Registration No.: 2C 2/54 (NBC)

Importer / Manufacturer: Sanofi Pasteur Ltd., Thailand/ Sanofi Pasteur S.A., France

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Intanza (15 microgram/strain)
Influenza vaccine (split virion, inactivated)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus (inactivated, split) of the following strains*:

A/California/7/2009 (H1N1) – derived strain used NYMC X-179A…………….15 micrograms HA**

A/Perth/16/2009 (H3N2) – like strain used NYMC X-187 derived from A/Victoria/210/2009
…………………………………………………………………………………………………………………………15 micrograms HA**

B/Brisbane/60/2008 ……………………………………………………………15 micrograms HA**
Per 0.1 ml dose

* propagated in fertilised hens’ eggs from healthy chicken flocks

** haemagglutinin

This vaccine complies with the WHO recommendations (Southern Hemisphere) for the 2012 season.

For a full list of excipients, see section 6.1.

Intanza (15 microgram/strain) contains residues of eggs such as ovalbumin.

3. PHARMACEUTICAL FORM

Suspension for injection.
Colourless and opalescent suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of influenza in individuals 60 years of age and over, especially in those who run an increased risk of associated complications.

The use of Intanza (15 microgram/strain) should be based on official recommendations.

4.2 Posology and method of administration

Posology
Individuals 60 years of age and over: 0.1 ml.
*Paediatric population*

Intanza (15 microgram/strain) is not recommended for use in children and adolescents below 18 years due to insufficient data on safety and efficacy.

*Method of administration*

Immunisation should be carried out by intradermal route.

The recommended site of administration is the region of the deltoid.

*Precaution to be taken before manipulating or administering the product*

For instructions for preparation of the medicinal product before administration, see section 6.6.

4.3 **Contraindications**

Hypersensitivity to the active substances, to any of the excipients, to residues of eggs, such as ovalbumin, and to chicken proteins.

The vaccine may also contain residues of the following substances: neomycin, formaldehyde and octoxinol 9.

Immunisation shall be postponed in subjects with febrile illness or acute infection.

4.4 **Special warnings and precautions for use**

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

Intanza (15 microgram/strain) should under no circumstances be administered intravascularly.

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

In case of presence of liquid at the injection site after vaccine administration, re-vaccination is not required.

Interference with serological testing: See section 4.5.

4.5 **Interaction with other medicinal products and other forms of interaction**

Intanza (15 microgram/strain) may be given at the same time as other vaccines. 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 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 disproves the false-positive ELISA test results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6 **Fertility, pregnancy and lactation**

This vaccine is intended for individuals 60 years of age and over. Therefore, this information is not applicable.
4.7 Effects on ability to drive and use machines

Intanza (15 microgram/strain) has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

a. Summary of the safety profile

The safety of Intanza (15 microgram/strain) has been assessed in 3 open-label randomised clinical trials, 3,372 vaccinees received an injection of Intanza (15 microgram/strain).

Safety evaluation was performed for all subjects during the first 3 weeks following vaccination and serious adverse reactions were collected during six months of follow-up for 2,974 subjects (population of two out of the three clinical trials).

The most common reactions occurring after vaccine administration were local reactions at injection site. Apparent local reactions after intradermal administration were more frequent than after intramuscular administration of an adjuvanted or non-adjuvanted comparator vaccine. Most reactions resolved spontaneously within 1 to 3 days after onset.

Systemic safety profile of Intanza (15 microgram/strain) is similar to the comparator vaccine, adjuvanted or non-adjuvanted, administered intramuscularly.

After repetitive yearly injections the safety profile of Intanza (15 microgram/strain) is similar to the previous injections.

b. Tabulated summary of adverse reactions

The data below summarizes the frequencies of the adverse reactions that were recorded following vaccination from clinical trials, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000), not known (cannot be estimated from available data).

<table>
<thead>
<tr>
<th>Organ class</th>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td></td>
<td></td>
<td>Paresthesia, neuritis</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td>Sweating</td>
<td>Pruritus, rash</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Myalgia</td>
<td></td>
<td>Arthralgia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Local reactions: redness*, induration, swelling, pruritus, pain</td>
<td>Malaise, shivering, fever, Local reactions: ecchymosis</td>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*In some cases, local redness lasted up to 7 days.
c. Potential adverse events

Based on the experience with trivalent inactivated influenza vaccines administered by intramuscular or deep subcutaneous injection, the following events may be reported:

**Blood and lymphatic system disorders**
Transient thrombocytopenia, transient lymphadenopathy

**Immune system disorders**
Allergic reactions, in rare cases leading to shock, angioedema

**Nervous system disorders**
Neuralgia, febrile convulsions, neurological disorders, such as encephalomyelitis and Guillain Barré syndrome

**Vascular disorders**
Vasculitis associated in very rare cases with transient renal involvement

**Skin and subcutaneous tissue disorders**
Generalised skin reactions including urticaria

4.9 **Overdose**

Overdose is unlikely to have any untoward effect.

5. **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: Influenza vaccines, ATC code: J07BB02

**Immunogenicity**

Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccinal immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6-12 months.

In a pivotal randomised comparative phase III trial, 2,606 subjects over 60 years of age received 0.1 ml of Intanza (15 microgram/strain) by intradermal route and 1,089 subjects over 60 years of age received 0.5 ml of a trivalent inactivated influenza vaccine administered by intramuscular route.

In this comparative trial the geometric mean titres (GMTs), seroprotection rate*, seroconversion or significant increase rate** and the geometric mean titre ratio (GMTR) for anti-HA antibody (measured by HI) were assessed according to predefined criteria.

Data were as follows (values in brackets show the 95% confidence intervals):

<table>
<thead>
<tr>
<th>Intradermal 15µg</th>
<th>A/H1N1</th>
<th>A/H3N2</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/New Caledonia/20/99</td>
<td>N = 2,585</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/Wisconsin/67/2005</td>
<td>N = 2,586</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/Malaysia/2506/2004</td>
<td>N = 2,582</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Intradermal 15µg

<table>
<thead>
<tr>
<th></th>
<th>Intradermal 15µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric mean of titre  (1/dil)</td>
<td>81.7 (78.0 ; 85.6)</td>
</tr>
<tr>
<td>Seroprotection rate (%) *</td>
<td>77.0 (75.3 ; 78.6)</td>
</tr>
<tr>
<td>Seroconversion or significant increase rate (%) **</td>
<td>38.7 (36.8 ; 40.6)</td>
</tr>
<tr>
<td>Geometric mean of titre ratio (GMTR)</td>
<td>3.97 (3.77 ; 4.18)</td>
</tr>
</tbody>
</table>

*Seroprotection = HI titre ≥ 40
** Seroconversion = negative pre-vaccination HI titre and post vaccination HI titre ≥ 40, Significant increase = positive pre-vaccination HI titre and at least a 4-fold increase in post-vaccination HI titre

GMTR: Geometric mean titre ratio of individual (post-/pre-vaccination titre).

Intanza (15 microgram/strain) is at least as immunogenic as the comparator trivalent inactivated influenza vaccine administered by intramuscular route for each of the 3 influenza strains in subjects from 60 years of age and over.

Across all three influenza strains, for the comparator intramuscular vaccine GMTs ranged between 34.8 (1/dil) and 181.0 (1/dil), seroprotection rates ranged between 48.9% and 87.9%, seroconversion or significant increase rates ranged between 30.0% and 46.9% and GMTRs ranged between 3.04 and 5.35-fold over baseline HI titres.

In a randomised comparative phase III trial, 398 subjects over 65 years of age received 0.1 ml of Intanza (15 microgram/strain) by intradermal route and 397 subjects over 65 years of age received 0.5 ml of a trivalent inactivated adjuvanted (MF-59 containing) influenza vaccine at the same dosage administered by intramuscular route.

Intanza (15 microgram/strain) is as immunogenic as the comparator trivalent adjuvanted (MF-59 containing) vaccine in terms of GMT for each of the 3 influenza strains with the SRH method and for 2 strains with the HI method.

### 5.2 Pharmacokinetic properties

Not applicable

### 5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on animal studies. The vaccine was immunogenic in mice and rabbits. In repeated-dose toxicity studies in rabbits there was no significant evidence of systemic toxicity. Nevertheless, single and repeated administrations led to transient local erythema and oedema. Genotoxicity and carcinogenic potential were not assessed because these studies are not appropriate for a vaccine. Fertility and toxicity studies to reproduction in females have not identified any specific potential hazard for humans.

### 6. PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients

Sodium chloride
Potassium chloride
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections

6.2 Incompatibilities

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

6.3 Shelf-life

1 year

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C). Do not freeze.
Keep the syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.1 ml of suspension in a pre-filled syringe (glass) with a Micro-Injection System, with attached micro-needle, equipped with an elastomer plunger stopper (chlorobutyl), a tip cap (thermoplastic elastomer and polypropylene) and a needle shielding system. Pack size of 1 or 10 or 20.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

The vaccine should be allowed to reach room temperature before use.

The vaccine should not be used if foreign particles are present in the suspension.

It is not necessary to shake the vaccine before use.

The Micro-Injection System for intradermal injection consists of a pre-filled syringe with a micro-needle (1.5 mm) and a needle shielding system.
The needle shielding system is designed to cover the micro-needle after use.

7. MARKETING AUTHORISATION HOLDER

Sanofi Pasteur Ltd., Bangkok

8. MARKETING AUTHORISATION NUMBER(S)

2C 2/54 (NBC)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZAION

06 May 2011
10. DATE OF REVISION OF THE TEXT

26 January 2012

Micro-Injection System
INSTRUCTIONS FOR USE

Please read the instruction before use

1/ REMOVE NEEDLE CAP

Remove the needle cap from the Micro-Injection System.

Do not purge air through the needle.

2/ HOLD MICRO-INJECTION SYSTEM BETWEEN THUMB & MIDDLE FINGER

Hold the system by placing the thumb and middle finger only on the finger pads; the index finger remains free.

Do not place fingers on the windows.

3/ INSERT NEEDLE RAPIDLY PERPENDICULAR TO THE SKIN

Insert the needle perpendicular to the skin, in the region of the deltoid, in a short, quick movement.

4/ INJECT USING THE INDEX FINGER

Once the micro-needle has been inserted, maintain a light pressure on the surface of the skin and inject using the index finger to push on the plunger. The vein test is unnecessary.

5/ ACTIVATE NEEDLE SHIELD BY PUSHING FIRMLY ON PLUNGER

Remove the needle from the skin.

Orient the needle away from you and others.

With the same hand, push very firmly with the thumb on the plunger to activate the needle shield.

You hear a click and a shield comes out to cover the needle.

Immediately dispose of the system in the nearest sharps collector.

Injection is considered successful whether or not the presence of a wheal is observed.

In case of presence of liquid at the injection site after vaccine administration, re-vaccination is not required.