SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Monovalent Influenza A (H1N1 2009) Virus Like Particle (VLP) Vaccine

2. COMPOSITION:

Each 0.5 mL dose of CadiFlu contains 15 µg of hemagglutinin antigen of purified influenza A/California/04/2009 (H1N1) VLPs (produced in Sf9 cells using recombinant baculovirus) in a phosphate buffer containing calcium chloride dihydrate, polysorbate 80, disodium hydrogen phosphate anhydrous, sodium dihydrogen phosphate monohydrate,sodium chloride and water for injection.

CadiFlu contains no egg proteins, antibiotics or preservatives

3. Dosage Form:

Sterile liquid for intramuscular injection

4. CLINICAL PARTICULARS

4.1 Indications

CadiFlu is indicated in individuals above 18 years of age for the active immunization against disease caused by influenza A/California/7/2009 (H1N1) pdm09 virus.

4.2 Dose and method of administration:

CadiFlu should be administered as a single 0.5 mL intramuscular injection in the region of the deltoid muscle. Do not mix with any other vaccine in the same syringe or vial.

4.3 Contraindications:

CadiFlu is contraindicated in individuals with known severe allergic reactions (e.g anaphylaxis), to the vaccine or any component of the vaccine.

4.4 Special warnings and Precautions for use:

Limitation of vaccine effectiveness:

The vaccine is intended to provide antibody responses potentially protective against influenza caused by A/California/07/2009 (H1N1)pdm09 like viruses. Protection against other influenza virus subtypes is not expected.

Vaccination with CadiFlu vaccine may not protect all recipients.

Preventing and managing allergic reactions:

If the individual has a history of Guillain-Barré syndrome, the decision to give CadiFlu should be based on careful consideration of the potential benefits and risks.

Prior to administration of CadiFlu, the healthcare provider should review the individual's prior immunization history for possible adverse effects, to determine the existence of any

contraindication to immunization with CadiFlu vaccine and to allow an assessment of benefits and risks. Appropriate medical treatment and medical supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

Altered immunocompetence:

If CadiFlu is administered to immunocompromised individuals, including persons receiving immunosuppressive therapy, the immune response may be diminished.

4.5 Drug Interactions:

Data evaluating the concomitant administration of CadiFlu with other vaccines are not available

4.6 Use in special population:

Pregnant and nursing mothers:

Pregnancy Category C: Animal reproduction studies have not been conducted with CadiFlu. It is also not known whether CadiFlu can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CadiFlu should be given to a pregnant woman only if clearly needed. It is not known whether CadiFlu is excreted in human milk. As many drugs are excreted in human milk, caution should be exercised when CadiFlu is administered to a nursing woman.

4.7 Undesirable effects:

CadiFlu has been evaluated for safety and immunogenicity in Phase I/II and Phase III clinical studies in the Indian population by Cadila Pharmaceuticals Limited, India. CadiFlu was found to be safe and immunogenic in both clinical trials.

The adverse events reported here are from the clinical trials conducted with CadiFlu (Monovalent Influenza A (H1N1 2009) Virus Like Particle (VLP) Vaccine). There was no significant difference (p=0.56) between the vaccine and placebo arms when subjects with adverse events were compared as whole.

The common adverse events in both vaccine and placebo groups were injection site reactions, including site pain (23.26% vs 18.92%) and local swelling (12.4% 12.16%). Other most common adverse events reported were headache (18.6% vs 16.22%) and joint pain (6.98% vs 8.11%). The adverse events were reported as mild and transient in nature and were similar between vaccine and placebo groups.

4.8 Overdose

No data are available on overdose with CadiFlu.

5. PHARMACOLOGICALS PROPERTIES

5.1 Pharmacodynamic properties:

Mechanism of Action:

Influenza viruses have 2 major envelope glycoproteins - haemagglutinin (HA) and neuraminidase (NA), and protection against clinical disease is mainly conferred by serum antibodies to these glycoproteins. HA is the major antigenic target of virus neutralizing antibodies. Antibody to HA blocks the attachment of virus to cell surfaces, and is measured by the ability of serum to inhibit the agglutination of red blood cells by virus, termed haemagglutination-inhibition or HAI. CadiFlu expresses recombinant HA of the influenza virus strain. A/California/04/2009, which is immunologically like A/California/07/2009, the prototype strain for the 2009 pandemic, and A(H1N1) persisting and causing human disease in 2015. Administration of this vaccine results in humoral antibody responses to this HA antigen which has been measured by HAI.

Immunogenicity:

In two clinical trials conducted in the Indian population, CadiFlu demonstrated rates of seroconversion (proportion of subjects with either a post-vaccination HI titer >1:40 from a pre-vaccination titer <1:10 or at least a four-fold increase from pre-vaccination HI titer >1:10 in antibody titer), seroprotection (proportion of vaccinees with post-vaccine reciprocal HAI titer >1:40, a value historically associated with reduced risk of disease) and Geometric Mean Ratio (GMR, the fold-increase in HAI titer from before to 21 days post vaccination) that were highly significant ($p<0.0001$ in each case) in the vaccine arm in comparison to the placebo arm. All three parameters fulfilled their targets: seroconversion rate =40%,seroprotection =70% and GMR =2.5.

Because viruses antigenically similar to A/California/04/2009 have continued to circulate in the population since 2009, and cause immune responses, it is important to understand the performance of Cadiflu in contrast to background changes in placebo recipients. This was done in the Phase III trial. In the Phase III trial, the GMR in vaccine-treated subjects was 11.69 in comparison with 1.32 in placebo-treated subjects ($p<0.0001$). The rate of seroconversion at day-21 post vaccination in the vaccine arm (65.55%, 95% CI: 60-70) was significantly greater than that in the placebo arm (8.1%, 95% CI: 3-12; $p <0.0001$).

Baseline pre-immunization seroprotection rates were 15.1% (95 % CI: 11-19) and 13.9% (95 % CI: 8-19) for the vaccine and placebo arms, respectively. However, 21 days post-vaccination, the seroprotection rate attained in the vaccine arm was of 73.2% (95% CI: 68 – 78) 21 days post-vaccination compared with a placebo seroprotection rate of 21% (95% CI: 14-27); ($p<0.0001$).

6. PHARMACEUTICAL PARTICLUARS

6.1 List of Excipients

- Calcium chloride Dihydrate
- Polysorbate 80
- Disodium hydrogen phosphate anhydrous
- Sodium dihydrogen phosphate monohydrate
- Sodium Chloride
- Water for injection

6.2 Incompatibilities:

In the absence of compatibility studies, CadiFlu must not be mixed with other medicinal products

6.3 Shelf life:

12 months when stored at 2-8 °C .

The expiry date is indicated on the container label

6.4 Special precautions for storage:

Store at 2-8 °C

Do not freeze. Discard if vaccine has been frozen.

Protect from light

6.5 Nature and contents of container:

2 ml, 13 mm neck USP Type I glass vial with rubber stopper and flip off seal containing 0.5 mL – Single dose vial

7. MARKETING AUTHORISATION

Cadila Pharmaceuticals Ltd.

1389, Trasad Road

Dholka-382225

Ahmedabad, Gujarat

8. MARKETING AUTHORISATION NUMBER(S)

MF-70/2015

9. DATE OF FIRST AUTHORISATION

12 Mar 2015