SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) is a monovalent vaccine produced using strains of NYMC X-179A, a reassortant strain prepared by New York Medical College using classical reassortant methodology from A/California/7/2009 (H1N1) virus and NYMC X-157 virus. The HA, NA and PB1 genes donated from A/California/7/2009 (H1N1)v and the other internal genes donated from A/PR/8/34 (H1N1).

Each vial of Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) contains a single dose of either 10 μg HA (haemagglutinin) antigen propagated in eggs respectively in a solution of 0.5 ml. This vaccine complies with the WHO recommendation and EU decision for the pandemic. For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection. The suspension is a colourless light opalescent liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of influenza in an officially declared pandemic situation (see sections 4.2 and 4.1). Pandemic influenza vaccine should be used in accordance with Official Guidance.

4.2 Posology and method of administration

Adults (18-49 years), elderly (≥ 50 years) and children and adolescents (3-17 years) of age: A single dose of 0.5 ml containing 10 μg HA antigen by intramuscular 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.

4.3 Contraindications

History of an anaphylactic (i.e. life-threatening) reaction to any of the constituents or trace residues (egg and chicken protein, ovalbumin) of this vaccine. If vaccination is considered to be necessary, facilities for resuscitation should be immediately available in case of need.
See section 4.4 for Special warnings and special precautions for use.

4.4 Special warnings and precautions for use

Caution is needed when administering this vaccine to persons with a known hypersensitivity (other than anaphylactic reaction) to the active substance, to any of the excipients, to thiomersal and to residues (egg and chicken protein, ovalbumin).

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

If the pandemic situation allows, immunisation shall be postponed in patients with severe febrile illness or acute infection.

SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) should under no circumstances be administered intravascularly.

Therefore, healthcare providers need to assess the benefits and potential risks of administering the vaccine in individuals with thrombocytopenia or any bleeding disorder that would contraindicate intramuscular injection unless the potential benefit outweighs the risk of bleedings.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

A protective immune response may not be elicited in all vaccinees (see section 5.1).

There are no safety, immunogenicity or efficacy data to support interchangeability of SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) with other H1N1 pandemic vaccines.

4.5 Interaction with other medicinal products and other forms of interaction

There are no data on co-administration of SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) with other vaccines.

However, if co-administration with another vaccine is considered, immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Following influenza vaccination, false-positive serology test results may be obtained by the ELISA method for antibody to human immunodeficiency virus-1 (HIV-1), hepatitis C
virus and, especially, HTLV-1. In such cases, the Western blot method is negative. These transitory false-positive results may be due to IgM production in response to the vaccine.

4.6 Pregnancy and lactation

There are currently no data available on the use of SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) in pregnancy. Data from pregnant women vaccinated with different inactivated non-adjuvanted seasonal vaccines do not suggest malformations or fetal or neonatal toxicity.

Animal studies with SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) have been completed to assess reproductive toxicity (see section 5.3).

The use of SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) may be considered during pregnancy if this is thought to be necessary, taking into account official recommendations.

A teratogenicity study in pregnant rats did not reveal any maternal, embryotoxic or fetotoxic potential.

It is not known whether SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

4.8 Undesirable effects

The SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) vaccine has undergone Phase I and Phase II/III studies.

The Phase I study was conducted in 50 healthy adults aged 18-49 years. The study compared two strengths 10 µg or 15 µg of the vaccine in a double-blind randomized fashion, when given in a single dose. The total follow up period was 42 days. A large Phase II/III study was initiated after successfully generating 30 day safety data in the Phase I study. The study was conducted in 330 healthy subjects [110 adults (18-49 years), 110 elderly (>50 years) and 110 children and adolescents (3-17 years)]. The study compared two strengths 10 µg or 15 µg of the vaccine in a double-blind randomized fashion. Two doses of the vaccines were given 21 days apart.
In the Phase I study, the vaccine was found safe in both dose strengths. The reported solicited reactions were pain/tenderness (24-36 %), body ache (8-12 %), chills (0-12%), diarrhoea (0-4%), fatigue (12-16 %), headache (8-24 %), malaise (12-16 %), myalgia (12-28 %), nausea (0-4%). The incidence was similar in both the study groups. Almost all the reactions were mild in intensity. All of them resolved without any sequelae within 2-3 days and did not require any treatment.

Few adverse events (accidental injury, cough and throat pain) were reported. The events were mild to moderate in severity. All the events resolved without any sequelae. None of them were causally related to the study vaccine. Two serious adverse events were reported. One subject had a dog bite and another had cholelithiasis. Both the events resolved without any sequelae. None of them were causally related to the study vaccine. No hematological, biochemical and urine parameter was affected. There was no effect on vital functions. The study showed that both the strengths of the vaccine are very safe.

In the larger Phase II/III study, the vaccine was again found safe. There was no serious adverse event. The reported solicited local reactions were pain/tenderness (10.6-12.7 %), erythema (0 - 0.3 %), induration (0-0.3 %), swelling (0.3-0.6%) and redness (0-0.6 %). The reported solicited systemic reactions were fever (0.3-01 %), headache (2.5-4.4%), body ache (2.5-4.7 %), irritability (0.3-1.0 %), nausea (0.6-1.6 %), loss of appetite (0-1.9 %), drowsiness (0.9-1.3 %), diarrhoea (0.3 %), fatigue (2.5-4.7 %), myalgia (0.9-1.9 %), chills (0.3-0.6 %) and malaise (0-1.3 %). The incidence was similar in both the study groups. Almost all the reactions were mild in severity and resolved without any sequelae within 2-3 days.

There were a few unsolicited event reported in both the groups. These were chicken pox, cold, cold and cough, cough, fever, headache, loose motion, maculopapular rash, vomiting with incidence ranging from 0.3% to 1%. The incidence was similar in both the groups. All of them resolved without any sequelae. None of them except a case of cold and cough was causally related to study vaccines. There was no effect on vital functions. The results showed that both the strengths of vaccine were very safe in all three age groups. Safety profile of the vaccine is in line with published literature. 1-5

4.9 Overdose
No case of overdose has been reported.
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccines, ATC Code J07BB02.

In the large Phase II/III study in 330 subjects, the following was evaluated: seroprotection rate: proportion of subjects with haemagglutination inhibition (HI) titre ≥ 1:40; seroconversion rate: proportion of subjects who were either seronegative at pre-vaccination and have a protective post-vaccination titre of ≥ 1:40, or who were seropositive at pre-vaccination and have a 4-fold increase in titre; and the pre- and post-vaccination geometric mean titres (GMT).

On Day 21 after a single dose of the vaccine, seroprotection rates were 96.3 % and 89.1 % with a single dose of 10 μg and 15 μg of dose respectively. The corresponding seroconversion was 91.9 % and 87.8 %. In 10 μg dose group, the post-vaccination GMT was 205.4 on Day 21 and for 15 μg dose, it was 180.9.

Seroprotection, seroconversion and GMT in both groups were significantly higher at Day 21 as compared to baseline. The vaccines were also found immunogenic in all three age groups (pediatrics, adults and elderly). The results are also in line with the licensed Inactivated H1N1/2009 vaccines.

Overall, the immunogenicity results clearly showed that the vaccine induces protective immunity in the majority of subjects in both dose strengths.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) underwent two single-dose and two repeated-dose toxicity studies in mice and rats. Single dose toxicity studies in Swiss albino mice and Wistar rats were carried out with a dose of 6 ug HA /mouse (equal to 2 times the human equivalent dose) and 15 ug HA per rat (equal to one human equivalent dose in absolute terms) respectively to find out the toxicity of the vaccine. The repeated dose toxicity studies in mice and rats were carried out with dose of 3 μg/mouse and 15 μg/rat given 3 times on Day 0, 7 and 14. All the studies evaluated the intended intramuscular route of vaccine administration.

In both the single-dose studies, no mortality or abnormal clinical signs were observed in the animals treated with the study vaccines during the observation period of 14 days. On necropsy, there were no gross or histopathological changes in any organ. Treatment related inflammatory changes were observed in mice of vaccine and vehicle treated groups.
In both the repeated-dose studies, no mortality or abnormal clinical signs were observed in the animals treated with the study vaccines during the observation period of 28 days. No alternation in growth was seen in vaccine and vehicle control group.

Haematological parameters and biochemistry did not reveal any treatment related effect during the study, at the termination of the treatment and at the end of the reversal period. The value of absolute and relative weight of organs (kidneys, liver, adrenals, testes, ovaries, epididymides, uterus, thymus, spleen, brain, heart and lung) treated with the vaccine were found to be comparable to those of the vehicle control group at termination of treatment and at the end of reversal period.

On necropsy, there were no gross or histopathological changes in any organ. Treatment related inflammatory changes were observed in animals of vaccine and vehicle control groups.

A teratogenicity study was also conducted on pregnant Wistar rats. Groups of thirty pregnant female rats were administered Influenza Vaccine (Whole virion, inactivated) Pandemic by intramuscular injection, at the doses of 0.5 ml/rat (day 5 of gestation), 1 ml/rat (0.5 ml on day 5 and on day 12 of gestation) and 1.5 ml/rat (0.5 ml on day 5, 12 and 18 of gestation) (equivalent to 1, 2 & 3 times the human dose). None of the animals died during the period of gestation. No maternal toxicity, embryotoxicity or fetotoxicity was observed at and upto the dose of 1.5 ml / rat. Influenza Vaccine (Whole virion, inactivated) Pandemic at the doses upto 1.5 ml / rat is not teratogenic in Wistar rat.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Al(OH):3 gel - Aluminium(Al+++) content NMT 1.25 mg/dose.
Phosphate buffered saline - Base

6.2 Incompatibilities

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

6.3 Shelf life

9 months

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Store in the original package in order to protect from light.
6.5 Nature and contents of container

Vaccine: 4 mL Clear glass vial of Type 1 USP (dimensions d=16.5, h= 40 mm) containing 0.5 mL suspension of product, stoppered and sealed with a 13 mm orange flip top cap

Pack: One vial accompanied by a syringe in a unit carton.

6.6 Special precautions for disposal and other handling

SII Influenza Vaccine (whole virion, Inactivated) A/H1N1 (Pandemic) consists of single dose vial containing the antigen 10 μg HA antigen in 0.5 ml suspension.

Instructions for administration of the vaccine:

1. Before withdrawing, the suspension should be shaken and inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.
2. The vial should be shaken prior to each administration.
3. Each vaccine dose of 0.5 ml (full dose) is withdrawn into a syringe for injection and administered intramuscularly. The vaccine should be allowed to reach room temperature before use.

Any unused product or waste material should be disposed as per the procedure of disposal of biohazardous waste.

7. MARKETING AUTHORISATION HOLDER

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