Influenza Vaccine (Human, Live Attenuated)

Pandemic (H1N1) (Freeze-Dried)

DESCRIPTION
Influenza Vaccine (Human, Live Attenuated) Pandemic (H1N1), freeze dried is a live monovalent vaccine for administration by intranasal spray. The influenza vaccine contains Influenza virus cultivated on embryonated eggs.

COMPOSITION
[Propagated in Embryonated hen eggs (SPF)]
Each single dose of 0.5 ml contains:
A/17/California/2009/38 > 10^7 EID_{50}
Gelatin (Partially hydrolyzed) 2.5%, Sorbitol 5%, 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 USP. 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.
Influenza Vaccine (Human, Live Attenuated) is supplied as a vial containing freeze-dried cake in USP type 1 glass vials. A ampoule/vial containing sterile water for inhalation as diluent, syringe (for reconstitution of multi dose vaccine vial), syringe (for administration) , needle free device and intranasal spray device are also supplied along with the vaccine.
The vaccine complies with the WHO recommendation and EU decision for the pandemic.

INDICATIONS
Influenza Vaccine (Human, Live Attenuated), Intranasal is indicated for the active immunization of individuals above 3 years of age against influenza disease caused by pandemic (H1N1) 2009 virus.
Prophylaxis of influenza in an officially declared pandemic situation (see sections Posology and method of administration and Pharmacodynamic properties).
Pandemic influenza vaccine 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 0.5/1.0 ml syringe and a spray device. The sprayer device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx. A single intranasal dose is recommended for people above 3 years of age.
Adults (18-49 years), elderly (⩾50 years) and children and adolescents (3-17 years) of age: A single dose of 0. 5 ml by intranasal route. A second dose of vaccine could be given after an interval of at least 21 days.
There is no clinical experience in children below 3 years of age.
For further information, see (Pharmacodynamic properties).
If the vaccine is not used immediately then it should be stored at 2-8°C for no longer than 6 hours. While storing the reconstituted vaccine, ensure that the administration syringe is locked on to the needle free transfer device and the combined unit is stored at 2 to 8°C to ensure that the opening created by the device is blocked and the syringe is also stored in a manner which prevents the proliferation of bio-burden. 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
Influenza Vaccine(Human,Live Attenuated) is contraindicated in individuals with a history of hypersensitivity, especially anaphylactic reactions, to eggs, egg proteins, gentamicin, gelatin, or arginine or with life-threatening reactions to previous influenza vaccinations.
Concomitant Pediatric and Adolescent Aspirin Therapy and Reye's syndrome
Influenza Vaccine(Human,Live Attenuated) is contraindicated in children and adolescents (3-17 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
Caution is needed when administrating this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance(s), to any of the excipients, and to residues e.g. eggs, chicken proteins, etc.
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.
Do not administer Influenza Vaccine(Human,Live Attenuated) to children <36 months of age since there is no clinical data available.
Influenza Vaccine(Human,Live Attenuated) should not be administered to any individuals with asthma or children < 5 years of age with recurrent wheezing because of the potential for increased risk of wheezing post vaccination unless the potential benefit outweighs the potential risk.
Do not administer Influenza Vaccine(Human,Live Attenuated) to individuals with severe asthma or active wheezing because these individuals have not been studied in clinical trials.
If Guillain-Barré syndrome has occurred within 6 weeks of any prior influenza vaccination, the decision to give Influenza Vaccine(Human,Live Attenuated) should be based on careful consideration of the potential benefits and potential risks.
If the pandemic situation allows, immunisation shall 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 with or 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 who are in contact with others with severely compromised immune systems, should not get Influenza Vaccine(Human,Live Attenuated).
Influenza Vaccine(Human,Live Attenuated) should under no circumstances be injected.
Administration of Influenza Vaccine(Human,Live Attenuated), to immunocompromised 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 immunocompromised persons. Antibody response in such patients may be insufficient.
The safety of Influenza Vaccine(Human,Live Attenuated) in individuals with underlying medical conditions that may predispose them to complications following wild-type influenza infection has not been established. Influenza Vaccine(Human,Live Attenuated) should not be administered unless the potential benefit outweighs the potential risk.

DRUG INTERACTIONS
Do not administer Influenza Vaccine (Human, Live Attenuated) to children or adolescents who are receiving aspirin therapy or aspirin-containing therapy (see Contraindications).
The concurrent use of Influenza Vaccine(Human,Live Attenuated) 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 Influenza Vaccine(Human,Live Attenuated), 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 Influenza Vaccine(Human,Live Attenuated) are administered concomitantly, revaccination should be considered when appropriate.
There are no data on co-administration of Influenza Vaccine(Human,Live Attenuated) 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 Influenza Vaccine(Human,Live Attenuated) with other intranasal preparations. The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.
Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique may disprove the false positive results and confirm the true results. The transient false positive reactions could be due to the IgM response by the vaccine.
Pregnancy and lactation
Data from vaccinations with unadjuvanted interpandemic trivalent vaccines in pregnant women do not indicate that adverse foetal and maternal outcomes were attributable to the vaccine.
Animal teratogenicity studies are ongoing with Influenza Vaccine(Human,Live Attenuated). It is not known whether Influenza Vaccine(Human,Live Attenuated) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Healthcare providers need to assess the benefit and potential risks of administering the vaccine to pregnant women.
It is not known whether Influenza Vaccine(Human,Live Attenuated) 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 Influenza Vaccine(Human,Live Attenuated) is administered to nursing mothers.

Effects on ability to drive and use machines
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, lacrimation, facial swelling.
Systemic : Headache, fatigue, myalgia, arthralgia, irritability, loss of appetite, sore throat, cough, diarrhoea.
The incidence was similar in both the study groups.
There were a few unsolicited event reported in both the groups and none of them were causally related to study vaccines.

OVERDOSE
No case of overdose has been reported.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Influenza Vaccine (Human, Live Attenuated) is a live monovalent vaccine for administration by intranasal spray. The influenza virus strain in Influenza Vaccine (Human, Live Attenuated) 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) (it does not produce classic influenza-like illness in the ferret model of human influenza infection). 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.
Immune mechanisms conferring protection against influenza following receipt of Intranasal 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. Likewise, naturally acquired immunity to wild-type influenza has not been completely elucidated. Serum antibodies and mucosal antibodies may play a role in prevention and recovery from infection. However, it is well known that there are no correlates of protection for live attenuated influenza vaccines.
Pharmacokinetic properties
Not applicable.
Preclinical safety data
Influenza Vaccine (Human, Live Attenuated) 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 Influenza Vaccine (Human, Live Attenuated).
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 Influenza Vaccine(Human,Live Attenuated).

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 Influenza Vaccine(Human,Live Attenuated), Intranasal has been administered, the sprayer should be disposed of 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 outer box.

STORAGE
Influenza Vaccine(Human,Live Attenuated) 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 (Human, Live Attenuated) Intranasal

PRESENTATION
Influenza Vaccine(Human, Live Attenuated) Pandemic (H1N1) is available as:
1 dose vial plus diluent (0.5 ml)
5 dose vial plus diluent (2.5 ml)

THE VACCINE VIAL MONITOR (Optional)

Inner square lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**

At a later time, inner square still lighter than outer circle.
If the expiry date has not passed, USE the vaccine.

Discard point:
Inner square matches colour of outer circle.
DO NOT use the vaccine.

Beyond the discard point:
Inner square darker than outer ring.
DO NOT use the vaccine.

Vaccine Vial Monitors (VVMs) are on the cap of Influenza Vaccine (Human, Live Attenuated) supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indication 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 ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

MOST IMPORTANT WARNING

1. Please ensure that the vaccine is administered by intranasal spray. In rare cases anaphylactic shock may occur in susceptible individual and for such emergency please keep handy 1:1000 adrenaline injection ready to be injected intramuscularly or subcutaneously. For treatment of severe anaphylaxis the initial dose of adrenaline is 0.1-0.5 mg (0.1-0.5ml of 1:1000 injection) given s/c or i/m. Single dose should not exceed 1 mg (1ml). For infants and children the recommended dose of adrenaline is 0.01mg/kg (0.01ml/kg of 1:1000 injection). Single paediatric dose should not exceed 0.5mg (0.5ml). This will help in tackling the anaphylactic shock/reaction effectively.

2. 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, Influenza Vaccine, Live Attenuated (Human) vaccination should be postponed at least till recovery.

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

Protection from birth onwards

ADMINISTRATION INSTRUCTIONS

PHASE I :
Reconstitution of the multi - dose vaccine

Retract the plunger of the reconstitution syringe to the half way mark and then install the needle free transfer device

Remove the flip top of the vial containing the diluent and insert the needle free transfer device with syringe.

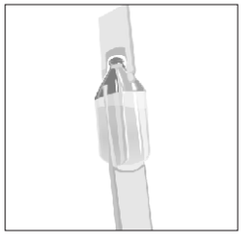
Invert the vial and syringe and release the plunger allowing the diluent to flow into the syringe.
Draw out the residual quantity of the diluent from the vial by further withdrawing the syringe plunger.

Remove the flip top of the vaccine vial.

Insert the needle free transfer device with the attached syringe into the vaccine vial.
Transfer the diluent into the vaccine vial by pushing the plunger of the syringe.

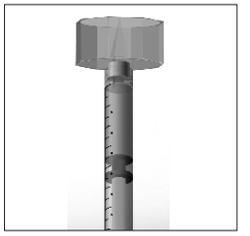
Remove the reconstitution syringe, leaving the needle free transfer device in place.
Shake the vial gently and allow it to stand till its contents are fully dissolved.
This completes the reconstitution of the vaccine.

PHASE I :
Reconstitution of the single dose vaccine

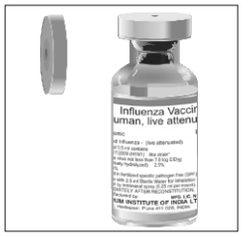


Tap the top of the diluent ampoule for the diluent to drip down. Twist off the top of the ampoule containing the diluent. Insert the tip of the syringe into the ampoule.

Invert the ampoule and syringe and draw out the entire quantity of the diluent into the syringe and remove the empty diluent ampoule.



Fix the Needle Free Transfer Device on the syringe containing the diluent.



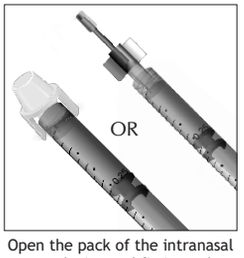
Remove the flip top of the vaccine vial.

Insert the needle free transfer device with the attached syringe into the vaccine vial.
Transfer the diluent into the vaccine vial by pushing the plunger of the syringe. Release the residual vacuum by detaching the syringe and refitting it.

Shake the vial gently and allow it to stand till its contents are fully dissolved.
This completes the reconstitution of the vaccine.

Phase II :
Administration of the multi - dose reconstituted vaccine

Insert the Administration syringe into the needle free transfer device on the vaccine vial.
Invert the vaccine vial and draw vaccine into the syringe upto the 0.25 ml mark.



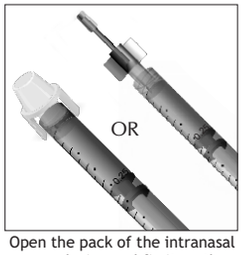
Open the pack of the intranasal spray device and fix it on the tip of the syringe.
The syringe now contains half dose i.e. 0.25 ml which is to be administered in one nostril of the recipient.

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.

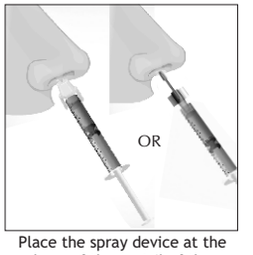
Repeat the above steps so as to draw the second half dose, refit the spray device and administer it into the second nostril of the recipient.
This completes the administration of 1 dose of vaccine to 1 recipient.
Repeat the above procedure using a fresh intranasal spray device for every recipient; but using the same administration syringe for all the remaining doses.

Phase II :
Administration of the single dose reconstituted vaccine

Invert the vaccine vial and draw vaccine into the syringe upto the 0.25 ml mark.



Open the pack of the intranasal spray device and fix it on the tip of the syringe.
The syringe now contains half dose i.e. 0.25 ml which is to be administered in one nostril of the recipient.



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.

Repeat the above steps so as to draw the second half dose, refit the spray device and administer it into the second nostril of the recipient.
This completes the administration of the single dose vaccine to 1 recipient.