COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Serinflu, suspension for injection 0.5 ml

influenza virus surface antigens (inactivated) (haemagglutinin and neuraminidase)

NL License RVG: 115203

Date: 24 July 2018

This module reflects the scientific discussion for the approval of Serinflu, suspension for injection 0.5 ml. The procedure was finalised on 27 January 2016. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
ERA	Environmental Risk Assessment
HA	Haemmagglutinin
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy
WHO	World Health Organisation

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Medicines Evaluation Board (MEB) of the Netherlands has granted a marketing authorisation for Serinflu, suspension for injection 0.5 ml, from Abbott Biologicals B.V.

The product is indicated for prophylaxis of influenza, especially in those who run an increased risk of associated complications.
Serinflu is indicated in adults and children from 6 months of age.
The use of Serinflu should be based on official recommendations.

A comprehensive description of the indications and posology is given in the SmPC.

This national procedure concerns a so-called full dossier application according to Article 8(3) of Directive 2001/83/EC, a dossier with administrative, chemical-pharmaceutical, pre-clinical and clinical data. The active component of Serinflu, suspension for injection 0.5 ml is considered to be well-known and the clinical pharmacology of influenza virus surface antigens inactivated (haemagglutinin and neuraminidase) has been extensively studied. Most of the data in the dossier of Serinflu, suspension for injection 0. 5 ml was already submitted in the dossier of Influvac, suspension for injection 0.5 ml (NL License RVG 22289).

This application cross-references the pre-clinical and clinical data approved for Influvac; therefore these have not been resubmitted with this application. No new non-clinical or clinical studies on efficacy and safety were submitted, as the active substances and pharmaceutical form on administration are essentially similar to those approved for the parent product Influvac suspension for injection 0.5 ml.

II. QUALITY ASPECTS

II.1 Introduction

Serinflu is a colourless clear liquid suspension for injection. The product contains the influenza virus surface antigens (haemagglutinin and neuraminidase) of the following strains:

- A/California/7/2009 (H1N1)pdm09-like strain (A/California/7/2009, X-181) — 15 micrograms HA
- A/Switzerland/9715293/2013 (H3N2)-like strain (A/Switzerland/9715293/2013, NIB-88) — 15 micrograms HA
- B/Phuket/3073/2013-like strain (B/Phuket/3073/2013, wild type) — 15 micrograms HA

0.5 ml of the vaccine suspension for injection contains 15 micrograms of the antigen haemagglutinin of each recommended virus strain.

The virus strains in the vaccine comply with the recommendation of the WHO and the CHMP (northern hemisphere) for the 2015/2016 season.

The suspension for injection is packed in a vial (glass type 1) closed with a bromobutyl rubber stopper and sealed with an aluminium cap.

The excipients are: potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, sodium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate and water for injections.

II.2 Drug Substance

The chemical-pharmaceutical documentation and Expert Report are of sufficient quality in view of the present European regulatory requirements.
The same drug substances, *i.e.* monovalent bulk of each virus strain, are used for Serinflu 0.5 ml as for Influvac 0.5 ml. Hence, the drug substance section is approvable.

II.3 Medicinal Product

Pharmaceutical development
The MAH has submitted an application for national marketing authorisation for its subunit inactivated trivalent seasonal influenza vaccine in a vial. The formulation production and composition of the final product is identical to the vaccine in prefilled syringe (Influvac).The MAH has made modifications to the registered Influvac manufacturing process of which the development is described. This is acceptable.

Manufacturing process
The manufacturing process of Serinflu is the same as Influvac. The only difference is the immediate packaging of Serinflu which is a single dose vial instead of a 1 mL Long Syringe. The glass (type I) and the rubber stopper material (bromobutyl rubber) which are in contact with the vaccine remain unchanged. The manufacturing process and specifications of the drug substance and finished product (Final Lot) remain unchanged

Control of excipients
The excipients are purchased to the Ph. Eur. specifications. The specifications are the same as for Influvac 0.5 ml. These specifications are acceptable.

Quality control of drug product
The MAH clarified that the specifications and registered storage conditions for Serinflu are identical as for Influvac. Data demonstrating has been provided showing that there is no difference in quality and stability between both products. The product specifications cover appropriate parameters for this dosage form and include tests for appearance, identity, content, visible particles, sub-visible particles, extractable volume, pH, sterility and bacterial endotoxins. Validations of the analytical methods have been presented. Batch analysis has been performed on three batches. The batch analysis results show that the finished products meet the specifications proposed.

Stability of drug product
The conditions used in the stability studies are according to the ICH stability guideline. The shelf life as claimed in the SPC of 12 months when stored in a refrigerator (+2°C to +8°C), 'do not freeze' and 'store in the original package in order to protect from light', is deemed acceptable and is identical to Influvac.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the MEB considers that Serinflu has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product. No post-approval commitments were made

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

The product is intended as a substitute for other products on the market. It is expected that the use of this formulation will replace other available products, and thus the amount of active substance emitted to the environment is not expected to increase.

III.2 Discussion on the non-clinical aspects

This product is identical to Influvac, which is available on the European market. No new preclinical data have been submitted. The MAH referred to the preclinical documentation included in the application for Influvac. Therefore, the application has not undergone additional preclinical assessment. This is acceptable for this type of application.

IV. CLINICAL ASPECTS

IV.1 Clinical efficacy

This application cross-references the clinical data approved for Influvac; therefore, these have not been resubmitted with this application.

IV.2 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Serinflu.

- Summary table of safety concerns as approved in RMP

Important identified risks	Hypersensitivity to the active substances or to any of the excipients
Important potential risks	Non-febrile convulsions Autoimmune disorders
Missing information	None

The MEB agreed that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

IV.3 Discussion on the clinical aspects

The active substance is well-known with established efficacy and tolerability. This application cross-references to the clinical data approved for Influvac. No new clinical studies on efficacy and safety were submitted as the active substance and pharmaceutical form on administration are identical to those approved for the parent product, which is acceptable.

V. USER CONSULTATION

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference to Influvac, suspension for injection 0.5 ml (NL License RVG 22289). The bridging report submitted by the MAH has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Serinflu, suspension for injection 0.5 ml has a proven chemical-pharmaceutical quality and is an approvable product identical to Influvac, suspension for injection 0.5 ml, except for the drug product container. Influvac is a well-known medicinal product with an established favourable efficacy and safety profile.

No new non-clinical or clinical studies on efficacy and safety were submitted, as the active substances and pharmaceutical form on administration are identical to those approved for the parent product Influvac 2012/2013, suspension for injection 0.5 ml.

The Board followed the advice of the assessors.

The MEB, on the basis of the data submitted, considered that essential similarity has been demonstrated for Serinflu with Influvac, and have therefore granted a marketing authorisation. The national procedure was finalised with a positive outcome on 27 January 2016.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
Type IAin: B.II.b.1.a B.II.b.1.c **Type II:** B.II.b.2.b **Type IB:** B.II.b.4.f **Type IA:** B.II.b.5.c **Type II:** B.II.e.1.b.2: I	- Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product: • Secondary packaging site • Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products, or for pharmaceutical forms manufactured by complex manufacturing processes - Change to importer, batch release arrangements and quality control testing of the finished product; replacement or addition of a site where batch control/testing takes place for a biological/immunological product and any of the test methods performed at the site is a biological/immunological method - Change in the batch size (including batch size ranges) of the finished product; the scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) - Change to in-process tests or limits applied during the manufacture of the finished product; deletion of a non-significant in-process test - Change in immediate packaging of the finished product; change in type of container or addition of a new container; sterile medicinal products and biological/immunological medicinal products	Y	24-10-2016	Approved	-
Type IB: B.I.a.2.a	Changes in the manufacturing process of the active substance; minor change in the manufacturing process o the active substance	-	24-05-2017	Approved	-
Type II: B.I.a.2.c	The change refers to a biological/immunological substance or use of a different chemically derived substance in the manufacture of a biological/immunological substance, which may have a significant impact on the quality, safety and efficacy of the medicinal product and is not related to a protocol	-	01-06-2017	Approved	-
Type IB: C.I.11.z	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan	-	19-07-2017	Approved	-
Type II: B.I.a.5.a	Changes to the active substance of a seasonal, pre- pandemic or pandemic vaccine against human influenza; replacement of the strain(s) in a seasonal, pre- pandemic or a pandemic vaccine against human influenza	Y	19-07-2017	Approved	-
Type II: B.I.a.5.a	Changes to the active substance of a seasonal, pre- pandemic or pandemic vaccine against human influenza; replacement of the strain(s) in a seasonal, pre- pandemic or a pandemic vaccine against human influenza	Y	03-01-2018	Approved	-