regarding co-administration of NASOVAC-S with other intranasal preparations. The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.
The vaccine is unlikely to produce an effect on the ability to drive and use machines.

**ADVERSE REACTIONS**

In clinical trials a few local and systemic reaction were observed. They were mild to moderate in severity and resolved without any sequelae.
Local : Nasal discomfort, stuffy nose, sneezing, runny nose, loss of smell, red eyes, chills, facial swelling.
Systemic : Fever, headache, fatigue, myalgia, arthralgia, irritability, loss of appetite, sore throat, cough, wheezing, nausea.

**OVERDOSE**

No case of overdose has been reported.

**PHARMACOLOGICAL PROPERTIES**

**Mechanism of Action**

Immune mechanisms conferring protection against influenza following receipt of live attenuated influenza vaccines are not fully understood, though it is well-established that these vaccines provide clinical protection to the majority of the vaccinees. Serum antibodies, mucosal antibodies, and influenza-specific T cells may play a role in prevention and recovery from infection. NASOVAC-S contains live attenuated influenza viruses that must infect and replicate in cells lining the nasopharynx of the recipient to induce immunity. Vaccine viruses capable of infection and replication can be cultured from nasal secretions obtained from vaccine recipients (shedding)

**Pharmacodynamic properties**

NASOVAC-S is a live trivalent vaccine for administration by intranasal spray. The influenza virus strain in NASOVAC-S is (a) cold-adapted (ca) (i.e., it replicates efficiently at 25°C, a temperature that is restrictive for replication of many wild-type influenza viruses); (b) temperature-sensitive (ts) (i.e., it is restricted in replication at 39°C, a temperature at which many wild-type influenza viruses grow efficiently); and (c) attenuated (att). The cumulative effect of the antigenic properties and the ca, ts, and att phenotypes is that the attenuated vaccine virus replicates in the nasopharynx to induce protective immunity.

**Pharmacokinetic properties**

Not applicable.

**Preclinical safety data**

Efficacy study of NASOVAC-S in naïve ferrets (which is an established model of influenza) using homologous influenza viruses as challenge was conducted. Viral load, viral shedding and pathological analysis showed reduced levels of all three parameters in vaccinated animals after challenge irrespective of the challenge virus clearly demonstrating high efficacy of NASOVAC-S for all the three strains.
NASOVAC-S has undergone Single-dose and Repeated-dose toxicity studies in mice and rats when administered intranasally. In single-dose studies, higher than normal doses of the vaccine were given to animals and they were observed for 14 days for toxic effects. No vaccine-related untoward effects were found in animals receiving NASOVAC-S.
In repeated-dose toxicity studies, three doses of higher than normal doses of the vaccine were given intranasally to animals on day 0, 7 and 14 and were subsequently sacrificed. Necropsy was done to assess adverse effects on any organs. No vaccine-related adverse effects were found in the study animals receiving NASOVAC-S.

**INCOMPATIBILITIES**

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

**INSTRUCTIONS FOR USE AND HANDLING AND DISPOSAL**

The vaccine should be allowed to reach room temperature before use. Shake before use.
Once NASOVAC-S, intranasal has been administered, the used vaccine devices and all its parts should be disposed off according to the standard procedures for medical waste (e.g., sharps container or biohazard container).

**SHELF-LIFE**

Do not exceed the expiry date printed on the label and packaging.

**STORAGE**

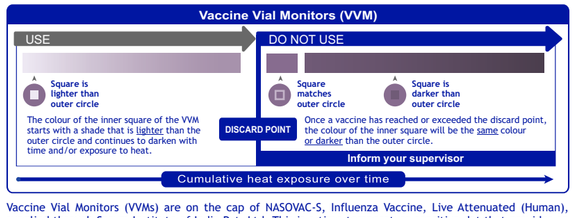
NASOVAC-S, Influenza Vaccine, Live Attenuated (Human) Intranasal SHOULD BE STORED IN A REFRIGERATOR AT 2 - 8°C (35-46°F) UPON RECEIPT AND UNTIL USE. THE PRODUCT MUST BE USED BEFORE THE EXPIRATION DATE ON THE LABEL. The cold chain (2 to 8°C) must be maintained when transporting Influenza Vaccine, Live Attenuated (Human) Intranasal.

**PRESENTATION**

NASOVAC-S Influenza Vaccine, Live Attenuated (Human) freeze dried, intranasal is available as:
1 dose vial plus diluent ( 0.5 ml)

NASOVAC-S is supplied as a vial containing freeze-dried cake in USP type 1 glass vials.
Vial containing sterile water for inhalation as diluent, syringe for administration, vial adapter, intranasal spray device and dose divider are also supplied along with the vaccine.

**THE VACCINE VIAL MONITOR (VVM) (Optional)**




Vaccine Vial Monitors (VVMs) are on the cap of NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indications of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

**MOST IMPORTANT WARNING**

1. Please ensure that the vaccine is administered by intranasal spray.
2. In rare cases anaphylactic shock may occur in susceptible individual. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis. As with the use of all vaccines, the vaccinees should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

**CAUTION: PEOPLE WHO SHOULD NOT TAKE THE VACCINE**

1. Those who are allergic to eggs
2. Children and adolescents (2-17 years of age) receiving aspirin and aspirin containing therapy. People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.

Revision date: 02/2021

Manufactured by:
**SERUM INSTITUTE OF INDIA PVT. LTD.**
212/2, Hadapsar, Pune 411028, INDIA
Protection from birth onwards

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Spanish

# Vacuna de la Influenza, Viva Atenuada (Humana)

## NASOVAC-S

Estacional, Trivalente

Fórmula 2020-21 Hemisferio Norte Liofilizada

**DESCRIPCIÓN**

NASOVAC-S (Vacuna de la Influenza, Viva Atenuada (Humana)), liofilizada es una vacuna trivalente, viva para la administración con atomizador nasal. NASOVAC-S contiene tres cepas del virus de la vacuna de A/H1N1, A/H3N2 y el virus de la influenza Tipo B que se cultiva en los huevos embrionados de gallina. Las tres cepas son antigénicamente similares a las cepas recomendadas por la Organización Mundial de Salud (O.M.S.) para 2020-21.

**COMPOSICIÓN**

[Propagada en los Huevos Embrionados de Gallina]
Cada frasco de dosis única (0,5 ml) contiene:

| | |
|---|---|
| Cepa A(H1N1) - A/17/Guangdong-Maonan/2019/211 (H1N1)* | No menos que $10^{7}$ $DIE_{50}$ |
| Cepa A(H3N2) - A/17/Hong Kong/2019/2573 (H3N2)* | No menos que $10^{7}$ $DIE_{50}$ |
| Cepa B - B/60 / Washington / 2019 / 3676* | No menos que $10^{6,5}$ $DIE_{50}$ |

* La especificidad antigénica de la hemaglutinina y la neuraminidasa es idéntica al virus del tipo salvaje, según recomendado por la Organización Mundial de Salud (OMS) para la vacuna de la influenza en la temporada de influenza en el hemisferio norte en 2020-2021 :

- Virus tipo A/Guangdong-Maonan/SWL 1536/2019 (H1N1) pdm09
- Virus tipo A/Hong Kong/2671/2019 (H3N2)
- Virus tipo B/Washington/02/2019 (Linaje B/Victoria)

Gelatina (parcialmente hidrolizada) 2,5%, Sorbitol 5%, L-Alanina 0,1%, L-Histidina 0,21%, Tricina 0,3%, L-Arginina Clorhidrato 1,6%, Hidrolizado de Lactoalbúmina 0,35%, Tampón de Fosfato Base Salina. Reconstituir con Agua Estéril para Inhalación IP. La vacuna no contiene conservantes.
Dosis: 0,5 ml intranasal (aplicar 0,25 ml por cada fosa nasal con atomizador) La punta colocada en el atomizador viene equipada con una boquilla que produce un rocío fino que se deposita en la nariz y la nasofaringe.
La vacuna cumple con las recomendaciones de la O.M.S.

**INDICACIONES**

NASOVAC-S está indicada en la inmunización activa de los individuos con más de 2 años para la prevención de la enfermedad de la influenza causada por dos virus del sub-tipo A y un virus de Influenza tipo B, que se espera circularán en la temporada de 2020-21. Se debe utilizar NASOVAC-S de conformidad con las directivas oficiales.

**POSOLOGÍA Y MÉTODOS DE ADMINISTRACIÓN**

Cada frasco de la vacuna liofilizada se reconstituye usando el contenido entero de agua estéril para inhalación que se suministra con la vacuna, usando la jeringa y adaptador de vial.
Una dosis de 0,5 ml se administra en la forma de 0,25 ml en cada fosa nasal usando una jeringa de 1,0 ml y un dispositivo atomizador. Retirar la vacuna reconstituida completa para su administración. El dispositivo atomizador crea un vapor fino que primariamente deposita la vacuna en la nariz y en la nasofaringe. Se recomienda una dosis intranasal para personas de más de 2 años.
Para más información (ver Propiedades Farmacodinámicas).
Usar inmediatamente después de la reconstitución. Si no se utiliza la vacuna inmediatamente se la debe guardar en la oscuridad a 2-8°C por no más de 6 horas.
Cualquier frasco que quede abierto al final de la sesión (dentro de seis horas de la reconstitución) debe ser descartado. El monitor de control de vial de la vacuna para este tipo de vacuna (ver figura) se encuentra adherido a la tapa del vial y debe desecharse cuando se está reconstituyendo la vacuna.
El diluente suministrado ha sido especialmente diseñado para usar con la vacuna. Se debe usar únicamente este diluente para reconstituir la vacuna. No usar diluentes de otros tipos de vacunas o de otros fabricantes. Usar un diluente incorrecto puede resultar en el daño a la vacuna y/o reacciones serias en personas que reciben la vacuna. El diluente no debe congelarse pero se debe mantenerlo frío.
El diluente y la vacuna reconstituida deben ser observados visualmente para la presencia de materia particulada extraña y/o variaciones en los aspectos físicos antes de la administración. En el evento de que se las observen, descartar el diluente o la vacuna reconstituida.

**CONTRAINDICACIONES**

**Hipersensibilidad**

NASOVAC-S está contraindicada en individuos con una historia de hipersensibilidad, especialmente reacciones anafilácticas a huevos, proteínas de huevos, gelatina o lactalbúmina o con otros componentes de la vacuna.

**Terapia concomitante Pediátrica y Adolescente con Aspirina y el Síndrome de Reyes**

NASOVAC-S está contraindicado en niños y adolescentes (de edad entre 2 - 17 años) recibiendo la terapia con aspirina o terapia con un medicamento que contenga la aspirina, debido a la asociación del Síndrome de Reyes con aspirina y la infección de influenza de tipo-salvaje.

**ADVERTENCIAS Y PRECAUCIONES**

NASOVAC-S no debe ser inyectado bajo ningún concepto.
Como en el caso de todas las vacunas, siempre debe estar disponible el tratamiento médico y la supervisión en el caso de un evento raro anafiláctico después de la administración de la vacuna.
NASOVAC-S no debe ser administrado en personas con la sibilancia activa.
Si la persona tiene una historia del síndrome de Gullain-Barré, la decisión de administrar NASOVAC-S debe basarse en la consideración cuidadosa de los beneficios potenciales y los riesgos potenciales.
La inmunización debe ser postergada en pacientes con una enfermedad febril severa o la infección aguda. La vacuna puede administrarse en personas con enfermedades menores (p.ej. la diarrea o la infección leve del tracto respiratorio superior con o sin la fiebre). Sin embargo si está presente la congestión nasal, ésta puede limitar la entrega de la vacuna en el revestimiento nasal y en este caso se debe considerar demorar la vacunación hasta que se reduzca la congestión nasal.
Las personas que ya sufren de la constipación, tos, fiebre, dolor corporal, o otros síntomas parecidos a la gripe deben ser clínicamente evaluadas y si fuera necesario se debe administrar el tratamiento apropiado. En tales casos la vacunación con NASOVAC-S debe ser postergada por lo menos hasta la recuperación.
La administración de NASOVAC-S en personas inmunocomprometidas debe ser basada en la consideración cuidadosa de los beneficios y riesgos potenciales. No hay datos clínicos disponibles sobre el uso de esta vacuna en personas inmunocomprometidas. La respuesta de anticuerpos en tales pacientes puede ser insuficiente.
No ha sido establecida la seguridad de NASOVAC-S en individuos con condiciones médicas subyacentes que tal vez les hagan más susceptibles a complicaciones siguientes a la infección tipo salvaje de la influenza. La decisión de administrar NASOVAC-S debe basarse en la evaluación detenida de los beneficios y riesgos potenciales.

**Gravidez y Lactancia**

Se ha realizado un estudio de desarrollo y de la toxicidad reproductiva en ratas que fueron administradas Nasovac (la Vacuna viva, atenuada para la pandemia de H1N1) una, dos o tres veces (durante el período de la organogénesis), equivalente a aproximadamente 2 dosis humanas por ocasión, por la instilación intranasal y no se reveló evidencia de la toxicidad materna, toxicidad fetal o teratogenecidad debido a Nasovac. No hay, de todos modos, estudios realizados sobre mujeres embarazadas. Debido al hecho de que los estudios animales no siempre pueden predecir la respuesta humana, Nasovac-S debe ser administrado durante el embarazo sólo si se necesita claramente.
No se sabe si NASOVAC-S se excreta en la leche humana. Por lo tanto, ya que algunos virus se excretan en la leche humana y adicionalmente debido a la posibilidad del desprendimiento del virus de la vacuna y la proximidad del bebé lactante con la madre, se debe ejercer la cautión si NASOVAC-S se administra en madres lactantes.

**INTERACCIONES MEDICAMENTOSAS**

No administrar NASOVAC-S en niños o adolescentes que están recibiendo la terapia con aspirina o con medicamentos que contienen la aspirina. (Ver Contraindicaciones)
El uso concurrente de NASOVAC-S con agentes antivirales que están activos contra los virus de la influenza A y/o B no ha sido evaluado. Sin embargo basado en el potencial de los agentes antivirales para reducir la eficacia de NASOVAC-S, no administrar esta vacuna hasta 48 horas después de la descontinuación de la terapia antiviral y los agentes antivirales no deben ser administrados hasta dos semanas después de la administración de esta vacuna a no ser que sea indicada médicamente. Si los agentes antivirales y NASOVAC-S se administran concomitantemente, se debe considerar la revacunación cuando sea apropiado.
No hay dados sobre la administración concomitante de NASOVAC-S con otras preparaciones intranasales. La respuesta inmunológica puede ser disminuida si el paciente está recibiendo el tratamiento con inmunosupresores. No es probable que la vacuna produzca algún efecto sobre la capacidad de conducir y utilizar máquinas.

**REACCIONES ADVERSAS**

En las pruebas clínicas se observaron unas pocas reacciones locales y sistémicas. Eran leves a moderadas en su severidad y se resolvieron sin secuelas.

Locales: Incomodidad nasal, nariz congestionada, rinorrea, pérdida de olfato, ojos enrojecidos, lagrimación, inflamación facial.
Sistémicas: Dolor de cabeza, fatiga, mialgia, artralgia, irritabilidad, pérdida del apetito, faringitis, tos, diarrhea.

**SOBREDOSIFICACIÓN**

No se ha comunicado ningún caso de la sobredosificación.

**PROPIEDADES FARMACOLÓGICAS**

**Mecanismo de Acción**

Los mecanismos inmunes que confieren la protección contra la influenza después de la administración de vacunas vivas, atenuadas contra la influenza todavía no se entienden completamente, aunque está bien establecido que estas vacunas brindan la protección clínica en la mayoría de los vacunados. Los anticuerpos séricos y mucosales y las células-T específicas para la influenza pueden jugar un papel en la prevención y la recuperación de la infección. NASOVAC-S contiene los virus vivos atenuados de influenza que deben infectar y replicar-se en las células que revisten la nasofaringe del vacunado para inducir la inmunidad. Los virus de la vacuna capaces de la infección y replicación pueden ser cultivados de las secreciones nasales obtenidas de los vacunados (excreción viral).

**Propiedades fármaco-dinámicas**

NASOVAC-S es una vacuna viva trivalente para administración usando un atomizador intranasal. La cepa del virus de la influenza en NASOVAC-S es (a) adaptada al frío (ca por sus siglas en inglés) (es decir se replica eficientemente a 25°C, una temperatura que limita la replicación en muchos virus de influenza de tipo salvaje); (b) sensible a la temperatura (ts por sus siglas en inglés) (es decir se restringe la replicación a 39°C, a una temperatura en la cual muchos virus de la influenza de tipo salvaje crecen eficientemente) ; y (c) atenuada (att). El efecto acumulativo de las propiedades antigénicas y los fenotipos ca, ts y att es que el virus de la vacuna atenuada se replica en la nasofaringe para inducir la inmunidad protectora.

**Propiedades Farmacocinéticas**

No se aplica.

**Datos de Seguridad Pre-clínica**

Se realizó un estudio de eficacia de NASOVAC-S en hurones sin tratamiento previo (lo cual es un modelo establecido de la influenza) usando los virus homologo de influenza como desafío. La carga viral, excreción viral y el análisis patológico mostraron niveles reducidos de todos los tres parámetros en los animales vacunados después del desafío sin consideración del hecho de que el virus de desafío claramente demostró la elevada eficacia de NASOVAC-S para todas las tres cepas.
NASOVAC-S ha sido sometido a estudios de toxicidad con dosis única y dosis repetidas en ratones y ratas, administrado por vía intranasal. En los estudios con dosis única, dosis más elevadas de la vacuna de lo normal fueron administradas en animales y se los observaron durante 14 días para los efectos tóxicos. No se notaron efectos inesperados relacionados a la vacuna en los animales que recibieron NASOVAC-S.
En los estudios de toxicidad con dosis repetidas, tres dosis de dosis más elevadas de lo normal de la vacuna fueron administradas intranasalmente en los animales el día 0,7 y 14 y ellos fueron sacrificados subsecuentemente. Se realizó la necropsia para evaluar los efectos adversos en cualquier órgano. No se encontraron efectos adversos relacionados a la vacuna en los animales del estudio que recibieron NASOVAC-S.

**INCOMPATIBILIDADES**

Dada la ausencia de los estudios de compatibilidad, este producto medicamentoso no debe ser mezclado con otros productos medicamentosos.

**INSTRUCCIONES PARA EL USO, MANIPULACIÓN Y LA ELIMINACIÓN**

La vacuna debe alcanzar la temperatura ambiental antes de ser usada. Agitar antes de usar.
Una vez que NASOVAC-S Intranasal haya sido administrada, los accesorios de la vacuna usada y todas sus partes deben ser descartados conforme los procesos estándares para los residuos bio-sanitarios (por ejemplo contenedor para objetos punzocortantes/ contenedores que representan peligros biológicos).

**VALIDEZ**

No exceder la fecha de vencimiento impresa en la caja externa.

**CONSERVACIÓN**

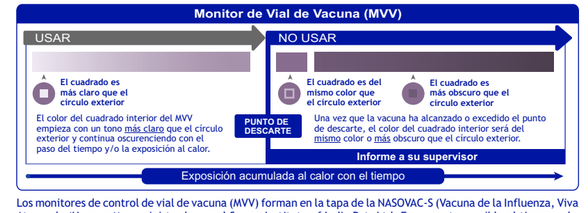
NASOVAC-S (Vacuna de la Influenza, Viva Atenuada (Humana)) Intranasal DEBE GUARDARSE EN UN REFRIGERADOR A 2 - 8°C (35 - 46°F) CUANDO SE LA RECIBE Y HASTA SU UTILIZACIÓN. EL PRODUCTO DEBE SER USADO ANTES DE LA FECHA DE VENCIMIENTO DECLARADA EN LA ETIQUETA. La cadena en frío (2 a 8°C) debe mantenerse durante el transporte de la Vacuna de la Influenza, Viva Atenuada (Humana) Intranasal.

**PRESENTACIÓN**

NASOVAC-S (Vacuna de la Influenza, Viva Atenuada (Humana)) Intranasal está disponible en la forma de:
Frasco de 1 dosis más diluente (0,5 ml)

NASOVAC-S se suministra en la forma de un vial que contiene una torta liofilizada en frascos de vidrio de USP tipo I. Se suministra también un vial que contiene agua estéril para inhalación como diluente, jeringa para administración, adaptador vial, dispositivo atomizador intranasal y separador de dosis junto con la vacuna.

**MONITOR DE VIAL DE VACUNA (MVV) (Opcional):**




Los monitores de control de vial de vacuna (MVV) forman en la tapa de la NASOVAC-S (Vacuna de la Influenza, Viva Atenuada (Humana)), suministrada por el Serum Institute of India Pvt. Ltd. Es un punto sensible al tiempo y la temperatura que indica el calor acumulado al cual haya sido expuesto el vial. Avisa al consumidor final cuando la exposición al calor ha podido degradar la vacuna fuera del nivel de aceptación.

La interpretación del MVV es fácil. Concentrarse en el cuadrado interno. Su color se cambiará progresivamente. Mientras el color de este cuadrado interior es más claro que el color del círculo exterior, se puede usar la vacuna. Tan pronto como el color del cuadrado interno se cambia al color del círculo exterior o un color más oscuro, desechar el vial.

**ADVERTENCIA MÁS IMPORTANTE**

1. Por favor asegure que la vacuna se administre por vía intranasal.
2. En raros casos puede ocurrir el choque anafiláctico en individuos susceptibles .El sostén en el tratamiento de la anafilaxia severa es el uso inmediato de adrenalina, que puede ser salvavidas. Debe ser usada ante la primera sospecha de la anafilaxia. Como con el uso de todas las vacunas, los vacunados deben estar bajo la observación por no menos de 30 minutos para la posibilidad de la ocurrencia de reacciones alérgicas rápidas. Hidrocortisona y anti-histamínicos también deben estar disponibles además de medidas de apoyo como la inhalación de oxígeno.

**CAUCIÓN: PERSONAS QUE NO DEBEN TOMAR LA VACUNA**

1. Aquellas personas que son alérgicas a los huevos.
2. Niños y adolescentes (entre 2 - 17 años) que reciben la aspirina y la terapia con aspirina. Las personas que ya sufren de la constipación, tos, fiebre, dolor corporal u otros síntomas parecidos a la gripe deben ser clínicamente evaluadas y si es necesario, se debe administrar el tratamiento apropiado. En tales casos la vacunación con NASOVAC-S debe ser postergada al menos hasta la recuperación.

Fecha de revisión: 02/2021

Fabricada por:
**SERUM INSTITUTE OF INDIA PVT. LTD.**
212/2, Hadapsar, Pune 411028, INDIA
Protección desde el nacimiento

French

# Vaccin Antigrippal, Vivant Atténué (Humain)

## NASOVAC-S

Saisonnier, Trivalent

Formule 2020-21 Hémisphère Nord Lyophilisé

**DESCRIPTION**

NASOVAC-S (Vaccin Antigrippal, Vivant Atténué (Humain)), lyophilisé est un vaccin trivalent vivant pour administration par pulvérisation intra-nasale. NASOVAC-S contient trois souches de virus de A/H1N1, A/H3N2 et le virus de la grippe de type B cultivé sur les œufs embryonnés. Ces trois souches sont antigéniquement analogues aux souches recommandées par l'Organisation Mondiale de la Santé (O.M.S.) pour 2020-21.

**COMPOSITION**

[Propagé sur œufs embryonnés de poulet]
Chaque flacon de dose unique (0,5 ml) contient:

| | |
|---|---|
| Souche A(H1N1) - A/17/Guangdong-Maonan/2019/211 (H1N1)* | Pas moins de $10^7$ $EID_{50}$ |
| Souche A(H3N2) - A/17/Hong Kong/2019/2573 (H3N2)* | Pas moins de $10^7$ $EID_{50}$ |
| Souche B - B/60/Washington/2019/3676* | Pas moins de $10^{6,5}$ $EID_{50}$ |

* La spécificité antigénique de l'Hémagglutinine et de la Neuraminidase identique au virus de type sauvage, comme recommandé par l'O.M.S. pour le vaccin antigrippal pour l'année 2020-21 saison de la grippe de l'hémisphère du nord :

- A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09 - comme le virus
- A/Hong Kong/2671/2019 (H3N2) - comme le virus
- B/Washington / 02 / 2019 - comme le virus (B/Victoria lineage)

Gélatine (partiellement hydrolysée) 2,5%, Sorbitol 5%, L-Alanine 0,1%, L-Histidine 0,21%, Tricine 0,3%, L-Arginine Chlorhydrate 1,6% Lactalbumine hydrolysat 0,35% une base physiologique tamponné par les phosphates. A reconstituer avec Eau Stérile pour Inhalation IP. Le vaccin ne contient pas d'agent de conservation.
Dose : 0,5 ml intranasale (pulvériser 0,25 ml dans chaque narine). La pointe attachée au pulvérisateur est équipée d'une canule qui produit une fine brume qui se dépose principalement dans le nez et le nasopharynx. Le vaccin est conforme aux exigences de l'O.M.S.

**INDICATIONS**

NASOVAC-S est indiqué pour l'immunisation active des personnes de plus de 2 ans pour la prévention de la maladie de la grippe causée par deux virus de la grippe de sous-type A et un virus de la grippe de type B dont on prévoit la circulation en 2020-21. NASOVAC-S doit être utilisé en conformité avec les directives officielles.

**POSOLOGIE ET MODE D'ADMINISTRATION**

Chaque flacon de vaccin lyophilisé est reconstitué par la teneur entier de l'eau stérile pour inhalation qui est fournie avec le vaccin, utilisant la seringue et adaptateur pour flacon.
Une dose de 0,5ml est administrée comme 0,25 ml dans chaque narine en utilisant une seringue de 1,0 ml et un appareil pulvérisateur. Retirer tout le vaccin reconstitué pour administration. L'appareil pulvérisateur crée une fine brume qui dépose le vaccin principalement dans le nez et le nasopharynx. Une dose intranasale unique est recommandée aux personnes ayant plus de 2 ans.
Pour plus d'information, voir (Propriétés Pharmacodynamiques).
Utilisez le vaccin immédiatement après la reconstitution. Si le vaccin n'est pas utilisé immédiatement il doit être conservé à l'abri à 2-8° C pour 6 heures maximum.
S'il y reste un récipient ouvert à la fin d'une session (en moins de six heures de reconstitution), jeter-le.
La pastille de contrôle du vaccin (voir l'image), pour ce type de vaccin est attaché au bouchon du flacon et doit être jetée lorsque le vaccin est en cours de reconstitution.
Le diluant fourni est spécialement conçu pour ce vaccin. Il ne faut utiliser que ce diluant pour reconstituer le vaccin. Ne pas utiliser les diluants conçus pour d'autres types de vaccins ou ceux fournis par d'autres fabricants. L'utilisation d'un diluant incorrect pourrait entrainer des dommages au vaccin et/ou des réactions graves chez ceux qui le reçoivent. Le diluant ne doit pas être congelé, mais doit être gardé au frais.
Le diluant et le vaccin reconstitué doivent être visuellement inspectés pour la présence des particules étrangères et/ou pour la variation des aspects physiques avant l'administration. Le cas échéant, jeter le diluant ou le vaccin reconstitué.

**CONTRE-INDICATIONS**

**Hypersensibilité**

NASOVAC-S est contre-indiqué chez les individus avec un antécédent d'hypersensibilité, surtout les réactions anaphylactiques aux œufs, aux protéines d'œufs, à la gélatine, ou à la lactalbumine ou aux autres composants du vaccin.

**Thérapie à l'Aspirine concomitante chez les Enfants et les Adolescents et Syndrome de Reye**

NASOVAC-S est contre-indiqué chez les enfants et les adolescents (2-17 ans) recevant une thérapie à l'aspirine ou une thérapie contenant l'aspirine à cause de l'association du syndrome de Reye avec l'aspirine et l'infection de la grippe de type sauvage.

**AVERTISSEMENTS ET PRÉCAUTIONS**

NASOVAC-S ne doit en aucun cas être injecté.
Comme pour tous les vaccins injectables, il est recommandé de toujours disposer d'un traitement médical approprié et de surveiller le sujet en cas d'une réaction anaphylactique rare suivant l'administration du vaccin.
Il ne faut pas administrer NASOVAC-S aux individus souffrant du cornage actif.
Si cas d'un antécédent du syndrome de Guillian-Barré, la décision d'administrer NASOVAC-S à cette personne doit être basée sur la considération prudente des bénéfices et des risques potentiels.
L'immunisation doit être retardée chez les personnes souffrant des maladies fébriles sévères ou d'une infection aigue.
Le vaccin pourrait être administré aux gens souffrant des maladies bénignes (par ex. Diarrhée ou infection des voies respiratoires supérieures sans fièvre). Cependant, en cas de congestion nasale qui limite le transfert du vaccin à la paroi nasale, considérer de retarder la vaccination jusqu'à ce que la congestion nasale soit réduite.
Ceux souffrant de rhume, de toux, de fièvre, de courbatures ou d'autres symptômes semblables à ceux de la grippe doivent être cliniquement évalués et le cas échéant, un traitement approprié doit être donné.
La vaccination avec NASOVAC-S doit être retardée au moins jusqu'au rétablissement.
L'administration de NASOVAC-S, aux personnes immunvulnérables doit être effectuée après la considération prudente du rapport bénéfices-risques. Il n'y a pas de données cliniques disponibles sur l'usage de ce vaccin chez les personnes immunodéprimées. La réponse d'anticorps chez de telles personnes pourrait être insuffisante.
La sureté de NASOVAC-S chez les personnes avec des conditions médicales sous-jacentes qui pourraient les prédisposer aux complications après l'infection de la grippe de type sauvage, n'est pas encore établie. NASOVAC-S ne doit être injecté que si les bénéfices potentiels l'emportent sur les risques éventuels.

**Grossesse Et Allaitement**

Une étude de toxicité reproductive et développementale a été effectuée chez les rats femelles qui ont reçu le Nasovac (Vaccin H1N1 pandémique Vivant atténué) soit une, deux ou trois fois (pendant la période de l'organogenèse), à environ 2 fois la dose humaine à chaque fois, par instillation intranasale. Cette étude n'a présenté aucun signe de toxicité maternelle, de foetotoxicité ou de tératogénicité dues au Nasovac. Cependant, aucune étude n'a été effectuée chez une femme enceinte. Puisque les études sur les animaux ne permettent pas toujours de prédire la réaction chez l'humain, Nasovac-S ne doit être administré pendant la grossesse que si absolument nécessaire.
Il n'est pas connu si NASOVAC-S est excrété dans le lait humain. Puisque quelques virus sont excrétés dans le lait humain et de plus, en raison de la possibilité d'excrétion du virus de vaccin, et la proximité du nouveau-né et la mère, il faut agir avec prudence si NASOVAC-S est administré aux mères allaitantes.

**INTERACTIONS MÉDICAMENTEUSES**

Ne pas administrer NASOVAC-S aux enfants ou aux adolescents qui reçoivent la thérapie à l'aspirine ou une thérapie contenant l'aspirine (voir contre-indications)
L'usage concurrent de NASOVAC-S avec des agents antiviraux qui sont actifs contre le virus de la grippe A et/ou B n'est pas encore évalué. Portant, les agents antiviraux pourraient réduire l'efficacité de NASOVAC-S. Il est donc recommandé d'administrer le vaccin seulement après 48 heures de la cessation de la thérapie antivirale, et les agents antiviraux ne doivent être administrés que 2 semaines après l'administration de ce vaccin, sauf si médicalement indiqué. Si NASOVAC-S et les agents antiviraux sont administrés de façon concomitante, il faut considérer la revaccination lors qu'on le juge approprié.
Il n'y a pas de données sur la co-administration de NASOVAC-S avec d'autres vaccins. Pourtant, si la co-administration avec un autre vaccin est indiquée, l'immunisation pourrait être effectuée. Il faut noter que les effets indésirables pourraient s'intensifier.
Il n'y a pas de données sur la co-administration de NASOVAC-S avec d'autres préparations intranasales. La réponse immunitaire pourrait diminuer si le patient subit un traitement immunodépresseur.
Il est peu probable que le vaccin produise un effet sur la capacité de conduite et d'utilisation des machines.

**EFFETS INDESIRABLES**

Pendant les essais cliniques, quelques réactions locales et systémiques ont été observées. Elles étaient bénignes ou modérées et se sont résolues sans séquelles.
Locales : malaise nasale, congestion nasale, éternuements, goutte au nez, perte d'odorat, rougeur des yeux, frissons, gonflement du visage.
Systémique: Fièvre, maux de tête, fatigue, myalgies, arthralgies, irritabilité, perte d'appétit, maux de gorge, toux, respiration sifflante, nausée.

**SURDOSAGE**

Aucun cas de surdosage n'est rapporté.

**PROPRIÉTÉS PHARMACOLOGIQUES**

**Mécanisme d'Action**

Bien que les mécanismes immunitaires qui confèrent une protection contre la grippe après la réception d'un vivant atténué contre la grippe ne soient pas totalement élucidées, il est bien établi que ces vaccins offrent une protection clinique à la majorité des vaccinés. Les anticorps sériques, les anticorps muqueux et les cellules T spécifiques à la grippe peuvent jouer un rôle dans la prévention et la récupération de l'infection. NASOVAC -S contient des virus vivants atténués de la grippe qui doit infecter et se répliquer dans les cellules qui tapissent le nasopharynx du destinataire pour induire une immunité. Les virus des vaccins capables d'infection et de réplication peuvent être cultivés à partir des sécrétions nasales obtenues auprès de sujets vaccinés (excrétion).

**Propriétés Pharmacodynamiques**

NASOVAC-S est un vaccin trivalent vivant pour administration par pulvérisation nasale. La souche du virus de la grippe dans NASOVAC-S est (a) adapté au froid (ca) (c.-à-d, il se réplique de manière efficace à 25 ° C, une température qui est restrictive pour la réplication de nombreux virus de la grippe de type sauvage); (b) sensible à la température (ts) (c'est à dire qu'elle est limitée dans la réplication à 39 ° C, une température à laquelle de nombreux virus grippaux de type sauvage se développent efficacement) et (c) atténué (att). L'effet cumulatif des propriétés antigéniques et les phénotypes ca, ts, et att est que le virus vaccinal atténué se réplique dans le nasopharynx pour induire une immunité protectrice.

**Propriétés Pharmacocinétiques**

Sans objet.

**Données de sureté préclinique**

Des études sur l'efficacité de NASOVAC -S ont été menées chez les furets naïfs (qui sont un modèle établi pour la grippe) en utilisant des virus de grippe homologues comme défi. La charge virale, l'excrétion virale et l'analyse pathologique ont montré des niveaux réduits de tous les trois paramètres chez les animaux vaccinés après l'épreuve quel que soit le virus de défi, démontrant clairement l'efficacité élevée de NASOVAC -S pour toutes les trois souches.
NASOVAC-S a fait l'objet des études de toxicité à dose unique et à doses répétées chez les souris et les rats lorsqu'il est administré par voie intranasale. Dans les études à dose unique, des doses supérieures aux doses normales du vaccin ont été administrées aux animaux et ils ont été observés pendant 14 jours pour les effets toxiques. Aucun effet indésirable lié au vaccin n'a été trouvé chez les animaux recevant NASOVAC-S.
Lors des études de toxicité à doses répétées, trois doses supérieures aux doses normales du vaccin ont été administrées par voie intranasale aux animaux au jour 0, 7 et 14 et ont ensuite été sacrifiés. L'autopsie a été effectuée pour évaluer les effets indésirables sur les
organes. Aucun effet indésirable lié au vaccin n'a été trouvé chez les animaux recevant NASOVAC-S.

**INCOMPATIBILITÉS**

En l'absence des études de compatibilité, ce médicament ne doit pas être mélangé avec d'autres médicaments.

**INSTRUCTIONS POUR LA MANIPULATION ET L'ELIMINATION**

Il faut laisser le vaccin atteindre la température ambiante avant son utilisation. Agiter bien avant de l'utiliser.
Une fois NASOVAC-S, intranasal est administré, les appareils vaccinaux utilisés doivent être éliminés conformément aux procédures normales pour les déchets médicaux (par exemple, conteneur pour instruments tranchants ou des conteneurs pour les produits qui sont nocifs à l'organisme).

**DURÉE DE CONSERVATION**

Ne pas dépasser la date de péremption imprimée sur la boite extérieure.

**CONSERVATION**

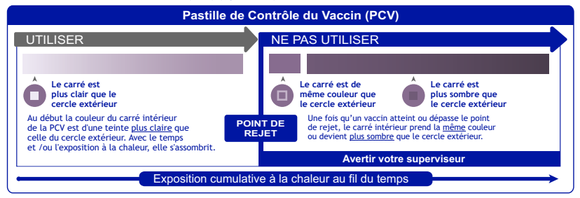
NASOVAC-S (Vaccin Antigrippal, Vivant Atténué (Humain)) Intranasal DOIT ÊTRE CONSERVÉ DANS UN REFRIGERATEUR À 2-8°C (35-46°F) DEPUIS SA RÉCÉPTION JUSQU'À SON UTILISATION. LE PRODUIT DOIT ÊTRE UTILISÉ AVANT LA DATE DE SA PÉRÉMPTION SUR L'ÉTIQUETTTE. La chaine du froid (2-8°C) doit être maintenue lors du transport du Vaccin Antigrippal, Vivant Atténué (Humain) Intranasal.

**PRÉSENTATION**

NASOVAC-S (Vaccin Antigrippal, Vivant Atténué (Humain)) lyophilisé, Intranasal est disponible comme suit:
Flacon de 1 dose plus diluant (0,5 ml)

NASOVAC-S est fourni dans des flacons en verre type I USP, contenant une pastille lyophilisée. Une flacon contenant de l'eau stérile pour inhalation en tant que diluant, une seringue pour administration, adaptateur pour flacon, un dispositif de pulvérisation intranasale et diviseur de dose sont également fournis avec le vaccin.

**PASTILLE DE CONTRÔLE DU VACCIN (PCV) (Optionnel):**




Les pastilles de contrôle du vaccin (PCV) sont sur le bouchon de NASOVAC-S (Vaccin Antigrippal, Vivant Atténué (Humain)), fourni par Serum Institute of India Pvt. Ltd. Il s'agit d'un point sensible au temps écoulé et à la température et indique la chaleur cumulative à laquelle le flacon a été exposé. Cela avertit l'utilisateur final au cas où l'exposition à la chaleur aurait dégradé le vaccin au delà d'un niveau acceptable.

L'interprétation de la PCV est facile. Il ne faut que se concentrer sur le carré intérieur. Sa couleur changera progressivement. Tant que la couleur de carré est plus claire que celle du cercle extérieur, on peut utiliser le vaccin. Lorsque le carré central est de la même couleur que le cercle extérieur ou plus foncé que le cercle extérieur, on doit jeter le flacon.

**EXTRÊMEMENT IMPORTANT**

1. S'assurer que le vaccin est administré uniquement par intranasale.
2. Dans de rares cas, le choc anaphylactique peut survenir chez les patients sensibles. L'utilisation immédiate d'Adrénaline est d'une importance vitale en cas d'anaphylaxie aiguë. Il faut l'utiliser dès les premiers signes de l'anaphylaxie. Comme pour tous les vaccins, les personnes vaccinées doivent être mises sous observation pendant au moins 30 minutes au cas où certaines réactions allergiques se produisent suite à l'administration du vaccin. L'Hydrocortisone et les anti-histaminiques doivent être également disponibles avec des mesures supplémentaires de soutien telles que l'inhalation d'oxygène.

**ATTENTION : PERSONNES QUI NE DOIVENT PAS RECEVOIR LE VACCIN**

1. Ceux qui sont allergiques aux œufs
2. Enfants et adolescents (2-17 ans) recevant de l'aspirine ou une thérapie contenant de l'aspirine. Ceux qui souffrent déjà de toux, fièvre, courbatures ou autres symptômes semblables à ceux de la grippe doivent être cliniquement évalués et le cas échéant, ils doivent recevoir un traitement approprié. Dans ces cas, la vaccination avec NASOVAC-S doit être reportée jusqu'à la récupération.

Date de révision : 02/2021


Fabriqué par :
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Protection dés la naissance

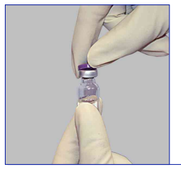

## RECONSTITUTION OF THE VACCINE
## RECONSTITUCIÓN DE LA VACUNA
## RECONSTITUTION DU VACCIN


Components for administration.
Allow the vaccine and diluent to attain room temperature.

Componentes para la administración.
Permitir que la vacuna y el diluyente atinjan la temperatura ambiente.

Composants pour l'administration.
Laissez le vaccin et le diluant atteindre la température ambiante.

1



Remove the flip top from the diluent vial.

Quitar la tapa flip-top del frasco del diluyente.

Enlevez la capsule amovible du flacon de diluant.

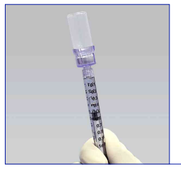
2

a) Connect the vial adapter onto the diluent vial by pushing it downwards until vial adapter is properly and solidly placed.
b) Connect the syringe to the vial adapter by completely screwing in clockwise direction.

a) Conectar el adaptador de ampolla en el frasco del diluyente empujándolo hacia abajo, hasta que el adaptador de ampolla esté bien colocado.
b) Conectar la jeringa al adaptador de ampolla, girándola en sentido horario hasta que esté bien sujeta.

a) Connectez l'adaptateur de flacon au flacon de diluant en le poussant vers le bas jusqu'à ce que l'adaptateur soit correctement et bien placé.
b) Connectez la seringue à l'adaptateur de flacon en vissant complètement dans le sens des aiguilles d'une montre.

3



Draw the entire contents of the diluent vial into the syringe.

Aspirar el contenido entero del frasco del diluyente dentro de la jeringa.

Retirez la teneur entière du flacon de diluant dans la seringue.

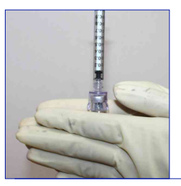
4

Remove the entire assembly (syringe connected to the adapter) from the diluent vial.

Retirar el conjunto entero (jeringa conectada al adaptador) del frasco del diluyente.

Enlevez l'assemblage entier (seringue connectée à l'adaptateur) du flacon de diluant.

5



Remove the flip top from the vaccine vial. Attach the syringe with vial adapter to the vaccine vial and allow the liquid to be drawn in. Assist by pushing the plunger if required. Disconnect the syringe from the vial adapter to break any residual vacuum.

Quitar la tapa tipo flip-off del vial de la vacuna. Colocar la jeringa en el adaptador del frasco y permitir la aspiración del líquido. Ayudar empujando el embolo si fuera necesario. Desconectar la del adaptador del frasco para romper el vacio residual.

Enlevez le capuchon du flacon de vaccin. Attachez la seringue avec l'adaptateur au flacon de vaccin et laissez le liquide entrer. Poussez le piston si nécessaire. Déconnectez la seringue de l'adaptateur de flacon pour casser tout vide résiduel.

6

Rotate the vial between the palms to dissolve its contents.

Girar el frasco entre las palmas de la mano para disolver el contenido.

Tournez le flacon entre les mains pour dissoudre le contenu.

7

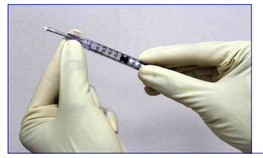
## ADMINISTRATION OF THE VACCINE
## ADMINISTRACIÓN DE LA VACUNA
## ADMINISTRATION DU VACCIN

Reconnect the syringe with the vial adapter and withdraw the entire reconstituted vaccine into the syringe.
Detach the syringe from the vial adapter.

Volver a conectar la jeringa con el adaptador del frasco y retirar todo la vacuna reconstituida en la jeringa.
Separe la jeringa del adaptador del frasco.

Reconnectez la seringue avec l'adaptateur de flacon et retirez tout le vaccin reconstitué dans la seringue.
Détachez la seringue de l'adaptateur de flacon.

1

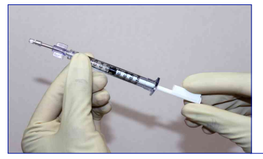


Fix the intranasal spray device on the tip of the syringe.

Colocar el dispositivo atomizador intranasal en el punto de la jeringa.

Fixez le dispositif de pulvérisation intranasale au bout de la seringue.

2



Fix the dose divider on the plunger of the syringe.

Colocar el separador de dosis en el émbolo de la jeringa.

Fixez le diviseur de dose sur le piston de la seringue.

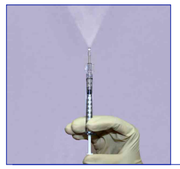
3

Place the intranasal spray device at the base of the nostril of the recipient sitting upright with his/her head slightly thrown back and push the plunger firmly in a single stroke to deliver the vaccine. 0.25 ml i.e. half of the dose is delivered.

Colocar el dispositivo atomizador intranasal en la apertura de la fosa nasal, con el recipiente sentado recto con la cabeza ligeramente inclinada y empujar el émbolo firmemente de una sola vez para entregar 0,25 ml de la vacuna, es decir se entrega la mitad de la dosis.

Placez le dispositif de pulvérisation à la base d'une narine du récipient qui est assis droit avec la tête légèrement inclinée vers l'arrière et poussez bien le piston d'un seul coup pour livrer le vaccin. 0,25 ml soit la moitié de la dose est administrée.

4



Draw back the plunger slightly and remove the dose divider. Repeat the above step to deliver the remaining 0.25 ml into the second nostril.

Tirar el émbolo un poco hacia atrás y quitar el separador de dosis. Repetir el paso arriba mencionado para entregar el 0,25 ml restante en la segunda fosa.

Retirez le piston un tout petit peu et enlever le diviseur de dose. Répétez l'étape précédente pour livrer la quantité restante soit 0,25 ml dans l'autre narine.

5


Manufactured by/ Fabricada por/Fabriqué par :
SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA

English

# Influenza Vaccine, Live Attenuated (Human)

# NASOVAC-S

Seasonal, Trivalent

2020-21 Formula Northern Hemisphere Freeze dried

**DESCRIPTION**

NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), freeze dried is a live trivalent vaccine for administration by intranasal spray. NASOVAC-S contains three vaccine virus strains of A/H1N1, A/H3N2 and Type B influenza virus cultivated on embryonated hen eggs. The three strains are antigenically similar to the strains recommended by the World Health Organization (W.H.O.) for 2020-21.

**COMPOSITION**

[Propagated in Embryonated hen eggs]
Each vial of single dose (0.5 ml) contains:

| | |
|---|---|
| A(H1N1) Strain- A/17/Guangdong-Maonan/2019/211 (H1N1)* | Not less than $10^7$ $EID_{50}$ |
| A(H3N2) Strain-A/17/Hong Kong/2019/2573 (H3N2)* | Not less than $10^7$ $EID_{50}$ |
| B Strain - B/60 / Washington /2019 /3676* | Not less than $10^{6.5}$ $EID_{50}$ |

* Antigenic specificity of Hemagglutinin and Neuraminidase identical to wild type virus as recommended by W.H.O. for influenza vaccine for the year 2020-21 Northern hemisphere influenza season:

- A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09 - like virus
- A/Hong Kong/2671/2019 (H3N2) - like virus
- B/Washington / 02 / 2019 - like virus (B/Victoria lineage)

Partially hydrolyzed gelatin 2.5%, Sorbitol 5.0%, L-Alanine 0.1%, L-Histidine 0.21%, Tricine 0.3%, L-Arginine hydrochloride 1.6%, Lactalbumin hydrolysate 0.35%, Phosphate buffer saline Base. Reconstitute with Sterile Water for Inhalation I.P. The vaccine contains no preservatives.
Dose: 0.5 ml intranasal (spray 0.25 ml per nostril). The tip attached to the sprayer is equipped with a nozzle that produces a fine mist that is primarily deposited in the nose and nasopharynx.
The vaccine complies with the W.H.O. recommendations.

**INDICATIONS**

NASOVAC-S is indicated in individuals above 2 years of age for the active immunization for the prevention of influenza disease caused by two influenza A subtype viruses and one influenza Type B virus which are expected to circulate in the 2020-21 season. NASOVAC-S should be used in accordance with official guidance.

**POSOLOGY AND METHOD OF ADMINISTRATION**

Each freeze-dried vaccine vial is reconstituted using the entire contents of sterile water for inhalation that is supplied along with the vaccine, using the supplied syringe and vial adapter.
A dose of 0.5 ml is administered as 0.25 ml per nostril using a 1.0 ml syringe and a spray device. Withdraw the entire reconstituted vaccine for administration. The spray device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx. A single intranasal dose is recommended for people above 2 years of age.
For further information, see (Pharmacodynamic properties).
Use immediately after reconstitution. If the vaccine is not used immediately then it should be stored in the dark at 2-8°C for no longer than 6 hours.
Any opened container remaining at the end of a session (within six hours of reconstitution) should be discarded.
The vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.
The diluent supplied is specially designed for use with the vaccine. Only this diluent must be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or from other manufacturers. Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen, but should be kept cool.
The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

**CONTRAINDICATIONS**

**Hypersensitivity**

NASOVAC-S is contraindicated in individuals with a history of hypersensitivity, especially anaphylactic reactions to eggs, egg proteins, gelatin, or Lactalbumin or with other vaccine components.

**Concomitant Pediatric and Adolescent Aspirin Therapy and Reye's syndrome**

NASOVAC-S is contraindicated in children and adolescents (2-17 years of age) receiving aspirin therapy or aspirin-containing therapy, because of the association of Reye's syndrome with aspirin and wild-type influenza infection.

**WARNINGS AND PRECAUTIONS**

NASOVAC-S should under no circumstances be injected.
As with all vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.
NASOVAC-S should not be administered to any individuals with active wheezing.
If the individual has a history of Guillain-Barré syndrome the decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.
Immunization should be postponed in patients with severe febrile illness or acute infection. The vaccine can be given to people with minor illnesses (e.g., diarrhea or mild upper respiratory tract infection without fever). However, if nasal congestion is present that might limit delivery of the vaccine to the nasal lining, then delaying of vaccination until the nasal congestion is reduced should be considered.
People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.
Administration of NASOVAC-S, to immune-compromised persons should be based on careful consideration of potential benefits and risks. There is no clinical data available on the use of this vaccine in immune-compromised persons. Antibody response in such patients may be insufficient.
The safety of NASOVAC-S in individuals with underlying medical conditions that may predispose them to complications following wild-type influenza infection has not been established. The decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.

**Pregnancy and lactation**

A developmental and reproductive toxicity study has been performed in female rats administered Nasovac (Live attenuated pandemic H1N1 vaccine) either once, twice or thrice (during the period of organogenesis), at approximately 2 human dose equivalents per occasion, by intranasal instillation and has revealed no evidence of maternal toxicity, fetotoxicity or teratogenicity due to Nasovac. There are however, no studies in pregnant women. Because animal studies are not always predictive of human response, Nasovac-S should be administered during pregnancy only if clearly needed.
It is not known whether NASOVAC-S is excreted in human milk. Therefore, as some viruses are excreted in human milk and additionally, because of the possibility of shedding of vaccine virus and the close proximity of a nursing infant and mother, caution should be exercised if NASOVAC-S is administered to nursing mothers.

**DRUG INTERACTIONS**

Do not administer NASOVAC-S to children or adolescents who are receiving aspirin therapy or aspirin-containing therapy (see Contraindications).
The concurrent use of NASOVAC-S with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for antiviral agents to reduce the effectiveness of NASOVAC-S, do not administer this vaccine until 48 hours after the cessation of antiviral therapy and antiviral agents should not be administered until two weeks after administration of this vaccine unless medically indicated. If antiviral agents and NASOVAC-S are administered concomitantly, revaccination should be considered when appropriate.
There are no data on co-administration of NASOVAC-S with other vaccines. However, if co-administration with another vaccine is indicated, immunisation may be carried. It should be noted that the adverse reactions may be intensified.
There are no data regarding co-administration of NASOVAC-S with other intranasal preparations. The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.
The vaccine is unlikely to produce an effect on the ability to drive and use machines.

**ADVERSE REACTIONS**

In clinical trials a few local and systemic reaction were observed. They were mild to moderate in severity and resolved without any sequelae.
Local : Nasal discomfort, stuffy nose, sneezing, runny nose, loss of smell, red eyes, chills, facial swelling.
Systemic : Fever, headache, fatigue, myalgia, arthralgia, irritability, loss of appetite, sore throat, cough, wheezing, nausea.

**OVERDOSE**

No case of overdose has been reported.

**PHARMACOLOGICAL PROPERTIES**

**Mechanism of Action**

Immune mechanisms conferring protection against influenza following receipt of live attenuated influenza vaccines are not fully understood, though it is well-established that these vaccines provide clinical protection to the majority of the vaccinees. Serum antibodies, mucosal antibodies, and influenza-specific T cells may play a role in prevention and recovery from infection. NASOVAC-S contains live attenuated influenza viruses that must infect and replicate in cells lining the nasopharynx of the recipient to induce immunity. Vaccine viruses capable of infection and replication can be cultured from nasal secretions obtained from vaccine recipients (shedding)

**Pharmacodynamic properties**

NASOVAC-S is a live trivalent vaccine for administration by intranasal spray. The influenza virus strain in NASOVAC-S is (a) cold-adapted (ca) (i.e., it replicates efficiently at 25°C, a temperature that is restrictive for replication of many wild-type influenza viruses); (b) temperature-sensitive (ts) (i.e., it is restricted in replication at 39°C, a temperature at which many wild-type influenza viruses grow efficiently); and (c) attenuated (att). The cumulative effect of the antigenic properties and the ca, ts, and att phenotypes is that the attenuated vaccine virus replicates in the nasopharynx to induce protective immunity.

**Pharmacokinetic properties**

Not applicable.

**Preclinical safety data**

Efficacy study of NASOVAC-S in naïve ferrets (which is an established model of influenza) using homologous influenza viruses as challenge was conducted. Viral load, viral shedding and pathological analysis showed reduced levels of all three parameters in vaccinated animals after challenge irrespective of the challenge virus clearly demonstrating high efficacy of NASOVAC-S for all the three strains.
NASOVAC-S has undergone Single-dose and Repeated-dose toxicity studies in mice and rats when administered intranasally. In single-dose studies, higher than normal doses of the vaccine were given to animals and they were observed for 14 days for toxic effects. No vaccine-related untoward effects were found in animals receiving NASOVAC-S.
In repeated-dose toxicity studies, three doses of higher than normal doses of the vaccine were given intranasally to animals on day 0, 7 and 14 and were subsequently sacrificed. Necropsy was done to assess adverse effects on any organs. No vaccine-related adverse effects were found in the study animals receiving NASOVAC-S.

**INCOMPATIBILITIES**

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

**INSTRUCTIONS FOR USE AND HANDLING AND DISPOSAL**

The vaccine should be allowed to reach room temperature before use. Shake before use.
Once NASOVAC-S, intranasal has been administered, the used vaccine devices and all its parts should be disposed off according to the standard procedures for medical waste (e.g., sharps container or biohazard container).

**SHELF-LIFE**

Do not exceed the expiry date printed on the label and packaging.

**STORAGE**

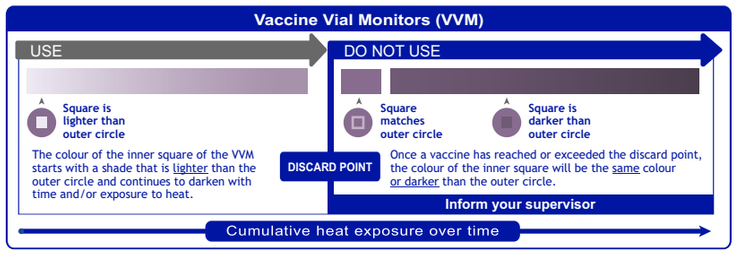
NASOVAC-S, Influenza Vaccine, Live Attenuated (Human) Intranasal SHOULD BE STORED IN A REFRIGERATOR AT 2 - 8°C (35-46°F) UPON RECEIPT AND UNTIL USE. THE PRODUCT MUST BE USED BEFORE THE EXPIRATION DATE ON THE LABEL. The cold chain (2 to 8°C) must be maintained when transporting Influenza Vaccine, Live Attenuated (Human) Intranasal.

**PRESENTATION**

NASOVAC-S Influenza Vaccine, Live Attenuated (Human) freeze dried, intranasal is available as:
1 dose vial plus diluent ( 0.5 ml)

NASOVAC-S is supplied as a vial containing freeze-dried cake in USP type 1 glass vials.
Vial containing sterile water for inhalation as diluent, syringe for administration, vial adapter, intranasal spray device and dose divider are also supplied along with the vaccine.

**THE VACCINE VIAL MONITOR (VVM) (Optional)**




Vaccine Vial Monitors (VVMs) are on the cap of NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indications of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

**MOST IMPORTANT WARNING**

1. Please ensure that the vaccine is administered by intranasal spray.
2. In rare cases anaphylactic shock may occur in susceptible individual. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis. As with the use of all vaccines, the vaccinees should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

**CAUTION: PEOPLE WHO SHOULD NOT TAKE THE VACCINE**

1. Those who are allergic to eggs
2. Children and adolescents (2-17 years of age) receiving aspirin and aspirin containing therapy. People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.

Revision date: 02/2021


Manufactured by:
**SERUM INSTITUTE OF INDIA PVT. LTD.**
212/2, Hadapsar, Pune 411028, INDIA


Protection from birth onwards

20017672/0

Portuguese

# Vacina da Influenza Viva, Atenuada (Humana)

# NASOVAC-S

Sazonal , Trivalente

Fórmula de 2020-2021 Hemisfério Norte Liofilizada

**DESCRIÇÃO**

NASOVAC-S, Vacina da Influenza, Viva, Atenuada, (Humana), liofilizada é uma vacina trivalente, viva, para a administração por spray intranasal. NASOVAC-S contém três estirpes do vírus da vacina de A/H1N1, A/H3N2 e o vírus da influenza Tipo B cultivadas nos ovos de galinha embrionados. As três estirpes são antigenicamente semelhantes às cepas recomendadas pela Organização Mundial de Saúde (OMS) para 2020-2021.

**COMPOSIÇÃO**

[Propagada em ovos de galinha embrionados]
Cada frasco com uma dose única de 0,5 ml contém:

| | |
|---|---|
| Estirpe A (H1N1) - A/17/Guangdong-Maonan/2019/211 (H1N1)* | Não inferior a $10^7$ $DIE_{50}$ |
| Estirpe A (H3N2) - A/17/Hong Kong/2019/2573 (H3N2)* | Não inferior a $10^7$ $DIE_{50}$ |
| Estirpe B - B/60/Washington/2019/3676* | Não inferior a $10^{6.5}$ $DIE_{50}$ |

* A especificidade antigénica da hemaglutinina e neuraminidase é idêntica ao vírus do tipo selvagem de acordo com a recomendação da OMS para a vacina contra a influenza para a temporada de influenza do hemisfério norte no ano 2020-2021:

- Vírus tipo A / Guangdong-Maonan/ SWL1536/2019 (H1N1) pdm09
- Vírus tipo A / Hong Kong/2671/2019 (H3N2)
- Vírus tipo B / Washington / 02/2019 - (linhagem B / Victoria)

Gelatina (parcialmente hidrolisada) 2,5%, Sorbitol 5,0%, L-Alanina 0,1%, L-Histidina 0,21%, Tricina 0,3%, Cloridrato de L-Arginina 1,6%, Hidrolisado de Lactalbumina 0,35%, Tampão de Fosfato base salina. Reconstituir com Água Estéril para Inalação IP. A vacina não contém conservantes.
Dose: 0,5 ml intranasal (aplicar 0,25 ml em cada fossa nasal com spray). A ponta acoplada ao spray está equipada com um bico que produz um vapor fino que se deposita principalmente no nariz e na nasofaringe.
A vacina está em conformidade com as recomendações da OMS.

**INDICAÇÕES**

NASOVAC-S está indicada na imunização ativa dos indivíduos com mais de 2 anos de idade para a prevenção da doença da influenza causada por dois vírus do subtipo A e um vírus da influenza de tipo B, que segundo as previsões circularão na temporada de 2020-2021. NASOVAC-S deve ser utilizada de conformidade com as orientações oficias.

**POSOLOGIA E MÉTODO DE ADMINISTRAÇÃO**

Cada frasco da vacina liofilizada é reconstituído usando o conteúdo inteiro de água estéril para inalação que é fornecida junto com a vacina, usando a seringa e o adaptador do frasco fornecidos.

Uma dose de 0,5 ml é administrada na forma de 0,25 ml em cada narina usando uma seringa de 1,0 ml e um dispositivo spray. Retire toda a vacina reconstituída para administração. O dispositivo spray cria um vapor fino que primariamente deposita a vacina no nariz e nasofaringe. Recomenda-se uma dose intranasal para pessoas de mais de 2 anos.

Para mais informação (veja Propriedades Farmacodinâmicas).
Use imediatamente depois da reconstituição. Se a vacina não for usada imediatamente, deve ser armazenada no escuro a 2 - 8°C por não mais de 6 horas.

Qualquer recipiente aberto que permaneça no final de uma sessão (dentro de seis horas após a reconstituição) deve ser descartado. O monitor do frasco da vacina (veja a figura) para este tipo de vacina é colocado na tampa do frasco e deve ser descartado quando a vacina está sendo reconstituída.
O diluente fornecido é especialmente desenvolvido para uso com a vacina. Apenas este diluente deve ser usado para reconstituir a vacina. Não use diluentes de outros tipos de vacinas ou de outros fabricantes. O uso de um diluente incorreto pode resultar em danos à vacina e/ou reações graves em pessoas que recebem a vacina. O diluente não deve ser congelado, mas deve ser mantido fresco.
O diluente e a vacina reconstituída devem ser inspecionados visualmente para a presença de partículas estranhas e/ ou variações dos aspetos físicos antes da administração. Se for observada a presença de qualquer delas, descarte o diluente ou a vacina reconstituída.

**CONTRAINDICAÇÕES**

**Hipersensibilidade**

NASOVAC-S é contraindicada em indivíduos com uma história de hipersensibilidade, especialmente reações anafiláticas a ovos, proteínas de ovo, gelatina ou lactalbumina ou com outros componentes da vacina.

**Terapia concomitante Pediátrica e Adolescente com Aspirina e a Síndrome de Reye**

NASOVAC-S é contraindicada em crianças e adolescentes (de idade entre 2 - 17 anos) que estão recebendo a terapia com aspirina ou a terapia com um medicamento que contenha a aspirina, devido à associação da Síndrome de Reye com a aspirina e a infecção por influenza de tipo selvagem.

**ADVERTÊNCIAS E PRECAUÇÕES**

NASOVAC-S não deve ser injetada em nenhuma circunstância.
Tal como acontece com todas as vacinas deve estar sempre disponível o tratamento médico apropriado e supervisão no caso dum evento anafilático raro após a administração da vacina.
NASOVAC-S não deve ser administrado em pessoas com a pieira ativa.
Se a pessoa tiver histórico de Síndrome de Guillain-Barré, a decisão de administrar NASOVAC-S deve ser baseada na avaliação cuidadosa dos benefícios e riscos potenciais.
A imunização deve ser adiada em pacientes com uma doença febril grave ou infecção aguda. A vacina pode ser administrada em pessoas com doenças leves (por exemplo: diarreia ou infecção leve do trato respiratório superior sem febre). No entanto se houver congestão nasal, isto pode limitar a entrega da vacina ao revestimento nasal. Neste caso deve ser considerado o adiamento da vacinação até a congestão nasal seja reduzida.
Pessoas que já sofrem de resfriado, tosse, febre, dores no corpo ou outros sintomas parecidos aos da gripe devem ser avaliadas clinicamente e se for necessário, deve ser administrado o tratamento adequado. Nesses casos a vacinação com NASOVAC-S deve ser adiada pelo menos até a recuperação.
A administração de NASOVAC-S em pessoas imunocomprometidas deve ser baseada na consideração cuidadosa dos benefícios e riscos potenciais. Não há dados clínicos disponíveis sobre o uso desta vacina em pessoas imunocomprometidas. A resposta de anticorpos em tais pacientes pode ser insuficiente.
A segurança de NASOVAC-S em indivíduos com condições médicas subjacentes que podem predispor a complicações após a infecção por influenza de tipo selvagem não foi estabelecida. A decisão de administrar NASOVAC-S deve ser baseada na consideração cuidadosa dos benefícios e riscos potenciais.

**Gravidez e Lactação**

Foi realizado um estudo de toxicidade reprodutiva e de desenvolvimento em ratas administradas com Nasovac (Vacina viva, atenuada para a pandemia de H1N1) uma, duas ou três vezes (durante o período da organogênese) equivalentes a aproximadamente 2 doses humanas por ocasião, por instilação intranasal e não foi revelada nenhuma evidência da toxicidade materna, toxicidade fetal ou a teratogenicidade devido à Nasovac-S. No entanto, não existem estudos em mulheres grávidas. Como os estudos em animais nem sempre são preditivos da resposta humana, Nasovac-S deve ser administrada durante a gravidez apenas se for claramente necessário.

Não se sabe se NASOVAC-S é excretado no leite humano. Por tanto, dado que alguns vírus se excretam no leite humano e adicionalmente, devido à possibilidade da excreção do vírus da vacina e a proximidade do lactante e a mãe, deve-se ter cuidado se NASOVAC-S for administrada a mães que amamentam.

**INTERAÇÕES MEDICAMENTOSAS**

Não administrar NASOVAC-S em crianças ou adolescentes que estejam recebendo terapia com aspirina ou terapia com medicamentos que contêm a aspirina. (Veja Contraindicações)

O uso concorrente de NASOVAC-S com agentes antivirais ativos contra o vírus da influenza A e/ou B não foi avaliado. No entanto, com base no potencial dos agentes antivirais para reduzir a eficácia de NASOVAC-S, não administre esta vacina até 48 horas depois da descontinuação da terapia antiviral e os agentes antivirais não devem ser administrados até duas semanas após a administração desta vacina, a menos que haja indicação médica. Se agentes antivirais e NASOVAC-S forem administrados concomitantemente, a revacinação deve ser considerada quando for apropriado.
No entanto, se for indicada a administração concomitante com outra vacina, a imunização pode ser feita. Deve-se notar que podem ser mais intensas as reações adversas.

Não existem dados sobre a administração concomitante de NASOVAC-S com outras preparações intranasais.

A resposta imunológica pode ser reduzida se o paciente estiver sob tratamento com imunossupressores. É improvável que a vacina tenha efeito sobre a capacidade de conduzir e utilizar máquinas.

**REAÇÕES ADVERSAS**
Nas provas clínicas, foram observadas algumas reações locais e sistêmicas. Eram de gravidade leve a moderada e resolveram sem quaisquer sequelas.
Locais: Desconforto nasal, nariz congestionada, espirros, coriza, perda de olfato, olhos avermelhados, calafrios, edema facial.
Sistêmicas: Febre, dor da cabeça, fadiga, mialgia, artralgia, irritabilidade, perda de apetite, dor de garganta, tosse, pieira, náusea.

**SOBRE DOSAGEM**
Não foi relatado nenhum caso da sobredosagem.

**PROPRIEDADES FARMACOLÔGICAS**

**Mecanismo de Ação**
Os mecanismos imunológicos que conferem proteção contra a influenza após a administração das vacinas, vivas, atenuadas contra a influenza ainda não são totalmente compreendidos, embora esteja bem estabelecido que estas vacinas fornecem a proteção clínica para a maioria dos vacinados. Os anticorpos séricos, anticorpos mucosos e as células-T específicas da influenza podem desempenhar um papel na prevenção e recuperação da infecção. NASOVAC-S contém vírus vivos atenuados da influenza que devem infectar e se replicar nas células que revestem a nasofaringe do vacinado para induzir a imunidade. Os vírus da vacina capazes de infecção e replicação podem ser cultivados a partir das secreções nasais obtidas dos vacinados (excreção).

**Propriedades farmacodinâmicas**
NASOVAC-S é uma vacina viva trivalente para administração com spray intranasal. A estirpe do vírus da influenza em NASOVAC-S é (a) adaptada ao frio (ca pela sua abreviatura em inglês) (isto é, replica-se eficientemente a 25ºC, uma temperatura que é restritiva para a replicação de muitos vírus da influenza tipo selvagem; (b) sensível à temperatura (ts pela sua abreviatura em inglês) (isto é a replicação é restrita à 39ºC, a uma temperatura na qual muitos vírus da influenza de tipo selvagem crescem eficientemente; e (c) atenuada (att). O efeito cumulativo das propriedades antigênicas e dos fenótipos ca, ts e att é que o vírus da vacina atenuada se replica na nasofaringe para induzir a imunidade protetora.

**Propriedades Farmacocinéticas**
Não é aplicável

**Dados de Segurança Pré-clínica**
Foi realizado um estudo de eficácia de NASOVAC-S em furões sem tratamento prévio (que é um modelo estabelecido da influenza) usando vírus de influenza homóloga como desafio. A carga viral, excreção viral e a análise patológica mostraram níveis reduzidos de todos os três parâmetros em animais vacinados após o desafio, sem consideração do fato do que o vírus de desafio claramente demostrou a alta eficácia de NASOVAC-S para todas as três estirpes.
NASOVAC-S foi submetido a estudos de toxicidade de dose única e dose repetida em camundongos e ratas, quando foi administrada por via intranasal. Em estudos de dose única, foram administradas doses superiores à dose normal da vacina aos animais e foram observados durante 14 dias quanto a efeitos tóxicos. Nenhum efeito adverso relacionado à vacina foi observado nos animais de estudo que receberam NASOVAC-S.
Em estudos de toxicidade de dose repetida, três doses de doses superiores à dose normal da vacina foram administradas por via intranasal em animais nos dias 0, 7 e 14 e eles foram subsequentemente sacrificados. A necropsia foi realizada para avaliar os efeitos adversos em quaisquer órgãos. Nenhum efeito adverso relacionado à vacina foi observado nos animais do estudo que receberam NASOVAC-S.

**INCOMPATIBILIDADES**
Na ausência de estudos de compatibilidade, este medicamento não deve ser misturado com outros produtos medicamentosos.

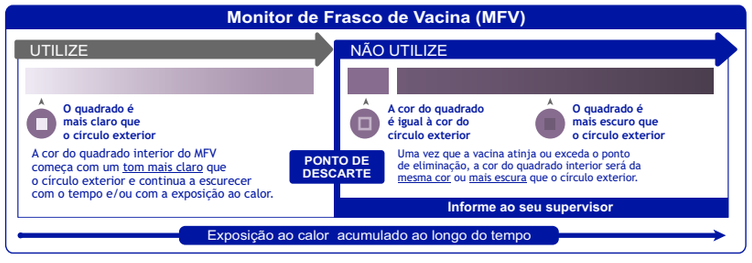
**INSTRUÇÕES PARA USO, MANUSEIO E DESCARTE**
A vacina deve atingir a temperatura ambiente antes de ser usada. Agite antes de usar.
Uma vez que NASOVAC-S Intranasal tenha sido administrada, os dispositivos da vacina usados e todas as suas partes devem ser descartados de conformidade com os procedimentos padrão para resíduos hospitalares (por exemplo, recipientes para objetos perfurocortantes/ recipientes que representam risco biológico)

**VALIDADE**
Não exceda a data de validade impressa no rótulo e na embalagem.

**CONSERVAÇÃO**
NASOVAC-S - Vacina da Influenza Viva, Atenuada (Humana) Intranasal DEVE SER ARMAZENADA NO REFRIGERADOR À 2 - 8ºC (35 - 46ºF) APÓS O RECEBIMENTO E ATÉ O SEU USO. O PRODUTO DEVE SER USADO ANTES DA DATA DE VENCIMENTO DECLARADA NO RÓTULO. A cadeia de frio (2 a 8ºC) deve ser mantida durante o transporte da Vacina da influenza Viva, Atenuada (Humana) Intranasal.

**APRESENTAÇÃO**
NASOVAC-S - Vacina da Influenza Viva, Atenuada (Humana) Intranasal está disponível na forma de:
Frasco de 1 dose mais diluente (0,5 ml)
NASOVAC-S é fornecida como frasco contendo um bolo liofilizado em frascos de vidro de USP tipo 1. Também são fornecidos, um frasco contendo água estéril para inalação como diluente, uma seringa para administração, adaptador para frasco, dispositivo spray intranasal e um dispositivo dosador junto com a vacina.

**MONITOR DE FRASCO DE VACINA (MFV) (Opcional)**




Os monitores de frasco da vacina (MFV) fazem parte da tampa da NASOVAC-S - Vacina da Influenza Viva, Atenuada (Humana) Intranasal fornecida pelo Serum Institute of India Pvt. Ltd. Este é um ponto sensível ao tempo e à temperatura que dá uma indicação do calor acumulado ao qual tem sido exposta a ampola. Isto adverte ao usuário final quando a exposição ao calor provavelmente degradou a vacina além de um nível aceitável.

A interpretação do MFV é muito simples. Concentre no quadrado central. A cor do quadrado mudará progressivamente. Enquanto a cor deste quadrado é mais clara do que a cor do círculo exterior, a vacina pode ser utilizada. Assim que a cor do quadrado central tiver a mesma coloração que a do círculo exterior ou também uma coloração mais escura do que a cor do círculo exterior, a ampola deve ser descartada.

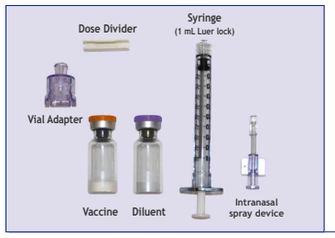
**ADVERTÊNCIA MAIS IMPORTANTE**
1. Assegure que a vacina seja administrada apenas por atomizador intranasal.
2. Em raros casos pode ocorrer o choque anafilático em indivíduos susceptíveis. O fator mais importante no tratamento da anafilaxia severa é o uso imediato de adrenalina, que pode salvar a vida. Deve ser usada ante a primeira suspeita da anafilaxia. Tal como acontece com todas as vacinas, todos os vacinados devem permanecer em observação pelo menos durante 30 minutos para a possibilidade da ocorrência de reações alérgicas rápidas. Também devem estar disponíveis hidrocortisona e anti-histamínicos além de outras medidas de apoio como a inalação de oxigénio.

**CAUÇÃO: PESSOAS QUE NÃO DEVEM TOMAR A VACINA**
1. Aqueles que são alérgicas a ovos.
2. Crianças e adolescentes (de idade de entre 2 -17 anos) recebendo aspirina e a terapia contendo aspirina. Pessoas que já sofrem de resfriado, tosse, febre, dores no corpo ou outros sintomas semelhantes aos da gripe devem ser clinicamente avaliadas e se necessário deve ser administrado o tratamento apropriado. Nesses casos, a vacinação com NASOVAC-S deve ser adiada pelo menos até a recuperação.

Data de revisão: 02/2021

*Fabricado por:*
**SERUM INSTITUTE OF INDIA PVT. LTD.**
212/2, Hadapsar, Pune 411028, INDIA
A proteção desde o nascimento

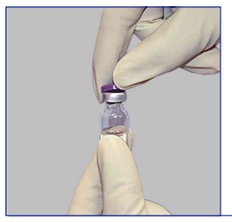
## RECONSTITUTION OF THE VACCINE
## RECONSTITUIÇÃO DA VACINA




Components for administration.
Allow the vaccine and diluent to attain room temperature.

Componentes para administração
Deixe a vacina e o diluente atingirem a temperatura ambiente.

1



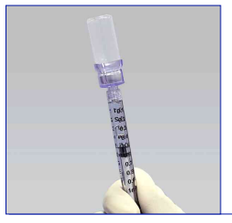
Remove the flip top from the diluent vial.

Remova a tampa tipo flip-top de frasco do diluente.

2

a) Connect the vial adapter onto the diluent vial by pushing it downwards until vial adapter is properly and solidly placed.
a) Conecte o adaptador da ampola ao frasco do diluente, empurrando-o até que o adaptador de frasco esteja bem encaixado.
b) Connect the syringe to the vial adapter by completely screwing in clockwise direction.
b) Conecte a seringa ao adaptador de frasco girando no sentido horário até que esteja firme.

3



Draw the entire contents of the diluent vial into the syringe.

Aspire todo o conteúdo do frasco de diluente para a seringa

4

Remove the entire assembly (syringe connected to the adapter) from the diluent vial.

Remova o conjunto inteiro (seringa acoplada ao adaptador) do frasco de diluente.

5

Remove the flip top from the vaccine vial.
Attach the syringe with vial adapter to the vaccine vial and allow the liquid to be drawn in. Assist by pushing the plunger if required.
Disconnect the syringe from the vial adapter to break any residual vacuum.

Remova a tampa flip-top do frasco da vacina. Fixe a seringa com o adaptador do frasco no frasco da vacina e deixe o líquido ser aspirado.
Auxilie empurrando o êmbolo se for necessário.

6

Rotate the vial between the palms to dissolve its contents.

Gire o frasco entre as palmas das mãos para dissolver seu conteúdo

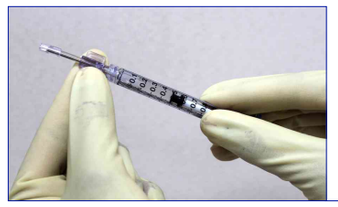
7

## ADMINISTRATION OF THE VACCINE
## ADMINISTRAÇÃO DA VACINA

Reconnect the syringe with the vial adapter and withdraw the entire reconstituted vaccine into the syringe. Detach the syringe from the vial adapter.

Volte a conectar a seringa com o adaptador do frasco e aspire toda a vacina reconstituída para a seringa. Separe a seringa do adaptador de frasco.

1



Fix the intranasal spray device on the tip of the syringe by completely screwing in clockwise direction.

Fixe o dispositivo de spray intranasal na ponta da seringa girando completamente no sentido horário

2

Fix the dose divider on the plunger of the syringe.

Fixe o dispositivo dosador no êmbolo da seringa.

3

Place the intranasal spray device at the base of the nostril of the recipient sitting upright with his/her head slightly thrown back and push the plunger firmly in a single stroke to deliver the vaccine. 0.25 ml i.e. half of the dose is delivered.

Coloque o spray intranasal na base da narina do receptor, sentado com a cabeça ligeiramente inclinada para trás e empurre o êmbolo firmemente de uma só vez para aplicar a vacina. 0,25 ml, ou seja, a metade da dose é entregue.

4

Draw back the plunger slightly and remove the dose divider. Repeat the above step to deliver the remaining 0.25 ml into the second nostril.

Puxe o êmbolo ligeiramente para trás e remova a dispositivo dosador. Repita o passo anterior para entregar o 0,25 ml restante na segunda narina.

5

English

# Influenza Vaccine, Live Attenuated (Human)

## NASOVAC-S

Seasonal, Trivalent

2020-21 Formula Northern Hemisphere Freeze dried

**DESCRIPTION**

NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), freeze dried is a live trivalent vaccine for administration by intranasal spray. NASOVAC-S contains three vaccine virus strains of A/H1N1, A/H3N2 and Type B influenza virus cultivated on embryonated hen eggs. The three strains are antigenically similar to the strains recommended by the World Health Organization (W.H.O.) for 2020-21.

**COMPOSITION**

[Propagated in Embryonated hen eggs]
Each vial of single dose (0.5 ml) contains:

| | | |
|---|---|---|
| A(H1N1) Strain-A/17/Guangdong-Maonan/2019/211 (H1N1)* | Not less than | $10^7$ $EID_{50}$ |
| A(H3N2) Strain-A/17/Hong Kong/2019/2573 (H3N2)* | Not less than | $10^7$ $EID_{50}$ |
| B Strain - B/60 / Washington /2019 / 3676* | Not less than | $10^{6.5}$ $EID_{50}$ |

* Antigenic specificity of Hemagglutinin and Neuraminidase identical to wild type virus as recommended by W.H.O. for influenza vaccine for the year 2020-21 Northern hemisphere influenza season:

- A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09 - like virus
- A/Hong Kong/2671/2019 (H3N2) - like virus
- B/Washington / 02 / 2019 - like virus (B/Victoria lineage)

Partially hydrolyzed gelatin 2.5%, Sorbitol 5.0%, L-Alanine 0.1%, L-Histidine 0.21%, Tricine 0.3%, L-Arginine hydrochloride 1.6%, Lactalbumin hydrolysate 0.35%, Phosphate buffer saline Base. Reconstitute with Sterile Water for Inhalation I.P. The vaccine contains no preservatives.
Dose: 0.5 ml intranasal (spray 0.25 ml per nostril). The tip attached to the sprayer is equipped with a nozzle that produces a fine mist that is primarily deposited in the nose and nasopharynx.
The vaccine complies with the W.H.O. recommendations.

**INDICATIONS**

NASOVAC-S is indicated in individuals above 2 years of age for the active immunization for the prevention of influenza disease caused by two influenza A subtype viruses and one influenza Type B virus which are expected to circulate in the 2020-21 season. NASOVAC-S should be used in accordance with official guidance.

**POSOLOGY AND METHOD OF ADMINISTRATION**

Each freeze-dried vaccine vial is reconstituted using the entire contents of sterile water for inhalation that is supplied along with the vaccine, using the supplied syringe and vial adapter.
A dose of 0.5 ml is administered as 0.25 ml per nostril using a 1.0 ml syringe and a spray device. Withdraw the entire reconstituted vaccine for administration. The spray device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx. A single intranasal dose is recommended for people above 2 years of age.
For further information, see (Pharmacodynamic properties).
Use immediately after reconstitution. If the vaccine is not used immediately then it should be stored in the dark at 2-8°C for no longer than 6 hours.
Any opened container remaining at the end of a session (within six hours of reconstitution) should be discarded.
The vaccine vial monitor (see figure), for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.
The diluent supplied is specially designed for use with the vaccine. Only this diluent must be used to reconstitute the vaccine. Do not use diluents from other types of vaccine or from other manufacturers. Using an incorrect diluent may result in damage to the vaccine and/or serious reactions to those receiving the vaccine. Diluent must not be frozen, but should be kept cool.
The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

**CONTRAINDICATIONS**

**Hypersensitivity**

NASOVAC-S is contraindicated in individuals with a history of hypersensitivity, especially anaphylactic reactions to eggs, egg proteins, gelatin, or Lactalbumin or with other vaccine components.

**Concomitant Pediatric and Adolescent Aspirin Therapy and Reye's syndrome**

NASOVAC-S is contraindicated in children and adolescents (2-17 years of age) receiving aspirin therapy or aspirin-containing therapy, because of the association of Reye's syndrome with aspirin and wild-type influenza infection.

**WARNINGS AND PRECAUTIONS**

NASOVAC-S should under no circumstances be injected.
As with all vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.
NASOVAC-S should not be administered to any individuals with active wheezing.
If the individual has a history of Guillain-Barré syndrome the decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.
Immunization should be postponed in patients with severe febrile illness or acute infection. The vaccine can be given to people with minor illnesses (e.g., diarrhea or mild upper respiratory tract infection without fever). However, if nasal congestion is present that might limit delivery of the vaccine to the nasal lining, then delaying of vaccination until the nasal congestion is reduced should be considered.
People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.
Administration of NASOVAC-S, to immune-compromised persons should be based on careful consideration of potential benefits and risks. There is no clinical data available on the use of this vaccine in immune-compromised persons. Antibody response in such patients may be insufficient.
The safety of NASOVAC-S in individuals with underlying medical conditions that may predispose them to complications following wild-type influenza infection has not been established. The decision to give NASOVAC-S should be based on careful consideration of the potential benefits and potential risks.

**Pregnancy and lactation**

A developmental and reproductive toxicity study has been performed in female rats administered Nasovac (Live attenuated pandemic H1N1 vaccine) either once, twice or thrice (during the period of organogenesis), at approximately 2 human dose equivalents per occasion, by intranasal instillation and has revealed no evidence of maternal toxicity, fetotoxicity or teratogenicity due to Nasovac. There are however, no studies in pregnant women. Because animal studies are not always predictive of human response, Nasovac-S should be administered during pregnancy only if clearly needed.
It is not known whether NASOVAC-S is excreted in human milk. Therefore, as some viruses are excreted in human milk and additionally, because of the possibility of shedding of vaccine virus and the close proximity of a nursing infant and mother, caution should be exercised if NASOVAC-S is administered to nursing mothers.

**DRUG INTERACTIONS**

Do not administer NASOVAC-S to children or adolescents who are receiving aspirin therapy or aspirin-containing therapy (see Contraindications).
The concurrent use of NASOVAC-S with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for antiviral agents to reduce the effectiveness of NASOVAC-S, do not administer this vaccine until 48 hours after the cessation of antiviral therapy and antiviral agents should not be administered until two weeks after administration of this vaccine unless medically indicated. If antiviral agents and NASOVAC-S are administered concomitantly, revaccination should be considered when appropriate.
There are no data on co-administration of NASOVAC-S with other vaccines. However, if co-administration with another vaccine is indicated, immunisation may be carried. It should be noted that the adverse reactions may be intensified.
There are no data regarding co-administration of NASOVAC-S with other intranasal preparations.
The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.
The vaccine is unlikely to produce an effect on the ability to drive and use machines.

**ADVERSE REACTIONS**

In clinical trials a few local and systemic reaction were observed. They were mild to moderate in severity and resolved without any sequelae.
Local : Nasal discomfort, stuffy nose, sneezing, runny nose, loss of smell, red eyes, chills, facial swelling.
Systemic : Fever, headache, fatigue, myalgia, arthralgia, irritability, loss of appetite, sore throat, cough, wheezing, nausea.

**OVERDOSE**

No case of overdose has been reported.

**PHARMACOLOGICAL PROPERTIES**

**Mechanism of Action**

Immune mechanisms conferring protection against influenza following receipt of live attenuated influenza vaccines are not fully understood, though it is well-established that these vaccines provide clinical protection to the majority of the vaccinees. Serum antibodies, mucosal antibodies, and influenza-specific T cells may play a role in prevention and recovery from infection. NASOVAC-S contains live attenuated influenza viruses that must infect and replicate in cells lining the nasopharynx of the recipient to induce immunity. Vaccine viruses capable of infection and replication can be cultured from nasal secretions obtained from vaccine recipients (shedding)

**Pharmacodynamic properties**

NASOVAC-S is a live trivalent vaccine for administration by intranasal spray. The influenza virus strain in NASOVAC-S is (a) cold-adapted (ca) (i.e., it replicates efficiently at 25°C, a temperature that is restrictive for replication of many wild-type influenza viruses); (b) temperature-sensitive (ts) (i.e., it is restricted in replication at 39°C, a temperature at which many wild-type influenza viruses grow efficiently); and (c) attenuated (att). The cumulative effect of the antigenic properties and the ca, ts, and att phenotypes is that the attenuated vaccine virus replicates in the nasopharynx to induce protective immunity.

**Pharmacokinetic properties**

Not applicable.

**Preclinical safety data**

Efficacy study of NASOVAC-S in naïve ferrets (which is an established model of influenza) using homologous influenza viruses as challenge was conducted. Viral load, viral shedding and pathological analysis showed reduced levels of all three parameters in vaccinated animals after challenge irrespective of the challenge virus clearly demonstrating high efficacy of NASOVAC-S for all the three strains.
NASOVAC-S has undergone Single-dose and Repeated-dose toxicity studies in mice and rats when administered intranasally. In single-dose studies, higher than normal doses of the vaccine were given to animals and they were observed for 14 days for toxic effects. No vaccine-related untoward effects were found in animals receiving NASOVAC-S.
In repeated-dose toxicity studies, three doses of higher than normal doses of the vaccine were given intranasally to animals on day 0, 7 and 14 and were subsequently sacrificed. Necropsy was done to assess adverse effects on any organs. No vaccine-related adverse effects were found in the study animals receiving NASOVAC-S.

**INCOMPATIBILITIES**

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

**INSTRUCTIONS FOR USE AND HANDLING AND DISPOSAL**

The vaccine should be allowed to reach room temperature before use. Shake before use.
Once NASOVAC-S, intranasal has been administered, the used vaccine devices and all its parts should be disposed off according to the standard procedures for medical waste (e.g., sharps container or biohazard container).

**SHELF-LIFE**

Do not exceed the expiry date printed on the label and packaging.

**STORAGE**

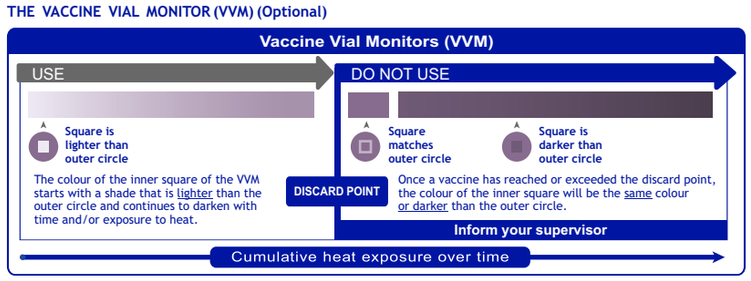
NASOVAC-S, Influenza Vaccine, Live Attenuated (Human) Intranasal SHOULD BE STORED IN A REFRIGERATOR AT 2 - 8°C (35-46°F) UPON RECEIPT AND UNTIL USE. THE PRODUCT MUST BE USED BEFORE THE EXPIRATION DATE ON THE LABEL. The cold chain (2 to 8°C) must be maintained when transporting Influenza Vaccine, Live Attenuated (Human) Intranasal.

**PRESENTATION**

NASOVAC-S Influenza Vaccine, Live Attenuated (Human) freeze dried, intranasal is available as:
1 dose vial plus diluent ( 0.5 ml)

NASOVAC-S is supplied as a vial containing freeze-dried cake in USP type 1 glass vials.
Vial containing sterile water for inhalation as diluent, syringe for administration, vial adapter, intranasal spray device and dose divider are also supplied along with the vaccine.

**THE VACCINE VIAL MONITOR (VVM) (Optional)**




Vaccine Vial Monitors (VVMs) are on the cap of NASOVAC-S, Influenza Vaccine, Live Attenuated (Human), supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indications of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.
The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the outer circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the outer circle or of a darker colour than the outer circle, then the vial should be discarded.

**MOST IMPORTANT WARNING**

1. Please ensure that the vaccine is administered by intranasal spray.
2. In rare cases anaphylactic shock may occur in susceptible individual. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis. As with the use of all vaccines, the vaccinees should remain under observation for not less than 30 minutes for possibility of occurrence of rapid allergic reactions. Hydrocortisone and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

**CAUTION: PEOPLE WHO SHOULD NOT TAKE THE VACCINE**

1. Those who are allergic to eggs
2. Children and adolescents (2-17 years of age) receiving aspirin and aspirin containing therapy. People already suffering from cold, cough, fever, bodyache or other flu-like symptoms should be clinically evaluated and if necessary, appropriate treatment should be given. In such cases, NASOVAC-S vaccination should be postponed at least till recovery.

Revision date: 02/2021


Manufactured by:
SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA


Protection from birth onwards

20017673/0

Russian

# Вакцина против гриппа, живая аттенуированная (человеческая)

## NASOVAC-S

против сезонного гриппа, трехвалентная

состав для эпидемического сезона гриппа 2020-2021 гг., для стран Северного полушария — лиофилизированная

**ОПИСАНИЕ**

NASOVAC-S, вакцина против гриппа, живая аттенуированная (человеческая), лиофилизированная, является живой трехвалентной вакциной для интраназального введения. NASOVAC-S содержит три вакцинных штамма вируса A/H1N1, A/H3N2 и вируса гриппа B, выращенных в культуре клеток куриных эмбрионов. Указанные три штамма антигенно идентичны штаммам, рекомендованным Всемирной организацией здравоохранения (ВОЗ) на эпидемический сезон гриппа 2020-2021 гг.

**СОСТАВ**

[штаммы, выращенные в культуре клеток куриных эмбрионов]
Каждый флакон (однократная доза, 0,5 мл) содержит:

| | |
|---|---|
| вирус гриппа A(H1N1) – штамм A/17/Guangdong-Maonan/2019/211 (H1N1)* | не менее $10^7$ $EID_{50}$ |
| вирус гриппа A(H3N2) – штамм A/17/Hong Kong/2019/2573 (H3N2)* | не менее $10^7$ $EID_{50}$ |
| вирус гриппа B – штамм B/60/Washington/2019/3676* | не менее $10^{6,5}$ $EID_{50}$ |

* Антигенная специфичность гемагглютинина и нейраминидазы идентична вирусу дикого типа, согласно рекомендациям ВОЗ для вакцин против гриппа для эпидемического сезона 2020-21 гг. для стран Северного полушария:

- вирус, подобный штамму A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09
- вирус, подобный штамму A/Hong Kong/2671/2019 (H3N2)
- вирус, подобный штамму B/Washington/02/2019 (B/викторианская линия)

желатин частично гидролизованный 2,5%, сорбитол 5,0%, L-аланин 0,1%, L-гистидин 0,21%, трицин 0,3%, L-аргинина гидрохлорид 1,6%, гидролизат лактальбумина 0,35%, фосфатный забуференный физиологический раствор. Восстанавливают стерильным раствором для ингаляции Фарм. Индии. Вакцина не содержит консервантов.
Способ введения: 0,5 мл интраназально (по 0,25 мл в каждый носовой ход). Распылитель оснащен съемной насадкой для создания мелкодисперсной взвеси, которая оседает преимущественно на слизистой оболочке носовой полости и носоглотки.
Вакцина соответствует рекомендациям ВОЗ.

**ПОКАЗАНИЯ К ПРИМЕНЕНИЮ**

Вакцина NASOVAC-S показана лицам старше 2 лет для активной иммунизации с целью профилактики гриппа, вызываемого двумя штаммами вируса гриппа A и одним штаммом вируса гриппа B, циркуляция которых ожидается в сезоне 2020-2021 гг. Вакцину NASOVAC-S следует применять в соответствии с официальными инструкциями по медицинскому применению лекарственного препарата.

**СПОСОБ ПРИМЕНЕНИЯ И ДОЗЫ**

Каждый флакон с лиофилизированной вакциной восстанавливают с использованием всего содержимого флакона со стерильным раствором для ингаляции, который поставляется вместе с вакциной, с использованием прилагаемого шприца и адаптера для флакона.
Дозу 0,5 мл вводят по 0,25 мл в каждый носовой ход с использованием шприца вместимостью 1,0 мл и распылителя. Для введения используют весь объем восстановленной вакцины. Распылитель предназначен для создания мелкодисперсной взвеси, которая оседает преимущественно на слизистой оболочке носовой полости и носоглотки. Однократное введение дозы вакцины интраназально рекомендуется лицам старше 2 лет.
Дополнительная информация приведена в разделе «Фармакодинамические свойства».
Используют немедленно после восстановления. Если вакцину не использовали сразу, ее следует хранить в темном месте при температуре 2-8°С не более 6 часов.
Открытые флаконы, оставшиеся в конце сеанса вакцинации (в течение шести часов после восстановления) необходимо утилизировать. Для данного типа вакцины используется контроль флакона с вакциной (см. рисунок), прикрепленный к колпачку флакона, его следует удалить при восстановлении вакцины.
Поставляемый растворитель специально разработан для использования с вакциной. Для восстановления вакцины используют только поставляемый растворитель. Не рекомендуется использовать растворители для других типов вакцин или других производителей. Использование несоответствующего растворителя может привести к негодности вакцины и/или тяжелым реакциям у вакцинированного. Растворитель не следует замораживать, но необходимо хранить в охлажденном виде.
Перед введением растворитель и восстановленную вакцину следует визуально проверить на наличие посторонних частиц и/или изменений внешнего вида. Если были обнаружены какие-либо отклонения от нормы, растворитель или восстановленную вакцину утилизируют.

**ПРОТИВОПОКАЗАНИЯ**

**Гиперчувствительность**

Введение вакцины NASOVAC-S противопоказано у лиц с гиперчувствительностью в анамнезе, особенно при наличии анафилактической реакции на яйца, яичный белок, желатин, лактальбумин или другие компоненты вакцины.

**Сопутствующая терапия аспирином и синдром Рея у пациентов детского и подросткового возраста**

NASOVAC-S противопоказан детям и подросткам (2-17 лет), получающим терапию аспирином или аспиринсодержащую терапию, из-за ассоциации синдрома Рея с аспирином и вируса гриппа дикого типа.

**ОСОБЫЕ УКАЗАНИЯ И МЕРЫ ПРЕДОСТОРОЖНОСТИ**

Ни при каких обстоятельствах не следует использовать инъекционный способ введения вакцины NASOVAC-S.
Как и в случае других вакцин, вакцинированные должны находиться под медицинским наблюдением, при этом в наличии должны быть все средства для оказания медицинской помощи в редких случаях возникновения анафилактической реакции после введения вакцины.
NASOVAC-S не следует применять у пациентов с синдромом бронхиальной обструкции.
При наличии в анамнезе синдрома Гийена-Барре, решение о применении вакцины NASOVAC-S должно быть основано на тщательном рассмотрении потенциальных преимуществ и рисков.
Вакцинацию следует отложить у лиц в острый период заболевания, сопровождающегося значительным повышением температуры. Незначительные расстройства (диарея или легкая форма респираторной инфекции с наличием незначительного повышения температуры или его отсутствием) как правило, не являются противопоказаниями к вакцинации. Однако, если заложенность носа может ограничить доставку вакцины к слизистой оболочке носа, следует рассмотреть возможность отсрочки вакцинации до тех пор, пока заложенность носа не уменьшится.
У лиц с симптомами простуды (кашель, повышение температуры, боль в мышцах) или других симптомов гриппа, следует провести клиническое обследование и, при необходимости, назначить соответствующее лечение. В указанных случаях введение вакцины NASOVAC-S следует отложить как минимум до выздоровления.
Решение о применении вакцины NASOVAC-S должно быть основано на тщательном рассмотрении потенциальных преимуществ и рисков. Отсутствуют доступные клинические данные о применении данной вакцины у лиц с ослабленным иммунитетом. Иммунный ответ у таких пациентов может быть недостаточным.
Безопасность вакцины NASOVAC-S у лиц с сопутствующими заболеваниями, предрасполагающими к возникновению осложнений после инфекции гриппа дикого типа, не установлена. Решение о применении вакцины NASOVAC-S должно быть основано на тщательном рассмотрении потенциальных преимуществ и рисков.

**Применение при беременности и кормлении грудью**

Исследование эмбриотоксичности и репродуктивной токсичности было проведено на самках крыс, которым вводили препарат Назовак (вакцина против пандемического гриппа H1N1 живая аттенуированная) один, два или три раза (в период органогенеза), в дозах примерно 2-кратно превышающих допустимые дозы для человека за одно введение, путем интраназальной инстилляции. Не было обнаружено токсического воздействия на материнский организм, эмбриотоксичности или тератогенности, связанных с применением вакцины Назовак. Однако, исследования у беременных женщин не проводили. Поскольку результаты исследований вакцины NASOVAC-S на животных не всегда позволяют предсказать влияние на репродуктивную функцию у человека, препарат следует применять во время беременности только в случае крайней необходимости.
Данные относительно возможного выделения препарата NASOVAC-S с грудным молоком отсутствуют. Поэтому, поскольку некоторые вирусы выделяются с грудным молоком и, кроме того, из-за возможности выделения вакцинного вируса и непосредственной близости грудного ребенка и матери, при применении вакцины NASOVAC-S у кормящих матерей следует проявлять осторожность.

**ВЗАИМОДЕЙСТВИЕ С ДРУГИМИ ЛЕКАРСТВЕННЫМИ ПРЕПАРАТАМИ**

NASOVAC-S противопоказан детям и подросткам, получающим терапию аспирином или аспиринсодержащую терапию (см. раздел «Противопоказания»).
Одновременное применение препарата NASOVAC-S с противовирусными лекарственными средствами, активными против вирусов гриппа A и/или B, не было исследовано. Однако, на основании способности противовирусных лекарственных средств снижать эффективность препарата NASOVAC-S, не рекомендовано применять данную вакцину за менее чем 48 часов после прекращения противовирусной терапии, также не следует применять противовирусные лекарственные средства в течение двух недель после введения данной вакцины, если отсутствуют медицинские показания. При необходимости, в случае одновременного применения противовирусных лекарственных средств и препарата NASOVAC-S, следует рассмотреть вопрос о ревакцинации.
Отсутствуют данные об одновременном применении вакцины NASOVAC-S и других вакцин. Однако, если показано одновременное применение с другой вакциной, вакцинация допускается. Следует отметить, что в таком случае нежелательные реакции могут быть более тяжелыми.
Отсутствуют данные об одновременном применении вакцины NASOVAC-S и других лекарственных препаратов для интраназального введения.
Иммунный ответ может быть снижен, если пациент получает терапию иммунодепрессантами.

Маловероятно, что применение вакцины повлияет на способность к управлению транспортными средствами и работе с механизмами.

**НЕЖЕЛАТЕЛЬНЫЕ РЕАКЦИИ**
В ходе клинических исследований были обнаружены некоторые местные и системные нежелательные реакции. Все они были легкой или средней степени тяжести и разрешились без каких-либо последствий.
Местные реакции: дискомфорт в области носа, заложенность носа, чихание, насморк, потеря обоняния, покраснение глаз, озноб, отек лица.
Системные реакции: повышение температуры, головная боль, утомляемость, миалгия, артралгия, раздражительность, потеря аппетита, боль в горле, кашель, хрипы, тошнота.

**ПЕРЕДОЗИРОВКА**
О случаях передозировки не сообщалось.

**ФАРМАКОЛОГИЧЕСКИЕ СВОЙСТВА**

**Механизм действия**
Иммунные механизмы, обеспечивающие защиту от гриппа после применения живых аттенуированных противогриппозных вакцин, до конца не изучены, хотя широко известно, что они обеспечивают защиту от клинических случаев у большинства вакцинированных. Гуморальные антитела, антитела слизистых оболочек и Т-клетки, специфичные для гриппа, вероятно играют роль в профилактике и восстановлении после инфекции. Вакцина NASOVAC-S содержит живые аттенуированные (ослабленные) штаммы вируса гриппа, которые должны обладать инфицирующими свойствами и размножаться в клетках, выстилающих носоглотку реципиента, чтобы вызвать иммунный ответ. Вакцинные вирусы, способные к инфицированию и репликации, можно культивировать из носового секрета, полученного от реципиентов вакцины (выделение вируса).

**Фармакодинамические свойства**
Препарат NASOVAC-S является живой трехвалентной вакциной для интраназального введения. Входящие в состав вакцины NASOVAC-S штаммы вируса гриппа являются (a) холодоадаптированными (ca), т. е. они эффективно реплицируются при 25°C, температуре, которая ограничивает репликацию многих вирусов гриппа дикого типа; (b) чувствительными к температуре (ts), т. е. их репликация ограничена при 39°C, температуре, при которой доказана активная репликация большинства вирусов гриппа дикого типа; и (c) аттенуированными (att). Кумулятивный эффект антигенных свойств и фенотипов (ca, ts и att) заключается в том, что ослабленный вакцинный вирус реплицируется в носоглотке, вызывая защитную иммунную реакцию.

**Фармакокинетические свойства**
Не применимо.

**Данные доклинической безопасности**
Было проведено исследование эффективности вакцины NASOVAC-S на невакцинированных хорьках (которые являются установленной моделью для вируса гриппа) с использованием гомологичных вирусов гриппа в качестве контрольного заражения. Результаты определения вирусной нагрузки, выделения вируса и гистологического исследования подтвердили снижение всех трех показателей у вакцинированных животных после заражения независимо от типа инфицирующего вируса, что достоверно подтверждает высокую эффективность вакцины NASOVAC-S против всех трех штаммов вируса.
Вакцина NASOVAC-S успешно прошла исследования токсичности при однократном и многократном введении на мышах и крысах при интраназальном введении. В исследованиях при однократном введении вакцины животным вводили дозы препарата, превышающие рекомендованные, и в течение 14 дней изучали токсическое воздействие. У животных, получавших препарат NASOVAC-S, не было обнаружено нежелательных реакций, связанных с применением вакцины.
В исследованиях токсичности при многократном введении три дозы вакцины, превышающие рекомендованную дозу, вводили животным интраназально на 0, 7 и 14 день и затем выводили из эксперимента. Гистологическое исследование проводили для оценки неблагоприятных воздействий на какие-либо органы. В ходе исследования у животных, получавших препарат NASOVAC-S, не было обнаружено неблагоприятных воздействий, связанных с применением вакцины.

**НЕСОВМЕСТИМОСТЬ**
В условиях отсутствия исследований совместимости, данный лекарственный препарат запрещено смешивать с другими лекарственными препаратами.

**ИНСТРУКЦИИ ПО ПРИМЕНЕНИЮ, ОБРАЩЕНИЮ И УТИЛИЗАЦИИ**
Перед использованием вакцину нагревают до комнатной температуры. Перед использованием вакцину необходимо встряхнуть.
После интраназального введения вакцины NASOVAC-S использованные изделия для введения вакцины и все их части должны быть утилизированы в соответствии со стандартными процедурами для медицинских отходов (например контейнер для острых предметов или контейнер для биологически опасных отходов).

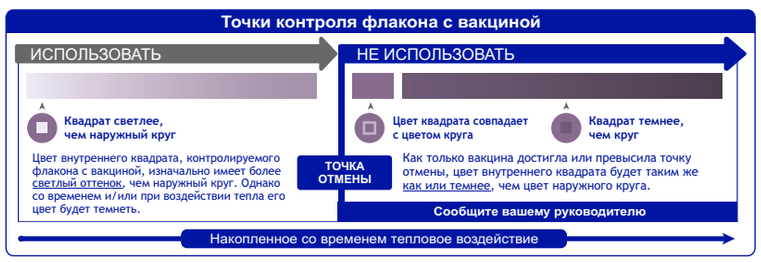
**СРОК ГОДНОСТИ**
Не используйте этот препарат после истечения срока годности, который указан на этикетке и упаковке.

**ХРАНЕНИЕ**
После получения и перед применением препарат NASOVAC-S (вакцина против гриппа, живая аттенуированная (человеческая) для интраназального введения) НЕОБХОДИМО ХРАНИТЬ В ХОЛОДИЛЬНОЙ КАМЕРЕ
ПРИ ТЕМПЕРАТУРЕ 2–8°C (35–46°F). НЕ ИСПОЛЬЗУЙТЕ ЭТОТ ПРЕПАРАТ ПОСЛЕ ИСТЕЧЕНИЯ СРОКА ГОДНОСТИ, КОТОРЫЙ УКАЗАН НА ЭТИКЕТКЕ. При транспортировке вакцины против гриппа, живой аттенуированной (человеческой) для интраназального введения необходимо поддерживать холодовую цепь (при температуре 2–8°C).

**ФОРМА ВЫПУСКА**
Форма выпуска препарата NASOVAC-S, вакцина против гриппа, живая аттенуированная (человеческая) лиофилизированная, для интраназального введения:
флакон с 1 дозой и растворитель (0,5 мл)

NASOVAC-S поставляется в стеклянных флаконах из прозрачного стекла класса I Фарм. США, содержащих лиофилизированный осадок.
Флакон, содержащий стерильный раствор для ингаляций в качестве растворителя, шприц для введения, адаптер для флакона, интраназальный распылитель и разделитель дозы также поставляются вместе с вакциной.

**ФЛАКОННЫЙ ТЕРМОРЕГУЛЯТОР (необязательный)**




На колпачке флакона препарата NASOVAC-S, вакцина против гриппа, живая аттенуированная (человеческая), поставляемого компанией «Серум Институт Оф Индия Пвт. Лтд.», находится флаконный термоиндикатор (ФТИ). Это точка, чувствительная к действию температуры и времени, которая показывает совокупное тепло, полученное флаконом. ФТИ предупреждает конечного пользователя, когда воздействие тепла может привести к ухудшению качества вакцины сверх допустимого уровня.
Интерпретация показаний ФТИ простая. Посмотрите на квадрат в центре. Его цвет изменяется с течением времени. Пока цвет этого квадрата светлее цвета внешнего круга, вакцину допускается использовать. Если цвет квадрата и внешнего круга одинаковый или цвет квадрата стал темнее цвета внешнего круга, вакцину использовать нельзя и ее необходимо утилизировать.

**ОСОБЫЕ УКАЗАНИЯ**
1. Единственным допустимым путем введения является интраназальное введение.
2. В редких случаях у людей, склонных к анафилаксии, может развиться анафилактический шок. Основным направлением в лечении тяжелой анафилактической реакции является немедленное введение адреналина, что может быть жизненно необходимым. Адреналин следует вводить при малейшем. подозрении на возникновение анафилактической реакции. Как и в случае других вакцин, вакцинированные должны находиться под медицинским наблюдением в течение не менее чем 30 минут на случай возможного возникновения немедленных или ранних аллергических реакций. Помимо вспомогательных мер, таких как, ингаляция кислорода, также всегда должны быть в наличии гидрокортизон и антигистаминные средства

**ВНИМАНИЕ: ПРОТИВОПОКАЗАНИЯ ДЛЯ ПРИМЕНЕНИЯ ВАКЦИНЫ**
1. Аллергическая реакция на яйца
2. Дети и подростки (2–17 лет), получающие терапию аспирином или аспиринсодержащую терапию. У лиц с симптомами простуды (кашель, повышение температуры, боль в мышцах) или других симптомов гриппа, следует провести клиническое обследование и, при необходимости, назначить соответствующее лечение. В указанных случаях введение вакцины NASOVAC-S следует отложить как минимум до выздоровления.

Дата пересмотра: 02/2021


Производитель:
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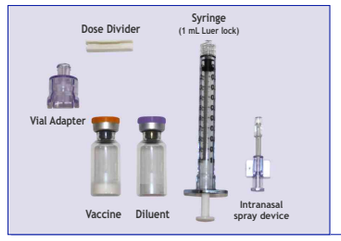
Защита с рождения

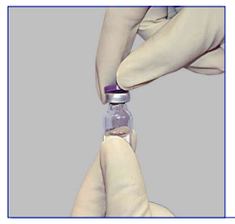
## RECONSTITUTION OF THE VACCINE
## ВОССТАНОВЛЕНИЕ ВАКЦИНЫ




Components for administration.
Allow the vaccine and diluent to attain room temperature.

Компоненты для введения вакцины.
Перед использованием вакцину и растворитель нагревают до комнатной температуры.

1



Remove the flip top from the diluent vial.

Снимите колпачок с флакона с растворителем.

2

a) Connect the vial adapter onto the diluent vial by pushing it downwards until vial adapter is properly and solidly placed.
a) Установите адаптер флакона на флакон с растворителем, надавив на него вниз, пока адаптер флакона не будет правильно и надежно закреплен.
b) Connect the syringe to the vial adapter by completely screwing in clockwise direction.
b) Подсоедините шприц к адаптеру флакона, полностью закрутив его по часовой стрелке.

3

Draw the entire contents of the diluent vial into the syringe.

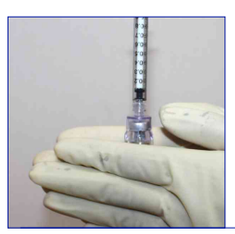
Наберите все содержимое флакона с растворителем в шприц.

4

Remove the entire assembly (syringe connected to the adapter) from the diluent vial.

Отсоедините адаптер флакона и прикрепленный шприц

5



Remove the flip top from the vaccine vial.
Attach the syringe with vial adapter to the vaccine vial and allow the liquid to be drawn in. Assist by pushing the plunger if required.
Disconnect the syringe from the vial adapter to break any residual vacuum.
Снимите колпачок с флакона с вакциной.
Подсоедините шприц с адаптером флакона к флакону с вакциной и введите растворитель. Для этого нажмите на поршень.
Отсоедините шприц от адаптера флакона, чтобы уравновесить давление с атмосферным.

6

Rotate the vial between the palms to dissolve its contents.

Перекатывайте флакон между ладонями до полного растворения содержимого.

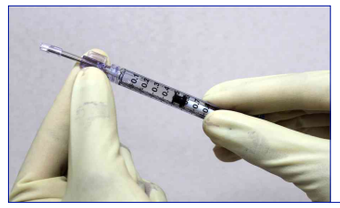
7

## ADMINISTRATION OF THE VACCINE
## ВВЕДЕНИЕ ВАКЦИНЫ

Reconnect the syringe with the vial adapter and withdraw the entire reconstituted vaccine into the syringe. Detach the syringe from the vial adapter.

Повторно подсоедините шприц к адаптеру флакона и наберите в шприц всю восстановленную вакцину. Отсоедините шприц от адаптера флакона.

1



Fix the intranasal spray device on the tip of the syringe by completely screwing in clockwise direction.

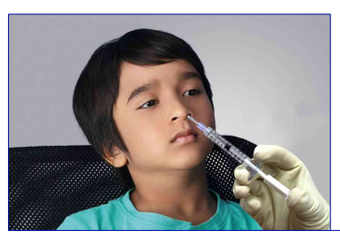
Закрепите интраназальный распылитель на наконечнике шприца, вращая его по часовой стрелке до упора.

2

Fix the dose divider on the plunger of the syringe.

Закрепите разделитель дозы на поршне шприца.

3



Place the intranasal spray device at the base of the nostril of the recipient sitting upright with his/her head slightly thrown back and push the plunger firmly in a single stroke to deliver the vaccine. 0.25 ml i.e. half of the dose is delivered.

Поднесите интраназальный распылитель вплотную к носовому ходу вакцинируемого, который сидит вертикально, со слегка запрокинутой головой, и одним движением сильно нажмите на поршень, чтобы ввести вакцину. Введите 0,25 мл раствора, т. е. половину дозы.

4

Draw back the plunger slightly and remove the dose divider. Repeat the above step to deliver the remaining 0.25 ml into the second nostril.

Слегка отведите назад поршень и снимите разделитель дозы. Повторите описанный выше шаг, чтобы ввести оставшиеся 0,25 мл вакцины во второй носовой ход.

5