CORE SPC/PL FOR TRIVALENT INFLUENZA VACCINES

Introduction

Requirements affecting the content of SPCs are to be found in a number of EU regulatory documents including Directive 2001/83/EC as amended[1] and in the European Commissions Guideline on the Summary of Product Characteristics. Guidance specific to composing SPCs for human vaccines appears in the Guideline on the Pharmaceutical Aspects of the Product Information for Human Vaccines (EMEA/CPMP/BWP/2758/02). There are also in existence a number of QRD group documents which provide guidance on drafting SPCs.

The function of the present document is to provide additional guidance on the composition of SPCs and package leaflets for inactivated, non-adjuvanted, influenza vaccines prepared using influenza viruses grown in fertilised hens' eggs.
SPCs and package leaflets 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 SPCs/PLs 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 SPC 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 SPC are given. These are written in normal font.
On some places a justification (in italic) concerning a proposal has been included.

The core package leaflet for trivalent influenza vaccines was agreed at the November 2008 CMD(h) meeting and reflects the results of consultation with target patient groups.

[1]Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (as amended)

REVISION OF THE CORE SPCFOR TRIVALENT INFLUENZA VACCINES

October 2003
Revision 2, December 2006

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 SPC.

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains*:

A/<Official strain> (H1N1) like strain (<actual strain>) <n> micrograms HA**
A/<Official strain> (H3N2) like strain (<actual strain>) <n> micrograms HA**
B/<Official strain> like strain (<actual strain>) <n> micrograms HA**
.....
per <n> ml dose
*** propagated in fertilised hens' eggs from healthy chicken flocks**
**** haemagglutinin**

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

For a full list of excipients see section 6.1.

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 in those who run an increased risk of associated complications.

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

Note: this is standard wording for vaccines.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Adults and children from 36 months: 0.5 ml.

Children from 6 months to 35 months: Clinical data are limited. Dosages of 0.25 ml or 0.5 ml have been used. The dose given should be according to the approved dosage for the respective vaccines.
For children, who have not previously been vaccinated, a second dose should be given after an interval of at least 4 weeks.

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

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 SPC.

For instructions for preparation, see section 6.6.

4.3 CONTRA-INDICATIONS
Hypersensitivity to the active substances, to any of the excipients and to {residues <product specific: e.g. eggs, chicken proteins>. <Invented name of vaccine> does not contain more than <n> microgram ovalbumin per dose. The vaccine may contain residues of the following substances <product specific>, e.g. antibiotics, thiomersal}.

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 the vaccine contains residues of thiomersal 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 (see section 4.3).

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. PREGNANCY AND LACTATION

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> may be used during lactation.

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

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 (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10000, <1/1000); very rare (<1/10000), including isolated reports.

Organ class	Very common >1/10	Common >1/100, <1/10	Uncommon >1/1,000, <1/100	Rare > 1/10,000, <1/1,000	Very rare <1/10,000
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, febril 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).

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 homologuous 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

6.2. INCOMPATIBILITIES
<In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products>
<This medicinal product must not be mixed with other medicinal products except those mentioned in 6.6>

6.3. SHELF-LIFE
<n> <months> or **<1 year>**

The value of n should not normally 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>
Unused vaccine and other waste material should be disposed of in compliance with local rules for the disposal of products of this nature.
The vaccine should be allowed to reach room temperature before use.
Shake before use.

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

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

CORE PACKAGE LEAFLET FOR TRIVALENT INFLUENZA VACCINES

November 2008

PACKAGE LEAFLET: INFORMATION FOR THE USER
<Product name>, suspension for injection in <Product specific>
Influenza vaccine <common name>

Read all of this leaflet carefully before you or your child is vaccinated.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist
- This vaccine has been prescribed for you or your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist

In this leaflet

1. WHAT <PRODUCT NAME> IS AND WHAT IT IS USED FOR

<Product name> is a vaccine. This vaccine helps to protect you or your child against influenza (flu), particularly in subjects who run a high risk of associated complications. The use of <Product name> should be based on official recommendations.

When a person is given the vaccine <Product name>, the immune system (the body's natural defence system) will produce its own protection (antibodies) against the disease. None of the ingredients in the vaccine can cause flu.

Flu is a disease that can spread rapidly and is caused by different types of strains that can change every year. Therefore, this is why you might need to be vaccinated every year. The greatest risk of catching flu is during the cold months between October and March. If you or your child was not vaccinated in the autumn, it is still sensible to be vaccinated up until the spring since you or your child runs the risk of catching flu until then. Your doctor will be able to recommend the best time to be vaccinated.

<Product name> will protect you or your child against the three strains of virus contained in the vaccine from about 2 to 3 weeks after the injection.

The incubation period for flu is a few days, so if you are exposed to flu immediately before or after your vaccination, you could still develop the illness.

The vaccine will not protect you against the common cold, even though some of the symptoms are similar to flu.

2. BEFORE <YOU> OR <YOUR CHILD> USE <PRODUCT NAME>

To make sure that <Product name> is suitable for you or your child, it is important to tell your doctor or pharmacist if any of the points below apply to you or your child. If there is anything you do not understand, ask your doctor or pharmacist to explain.

Do not use <Product name>
- If you or your child is allergic (hypersensitive) to the active substances, to any of the ingredients of <Product name>, <to eggs>, < to chicken proteins>, to < Product specific residue> (For other ingredients of <Product name>, see section 6 "Further information").
- If you or your child has an illness with a high temperature or acute infection, the vaccination shall be postponed until after you or your child has recovered.

Take special care with <Product name>
You should tell your doctor before vaccination if you or your child has a poor immune response (immunodeficiency or taking medicines affecting the immune system).

Your doctor will decide if you or your child should receive the vaccine.

If, for any reason, you or your child has a blood test within a few days following a flu vaccination, please tell your doctor. This is because false positive blood test results have been observed in a few patients who had recently been vaccinated.

As with all vaccines, <Product name> may not fully protect all persons who are vaccinated.

Using other medicines
- Please tell your doctor or pharmacist if you or your child is taking or has recently taken other vaccines or any other medicines, including medicines obtained without a prescription.
- <Product name> can be given at the same time as other vaccines by using separate limbs. It should be noted that the side effects may be stronger.
- The immunological response may decrease in case of immunosuppressant treatment, such as corticosteroids, cytotoxic drugs or radiotherapy.

Pregnancy and breast-feeding
Tell your doctor or pharmacist if you are pregnant or think you may be pregnant.

Limited data from flu vaccinations in pregnant women do not indicate that the vaccine would have harmful effects on the pregnancy or the baby. 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 the flu, administration of the vaccine is recommended, irrespective of their stage of pregnancy.

<Product name> may be used during breast-feeding.

Your doctor/pharmacist will be able to decide if you should receive <Product name>.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
The vaccine is unlikely to affect your ability to drive or use machines.

Important information about some of the ingredients of <Product name>
<Product specific>

3. HOW TO USE <PRODUCT NAME>

Dosage

Adults and children aged from 36 months receive one 0.5 ml dose.
Children from 6 months to 35 months may receive one 0.25 ml dose or one 0.5 ml dose.
If your child has not been previously vaccinated against flu, a second dose should be given after at least 4 weeks.

Method and/or route(s) of administration

Your doctor will administer the recommended dose of the vaccine as an injection into the muscle or deep under the skin.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, <Product name> can cause side effects, although not everybody gets them.

During clinical trials, the following side effects have been observed. Their frequencies have been estimated as Common: affects 1 to 10 users in 100.

- headache
- sweating
- muscular pain (myalgia), joint pain (arthralgia)
- fever, generally feeling unwell (malaise), shivering, fatigue
- local reactions: redness, swelling, pain, bruising (ecchymosis), hardness (induration) around the area where the vaccine is injected.

These reactions usually disappear within1-2 days without treatment.

Next to the above common side effects, the following side effects occurred after the vaccine came on the market:

- allergic reactions:
    - leading to medical emergency with a failure of the circulatory system to maintain adequate blood flow to the different organs (shock) in rare cases,
    - swelling most apparent in the head and neck, including the face, lips, tongue, throat or any other part of the body (angioedema) in very rare cases.
- skin reactions that may spread throughout the body including itchiness of the skin (pruritus, urticaria), rash
- blood vessel inflammation which may result in skin rashes (vasculitis) and in very rare cases in temporary kidney problems.
- pain situated on the nerve route (neuralgia), anomalies in the perception of touch, pain, heat and cold (paraesthesia), fits (convulsions) associated with fever, neurological disorders that may result in stiff neck, confusion, numbness, pain and weakness of the limbs, loss of balance, loss of reflexes, paralysis of part or all the body (encephalomyelitis, neuritis, Guillain-Barré Syndrom)
- temporary reduction in the number of certain types of particles in the blood called platelets; a low number of these can result in excessive bruising or bleeding (transient thrombocytopenia); temporary swelling of the glands in the neck, armpit or groin (transient lymphadenopathy)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist

5. HOW TO STORE <PRODUCT NAME>

Keep out of the reach and sight of children.

Do not use <Product name> after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

<Product specific storage conditions>

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

The active substance is < Product specific>*
A/<Official strain> (H1N1) like strain (<actual strain>) ..... <n>micrograms HA**
A/<Official strain> (H3N2) like strain (<actual strain>) ..... <n>micrograms HA**
B/<Official strain> like strain (<actual strain>) ..... <n>micrograms HA**

Per <Product specific> ml dose

* propagated in fertilised hens'eggs from healthy chicken flocks

** haemagglutinin

This vaccine complies with the WHO (World Health Organisation) recommendations (Northern hemisphere) and EU decision for the yyyy/yyyy season.

The other ingredients are <Product specific>

What <Product name> looks like and contents of the pack

<Product name> is {pharmaceutical form} presented (in {container} (content) {content of the package}

<Product specific>

Marketing Authorisation Holder and Manufacturer

<Manufacturer specific>

This medicinal product is authorised in the Member States of the EEA under the following names:

<Product specific>

This leaflet was last approved in {MM/YYYY}.

<Product specific>

The following information is intended for medical or healthcare professional only: