Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Adjuvanted Zoonotic Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe

A/turkey/Turkey/1/2005 (H5N1) like strain (NIBRG 23)

PLGB 47991/0013

Seqirus UK Ltd

LAY SUMMARY

Adjuvanted Zoonotic Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe A/turkey/Turkey/1/2005 (H5N1) like strain (NIBRG 23)

This is a summary of the Public Assessment Report (PAR) for Adjuvanted Zoonotic Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Adjuvanted Zoonotic Influenza Vaccine in this lay summary for ease of reading.

For practical information about using Adjuvanted Zoonotic Influenza Vaccine, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Adjuvanted Zoonotic Influenza Vaccine and what is it used for?
This application is the same as Aflunov suspension for injection in pre-filled syringe, PLGB 47991/0004 which is already authorised.

The Company responsible for Aflunov suspension for injection in pre-filled syringe has agreed that its scientific data can be used as the basis for the grant of an identical licence for Adjuvanted Zoonotic Influenza Vaccine.

Adjuvanted Zoonotic Influenza Vaccine is for use in adults from 18 years onwards, intended to be given in the context of outbreaks of zoonotic influenza viruses (coming from birds) with pandemic potential to prevent flu caused by viruses similar to the vaccine strain reported in section 6 of the PIL.

Zoonotic influenza viruses occasionally infect humans, and can cause disease ranging from mild upper respiratory infection (fever and cough) to rapid progression to severe pneumonia, acute respiratory distress syndrome, shock and even death. Human infections are primarily caused by contact with infected animals, but do not spread easily between people.

Adjuvanted Zoonotic Influenza Vaccine is intended also to be given when there is anticipation of a possible pandemic due to the same or a similar strain.

How does Adjuvanted Zoonotic Influenza Vaccine work?
When a person is given the vaccine, 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.

As with all vaccines, Adjuvanted Zoonotic Influenza Vaccine may not fully protect all persons who are vaccinated.

How is Adjuvanted Zoonotic Influenza Vaccine used?
The pharmaceutical form of this medicine is suspension for injection in pre-filled syringe and the route of administration is intramuscular injection into the muscle at the top of the upper arm (deltoid muscle).

A doctor or nurse will administer the vaccine in accordance with official recommendations.

Adults from 18 onwards:
One dose of 0.5 ml will be given. A second dose of 0.5 ml should be given after an interval of at least 3 weeks.

There is limited experience in elderly over 70 years of age.

Use in children
Children from 6 months to 17 years of age
There is limited experience in children between 6 months and 17 years of age.
Vaccination is currently not recommended in this age group.

Children aged less than 6 months of age
Vaccination is currently not recommended in this age group.

For further information on how Adjuvanted Zoonotic Influenza Vaccine is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning the medicine.

What benefits of Adjuvanted Zoonotic Influenza Vaccine have been shown in studies?
Adjuvanted Zoonotic Influenza Vaccine is considered identical to the previously authorised product with the same benefits and risks. No new studies have been provided for Adjuvanted Zoonotic Influenza Vaccine, however, reference is made to the studies for Aflunov suspension for injection in pre-filled syringe.

What are the possible side effects of Adjuvanted Zoonotic Influenza Vaccine?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Adjuvanted Zoonotic Influenza Vaccine is considered to be identical to the previously authorised product with the same benefits and risks.

Why was Adjuvanted Zoonotic Influenza Vaccine approved?
The MHRA decided that the benefits of Adjuvanted Zoonotic Influenza Vaccine are greater than the risks and recommended that this medicine is approved for use.

What measures are being taken to ensure the safe and effective use of Adjuvanted Zoonotic Influenza Vaccine?

As for all newly authorised medicines, a Risk Management Plan (RMP) has been developed for Adjuvanted Zoonotic Influenza Vaccine. The RMP details the important risks of Adjuvanted Zoonotic Influenza Vaccine, how these risks can be minimised, any uncertainties about Adjuvanted Zoonotic Influenza Vaccine (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Adjuvanted Zoonotic Influenza Vaccine:

Important identified risk	None
Important potential risk	Neuritis Convulsions Encephalitis (*encephalomyelitis*) Vasculitis Guillain-Barré Syndrome Demyelination Bell's palsy Immune thrombocytopenia
Missing information	Use in pregnancy and lactation

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Adjuvanted Zoonotic Influenza Vaccine are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Adjuvanted Zoonotic Influenza Vaccine

A marketing authorisation was granted in the Great Britain (consisting of England, Scotland, Wales) on 06 October 2023.

The full PAR for Adjuvanted Zoonotic Influenza Vaccine follows this summary.

This summary was last updated in June 2024.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Adjuvanted Zoonotic Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe (PLGB 47991/0013) could be approved.

The product is approved for the following indication:

- Active immunisation against H5 subtype of Influenza A virus.

The name of the active substance is A/turkey/Turkey/1/2005 (H5N1) like strain (NIBRG 23)

MF59C.1 is an oil-in-water emulsion with a squalene internal oil phase and a citrate buffer external aqueous phase. The surfactants, sorbitan trioleate and polysorbate 80, serve to stabilize the emulsion.

One of the effects of MF59 is to generate a local immunostimulatory environment at the injection site, which activates local immune cells. This results in maturation of resident dendritic cells (DCs), further recruitment and activation of immune cells into the injection site, enhanced antigen uptake, enhanced maturation of DCs and enhanced migration of APCs to the local draining lymph nodes. The effects of MF59 on human immune cells were assessed directly in vitro and it was found that following immunization, MF59 enhances the immune response at a range of points, including the induction of chemokines to increase recruitment of immune cells to the injection site, enhanced antigen uptake by monocytes at the injection site, and enhanced differentiation of monocytes into DCs, which represent the gold-standard cell type for priming naïve T cells. A particularly important feature of MF59 may be that it facilitates DCs migration into draining lymph nodes where they can trigger the adaptive immune response specific to the vaccine. Nevertheless, further studies are necessary to better define the mechanism of action of MF59.

So far there appears to be an impressive consistency between data obtained in vitro with human cells, and the in vivo data from mouse. These observations suggest that MF59 induces a local pro-inflammatory environment within the muscle, which promotes the induction of potent immune responses to co-administered vaccines. Overall, the justification for the use of MF59 as adjuvant is sufficiently supported.

This is a national abridged application approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as an informed consent application. The application cross-refers to the reference product Aflunov suspension for injection in pre-filled syringe, PLGB 47991/0004.

No new non-clinical or clinical data have been supplied and none are required for this informed consent application.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the application is for an identical version of an already authorised product, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A national marketing authorisation was granted in the Great Britain (consisting of England, Scotland, Wales) on 06 October 2023

II. EXPERT REPORT

The applicant cross-refers to the data for Aflunov suspension for injection in pre-filled syringe, Seqirus UK Ltd), to which this application is claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with that for Aflunov suspension for injection in pre-filled syringe, Seqirus UK Ltd) dated 07/2022.

PATIENT INFORMATION LEAFLET

A leaflet text and mock-up has been provided which has been aligned with that for Aflunov suspension for injection in pre-filled syringe, Seqirus UK Ltd), dated for 01/2021. The user test report submitted for PLGB 47991/0004 has been provided.

LABEL

Label text have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specification

The source of the active substance is in line with the cross-reference product. The proposed drug substance specification is consistent with the details registered for the cross-reference product.

IV.2. Drug Product

Name

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Adjuvanted Zoonotic Influenza Vaccine is available a type I glass pre-filled syringe (0.5ml) with a bromo-butyl rubber plunger stopper in pack sizes of 1 or 10 pre-filled syringes.

The appearance of the product is identical to that of the cross-reference product.

The proposed shelf life of the product is 2 years with the recommended storage conditions 'Store in a refrigerator (2°C – 8°C), do not freeze and store in the original package in order to protect from light'.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

Legal status

Prescription only medicine (POM).

Manufacturers
The proposed manufacturing sites are consistent with the details registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed product is consistent with the details registered for the cross-reference product.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference product and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference product.

TSE Compliance
No excipients of animal or human origin are used in the final products.

This product does not contain or consist of genetically modified organisms (GMO).

V. NON-CLINICAL ASPECTS
As this application is submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as an informed consent application) no new non-clinical data have been supplied and none are required.

VI. CLINICAL ASPECTS
As this application is submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as an informed consent application) no new clinical data have been supplied and none are required.

VII. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine risk minimisation measures, the following additional pharmacovigilance activities have been proposed:

Summary of important risks

Neuritis	
Risk minimisation measures	Routine risk minimisation measures: Neuritis is described in: *Foclivia SmPC: Section 4.8* *Foclivia PL: Section 4* Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)*

	Neuritis targeted follow-up questionnaire
Convulsions	
Risk minimisation measures	Routine risk minimisation measures: Convulsions are described in: *Foclivia SmPC: Section 4.4 and 4.8* *Foclivia PL: Section 2 and 4* Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Convulsions targeted follow-up questionnaire*
Encephalitis (*encephalomyelitis*)	
Risk minimisation measures	Routine risk minimisation measures: Neurological disorders, such as Encephalomyelitis, are described in: *Foclivia SmPC: Section 4.8* *Foclivia PL: Section 4* Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Encephalitis (encephalomyelitis) targeted follow-up questionnaire*
Vasculitis	
Risk minimisation measures	Routine risk minimisation measures: Vasculitis is described in: *Foclivia SmPC: Section 4.8* *Foclivia PL: Section 4* Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Vasculitis targeted follow-up questionnaire*
Guillain-Barré Syndrome	
Risk minimisation measures	Routine risk minimisation measures: Guillain-Barré syndrome is described in: *Foclivia SmPC: Section 4.8* *Foclivia PL: Section 4* Additional risk minimisation measures: *No additional measures*

Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Guillain-Barré Syndrome targeted follow-up questionnaire*
Demyelination	
Risk minimisation measures	Routine risk minimisation measures: None; included as a potential safety concern based on pharmacological class effects Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Demyelination targeted follow-up questionnaire*
Bell's palsy	
Risk minimisation measures	Routine risk minimisation measures: None; included as a potential safety concern based on pharmacological class effects Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Bell's Palsy targeted follow-up questionnaire*
Immune thrombocytopenia	
Risk minimisation measures	Routine risk minimisation measures: None; included as a potential safety concern based on pharmacological class effects Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Immune thrombocytopenia targeted follow-up questionnaire*
Use in pregnancy and lactation	
Risk minimisation measures	Routine risk minimisation measures: Pregnancy and breast-feeding are described in *Foclivia SmPC: Section 4.6* *Foclivia PL: Section 2* Additional risk minimisation measures: *No additional measures*
Additional Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reaction reporting and signal detection: *S-PSUR (in situation of pandemic)* *Pregnancy Reporting/Outcome form* Additional pharmacovigilance activities: *V87_27OB (pregnancy registry)*

This is acceptable.

VIII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference product and positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product.

In accordance with legal requirements, the current approved GB versions of the SmPC and PIL for this product are available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**