Influenza Vaccine, Live Attenuated (Human) NASOVAC-S Seasonal, Trivalent Freeze dried 2014 Formula Southern Hemisphere

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 2014.

COMPOSITION
Propagated in Embryonated hen eggs Each vial of single dose (0.5 ml) contains:
A/H1N1 Strain - A/California/09/2009 (H1N1)* Not less than 10^7 EID
A/H3N2 Strain - A/Texas/2012/30 (H3N2)* Not less than 10^7 EID
B Strain - B/Massachusetts/2012/10* Not less than 10^5 EID
* Antigenic specificity of Hemagglutinin and Neuraminidase identical to wild type virus as recommended by W.H.O. for influenza vaccine for the year 2014 Southern hemisphere influenza season:
- A/California/7/2009 (H1N1)pdm09 - like virus
- A/Texas/50/2012 (H3N2)-like virus
- B/Massachusetts/2/2012 - like virus

Drugs
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 Injection USP. The vaccine contains 0.3 ml of vaccine:
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 contains 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 2014 season. NASOVAC-S should be used in accordance with official guidance.

POSOLGY AND METHOD OF ADMINISTRATION
Each pre-diluted vaccine vial is reconstituted taking the entire contents of sterile water for injection that is supplied along with the vaccine, using the supplied syringe and plastic draw up needle. A dose of 0.5 ml is administered as 0.25 ml per nostril using a 1.0 ml syringe and a spray device. 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.
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 virus 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 Reyes'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 Reyes 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 fetal malformations 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 not be given.

Administration of NASOVAC-S, to immune-compromised persons should be based on careful consideration of the potential benefits and risks.

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 not been established. 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
Immun mechanism 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 vaccines. 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 (c.a.), i.e., it replicates efficiently at 25ºC, a temperature that is restrictive for replication of poorly wild type influenza viruses; (b) temperature-sensitive (ts) i.e., it is restricted in replication at 39ºC, a temperature at which many wild-type influenza viruses grow efficiently; and (c) attenuated (atts). The cumulative effect of the antigenic properties and the ca, ts, and at phenotypes that is the attenuated vaccine virus replicates in the nasopharynx to induce protective immunity.

Pharmacokinetic properties
Not applicable.

Preclinical safety data
Preclinical study of NASOVAC-S in naive 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.

An ampoule/vial containing sterile water for inhalation as diluent, syringe for administration, plastic needle, 5 dose concentration and least till expiry date.

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Most Important Warning
1. Please ensure that the vaccine is administered by intranasal spray.
2. In rare cases the nebulizer may have a sterile fluid be supplied in the vial. This fluid should be discarded.

Special storage conditions: The vaccine should be stored at 2-8°C (35-46°F) and transported in a cold chain (2-8°C).

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 therapy or aspirin-containing therapy.
3. 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.

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**RECONSTITUTION OF THE VACCINE**

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

1. Fix the plastic draw-up needle on the syringe.
2. Tap / Jerk the diluent to ensure that the water trapped at the top descends into the ampoule body.
3. Twist off the top of the diluent ampoule and draw entire contents of the diluent into the syringe.
4. Snap off the vaccine vial flip top and pierce the stopper of the vial with the syringe containing diluent to reconstitute the vaccine. Disconnect the syringe from the needle to break any residual vacuum.
5. Rotate the vial between the palms to dissolve its contents.

**ADMINISTRATION OF THE VACCINE**

Reconnect the syringe with the needle and withdraw 0.5 ml of the reconstituted vaccine into the syringe.

1. Replace the needle with the intranasal spray device.
2. Fix the dose divider on the plunger of the syringe.
3. Place the spray device at the base of the nostril of the recipient sitting upright with his 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.
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.

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