

HNVAC, Human Inactivated Influenza A(H1N1) Virus Vaccine (Adsorbed)
SUMMARY of PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Human Inactivated Influenza A(H1N1) Virus Vaccine (Adsorbed), **HNVAC**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Formula: The vaccine product contains the following ingredients:

S. No.	Ingredient		Function
1.	HA equivalent of Purified, Inactivated Influenza A(H1N1) Virus Bulk		Active Biological Ingredient
2.	Al(OH) ₃ gel as Al ⁺⁺⁺ (Adjuvant)		Adjuvant
3.	Thiomersal (Preservative)		Preservative
4.	Di-sodium hydrogen orthophosphate	Phosphate Buffered Saline	Buffer solution to maintain pH and osmolality
5.	Sodium dihydrogen orthophosphate		
6.	Sodium chloride		

Quantitative Formula: Each dose of 0.5 mL contains:

S. No.	Ingredient		Quantity
1.	HA equivalent of Purified, Inactivated Influenza A(H1N1) Virus Bulk		≥15 µg
2.	Al(OH) ₃ gel as Al ⁺⁺⁺ (Adjuvant)		0.25 mg
3.	Thiomersal (Preservative)		0.025 mg
4.	Di-sodium hydrogen orthophosphate	Phosphate Buffered Saline	qs per dose
5.	Sodium dihydrogen orthophosphate		
6.	Sodium chloride		

3. PHARMACEUTICAL FORM

Vaccine

Category: Active Immunizing Agent.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Vaccine is indicated for active immunization of persons of age 18 years to 65 years against influenza disease caused by pandemic influenza A (H1N1) 2009 virus.

4.2 Posology and method of administration

The recommended dose for Human Inactivated Influenza A(H1N1) Virus Vaccine (Adsorbed), **HNVAC** is 0.5 mL.

Vaccine should be administered by **intramuscular** injection. The site of injection should be prepared with a suitable antiseptic.

4.3 Contraindications

Do not administer the Human Inactivated Influenza A (H1N1) 2009 Vaccine, **HNVAC**, to anyone with a known history of severe hypersensitivity to any component of the vaccine or life-threatening reactions after previous administration of any influenza vaccine.

4.4 Special warnings and precautions for use

Guillain-Barré Syndrome

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of any prior influenza vaccine, the decision to give should be based on careful consideration of the potential benefits and risks.

Altered Immunocompetence

Immunocompromised patients may have a reduced immune response to Human Inactivated Influenza A (H1N1) 2009 Vaccine, **HNVAC**

Preventing and Managing Allergic Reactions

Prior to administration of Human Inactivated Influenza A (H1N1) 2009 Vaccine, **HNVac** the healthcare provider should review the patient's prior immunization history for possible adverse events, to determine the existence of any contraindication to immunization with **HNVac** and to allow an assessment of benefits and risks. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

It is current practice in vaccination to coadminister different vaccines during the same session. If **HNVac** to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

4.6 Pregnancy and lactation

Safety and effectiveness of **HNVac** have not been established in pregnant women and nursing mothers. Therefore this vaccine is not recommended to pregnant or lactating women.

4.7 Effects on ability to drive and use machines

Not Applicable.

4.8 Undesirable effects

Based on adverse event information from clinical trials, some vaccinated subjects develop local pain, redness and swelling. These are mild in nature and last for 24-48 hours. Small proportion of vaccinees may develop fever which is mild, last for a day or two. The other minor symptoms are itching, allergy, sore-throat, lower limb pain, nausea and malaise.

4.9 Overdose

Not Recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Clinical trials in Healthy individuals provided/ demonstrated safety and immunogenicity of Human Inactivated Influenza A (H1N1) 2009 Vaccine, **HNAC** by intramuscular route of administration. The antibody titres were significantly greater than the minimum prescribed protective level. No serious vaccine related adverse reactions were observed in any of the volunteers during the clinical trial.

5.2 Pharmacokinetic properties

Evaluation of Pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical Toxicity studies on “**HNAC**” were conducted using three species of animals i.e., Mice, Rats and Rabbits. In order to prove the safety of “**HNAC**” in experimental animals, the following studies were conducted:

- a. Single dose intramuscular toxicity study in Wistar Rats
- b. Single dose intramuscular toxicity study in Swiss Albino Mice
- c. 14-day intramuscular toxicity study in Wistar rats
- d. 14-day intramuscular toxicity study in New Zealand White Rabbits
- e. 28-day intramuscular toxicity study in Wistar rats
- f. 28-day intramuscular toxicity study in New Zealand White Rabbits

In summary, animals were injected with human equivalent doses considering 15 µg / 60 kg body weight, according to standard guidelines. It should be noted therefore that the animals injected repeatedly were administered up to 280 times the human equivalent dose of the formulated vaccine. In fact the above doses amounted to 45 and 90 actual human doses (not human equivalent doses) in rats and rabbits, respectively. The results of the studies indicated that there were no immediate hypersensitivity or anaphylactic reactions. No treatment-related effects on mortality, clinical observations, body weight, food consumption, water consumption, coagulation, haematology, clinical chemistry, necropsy, organ weights or gross pathology were observed in all the animals, whether it was acute dosing or repeated dosing for 14 or 28 days. Gross pathology findings did not

reveal any local reaction or inflammation at the site of repeated injection. Neither was any abnormality observed in any of the organs, including brain, heart, liver, kidneys, lungs, testes and ovaries. In addition, we did not observe nodule formation either at the site of injection or anywhere else in the body for any of the animals in any of the studies. Further, none of the organs, including liver, kidneys, spleen, lung, brain, heart and lymph nodes showed any abnormalities in histopathological studies of the 14-day and 28-day repeat dose toxicology studies.

Results of the studies have indicated that there were no treatment-related effects on mortality, clinical observation, body weight, food consumption, water consumption, haematology or clinical chemistry in animals. Based on the toxicity studies it is confirmed that “HNVAC” is safe for intramuscular injection.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Aluminium hydroxide gel as Al⁺⁺⁺ and Thiomersal.

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

Two years (when stored at 2°-8° C).

6.4 Special precautions for storage

The HNVAC shall be stored between 2°-8°C and transported in same conditions. HNVAC shall not frozen.

When stored under prescribed conditions the vaccine retains its potency for 24 months.

6.5 Nature and contents of container

5 mL vial contains 10 doses x 0.5 mL

0.5 mL vial contains 1 dose x 0.5 mL

0.5 mL PFS contains 1 dose x 0.5 mL

6.5 Special precautions for disposal

Discard the vaccine if particulate matter observed.

7. MARKETING AUTHORIZATION PREQUALIFICATION HOLDER

Name of the Company: Bharat Biotech International Limited

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8. MARKETING AUTHORIZATION NUMBER(S)

9432/M3B/2010 dated 11.10.10

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

We got marketing authorization for **HNVAC** on 11th October 2010 for 0.5 mL and 5.0 mL presentation in vials. However, for pre-filled syringes market authorization is still awaited.