

CORE SmPC FOR TRIVALENT INFLUENZA VACCINES

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Introduction

Requirements affecting the content of SmPCs are to be found in a number of EU regulatory documents including Directive 2001/83/EC as amended¹ and in the European Commissions Guideline on the Summary of Product Characteristics. Guidance specific to composing SmPCs for human vaccines appears in the Guideline on the Pharmaceutical Aspects of the Product Information for Human Vaccines (EMA/CPMP/BWP/2758/02). There are also in existence a number of QRD group documents which provides guidance on drafting SmPCs.

The function of the present document is to provide additional guidance on the composition of SmPCs for inactivated, non-adjuvanted, influenza vaccines prepared using influenza viruses grown in fertilised hens' eggs.

SmPCs for live influenza vaccines, and for influenza vaccines produced using cell cultures as virus propagation substrates, fall outside the scope of the document.

In effect, this means that SmPCs for vaccines complying with the following PhEur monographs are affected:

- Influenza vaccine (split virion, inactivated) [Monograph 0158]
- Influenza vaccine (surface antigen, inactivated) [Monograph 0869]
- Influenza vaccine (whole virion, inactivated) [Monograph 0159]

Standard text to be used in the SmPC is denoted using bold font.

Pieces of text which cannot be specified in the guideline and which therefore need to be generated on a product-specific basis are delimited using the characters < >.

Sometimes no concrete text proposal has been formulated, but instead items of guidance related to specific sections in the SmPC are given. These are written in normal font.

On some places a justification (in italic) concerning a proposal has been included.

1. NAME OF THE MEDICINAL PRODUCT

The standard requirement is for the invented name of the medicinal product, the strength and the pharmaceutical form to appear.

However, in the case of influenza vaccines, the strength (the haemagglutinin (HA) content for each strain present in the vaccine) should be omitted from the invented name in the SmPC.

The common name should be that of the monograph in the European Pharmacopoeia with which the vaccine complies.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Whole influenza virus (inactivated)> <Influenza virus (inactivated, split)><Influenza virus surface antigens (haemagglutinin and neuraminidase)> of the following strains*:

A/<Official strain> (H1N1) *** <n> micrograms HA**

A/<Official strain> (H3N2) *** <n> micrograms HA**

B/<Official strain> *** <n> micrograms HA**

per <n> ml dose

* propagated in fertilised hens' eggs from healthy chicken flocks

** haemagglutinin

- ***
- 1) When the official strain is directly used: nothing added.
 - 2) When the strain used is a like strain to the official one: -like strain used (<actual strain >)
 - 3) When the strain used is derived from the official one: -derived strain used (<actual strain >)
 - 4) When the strain used is derived from a strain like to the official one: -like strain used (<actual strain >) derived from <like strain>

Illustrative examples:

1) and 2) usually concern the B strain whereas 3) and 4) are related to A/H1N1 and A/H3N2 strains which are derived strains (from the official strain or from a like strain to the official strain).

1) When the official strain is directly used: nothing is added.

B/Brisbane/60/2008

(example issued from the NH 2010-2011 season)

2) When the strain used is a like strain to the official one: -like strain used (<actual strain>)

B/Florida/4/2006-like strain used (B/Brisbane/3/2007)

(example issued from the NH 2008-2009 season)

3) When the strain used is derived from the official one: -derived strain used (<actual strain>)

A/California/7/2009 (H1N1)-derived strain used (NYMC X-181)

(example issued from the NH 2010-2011 season)

4) When the strain used is derived from a strain like to the official one: strain used (<actual strain>) derived from <like strain>

A/Perth/16/2009 (H3N2)-like strain used (NYMC X-187) derived from A/Victoria/210/2009

(example issued from the NH 2010-2011 season)

This vaccine complies with the WHO recommendation (northern hemisphere) and EU decision for the <year/year> season.

<Excipients:>

“If the vaccine contains thiomersal as preservative, the amount should be stated here.”

For a full list of excipients see section 6.1.

In case that the vaccine contains traces of special relevance the following statement should be inserted:

<Invented name of the vaccine> may contain traces of eggs such as ovalbumin, <to be completed for other residues> which are used during the manufacturing process (see section 4.3).

3. PHARMACEUTICAL FORM

The full European Pharmacopoeia standard term should be used and a brief description of the product should follow.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Prophylaxis of influenza, especially those who run an increased risk of associated complications.

<Invented name of vaccine> is indicated in adults <and children from 6 months of age>.

Note: the end of sentence may only be included in case the product has been accepted for use in children (or in case data in children are available).

The use of <invented name of vaccine> should be based on official recommendations.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Adults: 0.5 ml.

Paediatric population

<Children from 36 months onwards: 0.5 ml

Children from 6 months to 35 months: Clinical data are limited. Dosages of 0.25 ml or 0.5 ml may be given. <The dose given should be in accordance with the existing national recommendations> >

<For children who have not previously been vaccinated, a second dose should be given after an interval of at least 4 weeks.>

Children less than 6 months: the safety and efficacy of <Invented name of vaccine> in children less than 6 months have not been established.

<No data are available> or <Currently available data are described in section <4.8><5.1><5.2> but no recommendation on a posology can be made>

There have been differences in children dosage between Member States and no sound evidence is available to justify a specific dosage.

Method of administration

Immunisation should be carried out by intramuscular or deep subcutaneous injection.

A text like “Immunodeficient patients are recommended to be immunised twice with an interval of at least 4 weeks” should not be included in the SmPC.

Precautions to be taken before handling or administering the medicinal 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 <such as product specific: <thiomersal>> or to any component that may be present as traces such as eggs (ovalbumin, chicken proteins), <antibiotic>, <formaldehyde>.....

Immunisation shall be postponed in patients 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.

<Invented name of the vaccine> should under no circumstances be administered intravascularly.

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

If thiomersal is used in the manufacturing process which results in levels of thiomersal ≥ 40 ng per dose, the following should be mentioned:

<Thiomersal (an organomercuric compound) has been used in the manufacturing process of this medicinal product and residues of it are present in the final product. Therefore, sensitisation reactions may occur.>

For levels of thiomersal < 40 ng per dose or undetectable levels, no statements are recommended for inclusion.

Interference with serological testing
See section 4.5.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

<Invented name of the vaccine> 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

Pregnancy

~~The limited data from vaccinations in pregnant women do not indicate that adverse fetal and maternal outcomes were attributable to the vaccine. The use of this vaccine may be considered from the second trimester of pregnancy. For pregnant women with medical conditions that increase their risk of complications from influenza, administration of the vaccine is recommended, irrespective of their stage of pregnancy.~~

| ~~<Invented name of the vaccine>~~ Inactivated influenza vaccines can be used in all stages of pregnancy. Larger datasets on safety are available for the second and third trimester, compared with the first trimester; however, data from worldwide use of inactivated influenza vaccines do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

| ~~Animal studies do not indicate reproductive toxicity (see section 5.3)~~

Breastfeeding

<Invented name of the vaccine> may be used during breastfeeding.

Fertility

No fertility data are available.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

<Invented name of the vaccine> has no or negligible influence on the ability to drive and use machines.

4.8. UNDESIRABLE EFFECTS

ADVERSE REACTIONS OBSERVED FROM CLINICAL TRIALS

The safety of trivalent inactivated influenza vaccines is assessed in open label, uncontrolled clinical trials performed as annual update requirement, including at least 50 adults aged 18 - 60 years of age and at least 50 elderly aged 61 years or older. Safety evaluation is performed during the first 3 days following vaccination.

The following undesirable effects have been observed during clinical trials with the following frequencies:

very common ($>1/10$); common ($\geq 1/100, <1/10$); uncommon ($\geq 1/1,000, <1/100$)

Tabulated list of adverse reactions.

Organ class	Very common $\geq 1/10$	Common $\geq 1/100,$ $<1/10$	Uncommon $\geq 1/1,000, <1/100$
Nervous system disorders		Headache*	
Skin and subcutaneous tissue disorders		Sweating*	
Musculoskeletal and connective tissue disorders		Myalgia, arthralgia*	
General disorders and administration site conditions		Fever, malaise, shivering, fatigue. Local reactions: redness, swelling, pain, ecchymosis, induration*	

* These reactions usually disappear within 1-2 days without treatment.

ADVERSE REACTIONS REPORTED FROM POST-MARKETING SURVEILLANCE

Adverse reactions reported from post marketing surveillance are, next to the reactions which have also been observed during the clinical trials, the following:

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, paraesthesia, febrile convulsions, neurological disorders, such as encephalomyelitis, neuritis 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 pruritus, urticaria or non-specific rash

If the vaccine contains thiomersal as a preservative the following should be mentioned:

<This medicinal product contains thiomersal (an organomercuric compound) as a preservative and therefore it is possible that sensitisation reactions may occur (see Section 4.3).>

If the vaccine contains thiomersal as a residue from the manufacturing process which results in levels ≥ 40 ng per dose the following should be mentioned:

<This medicinal product contains thiomersal (an organomercuric compound) as a residue from the manufacturing process and therefore it is possible that sensitisation reactions may occur (see section 4.4.). >

4.9 OVERDOSE

Overdosage is unlikely to have any untoward effect.

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Influenza vaccine, ATC Code: <J07BB01> or <J07BB02>
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.

5.2. PHARMACOKINETIC PROPERTIES

Not applicable

5.3. PRECLINICAL SAFETY DATA

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Product specific

According to the recommendation given by the Guideline on Summary of Product Characteristics, residues of production should not be stated in this Section.

6.2. INCOMPATIBILITIES

See corresponding Section in the current template on SmPC.

6.3. SHELF LIFE

<n> <months> or <1 year>

The value of n should not be greater than eleven.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

<Product specific>.

6.5. NATURE AND CONTENTS OF THE CONTAINER

Standard guidance on composing the entry under this section should be followed. Examples of entries are given in attachment 3 of the Guideline on pharmaceutical aspects of the product information for human vaccines (EMEA/CPMP/BWP/2758/02).

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL <AND OTHER HANDLING>

The vaccine should be allowed to reach room temperature before use.
Shake before use. Inspect visually prior to administration

Where a single dose 0.5 ml syringe is to be used for administration of a 0.25 ml dose, specific instructions should be added. See also section 4.2.

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

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT