PASS INFORMATION

Title	Prospective non-interventional cohort study to assess safety and tolerability of Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects
Protocol version identifier	v01
Date of last version of protocol	29 October 2014

EU PAS register number	
Active substance	15µg HA per 0.5 ml vaccine per the following influenza virus strains: - Influenza virus Type A H1N1, whole virion, inactivated [A/California/7/2009(H1N1) derived NYMC X-179A reassortant strain] [1] - Influenza virus Type A H3N2, whole virion, inactivated [A/Texas/50/2012 derived NYMC X-223A reassortant strain][1] - Influenza virus Type B, whole virion, inactivated [B/Massachusetts/2/2012 (wild-type) strain][1] [1]Strains recommended by the BWP ad-hoc influenza Working Party of the CHMP to be incorporated in trivalent vaccines used in the upcoming seasonal epidemics on the Northern Hemisphere ATC code: J07BB01
Medicinal product	Fluval AB suspension for injection (influenza vaccine, whole virion, inactivated) for season 2014/2015 (i.e. Fluval AB 2014/2015 vaccine in the followings)
Product reference	-
Procedure number	FluvalAB-H-17
Marketing authorisation holder(s)	Omninvest Ltd.
Joint PASS	No

Title	Prospective non-interventional cohort study to assess safety and tolerability of Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects
Protocol version identifier	v01
Date of last version of protocol	29 October 2014

Research question and objectives	The aim of this observational study, is to detect a potential increase in reactogenicity and allergic events that is intrinsic to the product in near real-time as part of the active surveillance of subjects vaccinated with Fluval AB vaccine containing influenza virus strains recommended for the 2014/2015 seasonal epidemics in accordance with the Summary of Product Characteristics. **Objective**: The objective of the study is to evaluate the occurrence of adverse events (AEs) in vaccinated subjects participating in the study and to rapidly detect any clinically significant change (compared to what was known or expected with the previous vaccine composition) in the frequency and severity of AEIs in vaccinated subjects participating in the study that may indicate a potential for more serious risks as exposure to the vaccine increases.
Country(-ies) of study	Hungary
Author	Orsolya Gyurján PharmD Hungary-2040 Budaörs, Fodros u. 45/B Email: orsolya.gyurjan@omninvest.hu Telephone: +36 20 419 7063

MARKETING AUTHORIZATION HOLDER(S)

Marketing authorisation holder(s)	Omninvest Ltd. Hungary-2097 Pilisborosjenő, Fő u. 7. Email: ndezso@omninvest.hu Telephone: +36 26 336 597 Fax: +36 26 536 051
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1. TABLE OF CONTENTS

2. LIST OF ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
AEI	Adverse Event of Interest
GCP	Good Clinical Practice
GYEMSZI-OGYI	Gyógyszerészeti és Egészségügyi Minőség- és Szervezetfejlesztési Intézet - Országos Gyógyszerészeti Intézet
HLT	High Level Term
MedDRA	Medical Dictionary for Regulatory Affairs
PRAC	Pharmacovigilance Risk Assessment Committee
PT	Preferred Term
SmPC	Summary of Product Characteristics
SOC	System Organ Class
ETT-TUKEB	Egészségügyi Tudományos - Tanács Tudományos és Kutatásetikai Bizottság
WHO	World Health Organisation

3. RESPONSIBLE PARTIES

TITLE: Prospective non-interventional cohort study to assess safety and tolerability of Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects

Undersigned below agree to adhere to the Study Protocol as approved by the Competent Authority (GYEMSZI-OGYI) and Ethics Committee (ETT-TUKEB). This study will be conducted in accordance with local ethical and legal requirements.

Name/Position: Date: Signature:

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4. ABSTRACT

Title	**Prospective non-interventional cohort study to assess safety and tolerability of a Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects**
Version	v01
Date	29 October, 2014

Name and affiliation of main author	Orsolya Gyurján PharmD Deputy QPPV, Omninvest Ltd.
Rationale and background	Seasonal influenza vaccines present several specific challenges for pharmacovigilance. These include mass immunisation in large population cohorts in a relatively short and fixed time period each year, seasonal factors (e.g. differentiating seasonal peaks in background illness from vaccine-induced effects) and multiplicity of seasonal vaccine products on the market with need for product-specific surveillance.
Research question and objectives	The aim of this observational study, which will be initiated after Fluval AB 2014/2015 seasonal influenza vaccine is licensed and used in a mass vaccination campaign, is to is to detect a potential increase in reactogenicity and allergic events that is intrinsic to the product in near real-time.
Study design	Defined cohorts of children and adults will be actively followed-up seven (7) days after immunisation for AEs following vaccination, with the aim to detect eventual changes (compared to the safety profile defined in the Summary of Product Characteristics) in the frequency and severity of defined AEIs.
Population	A total of six hundred (600) subjects will be observed in the study in order to achieve at least five hundred (500) evaluable male and female subjects (one hundred (100-100) per age group) in accordance with the provisions of guide Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU. Age groups are defined as follows: 3-5, 6-12, 13-17, 18-65 years and over 65 years. Relevant information on AEs will be collected during a follow-up phone contact seven (7) days after vaccination. Subjects in this study will be vaccinated in compliance with national vaccination policy decisions in Hungary and standard practice.

Title	**Prospective non-interventional cohort study to assess safety and tolerability of a Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects**
Version	v01
Date	29 October, 2014

Variables	The occurrence rates of reactogenicity endpoints of interest (AEIs) as well as other reported AEs will be evaluated. The following of reactogenicity endpoints are defined: - Vaccinaton site pain - Vaccination site erythema - Vaccination site swelling - Vaccination site induration - Vaccination site numbness - Fatigue - Headache - Fever - Hyperhidrosis - Malaise - Chills - Myalgia - Arthralgia - Nausea
Data sources	Data Report Forms will be available for data recording. However, source data will be available to document the existence of the subject and substantiate integrity of study data collected and will include the original documents related to the study.
Study size	Six hundred (600) subjects will be vaccinated with Fluval AB vaccine containing influenza virus strains recommended for the 2014/2015 seasonal epidemics in accordance with the Summary of Product Characteristics and participate in the study, evaluated in order to achieve at least five hundred (500) evaluable subjects giving at least one hundred (100) male and female vaccinated subjects in each defined age groups (3-5, 6-12, 13-17, 18-65 years and over 65 years), according to Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU EMA/PRAC/222346/2014.

Title	**Prospective non-interventional cohort study to assess safety and tolerability of a Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects**
Version	v01
Date	29 October, 2014

Data analysis	All individual data will be listed. Every subject who has already been vaccinated and involved in the study will be included in the statistical analysis. The assessment of safety and tolerability will be primarily based on the occurrence of adverse reactions compared to what was already known or expected with Fluval AB vaccine (according to the SmPC) in the frequency and severity of expected adverse reactions that may indicate a potential for more serious risks as exposure to the vaccine increases.
Milestones	Planned milestones of the study: 1. Vaccination: N/A 2. Follow up: Seven (7) days after vaccination 3. Expedited Summary Safety Report: Within 1 (one) months after the start of data collection 4. Final Study Report: Within 6 (six) months from the termination of data collection

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

Milestone	Planned date
1. Vaccination	N/A
2. Follow up	Seven (7) days after vaccination
3. Expedited Summary Safety Report	Within 1 (one) months after the start of data collection
4. Final Study Report	Within 6 (six) months from the termination of data collection

7. RATIONALE AND BACKGROUND

Influenza is a viral infection that affects mainly the nose, throat, bronchi and, occasionally, lungs. Infection usually lasts for about a week, and is characterized by sudden onset of high fever, aching muscles, headache and severe malaise, non-productive cough, sore throat and rhinitis. Most infected people recover within one to two weeks without requiring medical treatment. Prophylaxis of influenza by vaccination is considered the first and best way of protection. The National Centre for Epidemiology recommends that sub-populations at risk of severe complications on influenza are vaccinated yearly.

Seasonal influenza vaccines present several specific challenges for pharmacovigilance. These include mass immunisation in large population cohorts in a relatively short and fixed time period each year, seasonal factors (e.g. differentiating seasonal peaks in background illness from vaccine-induced effects) and multiplicity of seasonal vaccine products on the market with need for product-specific surveillance. There have also been examples when product-specific (or batch-specific) changes in quality specifications, arising from changes to a manufacturing process during the product life-cycle, have led to an unexpected change in reactogenicity or other adverse immune response. Due to these challenges, pharmacovigilance systems for influenza vaccines need capability to rapidly detect and evaluate potential new safety concerns each influenza season. The aim is to mitigate risks before the peak period of seasonal immunisation (i.e. at least within the first month after the start of immunisation). Although no strain change is proposed for the 2014-2015 influenza season, MAHs are still expected to begin the process of implementing enhanced surveillance – of which active part is performed by the present PASS study regarding to Fluval AB 2014/2015 vaccine.

8. RESEARCH QUESTION AND OBJECTIVES

The aim of this observational study, which will be initiated after Fluval AB 2014/2015 seasonal influenza vaccine is licensed and used in a mass vaccination campaign, is to is to detect a potential increase in reactogenicity and allergic events that is intrinsic to the product in near real-time.

Objective:

The objective of the study is to estimate the occurrence of adverse events in vaccinated subjects participating in the study and to rapidly detect a clinically significant change (compared to what was known or expected with the previous vaccine composition) in the frequency and severity of AEIs in vaccinated subjects participating in the study that may indicate a potential for more serious risks as exposure to the vaccine increases.

9. RESEARCH METHODS

9.1. Study design

This is a prospective, non-interventional, cohort, non-randomized, observational open study.

The aim of the vaccination is to reduce the morbidity associated with seasonal influenza infection. Defined cohorts of children and adults previously vaccinated with a single dose of Fluval AB suspension for injection (influenza vaccine, whole virion, inactivated, adjuvanted) will be actively followed-up seven (7) days after immunisation for AEs following vaccination, with the aim to detect eventual changes (compared to the safety profile defined in the Summary of Product Characteristics) in the frequency and severity of defined AEIs.

9.2. Setting

The sample size was determined in accordance with the provisions of guide 'Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU' stating that a total of at least one hundred (100) male and female vaccinated subjects in each defined age groups (3-5, 6-12, 13-17, 18-65 years and over 65 years) should be evaluated. Considering approximately ~17% of drop-out (one out of six participants), in total six hundred (600) subjects will be vaccinated with Fluval AB vaccine containing influenza virus strains recommended for the 2014/2015 seasonal epidemics in accordance with the Summary of Product Characteristics and participate in the study in order to achieve at least five hundred (500) evaluable subjects (one hundred-one hundred (100-100) subjects per each age group respectively).

Relevant information on AEs will be collected during a follow-up phone contact seven (7) days after vaccination.

Subjects in this study will be vaccinated in compliance with national vaccination policy decisions in Hungary and standard practice.

9.2.1. Vaccination

The inclusion of subjects in this study will follow national vaccination policy decisions in Hungary and standard practise. Inclusion criteria consist of the following:

- subjects who have already received a dosage of Fluval AB 2014/2015 vaccine according to the SmPC and
- subjects willing to participate in the study expressed by signing the patient information and informed consent and forms.

9.2.2. Subject identification

When inclusion is performed subjects will be assigned a subject identification code (subject number) which will ensure unambiguous identification throughout the study.

Subject identification code will be generated as follows: *H17-VV-A-NNN*

H17: mandatory, abbreviated code of the study
VV: code of the study centre (kindly refer to Annex 1)
A: age group identifier, generated as follows:
- for children aged 3-5 years: 1
- for children aged 6-12 years: 2
- for adolescents aged 13-17 years: 3
- for non-elderly adults aged 18-65 years: 4
- for elderly subjects aged over 65 years: 5

NNN: serial number per age group

9.2.3. Follow up

Patient follow-up will be performed seven (7) days after vaccination by phone contact with respect to AEs following vaccination. AEs will be recorded on Data Report Forms regarding to occurrence and severity.

A clear concise reason should be recorded in the Data Report Form for subjects ending the study prematurely. All study data from withdrawals should be retained.

9.3. Variables

The occurrence rates of reactogenicity endpoints of interest (AEIs) as well as other reported AEs will be evaluated. The following of reactogenicity endpoints are defined:

- Vaccinaton site pain
- Vaccination site erythema
- Vaccination site swelling
- Vaccination site induration
- Vaccination site numbness
- Fatigue
- Headache
- Fever
- Hyperhidrosis
- Malaise
- Chills
- Myalgia
- Arthralgia
- Nausea

9.4. Data sources

Data Report Forms will be available for data recording. However, source data will be available to document the existence of the subject and substantiate integrity of study data collected and will include the medical records of the subject and records related to vaccination.

9.5. Study size

According to Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU EMA/PRAC/222346/2014: " The PASS should be designed and put in place with defined cohorts of children and adults actively followed-up at 7 days (or up to 14 days for a live attenuated vaccine) after immunisation for the stated AEIs. As a guide, the goal should be to detect a clear change (compared to defined baseline) in the frequency and/or severity of defined local and general events in at least one hundred (100) vaccinated subjects in each defined age groups (e.g. those aged 6 months to 5 years, 6 to 12 years, 13 to 18 years, ≥ 18 years-65 years and > 65 years)."

At least one hundred (100) male and female vaccinated subjects in each defined age groups (3-5, 6-12, 13-17, 18-65 years and over 65 years) will be vaccinated and participate in the PASS, that data can be evaluated: considering approximately ~17% of drop-out (one out of six participants), in total six hundred (600) subjects will be vaccinated in order to achieve at least five hundred (500) evaluable subjects (one hundred-one hundred (100-100) subjects per each age group respectively).

9.6. Data management

During the course of this study, investigators will record AEs by telephone follow up. Data collected on each study subject will be recorded on Data Report Forms. The investigator is responsible for ensuring that all sections of each Data Report Form are completed correctly, and that entries can be verified against source data. The study monitor will review the Data Report Forms and check them for completeness and conformity. Control checks on the data included in the database will be performed at the end of the study. Clean data sets will be provided for statistical analysis and reporting.

Data Report Forms are expected to ensure awareness of the sponsor of the occurrence and severity of AEIs. Further processing of the recorded events (including further data collection and follow-up) will be performed throughout the routine Pharmacovigilance procedures of the manufacturer of Fluval AB suspension for injection, outside the scope of this study.

9.7. Data analysis

Data analysis will be based on and presented according to the 'Guidance for the format and content of the final study report of non-interventional post-authorization safety studies (EMA/48663/2013)'. All individual data will be listed. All subjects having completed the follow-up will be included in the statistical analysis.

All AEs will be coded using the latest approved version of MedDRA. The occurrence rates of AEs will be stratified per age groups and gender; summarized by System Organ Class (SOC), High Level Term (HLT) and Preferred Term (PT); and compared to that expected for Fluval AB vaccine (according to the SmPC), in order to evaluate the potential for an increased risk related to vaccination therewith, than already known.

9.8. Quality control

The study monitor will review Data Report Forms and check them for completeness and conformity. Omninvest Ltd., as sponsor of this study, is responsible for assuring proper study conduct in regard to protocol adherence and validity of the data recorded on the Data Report Forms. Omninvest Ltd. shall assign a study monitor to this study. His/her duties are to assist the investigator in the maintenance of complete, legible, well-organized, and easily retrievable data. In addition, the monitor will ensure that the investigator understands all applicable regulations concerning the study. The investigator agrees to allow the monitor direct access to all study data of the study subjects for the above purposes and agrees to assist the monitor in these activities. The investigator accepts that the monitor will visit the clinic to review and verify the data collected. The monitor will regard all information that is supplied to him or her as strictly confidential.

The sponsor will archive and retain all documents pertaining to the study for the lifetime of the product.

9.9. Limitations of the research methods

Not applicable.

9.10. Other aspects

Not applicable.

10. PROTECTION OF HUMAN SUBJECTS

The study will be conducted with the approval of National Institute of Pharmacy, Hungary (i.e. GYEMSZI-OGYI) and of Ethics Committee, Hungary (i.e. ETT-TUKEB).

Each subject will be identified by subject identification codes (subject numbers) after having entered the study which will ensure unambiguous identification throughout the study. Codes will not contain any personal data or data contributing to the identification of participants. All information gathered during the conduct of the study will be managed in line with terms of privacy in line with provisions of Hungarian laws (i.e. 1997. évi XLVII. törvény az egészségügyi és a hozzájuk kapcsolódó személyes adatok kezeléséről és védelméről and 2011. évi CXII. törvény az információs önrendelkezési jogról és az információszabadságról).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS / ADVERSE REACTIONS

Data Report Forms are expected to ensure awareness of the sponsor of the occurrence and severity of AEIs.

Further processing of the recorded events (including further data collection and follow-up) will be performed throughout the routine Pharmacovigilance procedures of the manufacturer of Fluval AB suspension for injection, outside the scope of this study.

Definition of Adverse Events (AEs)

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. This definition includes any occurrence that is new in onset, aggravated/deteriorated in severity or frequency from the baseline condition.

Abnormal results of diagnostic procedures including laboratory test abnormalities are considered AEs if they:
- result in discontinuation from the trial;
- require treatment or any other therapeutic intervention;
- require further diagnostic evaluation (excluding a repetition of the same procedure to confirm the abnormality);
- are associated with clinical signs or symptoms judged by the investigator to have a significant clinical relevance.

Definition of Adverse Events of Interest (AEIs)

Adverse Events of Interest (AEIs) are the following predefined reactogenicity endpoints of the study: vaccination site pain, vaccination site erythema, vaccination site swelling, vaccination site induration, vaccination site numbness, fatigue, headache, fever, hyperhidrosis, malaise, chills, myalgia, arthralgia, nausea.

Definition for the assessment of severity

- Mild: transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.
- Moderate: mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required.
- Severe: marked limitation in activity; some assistance usually required; medical intervention/therapy required, hospitalization possible.
- Life threatening: extreme limitation in activity; significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care probable.

Definition of age groups

Subgroups are defined according to age groups, as follows:

- Children aged between 3-5 years: A patient is belonging to age group of 3-5 years, if he/she has already been turning 3, but has not yet been turning 6 on the day of enrolment.
- Children aged between 6-12 years: A patient is belonging to age group of 6-12 years, if he/she has already been turning 6, but has not yet been turning 13 on the day of enrolment.
- Adolescents aged between 13-17 years: A patient is belonging to age group of 13-17 years, if he/she has already been turning 13, but has not yet been turning 18 on the day of enrolment.
- Adults aged between 18-65 years: A patient is belonging to age group 18-59 years, if he/she has already been turning 18, but has not yet been turning 66 on the day of enrolment.
- Elders aged over 65 years: A patient is belonging to age group over 65 years, if he/she has already been turning 66 on the day of enrolment.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

Information concerning the study drug, patent applications, processes, unpublished scientific data and other pertinent information is confidential and remains the property of Omninvest Ltd. Details should be disclosed only to the persons involved in the approval or conduct of the study. The investigator may use this information for the purpose of the study only. It is understood by the investigator that the company will use the information obtained during the study in connection with the development of the vaccine and therefore may disclose it as required to other investigators or to regulatory agencies. In order to allow for the use of the information derived from this study, the investigator understands that he has an obligation to provide the sponsor with all data obtained during the study.

Information of AEs regarding to occurrence and severity will be reported within one (1) month after stating the data collection to the National Institute of Pharmacy, Hungary (i.e. GYEMSZI-OGYI). Provisions on Expedited Summary Safety Report laid down in the 'Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU' (EMA/PRAC/222346/2014).

A Study Report 'Guidance for the format and content of the final study report of non-interventional post-authorization safety studies (EMA/48663/2013)' will be generated within six (6) months after the termination of data collection.

Further information on AEs will be communicated to the competent authorities in accordance with the Hungarian and European Union legislation of reporting in spontaneous environment.

13. REFERENCES

1. *2005. évi XCV. Törvény* - az emberi alkalmazásra kerülő gyógyszerekről és egyéb, a gyógyszerpiacot szabályozó törvények módosításáról
2. *1997. évi XLVII. törvény az egészségügyi és a hozzájuk kapcsolódó személyes adatok kezeléséről és védelméről*
3. *2011. évi CXII. törvény az információs önrendelkezési jogról és az információszabadságról*
4. *1997. évi törvény az egészségügyről*
5. *52/2005. (XI. 18) EüM rendelet* – az emberi alkalmazásra kerülő gyógyszerek forgalomba hozataláról
6. *23/2002. (V.9.) EüM rendelet* – az embereken végzett orvostudományi kutatásokról
7. *Council Regulation (EEC) 2309/93* – laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products. Amended by Commission Regulation (EC) 649/98, amending the Annex to Council Regulation (EEC) No 2309/93. The Council of the European Communities. 1993 July
8. EMEA/359381/2009 (2009). *CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine.* European Medicines Agency, EMA. 2009, September
9. EMA/PRAC/222346/2014 (2014). *Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU*. European Medicines Agency, EMA. 2014 April
10. EMA/488220/2012 (2013). *Guideline on good pharmacovigilance practices (GVP). Product. or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases.* European Medicines Agency, EMA. 2013 December
11. EMA/813938/2011 Rev 1 (2013). *Guideline on good pharmacovigilance practices (GVP) Module VIII. Post- authorization safety studies (Rev 1).* European Medicines Agency, EMA. 2013 April
12. EMA/623947/2012 (2012). *Guidance on the format and content of the protocol of non-interventional post-authorization safety studies.* European Medicines Agency, EMA. 2012 September
13. EMA/48663/2013 (2013). *Guidance for the format and content of the final study report of non-interventional post-authorization safety studies.* European Medicines Agency, EMA. 2013 July

ANNEX 1. LIST OF STAND-ALONE DOCUMENTS

Number	Doc. Ref. No.	Date	Title[1]
1	List of investigators v01	29 October 2014	List of investigators
2	FluvalAB-H-17 Data Report Form v01	29 October 2014	Data Report Form
3	FluvalAB-H-17 Patient Information for children v01	29 October 2014	Patient Information for children
4	FluvalAB-H-17 Patient Information for adolescents v01	29 October 2014	Patient Information for adolescents
5	FluvalAB-H-17 Patient Information for parents / legal representatives) v01	29 October 2014	Patient Information for parents / legal representatives)
6	FluvalAB-H-17 Patient Information for adults v01	29 October 2014	Patient Information for adults
7	FluvalAB-H-17 Informed Consent for children v01	29 October 2014	Informed Consent for children
8	FluvalAB-H-17 Informed Consent for adolescents v01	29 October 2014	Informed Consent for adolescents
9	FluvalAB-H-17 Informed Consent for parents / legal representatives) v01	29 October 2014	Informed Consent for parents / legal representatives)
10	FluvalAB-H-17 Informed Consent for adults v01	29 October 2014	Informed Consent for adults

[1] Documents are not incorporated into the text, are maintained separately from the study protocol.

ANNEX 2. ENCePP CHECKLIST FOR STUDY PROTOCOLS

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Doc.Ref. EMA/540136/2009

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

ENCePP Checklist for Study Protocols (Revision 2, amended)

Adopted by the ENCePP Steering Group on 14/01/2013

The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) welcomes innovative designs and new methods of research. This Checklist has been developed by ENCePP to stimulate consideration of important principles when designing and writing a pharmacoepidemiological or pharmacovigilance study protocol. The Checklist is intended to promote the quality of such studies, not their uniformity. The user is also referred to the ENCePP Guide on Methodological Standards in Pharmacoepidemiology which reviews and gives direct electronic access to guidance for research in pharmacoepidemiology and pharmacovigilance.

For each question of the Checklist, the investigator should indicate whether or not it has been addressed in the study protocol. If the answer is "Yes", the page number(s) of the protocol where this issue has been discussed should be specified. It is possible that some questions do not apply to a particular study (for example in the case of an innovative study design). In this case, the answer 'N/A' (Not Applicable) can be checked and the "Comments" field included for each section should be used to explain why. The "Comments" field can also be used to elaborate on a "No" answer.

This Checklist should be included as an Annex by marketing authorisation holders when submitting the protocol of a non-interventional post-authorisation safety study (PASS) to a regulatory authority (see the Guidance on the format and content of the protocol of non-interventional post-authorisation safety studies). Note, the Checklist is a supporting document and does not replace the format of the protocol for PASS as recommended in the Guidance and Module VIII of the Good pharmacovigilance practices (GVP).

Study title:
Prospective non-interventional cohort study to assess safety and tolerability of Fluval AB 2014/2015 trivalent seasonal influenza vaccine in children, adolescents, adults and elderly subjects

Study reference number:
FluvalAB-H-17

Section 1: Milestones	**Yes**	**No**	**N/A**	**Page Number(s)**
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[1]	☐	☐	☒	
1.1.2 End of data collection[2]	☒	☐	☐	11
1.1.3 Study progress report(s)	☐	☐	☒	
1.1.4 Interim progress report(s)	☒	☐	☐	11
1.1.5 Registration in the EU PAS register	☒	☐	☐	1
1.1.6 Final report of study results.	☒	☐	☐	11

Comments:
None.

[1] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[2] Date from which the analytical dataset is completely available.

Section 2: Research question	Yes	No	N/A	Page Number(s)
2.1 Does the formulation of the research question and objectives clearly explain:				
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	13
2.1.2 The objective(s) of the study?	☒	☐	☐	13
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	14
2.1.4 Which formal hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

None.

Section 3: Study design	Yes	No	N/A	Page Number(s)
3.1 Is the study design described? (e.g. cohort, case-control, randomised controlled trial, new or alternative design)	☒	☐	☐	14
3.2 Does the protocol specify the primary and secondary (if applicable) endpoint(s) to be investigated?	☒	☐	☐	13
3.3 Does the protocol describe the measure(s) of effect? (e.g. relative risk, odds ratio, deaths per 1000 person-years, absolute risk, excess risk, incidence rate ratio, hazard ratio, number needed to harm (NNH) per year)	☒	☐	☐	14

Comments:

None.

Section 4: Source and study populations	Yes	No	N/A	Page Number(s)
4.1 Is the source population described?	☒	☐	☐	14
4.2 Is the planned study population defined in terms of:				
4.2.1 Study time period?	☒	☐	☐	11
4.2.2 Age and sex?	☒	☐	☐	14, 16
4.2.3 Country of origin?	☐	☐	☒	
4.2.4 Disease/indication?	☒	☐	☐	1,14
4.2.5 Co-morbidity?	☒	☐	☐	29
4.2.6 Seasonality?	☒	☐	☐	29
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	14

Comments:

None.

Section 5: Exposure definition and measurement	Yes	No	N/A	Page Number(s)
5.1 Does the protocol describe how exposure is defined and measured? (e.g. operational details for defining and categorising exposure)	☒	☐	☐	14, 29
5.2 Does the protocol discuss the validity of exposure measurement? (e.g. precision, accuracy, prospective				

Section 5: Exposure definition and measurement	Yes	No	N/A	Page Number(s)
ascertainment, exposure information recorded before the outcome occurred, use of validation sub-study)	☐	☐	☒	
5.3 Is exposure classified according to time windows? (e.g. current user, former user, non-use)	☒	☐	☐	14, 15
5.4 Is exposure classified based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.5 Does the protocol specify whether a dose-dependent or duration-dependent response is measured?	☐	☐	☒	

Comments:

Biological mechanism of action, pharmacokinetics, pharmacodynamics of the drug, dose-dependent and duration dependent response are not addressed.

Section 6: Endpoint definition and measurement	Yes	No	N/A	Page Number(s)
6.1 Does the protocol describe how the endpoints are defined and measured?	☒	☐	☐	13, 14
6.2 Does the protocol discuss the validity of endpoint measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, prospective or retrospective ascertainment, use of validation sub-study)	☐	☐	☒	

Comments:

None.

Section 7: Confounders and effect modifiers	Yes	No	N/A	Page Number(s)
7.1 Does the protocol address known confounders? (e.g. collection of data on known confounders, methods of controlling for known confounders)	☐	☐	☒	
7.2 Does the protocol address known effect modifiers? (e.g. collection of data on known effect modifiers, anticipated direction of effect)	☒	☐	☐	29

Comments:

None.

Section 8: Data sources	Yes	No	N/A	Page Number(s)
8.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
8.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview, etc.)	☒	☐	☐	16
8.1.2 Endpoints? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics, etc.)	☒	☐	☐	16, 19
8.1.3 Covariates?	☒	☐	☐	15
8.2 Does the protocol describe the information available from the data source(s) on:				
8.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☒	☐	☐	16
8.2.2 Endpoints? (e.g. date of occurrence, multiple event, severity measures related to event)	☒	☐	☐	16, 19
8.2.3 Covariates? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, life style, etc.)	☒	☐	☐	15

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Section 8: Data sources	Yes	No	N/A	Page Number(s)
8.3 Is a coding system described for:				
8.3.1 Diseases? (e.g. International Classification of Diseases (ICD)-10)	☐	☐	☒	
8.3.2 Endpoints? (e.g. Medical Dictionary for Regulatory Activities (MedDRA) for adverse events)	☒	☐	☐	17
8.3.3 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC)Classification System)	☒	☐	☐	1, 29
8.4 Is the linkage method between data sources described? (e.g. based on a unique identifier or other)	☒	☐	☐	14

Comments:

None.

Section 9: Study size and power	Yes	No	N/A	Page Number(s)
9.1 Is sample size and/or statistical power calculated?	☒	☐	☐	14

Comments:

None.

Section 10: Analysis plan	Yes	No	N/A	Page Number(s)
10.1 Does the plan include measurement of excess risks?	☒	☐	☐	15
10.2 Is the choice of statistical techniques described?	☒	☐	☐	13
10.3 Are descriptive analyses included?	☐	☐	☒	
10.4 Are stratified analyses included?	☒	☐	☐	16, 17
10.5 Does the plan describe methods for adjusting for confounding?	☐	☐	☒	
10.6 Does the plan describe methods addressing effect modification?	☐	☐	☒	

Comments:

None.

Section 11: Data management and quality control	Yes	No	N/A	Page Number(s)
11.1 Is information provided on the management of missing data?	☒	☐	☐	16
11.2 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	21
11.3 Are methods of quality assurance described?	☒	☐	☐	17
11.4 Does the protocol describe possible quality issues related to the data source(s)?	☒	☐	☐	17
11.5 Is there a system in place for independent review of study results?	☒	☐	☐	18, 21

Comments:

None.

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Section 12: Limitations	Yes	No	N/A	Page Number(s)
12.1 Does the protocol discuss: 12.1.1 Selection biases? 12.1.2 Information biases? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods)	☐ ☐	☐ ☐	☒ ☒	
12.2 Does the protocol discuss study feasibility? (e.g. sample size, anticipated exposure, duration of follow-up in a cohort study, patient recruitment)	☒	☐	☐	14, 15
12.3 Does the protocol address other limitations?	☐	☐	☒	

Comments:

None.

Section 13: Ethical issues	Yes	No	N/A	Page Number(s)
13.1 Have requirements of Ethics Committee/Institutional Review Board approval been described?	☒	☐	☐	6, 21
13.2 Has any outcome of an ethical review procedure been addressed?	☒	☐	☐	6
13.3 Have data protection requirements been described?	☒	☐	☐	18

Comments:

None.

Section 14: Amendments and deviations	Yes	No	N/A	Page Number(s)
14.1 Does the protocol include a section to document future amendments and deviations?	☒	☐	☐	10

Comments:

None.

Section 15: Plans for communication of study results	Yes	No	N/A	Page Number(s)
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	21
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	21

Comments:

None.

Name of the main author of the protocol: ORSOLYA GYURKÁN PHARMD

Date: 29/10/2014

Signature: _____

ANNEX 3. ADDITIONAL INFORMATION

ANNEX 3.1 Summary of Product Characteristics (Hungarian)

1. A GYÓGYSZER NEVE

Fluval AB szuszpenziós injekció
influenza vakcina (teljes vírus, inaktivált, adjuvált)
(a 2014/2015-es szezonra)

2. MINŐSÉGI ÉS MENNYISÉGI ÖSSZETÉTEL

1 adag (0,5 ml) vakcina összetétele a 2014/2015-es szezonra:

A vakcina formaldehiddel inaktivált, teljes virion* tartalmaz az alábbi antigénösszetétellel:

A/California/7/2009(H1N1) eredetű NYMC X-179A reasszortáns törzs	min.15µg HA**
A/Texas/50/2012 (H3N2) eredetű NYMC X-223A reasszortáns törzs	min.15µg HA**
B/Massachusetts/2/2012 (vad típus)	min.15µg HA**

* tojáson szaporított
** hemagglutinin

A vakcina megfelel az Egészségügyi Világszervezet (WHO) és az Európai Gyógyszerügynökség (EMA) 2014/2015-es szezonra vonatkozó ajánlásának.

1 dózis max. 1µg ovalbumint, 0,5 µg gentamicint, neomicint, vankomicint és ciprofloxacint tartalmaz.

Adjuváns: Alumínium-foszfát gél (max. 0,625 milligramm Al^{3+})

Ismert hatású segédanyagok: Tiomerzál (max. 53 mikrogramm)

A segédanyagok teljes listáját lásd a 6.1 pontban.

3. GYÓGYSZERFORMA

Szuszpenziós injekció.
Fehéres, enyhén opaleszkáló szuszpenzió.

4. KLINIKAI JELLEMZŐK

4.1 Terápiás javallatok

Influenza profilaxisa 3 éves kortól. Különösen ajánlott azok részére, akiknél az influenza fertőzés vagy az ahhoz társuló szövődmények nagy kockázatot jelentenek.

Az oltóanyag azon influenzatörzsek okozta megbetegedésektől véd, amelyek antigénszerkezete ugyanolyan, vagy hasonló a vakcinába beépített prototípus törzsekhez. Egyéb kórokozók által kiváltott influenzaszerű megbetegedések ellen nem nyújt védelmet.

A vakcinát a hivatalos útmutatásoknak megfelelően kell alkalmazni.

4.2 Adagolás és alkalmazás

Adagolás

18 éven felüli felnőttek és idősek: 1 × 0,5 ml

Gyermekek:
12-18 éves serdülők: 1 × 0,5 ml
3-12 éves gyermekek: 1 × 0,25 ml

A Fluval AB vakcina biztonságosságát és hatásosságát 3 évesnél fiatalabb gyermekek esetében nem igazolták.

Az immunizálás egyszeri oltással történik.

Az alkalmazás módja

Az oltóanyagot a mellékelt steril fecskendővel és tűvel a bőr dezinficiálását követően intramuszkulárisan kell a felkar deltaizmába beadni.

A 3-12 éves gyermekek oltása esetében a felrázott oltóanyag teljes mennyiségét a mellékelt steril tűvel és fecskendővel fel kell szívni, majd a fecskendőt függőleges helyzetben tartva annyi oltóanyagot kell kinyomni a fecskendőből, hogy a fecskendőben maradó oltóanyag mennyisége 0,25 ml legyen. A fecskendőben maradó 0,25 ml oltóanyagot a bőr dezinficiálását követően intramuszkulárisan kell a felkar deltaizmába beadni.

A vakcina intravaszkuláris beadása tilos!

A védettség általában 2-3 hét alatt fejlődik ki és több hónapig tart, ezért célszerű az oltást a járványidőszakot megelőzően elvégezni.

Óvintézkedések a gyógyszer felhasználása vagy alkalmazása előtt

A gyógyszer alkalmazás előtti előkészítésére vonatkozó utasításokat lásd a 6.6 pontban.

4.3 Ellenjavallatok

A készítmény hatóanyagaival vagy a 6.1 pontban felsorolt bármely segédanyagával, mint például a tiomerzállal vagy bármely olyan összetevővel, amely nyomokban jelen lehet, mint pl. tojással (ovalbumin), formaldehiddel, gentamicinnel, neomicinnel, vankomicinnel, illetve ciprofloxacinnal szembeni túlérzékenység.

Bármely vakcinával történt oltás következtében kialakult súlyos alábbi szövődmény előfordulása a kórelőzményben: enkefalitisz/enkefalopátia, nem lázas konvulzió, Guillain-Barré szindróma, vaszkulitisz, neuritisz, faciális parézis.

Akut, lázas megbetegedés esetén az oltóanyag csak a tünetek elmúlta után 2-3 nappal adható.

3 évnél fiatalabb gyermeknél alkalmazása ellenjavallt (lásd 4.2 pont).

4.4 Különleges figyelmeztetések és az alkalmazással kapcsolatos óvintézkedések

Mint minden injektábilis vakcina esetében, megfelelő orvosi háttérnek kell készenlétben állnia az esetlegesen előforduló anafilaxiás reakció kezelésére.

A Fluval AB szuszpenziós injekciót semmilyen körülmények között nem szabad intravaszkulárisan beadni!

Endogén vagy iatrogén okból immunszupprimált betegekben elégtelen lehet az immunválasz.

A vakcinát fokozott elővigyázattal kell alkalmazni olyan személyek esetében, akiknél ismert fokozott görcskészség áll fenn lázas állapot esetén, mivel a vakcina mellékhatásaként láz jelentkezhet. Ilyen esetben javasolt az oltott személy vakcinációt követő fokozott megfigyelése, illetve a láz megelőzése.

4.5 Gyógyszerkölcsönhatások és egyéb interakciók

A Fluval AB szuszpenziós injekció együttes alkalmazásáról a Fluval P szuszpenziós injekcióval rendelkezésre állnak adatok. A 18 évesnél idősebb személyek részvételével elvégzett klinikai vizsgálatok eredménye alapján a Fluval P vakcina a Fluval AB szezonális influenza elleni vakcinával külön-külön végtagokon oltva egy időben alkalmazható.

Influenza vakcinációt követően, HIV 1, hepatitisz C és különösen HTLV 1 antitestekre vonatkozóan ELISA módszerrel végzett szerológiai vizsgálatokban téves pozitív eredmények fordultak elő.
Western Blot technika alkalmazásával az ELISA módszerrel kapott fals pozitív eredmények kiszűrhetők. Az átmeneti fals pozitív eredményeket a vakcina által kiváltott IgM ellenanyag válasz okozhatja.

Gyermekek

Interakciós vizsgálatokat csak felnőttek körében végeztek.

4.6 Termékenység, terhesség és szoptatás

Terhesség

A terheseken végzett oltásokból származó kevés adat nem utal a vakcinálásnak tulajdonítható nemkívánatos magzati vagy anyai következményekre.
Terhes nők oltása az influenza megbetegedés és következményeinek, valamint a védőoltás nem kívánt mellékhatásainak mérlegelése alapján javasolt.

Szoptatás

A Fluval AB szuszpenziós injekció szoptatás alatt alkalmazható.

Termékenység

Nem állnak rendelkezésre termékenységre vonatkozó adatok.

4.7 A készítmény hatásai a gépjárművezetéshez és a gépek kezeléséhez szükséges képességekre

A Fluval AB szuszpenziós injekció nem, vagy csak elhanyagolható mértékben befolyásolja a gépjárművezetéshez és a gépek kezeléséhez szükséges képességeket.

4.8 Nemkívánatos hatások, mellékhatások

Az oltóanyag elölt vírust tartalmaz, ezért az oltás következményeként a vakcinától nem alakulhat ki influenza fertőzés. Az oltást követő légúti betegség véletlen egybeesés következménye, és más légúti kórokozó válthatja ki. A leggyakoribb mellékhatás az oltást követően a beadás helye körül kialakuló bőrpír, ami általában 48 órán belül megszűnik.

Klinikai vizsgálatokban megfigyelt nemkívánatos hatások

A trivalens inaktivált influenza vakcina biztonságos alkalmazását az éves felújítási követelmények részeként kontrollcsoport nélküli nyílt vizsgálatokban értékelték, amelyekben évenként legalább ötven 18 és 60 év közötti felnőtt és ötven idős korú (61 éves és idősebb) vesz részt.

A jelentett mellékhatások előfordulási gyakoriságuk szerint:
Nagyon gyakori (≥1/10)
Gyakori (≥1/100 – <1/10)
Nem gyakori (≥1/1000 – <1/100)
Ritka (≥1/10 000 – <1/1000)
Nagyon ritka (<1/10 000)
Nem ismert (a rendelkezésre álló adatokból nem állapítható meg)

Szervrendszer	**Nagyon gyakori ≥1/10**	**Gyakori ≥1/100 – <1/10**	**Nem gyakori ≥1/1000 – <1/100**	**Ritka ≥1/10 000 – <1/1000**	**Nagyon ritka <1/10 000**
Emésztőrendszeri betegségek és tünetek			Hányinger		
A csont- és izomrendszer, valamint a kötőszövet betegségei és tünetei		Izomfájdalom Ízületi fájdalom			
Általános tünetek, az alkalmazás helyén fellépő reakciók	Helyi fájdalom	Helyi bőrpír, duzzanat, induratio, zsibbadás Fáradékonyság Fejfájás Láz Verítékezés Rossz közérzet	Helyi érzékenység Hidegrázás		

Gyermekek

A Fluval AB biztonságosságát és hatásosságát vizsgáló klinikai vizsgálati csoportba 9 fő 3-12 év közötti gyermeket és 10 fő 12-18 év közötti serdülőt vontak be.

Az észlelt nemkívánatos eseményeket az alábbi táblázat tartalmazza előfordulási gyakoriság és szervrendszer szerinti csoportosításban:

Szervrendszer	**Nagyon gyakori ≥1/10**	**Gyakori ≥1/100 – <1/10**	**Nem gyakori ≥1/1000 – <1/100**	**Ritka ≥1/10 000 – <1/1000**	**Nagyon ritka <1/10 000**
Emésztőrendszeri betegségek és tünetek		Hasmenés			
Általános tünetek, az alkalmazás helyén fellépő reakciók	Helyi fájdalom* Fejfájás*	Karzsibbadás* Láz Fáradékonyság*			

*Valamennyi tünet enyhe volt és 2-3 napon belül spontán megszűnt.

A forgalomba hozatalt követő megfigyelések

A fentieken kívül az alábbi nemkívánatos eseményeket jelentették:

Immunrendszeri betegségek és tünetek:
Allergiás reakciók, ITP-ben (Idiopátiás Trombocitopéniás Purpura) szenvedő páciensnél a vérlemezke-szám csökkenése

Idegrendszeri betegségek és tünetek:
Parsonage-Turner szindróma, felső végtagi parézis, nervus trochlearis parézis, neuritis

Emésztőrendszeri betegségek és tünetek:
Nyelési nehezítettség, diarrhoea*, nausea*, vomitus*

A bőr és a bőr alatti szövet betegségei és tünetei:
Bőr égő érzése, kiütés, viszketés, urtikária, arc bőrpír, ecchymosis*

*A Fluval P szuszpenziós injekcióval történt együttadáskor jelentkező nemkívánatos események.

Általános tünetek, az alkalmazás helyén fellépő reakciók:
Elesettség, gyengeség, hőemelkedés, arc duzzanat, szem duzzanat, oltási hely melegség, haematoma.

Egyéb, a szakirodalom szerint lehetséges szövődmények: enkefalopátia, Guillain Barré szindróma (GBS), Gianotti-Crosti szindróma.

Gyermekek

A 3-12 éves korosztályban 1-1 oltási reakciót jelentettek, melyek enyhe lefolyásúak voltak és 2-3 napon belül spontán elmúltak.

Általános tünetek, az alkalmazás helyén fellépő reakciók:
Oltási hely bőrpír, izomfájdalom

Ez a gyógyszerkészítmény tiomerzált (szerves higanyvegyületet) tartalmaz tartósítószerként, ezért érzékenységi reakciók előfordulhatnak (lásd 4.3 pont).

Feltételezett mellékhatások bejelentése
A gyógyszer engedélyezését követően lényeges a feltételezett mellékhatások bejelentése, mert ez fontos eszköze annak, hogy a gyógyszer előny/kockázat profilját folyamatosan figyelemmel lehessen kísérni.
Az egészségügyi szakembereket kérjük, hogy jelentsék be a feltételezett mellékhatásokat a hatóság részére az V. függelékben található elérhetőségek valamelyikén keresztül.

4.9 Túladagolás

A vakcina túladagolásával kapcsolatosan nem áll rendelkezésre adat.

5. FARMAKOLÓGIAI TULAJDONSÁGOK

5.1 Farmakodinámiás tulajdonságok

Farmakoterápiás csoport: Influenza vakcina, ATC kód: J07BB01

A szerológiai védelem általában 2-3 hét alatt kialakul. Az oltás utáni immunitás tartama homológ vírustörzsekkel vagy a vakcinában alkalmazott törzsekhez közelálló törzsekkel szemben különböző lehet, általában több hónap.

A vakcina megfelel az Európai Gyógyszerügynökség által meghatározott immunogenitási kritériumoknak.

5.2 Farmakokinetikai tulajdonságok

Nem értelmezhető.

5.3 A preklinikai biztonságossági vizsgálatok eredményei

Nem releváns.

6. GYÓGYSZERÉSZETI JELLEMZŐK

6.1 Segédanyagok felsorolása

Alumínium-klorid-hexahidrát,
trinátrium-foszfát-dodekahidrát,
kálium-klorid,
tiomerzál,
dinátrium-hidrogén-foszfát-dihidrát,
kálium-dihidrogén-foszfát,
nátrium-klorid,
injekcióhoz való víz.

6.2 Inkompatibilitások

Kompatibilitási vizsgálatok hiányában ez a gyógyszer nem keverhető más gyógyszerekkel.

6.3 Felhasználhatósági időtartam

2015. szeptember
Felbontás után a vakcinát haladéktalanul fel kell használni.

6.4 Különleges tárolási előírások

Hűtőszekrényben (2°C - 8°C) tárolandó.
Nem fagyasztható!
A fénytől való védelem érdekében az eredeti csomagolásban tárolandó.
A vakcina első felbontására vonatkozó tárolási előírásokat lásd a 6.3 pontban.

6.5 Csomagolás típusa és kiszerelése

0,5 ml szuszpenzió törőponttal ellátott, üveg (I. típusú) ampullába töltve.

Egy adag:
Egy ampulla, egy steril fecskendő és egy tű dobozban.

Húsz ampulla dobozban.

6.6 A megsemmisítésre vonatkozó különleges óvintézkedések és egyéb, a készítmény kezelésével kapcsolatos információk

Az oltóanyagot beadás előtt hagyni kell szobahőmérsékletűre melegedni.
Az ampulla felnyitása előtt győződjön meg annak sértetlenségéről.
Az ampulla felnyitás előtt felrázandó!
Felrázás után ellenőrizze, hogy a szuszpenzió homogén-e.
Nem homogén oltóanyag felhasználása tilos!

Bármilyen fel nem használt gyógyszer, illetve hulladékanyag megsemmisítését a gyógyszerekre vonatkozó előírások szerint kell végrehajtani.

Megjegyzés: ✠ (egykeresztes)
Osztályozás: II. csoport
Kizárólag orvosi rendelvényhez kötött gyógyszer (V).

7. A FORGALOMBA HOZATALI ENGEDÉLY JOGOSULTJA

OMNINVEST Oltóanyagtermelő és Kutatásfejlesztő Kereskedelmi Kft., 2097 Pilisborosjenő, Fő u. 7.

8. A FORGALOMBA HOZATALI ENGEDÉLY SZÁMA(I)

OGYI-T-8998/01 1×
OGYI-T-8998/02 20×

9. A FORGALOMBA HOZATALI ENGEDÉLY ELSŐ KIADÁSÁNAK/ MEGÚJÍTÁSÁNAK DÁTUMA

A forgalomba hozatali engedély első kiadásának dátuma: 2003. augusztus 05.

A forgalomba hozatali engedély legutóbbi megújításának dátuma: 2009. május 11.

10. A SZÖVEG ELLENŐRZÉSÉNEK DÁTUMA

2014. október 18.