Summary Report of Benefit-Risk Assessment

AREXVY POWDER AND SUSPENSION FOR INJECTION 120MCG/0.5ML

NEW DRUG APPLICATION

Active Ingredient(s)	RSVPreF3 antigen
Product Registrant	GlaxoSmithkline Pte Ltd.
Product Registration Number	SIN17008P
Application Route	Abridged evaluation
Date of Approval	10 May 2024

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Table of Contents

A INTRODUCTION 3
B ASSESSMENT OF PRODUCT QUALITY 3
C ASSESSMENT OF CLINICAL EFFICACY 4
D ASSESSMENT OF CLINICAL SAFETY 8
E ASSESSMENT OF BENEFIT-RISK PROFILE 10
F CONCLUSION 11
APPROVED PACKAGE INSERT AT REGISTRATION 12

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A INTRODUCTION

Arexvy is indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 60 years of age and older.

Arexvy is a recombinant protein vaccine with RSVPreF3 antigen, an engineered version of the trimeric RSV F surface glycoprotein, stabilised in a prefusion conformation, adjuvanted by AS01E.

Arexvy is available as a powder and suspension for suspension for injection containing 120mcg/0.5mL of recombinant respiratory syncytial virus pre-fusion F protein (RSVPreF3) antigen. The product contains an antigen vial and an adjuvant vial. Other than the RSVPreF3, the antigen vial contains trehalose dihydrate, polysorbate 80, potassium dihydrogen phosphate and dipotassium phosphate. The AS01E adjuvant vial contains a suspension of Quillaja saponaria Molina, fraction 21 (QS-21), 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL), dioleoyl phosphatidylcholine, cholesterol, sodium chloride, disodium phosphate, anhydrous, potassium dihydrogen phosphate and water for injections.

B ASSESSMENT OF PRODUCT QUALITY

The drug substance, RSVPreF3, and the antigen vial for Arexvy Powder and Suspension for Suspension for Injection 120mcg/0.5mL are manufactured at [redacted]. The adjuvant vial is manufactured at both [redacted] and [redacted].

Drug substance:

Adequate controls have been presented for the cell banks. The in-process control tests and acceptance criteria applied during the manufacturing of the drug substance are considered appropriate. The drug substance manufacturer is compliant with Good Manufacturing Practice (GMP). Process validation was conducted on three consecutive production-scale batches.

The characterisation of the drug substance and its impurities has been appropriately performed. Potential and actual impurities are adequately controlled in the manufacturing process.

The drug substance specifications were established in accordance with ICH Q6B, and the impurity limits have been appropriately qualified. The analytical methods used were adequately described and non-compendial methods have been validated in accordance with ICH guidelines, with information on the reference standards used for identity, assay and impurities testing presented.

The stability data presented was adequate to support the storage of the drug substance at -45°C with a shelf life of 24 months. The packaging consists of 1,000 mL high-density polyethylene bottles closed by polypropylene screw caps.

Drug product:

The manufacturing process of the antigen vial involves homogenisation of the formulated drug substance, followed by sterile filtration, aseptic filling and lyophilisation. The manufacturing

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process of the adjuvant vial involves formulation, sterile filtration and aseptic filling. These are considered to be standard manufacturing processes.

The manufacturing sites are compliant with GMP. Proper development and validation studies were conducted. It has been demonstrated that the manufacturing process is reproducible and consistent. Adequate in-process controls are in place. The specifications have been established in accordance with ICH Q6B, and impurity limits were adequately qualified. The analytical methods used were adequately described and non-compendial methods have been validated in accordance with ICH guidelines, with information on the reference standards used for identity, assay and impurities testing presented.

The stability data submitted was adequate to support the approved shelf-life of 36 months at 2-8°C, with protection from light. The shelf life after reconstitution is up to 4 hours at below 25°C or at 2-8°C. The container closure system for both the antigen and adjuvant are [redacted] Type I glass vials with rubber stoppers and aluminium caps.

C ASSESSMENT OF CLINICAL EFFICACY

The clinical efficacy of Arexvy for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in adults 60 years of age and older was based primarily on one pivotal Phase 3 study RSV OA=ADJ-006, three phase 3 supportive studies (Study RSV OA=ADJ-004, Study RSV OS=ADJ-007 and RSV OA=ADJ-009) and one phase1/2 dose-finding study (Study RSV OA=ADJ-002).

Study RSV OA=ADJ-002 was a phase 1/2, randomised, placebo-controlled, observer-blind, multi-centre study designed for selection of dose and formulation of RSVPreF3 vaccine. The study consisted of two parts (Part A and B). Part A comprised of 3 non-adjuvanted formulation groups for three dose levels (30 µg, 60 µg, and 120 µg) and a placebo group with1:1:1:1 randomisation. Part B expanded to 10 parallel groups with 1:1:1:1:1:1:1:1:1:1 randomisation, investigating the three dose levels with or without adjuvant ($ASO1_E$ or $ASO1_B$[1]) and a placebo group. The vaccine was administered intramuscularly in a 2-dose schedule (0, 2-month) to young adults aged 18-40 years (in part A) and older adults aged 60-80 years (in part B). The study demonstrated a dose-dependent increase in neutralising antibody titres from the baseline of 4.5 to 8.0-fold across the dose range of 30µg to 120µg, regardless of whether the vaccine was adjuvanted or not. The adjuvanted formulations did not produce an increase in neutralising antibody titres for the respective doses compared to the non-adjuvanted formulations. However, the adjuvanted formulations elicited higher cell-mediated immunity, with a 2.2 to 3.2-fold increase in geometric mean levels of RSVPreF3 specific poly-positive CD4+ T cells, compared to a 1.7 to 2.0-fold increase in the unadjuvanted formulation. There was no significant boosting in neutralising antibody titres observed with the second dose compared to the titres observed with the first dose in all the dose groups, suggesting that a single dose would be adequate to achieve the optimal immune response. $ASO1_E$ adjuvanted formulations exhibited fewer adverse events compared to $ASO1_B$ adjuvanted formulations. Based on these results, a single dose of 120µg RSVPreF3/$AS01_E$ was selected for further development.

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[1] *Adjuvant system 1 (ASO1) is a liposome based adjuvant formulation containing monophosphoryl lipid A (MPL) and Quillaja Saponaria (QS-21) developed by GSK. ASO1B contains 50 µg MPL and 50 µg QS-21. ASO1E is the lower dose version containing 25 µg MPL and 25 µg QS-21.*

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Pivotal study RSV OA=ADJ-006 is an ongoing phase 3 trial assessing the efficacy and safety of a single dose and annual revaccination of the RSVPreF3 vaccine in adults aged 60 years and above. This was a multi-regional study involving multiple European countries, US, Japan, and South Korea in the Northern Hemisphere (NH), as well as Australia, New Zealand, and South Africa in the Southern Hemisphere (SH). The study was initiated in May 2021 and the primary efficacy analysis was based on data cut-off date in April 2022 to cover the first RSV seasons in both NH and SH. The placebo-controlled design was deemed appropriate given the absence of an approved RSV vaccine at the time. The study included subjects with risk factors for severe RSV infection, such as chronic heart or lung disease, certain other underlying medical conditions, and residence in long-term care facilities. The Charlson Comorbidity Index was used to categorise participants into low/medium and high-risk groups, ensuring inclusion of individuals with varying comorbidity levels. Overall, the study design was considered acceptable for its intended purpose.

The primary efficacy endpoint of Study RSV OA=ADJ-006 was vaccine efficacy (VE) defined as the first occurrence of qRT-PCR-confirmed RSV-A and/or B-associated lower respiratory tract disease (LRTD) 15 days post-vaccination during the first season, confirmed by an external adjudication committee. The secondary endpoints included VE against RSV-confirmed LRTD by RSV subtype, age groups, baseline comorbidities, and frailty status. Additional endpoints evaluated efficacy against severe RSV-confirmed LRTD, RSV-confirmed acute respiratory infection (ARI), any ARI and any LRTD regardless of cause, and human metapneumovirus (hMPV)-confirmed LRTD. The study also assessed the prevention of hospitalisations and complications related to respiratory diseases. Immunogenicity endpoints were assessed in a subset of 1800 subjects (~7% of the total population). Immunogenicity assays used were neutralisation assays for the determination of functional antibodies against RSV-A and RSV-B and Enzyme-linked immunosorbent assay (ELISA) for measurement of IgGs binding to the RSVPreF3 protein. Cell mediated immunity was characterised by the evaluation of the RSVPreF3-specific CD4+ and CD8+ T-cell frequencies using intracellular cytokine staining assay performed on peripheral blood mononuclear cell samples. The immunogenicity endpoints included percentage of participants with RSVPreF3- specific IgGs above pre-defined assay cut-offs (25 Elisa Units/ml), neutralising antibody (nAbs) geometric mean titres (GMTs), and mean geometric increase in titres from baseline.

The original sample size for the study was determined assuming an attack rate of RSV confirmed LRTD around 0.6% during the first season. Due to the potential impact of the COVID-19 pandemic measures on RSV circulation and difficulty in estimating the attack rate for Season 1, the sample size was increased to 23,000 in the NH assuming a lower attack rate of 0.42% to mitigate risks of reduced RSV incidence. The efficacy of the RSVPreF3 OA investigational vaccine against RSV-confirmed LRTD was demonstrated if the lower limit of the 2-sided confidence interval of vaccine efficacy was above 20%. The primary analysis was planned after accruing at least 56 externally adjudicated RSV-confirmed LRTD cases. An optional interim analysis was planned if the required number of events was not achieved at the end of Season 1 in the NH. The interim analysis was considered the final analysis if the pre-defined criteria for efficacy were met. Multiplicity was adjusted for the interim analysis and the data was assessed for 96.95% CI. The VE for the subsequent seasons is still ongoing. Secondary endpoints were not adjusted for multiplicity at this interim analysis and were considered exploratory.

The modified exposed set (mES) included 24,960 subjects (12,466 RSVPreF3, 12,494 placebo). Participants were predominantly from North America (37.7%) and Europe (47.4%), with smaller representations from Asia (7.0%) and the Southern Hemisphere (7.8%). The cohort was mostly White (79.4%), with 8.7% Black or African American and 7.6% Asian. The

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median age was 69 years, with 74.5% aged 65 or older, 44.1% aged 70 or older and 8.2% aged 80 years or older. The study population had a balanced gender distribution with 51.7% females. Most participants (98.8%) lived in the general community, with a small minority (1.2%) living in a long-term care facility. Frailty assessment by Gait speed test showed 38.3% as pre-frail and 1.5% as frail. Comorbidities were present in 39.3% of participants, with 33.5% categorised as high risk. Cardiorespiratory and endocrine-metabolic conditions were reported at rates similar to the general population. Overall, the mES participants' demographic and baseline characteristics comprehensively represented the target population, encompassing the relevant age group and comorbidity statuses.

The study demonstrated a VE of 82.6% (96.95% CI: 57.89, 94.08) against symptomatic RSV RT-PCR confirmed LRTD during the first RSV season. This season predominantly included season 1 of the Northern Hemisphere and part of season 1 of the Southern Hemisphere, with a median follow-up of 6.7 months. Various sensitivity analyses supported the primary efficacy results. The VE against LRTD was consistent across RSV subtypes, with 84.6% (95% CI: 32.1-98.3) for RSV-A and 80.9% (95% CI: 49.4-94.3) for RSV-B.

Consistent VE was observed across various subgroups. High VE was demonstrated in participants with at least one chronic medical condition (94.6%; 95% CI: 65.9-99.9), those without chronic conditions (72.5%; 95% CI: 30.0-90.9), and those classified as pre-frail at baseline (92.9%; 95% CI: 53.4-99.8). However, VE was inconclusive in adults 80 years and older (33.8%; 95% CI: -477.7-94.5) and those classified as frail at baseline (14.9%; 95% CI: -6638.7-98.9) due to insufficient event rates. Despite inconclusive vaccine efficacy results in some subgroups due to low event rates, comparable immunogenicity (mean geometric increase of RSV-A/RSV-B neutralizing antibody titres) across all age groups and frailty statuses suggest similar efficacy in these subgroups.

The study demonstrated high VE against complications from RSV-confirmed respiratory disease (88.86%; 95% CI: 19.58, 99.75) and severe RSV-confirmed LRTD (94.10%; 95% CI: 62.37, 99.86). However, these results require careful interpretation. Severe disease events were primarily based on investigator determination rather than objective criteria for supportive respiratory therapy, with only 2 patients in the placebo arm and none in the vaccine arm requiring such therapy. Consequently, the reported VE against severe disease may not accurately represent VE against the objective definition. No conclusion could be drawn on VE against hospitalisation due to RSV-confirmed respiratory disease. In terms of durability of vaccine, VE analysis 2 throughout season 1 of the Southern Hemisphere, with a median follow-up of 11 months, demonstrated sustained VE of 78.9%, indicating long-term protection.

Secondary immunogenicity analyses from the pivotal study and Study 004 showed a 7 to 10-fold mean geometric increase in nAbs against both RSV-A and RSV-B viruses. Study-004 revealed a waning of nAbs at 6 months, though titres remained above pre-vaccination levels. Lower VE against acute respiratory infection (ARI) in subjects vaccinated 2-5 months before the season start (VE: 63.09%; 95% CI: 36.38, 79.42) compared to those vaccinated one month prior (VE: 81.92%; 95% CI: 61.17, 92.65). Longer-term follow-up is needed to assess the potential need for a booster dose.

The study did not indicate any vaccine-mediated enhancement of disease. Despite administration 5-6 months before the season's start and some waning of antibody titres at 6 months, no enhanced disease was observed in the vaccine arm during the 11-month follow-up in view that there was no imbalance in severe disease between vaccine and placebo arms. However, the available clinical data lacked information on long-term protection duration, revaccination requirements, or use in immunocompromised subjects.

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Efficacy results from pivotal study RSV OA=ADJ-006

Endpoints	RSVPreF3 (N=12,466)	Placebo (N=12,494)
Primary efficacy endpoint (Interim VE analysis)- data lock point: 11 April 2022		
RSV-confirmed LRTD events Incidence Event rate (per 1000)	7 1.0	40 5.8
VE (96.95% CI) p-value (Poisson method)	82.58% (96.95% CI: 57.89,94.08) <0.0001	
Secondary efficacy endpoints (descriptive)		
RSV A-confirmed LRTD events RSV B-confirmed LRTD events	2 5	13 26
VE (95% CI) against RSAV-A VE (95% CI) against RSV-B	84.6 % (95% CI: 32.1-98.3) 80.9% (95% CI: 49.4-94.3)	
RSV confirmed LRTD events by age RSV-associated LRTD in ≥65 YOA RSV-associated LRTD in ≥70 YOA RSV-associated LRTD in ≥80 YOA RSV-associated LRTD in 60-69 YOA RSV-associated LRTD in 70-79 YOA	 5/9258 3/5503 2/1016 4/6963 1/4487	 29/9325 19/5515 3/1028 21/6979 16/4487
VE % (95%CI) by age RSV-associated LRTD in ≥65 YOA RSV-associated LRTD in ≥70 YOA RSV-associated LRTD in ≥80 YOA RSV-associated LRTD in 60-69 YOA RSV-associated LRTD in 70-79 YOA	 82.7 (95% CI: 54.9, 94.8) 84.4 (95% CI: 46.9, 97.0) 33.8 (95% CI: -477.7,94.5) 80.96 (95% CI: 43.56, 95.25) 93.81 (95% CI: 60.15, 99.85)	
RSV confirmed LRTD by co-morbidities No pre-existing co-morbidities At least 1 pre-existing comorbidity of interest At least 1 pre-existing cardiorespiratory condition	 6/7529 1/4937 1/2496	 22/7633 18/4861 12/2421
VE % (95%CI) by co-morbidities No pre-existing co-morbidities At least 1 pre-existing comorbidity of interest At least 1 pre-existing cardiorespiratory condition	 72.5 (95% CI: 30.0-90.9) 94.6 (95% CI: 65.9-99.9) 92.1 (95% CI: 46.7-99.8)	
VE against first occurrence of RT-PCR-confirmed RSV ARI up to VE Analysis 1 (mES)	71.71% (95% CI:56.23,82.27)	
VE against severe RSV-confirmed LRTD (Definition 1 and 2)	94.10% (95% CI: 62.37, 99.86)	
VE against complications due to RSV-confirmed respiratory disease	88.86% (95% CI: 19.58, 99.75)	
VE against first occurrence of RT-PCR-confirmed RSV LRTD up to end of season 1 in Southern Hemisphere (VE analysis 2)		
RSV-confirmed LRTD	10/12469	47/12498
VE (95% CI)	78.86% (95% CI: 57.61, 90.48	

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Supportive studies:

Study RSV OA=ADJ-007 was a randomised, controlled, open-label, multicentre study to assess the humoral immune response, reactogenicity and safety of a single dose of RSVPreF3 OA vaccine when co-administered with unadjuvanted quadrivalent influenza vaccine (FLU-QIV) or given separately in adults aged 60 years and older. A total of 885 participants received the study intervention with 442 participants in the co-administration group and 443 participants in the control group. The primary objective was to demonstrate non-inferiority of both vaccines when co-administered compared to when administered separately. This was assessed using a pre-defined non-inferiority criterion that the upper limit (UL) of 95% CI of the GMT ratio (Control group/ Co-administration group) should be less than 1.5, which is accepted as a standard approach in vaccine non-inferiority studies. Non-inferiority of the immune responses in terms of RSV-A NAb titres was demonstrated as the UL of the 95% CI for the GMT ratio was less than the pre-defined criterion of 1.5 (1.27 [95% CI: 1.12, 1.44]). Similarly, non-inferiority was met in terms of hemagglutination inhibition (HI) antibody titres for each of the 4 FLU-QIV with the ULs of the 95% CIs for the GMT ratios less than the pre-defined criterion of 1.5 (1.17 [95% CI: 1.02, 1.35] for Flu A/Hong Kong/H3N2, 1.22 [95% CI: 1.03, 1.44] for Flu A/Victoria/H1N1, 1.17 [95% CI: 1.04, 1.32] for Flu B/Phuket/Yamagata, and 1.10 [95% CI: 0.95, 1.26] for Flu B/Washington/Victoria). The co-administration group showed numerically lower titres for most antigens, with the lower limit of 95% CI of GMT ratios exceeded 1, except for the Flu B/Washington/Victoria strain. This observed immune interference is expected in vaccine co-administration. However, as non-inferiority criteria were met, the overall effectiveness is presumed to be maintained. These findings supported the inclusion of co-administration data in the package insert, with a proposed addition noting the lower antibody responses and lack of data on concomitant administration with other vaccines.

The supportive phase 3 RSV OA=ADJ-009 study was a randomised (1:1:1), double-blind trial evaluating the lot-to-lot consistency of three RSVPreF3 OA lots in adults ≥60 years old. It assessed humoral immune response, reactogenicity, and safety of a single dose administration (n=757). The primary endpoint evaluated geometric mean concentration (GMC) ratios at 30 days post-vaccination for each pair of vaccine lots. Lot-to-lot consistency was successfully demonstrated, with the 95% confidence intervals on the group GMC ratios meeting the pre-defined limit of [0.67, 1.5].

Overall, VE of 82.6% against RSV-A/RSV-B RT-PCR confirmed LRTD was demonstrated with consistent efficacy against individual virus subtypes and subjects with at least 1 co-morbidity who have higher risk of severe disease. A 7 to 10-fold mean geometric increase was demonstrated in neutralising antibody titres against both RSV-A and RSV-B viruses. Non-inferior immune responses were observed when co-administered with influenza vaccine. Due to the efficacy study's follow-up for only one season, a registration condition was imposed requiring submission of completed two-season efficacy data.

D ASSESSMENT OF CLINICAL SAFETY

The safety population consisted of 15,745 subjects aged 60 years and above who received a single dose of the vaccine in the pivotal phase 3 study RSV OA=ADJ-006 and the three supportive phase 3 studies (Study 004, 007, 009), with a median follow-up duration of 7.9 months.

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Overview of solicited and unsolicited adverse events after vaccination (Pivotal study RSV OA=ADJ-006)

Solicited AEs	**RSVPreF3 OA (N=879)**	**Placebo (N=878)**
Any solicited AE	632 (71.9%)	245 (27.9%)
Local solicited AEs	547 (62.2%)	88 (10.0%)
Systemic adverse events	434 (49.4%)	204 (23.2%)
Unsolicited AEs	**RSVPreF3 OA (N=12467)**	**Placebo (N=12499)**
Any unsolicited AE within 30 days post-vaccination	8411 (33%)	3732 (17.8%)
Any Grade 3 unsolicited adverse event within 30 days post-vaccination	336 (2%)	207 (1.3%)
Any related unsolicited adverse event within 30 days post-vaccination	5584 (24.9%)	1146 (5.8%)
Any Grade 3 related unsolicited adverse event within 30 days post-vaccination	165 (0.9%)	41 (0.2%)
Any medically attended unsolicited adverse event within 30 days post-vaccination	879 (5.5%)	871 (5.5%)
Any non-serious medically attended unsolicited adverse event within 30 days post-vaccination	782 (4.9%)	758 (4.9%)
Any serious adverse event up to 6 months post-vaccination	643 (4.2%)	656 (4.0%)
Any related serious adverse event to DLP (30 April 2022)	12 (0.1%)	7 (0.1%)
Any related pIMD up to DLP	7 (0.1%)	5 (0.0)
Deaths up to DLP	58 (0.4%)	64 (0.5%)

Local reactogenicity events included injection site pain, swelling, and redness which were observed in 62.2% of the vaccine recipients and 10.0% of the placebo recipients. Systemic reactogenicity events included fatigue, arthralgia, fever, headache, and myalgia which were observed in 49.4% of the vaccine recipients and 23.2% of the placebo recipients. Most events were mild to moderate, with Grade 3 local solicited events in 1.5% of the vaccine group and Grade 3 systemic solicited events in 3.3%. The median duration of events ranged from 1 to 4 days.

In terms of adverse events of special interest (AESI), two cases of Bell's palsy were reported in the studies: one case occurred 41 days after vaccination (serious), and the other occurred 196 days after vaccination (non-serious). The first case was also associated with concomitant Herpes infection thus confounding the etiology. The second case, due to the time of onset, was considered unlikely to be due to vaccination. The incidence was observed to fall within the background rate for Bell's palsy.

Two cases of acute disseminated encephalomyelitis (ADEM) were observed in the clinical study ADJ-007, but the causality could not be established due to the co-administration of the influenza vaccine, which confounded the assessment. Furthermore, there were no MRI or CSF findings for these two cases to confirm the diagnosis of ADEM.

A single case of Guillain-Barre syndrome (GBS) possibly related to the vaccine was observed in study ADJ-004, occurring 9 days after vaccination. As it was a single case, the causality due to vaccination could not be conclusively determined.

Neurologic complications associated with RSV infections are more frequently observed in children than in adults. The occurrence of these neurologic events with multiple RSV vaccines has raised uncertainty about whether it might be attributed to an artefact or it indicates an increased risk associated with RSV vaccination. Hence, further post-market monitoring and surveillance would be necessary to better characterise the neurological safety profile of the vaccine. Information on these neurologic events has been included in the package insert to ensure healthcare providers and patients are aware of this potential risk.

A higher number of cases of atrial fibrillation was observed in the vaccine arm (10 cases) compared to the placebo arm (4 cases) in the study ADJ-006. However, as all the cases except one had pre-existing risk factors, the association of the vaccine to atrial fibrillation is yet to be established. Post-market surveillance will be necessary to further determine the real incidence and causality of these adverse events associated with vaccination.

Events of immune-mediated disorders such as gout, psoriasis, pancytopenia, Grave's disease, and arthritis were noted, which occurred in the context of participants underlying conditions. pIMDs have been included in the risk management plan and the package insert. Overall, the AESIs observed in the studies were generally single events. However, given that RSV infection itself is also associated with these risks, the causality of these events due to the RSV vaccine could not be excluded.

There were 49 deaths occurred in the vaccine arm and 58 deaths in the placebo arm. Three events of the deaths (1 cardiopulmonary failure in RSVPreF3 group, 1 case of pulmonary embolism and I unknown in placebo) were considered related to the treatment by the investigator. The death events were considered related to background comorbidities or old age in both the arms. No imbalance in the causes of deaths was observed.

Taken together, while the reactogenicity events were consistent with other vaccines, AESIs were noted in the studies, including GBS, atrial fibrillation, and pIMDs. The causal relationship between these events and the vaccine could not be definitively established based on the available data. Hence, further follow-up and monitoring in the post-authorisation phase would be necessary. Information about these adverse events has been incorporated into the package insert.

E ASSESSMENT OF BENEFIT-RISK PROFILE

RSV typically causes acute upper respiratory tract infection. However, older adults, specifically in those with underlying co-morbidities, may have a higher risk of developing severe LRTD.

The efficacy of Arexvy in preventing LRTD caused by RSV-A and RSV-B subtypes in adults aged 60 and above was demonstrated in the pivotal Study RSV OA=ADJ-006. This study followed participants for one complete season and was ongoing for the subsequent season. The overall vaccine efficacy (VE) against RSV-confirmed LRTD was 82.6% (96.95% CI: 57.89, 94.08). Consistent efficacy was demonstrated against both RSV-A (VE 84.6%; 95% CI: 32.1-98.3) and RSV-B (VE 80.9%; 95% CI: 49.4-94.3). Events due to RSV-A and RSV-B were well balanced in the study and the observed VE against both RSV subtypes is reassuring as RSV epidemiology might be characterised by alternating patterns of subtype predominance across seasons.

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The study population included a diverse older adult population from various geographic areas, allowing for the extrapolation of results to the target population of adults aged 60 years and above. Consistent efficacy was observed in subgroups of interest including those at high risk of developing severe RSV LRTD, including those with at least one comorbidity of interest (94.61%; 95% CI: 65.88, 99.87) or pre-frail status (92.92%; 95% CI: 53.44, 99.83) supporting its use to prevent the majority of RSV-associated LRTD cases in this vulnerable population.

As the data covered only one season, the registration of the vaccine is subject to the condition to submit efficacy data for the second season to ensure consistent efficacy.

While VE was not conclusive in older subjects ≥80 years of age or frail subjects due to the low number of events, the comparable immune responses in these subgroups to the overall population was reassuring. The immune responses were consistent across the pivotal studies and the supportive studies demonstrating 7 to 10-fold increase in neutralising antibody titres post-vaccination which was consistent with that observed in natural infection.

No signal of vaccine-induced enhanced disease was observed. However, the duration of protection and need for booster doses were not assessed.

Co-administration with a seasonal quadrivalent influenza vaccine did not interfere with immune responses to either vaccine.

The vaccine showed higher reactogenicity than placebo, with generally mild and transient symptoms. Local reactions (pain, swelling, redness) were observed in 62.2% of vaccine recipients versus 10.0% of placebo recipients, while systemic symptoms (fatigue, arthralgia, fever, headache, myalgia) occurred in 49.4% versus 23.2%, respectively.

A higher incidence of atrial fibrillation was noted in the vaccine arm, mostly in subjects with pre-existing risk factors. No serious hypersensitivity cases were reported. A single case of GBS was noted in Study-004, possibly related to the vaccine. This neurologic adverse event, along with atrial fibrillation and potential immune-mediated disorders, require post-approval pharmacovigilance monitoring and have been included in the package label.

Overall, the vaccine demonstrated high efficacy against RSV-associated LRTD, including in the high-risk subgroups. While the safety profile was generally acceptable, specific adverse events were identified for ongoing monitoring. Long-term follow-up and post-marketing surveillance are crucial to characterise the protection duration, assess booster dose needs, and detect rare adverse events. Considering that the vaccine is indicated for targeted populations aged 60 years and above who may have a higher risk of developing severe disease and require hospitalisation, on balance the benefit-risk profile for this population was deemed positive.

F CONCLUSION

Based on the review of quality, safety and efficacy data, the benefit-risk balance of Arexvy for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 60 years of age and older was deemed favourable and approval of the product registration was granted on 10 May 2024.

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AREXVY

Respiratory Syncytial Virus (RSV) Vaccine (recombinant, AS01$_E$ adjuvanted)

Powder and suspension for suspension for injection

QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 mL) contains 120 micrograms of RSVPreF3[1] antigen adjuvanted with AS01$_E$[2].

[1] Respiratory syncytial virus (RSV) glycoprotein F stabilized in the pre-fusion conformation (RSVPreF3) produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cells.

[2] The GlaxoSmithKline proprietary AS01$_E$ Adjuvant System is composed of the plant extract *Quillaja saponaria* Molina, fraction 21 (QS-21) (25 micrograms) and 3-O-desacyl-4'-monophosphoryl lipid A (MPL) from *Salmonella minnesota* (25 micrograms).

The powder is white.
The suspension is an opalescent, colourless to pale brownish liquid.

CLINICAL INFORMATION

Indications

Arexvy is indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 60 years of age and older.

Consideration should be given to official vaccine recommendations on the appropriate use.

Dosage and Administration

Consideration should be given to official vaccine recommendations for immunisation schedules.

Posology

Arexvy is administered as a single dose of 0.5 mL.

The need for revaccination has not been established.

Paediatric population

The safety and efficacy of Arexvy in children have not been established.

Method of Administration

Arexvy is for intramuscular injection only, preferably in the deltoid muscle.

For instructions on reconstitution of the medicinal product before administration, see *Use and Handling*.

Contraindications

Hypersensitivity to the active substances or to any component of the vaccine (see *Qualitative and quantitative composition* and *List of Excipients*).

Warnings and Precautions

Prior to immunisation

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.

As with other vaccines, vaccination with Arexvy should be postponed in individuals suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with the vaccination process itself. It is important that procedures are in place to avoid injury from faints.

In order to improve the traceability of vaccines, the name and the batch number of the administered product should be clearly recorded.

Precautions for use

Do not administer the vaccine intravascularly or intradermally. No data are available on subcutaneous administration of Arexvy.

As with other vaccines administered intramuscularly, Arexvy should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these individuals.

Systemic immunosuppressive medications and immunodeficiency

Safety and immunogenicity data on Arexvy are not available for immunocompromised individuals. Patients receiving immunosuppresive treatment or patients with immunodeficiency may have a reduced immune response to Arexvy.

Interactions

Use with other vaccines

Arexvy can be given concomitantly with inactivated seasonal influenza vaccine *(*see *Pharmacodynamic Effects)*.

If Arexvy is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

No data are available for concomitant administration with other vaccines.

Pregnancy and Lactation

Fertility

There are no data on the effects of Arexvy on human fertility. Effects on male or female fertility have not been evaluated in animal studies.

Pregnancy

There are no data from the use of Arexvy in pregnant women from clinical trials.

After administration of an investigational unadjuvanted RSV vaccine that contained the same RSVPreF3 antigen as Arexvy to 3,557 pregnant women in a randomized controlled clinical trial, an increase in preterm births was observed compared to placebo (6.8% versus 4.9%, respectively). Currently no conclusion on a causal relationship between administration of unadjuvanted RSVPreF3 and preterm birth can be drawn.

Arexvy is not recommended during pregnancy.

Lactation

There are no data on the excretion of Arexvy in human or animal milk. Arexvy is not recommended in breast-feeding/lactating women.

Effects on Ability to Drive and Use Machines

No studies on the effects of Arexvy on the ability to drive and use machines have been performed. Some of the effects mentioned under *Adverse reactions* (e.g. fatigue) may temporarily affect the ability to drive or use machines.

Adverse Reactions

The safety profile presented below is based on a placebo-controlled Phase III clinical study, RSV-OA=ADJ-006 (conducted in Europe, North America, Asia and Southern hemisphere) in adults ≥ 60 years of age in which 12,467 adults received one dose of Arexvy and 12,499 received placebo.

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to <1/1,000

Very rare <1/10,000

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Uncommon	lymphadenopathy
Immune system disorders	Uncommon	hypersensitivity reactions (such as rash)
Nervous system disorders	Very common	headache
Respiratory, thoracic, and mediastinal disorders	Common	rhinorrhea
Gastrointestinal disorders	Uncommon	Nausea, abdominal pain, vomiting
Musculoskeletal and connective tissue disorders	Very common	myalgia, arthralgia
General disorders and administration site conditions	Very common	injection site pain, fatigue
	Common	injection site erythema, injection site swelling, fever, chills
	Uncommon	injection site pruritus
		pain, malaise

Solicited Adverse Reactions

In RSV-OA=ADJ-006 study, a subset of study participants (solicited safety set) was monitored for solicited adverse reactions using standardized paper diary cards during the 4 days (i.e., day of vaccination and the next 3 days) following a dose of Arexvy or placebo; 879 participants received Arexvy and 874 participants received placebo. The other study participants did not prospectively record solicited reactions on a diary card but may have reported them as unsolicited adverse reactions.

The reported frequences of specific solicited local (administration site) and systemic adverse reactions (per participant) are presented in Table 1.

Table 1: Percentage of Participants with Solicited Local Adverse Reactions and Systemic Adverse Reactions within 4 Days of Vaccination in Adults 60 Years of Age and Older (Solicited Safety Set with 4-Day Diary Card)

Local Adverse Reactions	**Arexvy % N = 879**	**Placebo[a] % N = 874**
Pain, Any[b]	60.9	9.3
Pain, Grade 3[b]	1	0
Erythema, >20 mm	7.5	0.8
Erythema, >100 mm	0.2	0
Swelling, >20 mm	5.5	0.6
Swelling, >100 mm	0.2	0
Systemic Adverse Reactions	**N = 879**	**N = 878**
Fatigue, Any[c]	33.6	16.1
Fatigue, Grade 3[c]	1.7	0.5
Myalgia, Any[c]	28.9	8.2

Myalgia, Grade 3[c]	1.4	0.3
Headache, Any[c]	27.2	12.6
Headache, Grade 3[c]	1.3	0
Arthralgia, Any[c]	18.1	6.4
Arthralgia, Grade 3[c]	1.3	0.6
Fever, ≥38.0°C/100.4°F[d]	2.0	0.3
Fever, >39.0°C/102.2°F[d]	0.1	0.1

N = Exposed set for solicited safety set included all participants with at least 1 documented dose.
[a] Placebo was a saline solution.
[b] Any grade pain: Defined as any pain neither interfering with nor preventing normal everyday activities (Grade 1), painful when limb is moved and interferes with everyday activities (Grade 2), or significant pain at rest and prevents normal everyday activities (Grade 3).
[c] Any grade fatigue, myalgia, headache, arthralgia: Defined as event easily tolerated (Grade 1), interfering with normal activity (Grade 2), or preventing normal activity (Grade 3).
[d] Temperature taken by any route (oral, axillary, or tympanic).

In the solicited safety set, the local administration site adverse reactions reported with Arexvy had a median duration of 2 days, and the systemic adverse reactions reported with Arexvy had a median duration ranging between 1 and 2 days.

Unsolicited Adverse Events

In all participants from RSV-OA=ADJ-006 study, unsolicited adverse events were monitored using paper diary cards during the 30-day period following vaccination (day of vaccination and the next 29 days).

Among participants in the solicited safety set, (Arexvy, n = 879 or placebo, n = 878), unsolicited adverse events occurring within 30 days after vaccination were reported in 14.9% and 14.6% of participants who received Arexvy and placebo, respectively.

In the exposed set, 24,966 participants 60 years of age and older, received at least 1 dose of Arexvy (n = 12,467) or placebo (n = 12,499). Unsolicited adverse events occurring within 30 days of vaccination were reported in 33.0% and 17.8% of participants, respectively. The higher frequency of reported unsolicited adverse events among participants who received Arexvy, compared to participants who received placebo, was primarily attributed to events that are consistent with adverse reactions solicited among participants in the reactogenicity subset.

Within 30 days after vaccination, atrial fibrillation was reported in 10 participants who received Arexvy and 4 participants who received placebo (of which 7 events in Arexvy arm and 1 event in placebo arm were serious); the onset of symptoms ranged from 1 to 30 days post vaccination. The currently available information on the atrial fibrillation is insufficient to determine a causal relationship to the vaccine. There were no other notable patterns or numerical imbalances between groups for specific categories of unsolicited adverse events.

Serious Adverse Events

In RSV-OA=ADJ-006 study, participants were monitored for all serious adverse events (SAEs) that occured during the 6-month period following administration of Arexvy (n = 12,467) or placebo (n = 12,499). SAEs with onset within 6 months following vaccination

were reported at similar rates in participants who received Arexvy (4.2%) or placebo (4.0%). Serious events of atrial fibrillation were reported in 13 participants who received Arexvy and 15 participants who received placebo within 6 months after vaccination.

Deaths

From vaccination through the first analysis of the ongoing RSV-OA=ADJ-006 study, adverse events leading to death were reported for 49 participants (0.4%) who received Arexvy (n = 12,467) and 58 participants (0.5%) who received placebo (n = 12,499). Based on available information, there is no evidence of causal relationship to Arexvy. Causes of death among participants were consistent with those generally reported in adult and elderly populations.

Potential Immune-Mediated Diseases

In RSV-OA=ADJ-006 study, participants were monitored for all potential immune-mediated diseases (pIMDs) that occurred during the 6-month period following administration of Arexvy (n = 12,467) or placebo (n = 12,499). New onset pIMDs or exacerbation of existing pIMDs within 6 months following vaccination were reported for 0.3% of participants who received Arexvy and 0.3% of participants who received placebo. There were no notable imbalances between study groups in individual pIMDs reported.

Serious Adverse Events Reported From Other Studies

RSV-OA=ADJ-004: Guillain-Barré syndrome beginning 9 days after Arexvy vaccination was reported in a participant enrolled in a study site in Japan.

Overdosage

Insufficient data are available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC code - J07BX05, respiratory syncytial virus vaccines

Mechanism of action

The risk of developing RSV-associated LRTD increases with age and with presence of underlying comorbidities. Arexvy induces the functional humoral immune responses against the RSV-A and RSV-B subtypes and the antigen-specific cellular immune responses which contribute to protect against RSV-associated LRTD (see *Immunogenicity of Arexvy*).

In a Phase I/II clinical trial, formulation adjuvanted with AS01$_E$ showed the ability to restore RSVPreF3-specific CD4+ T cells in adults 60 to 80 years of age to levels similar to those observed in young adults, despite lower baseline levels in the older adults.

Non-clinical data show that $AS01_E$ induces a local and transient activation of the innate immune system through specific molecular pathways. The adjuvant effect of $AS01_E$ is the result of interactions between MPL and QS-21 formulated in liposomes. This facilitates the recruitment and activation of antigen presenting cells carrying vaccine-derived antigens in the draining lymph node, which in turn leads to the generation of RSVPreF3-specific CD4+ T cells and induction of RSV-A and RSV-B neutralizing antibody responses. In addition, RSVPreF3 formulated with $AS01_E$ can elicit specific binding antibodies directed to site Ø, a highly neutralizing sensitive epitope, exposed only on the pre-fusion conformation of the F protein.

Pharmacodynamic effects

Efficacy of Arexvy

Efficacy of Arexvy against RSV-associated LRTD in adults 60 years and older was evaluated in RSV-OA=ADJ-006, an ongoing, Phase III, randomised, placebo-controlled, observer-blind clinical study conducted in 17 countries from Northern and Southern Hemispheres. Participants are planned to be followed for up to 36 months.

The study excluded participants who were immunocompromised. Participants with pre-existing, chronic, stable disease such as diabetes, hypertension, or cardiac disease were allowed to participate in the study if considered by the investigator as medically stable at the time of vaccination.

The primary population for efficacy analysis (referred to as the modified Exposed Set, included adults 60 years of age and older receiving 1 dose of Arexvy or placebo and who did not report an RSV-confirmed acute respiratory illness (ARI) prior to Day 15 after vaccination) included 24,960 participants randomised equally to receive 1 dose of Arexvy (N = 12,466) or placebo (N = 12,494). At the time of the primary efficacy analysis, participants had been followed for the development of RSV-associated LRTD for up to 10 months (median of 6.7 months).

At baseline, 39.3% of participants had at least one comorbidity of interest; 19.7% of participants had an underlying cardiorespiratory condition (COPD, asthma, any chronic respiratory/pulmonary disease, or chronic heart failure) and 25.8% of participants had endocrinometabolic conditions (diabetes, advanced liver or renal disease).

Using the Gait speed test, 38.3% of participants were ranked as pre-frail (0.4-0.99m/s walking speed) and 1.5% as frail (<0.4 m/s walking speed or who were not able to perform the test).

Efficacy against RSV-associated LRTD

The primary objective was to demonstrate the efficacy of Arexvy in the prevention of a first episode of confirmed RSV-A and/or B associated LRTD during the first season. Confirmed RSV cases were determined by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) on nasopharyngeal swab. LRTD was defined based on the following criteria: the participant must have experienced at least 2 lower respiratory symptoms/signs including at least 1 lower respiratory sign for at least 24 hours, or experienced at least 3 lower respiratory symptoms for at least 24 hours. Lower respiratory symptoms included: new or increased sputum, new or increased cough, new

or increased dyspnea (shortness of breath). Lower respiratory signs included: new or increased wheezing, crackles/ronchi, respiratory rate ≥20 respirations/min, low or decreased oxygen saturation (O_2 saturation <95% or ≤90 % if baseline is <95%) or need for oxygen supplementation.

Compared with placebo, Arexvy significantly reduced the risk of developing RSV-associated LRTD by 82.58% (96.95% CI: [57.89, 94.08]) in participants 60 years of age and older, which met the pre-specified success criterion for the primary study objective (Table 2). High vaccine efficacy against RSV-LRTD is observed through the median follow-up period of 6.7 months.

The vaccine efficacy against RSV A-associated LRTD cases and RSV B-associated LRTD cases was 84.62% (95% CI [32.08, 98.32]) and 80.88% (95% CI [49.40, 94.27]), respectively.

Table 2. Efficacy Analysis: First RSV-associated LRTD Overall, by Age and co-morbidity subgroups in RSV-OA=ADJ-006 (modified Exposed Set)

Subgroup	Arexvy			Placebo			% Efficacy (CI)[a]
	N	n	Incidence Rate per 1,000 Person-Years	N	n	Incidence Rate per 1,000 Person-Years	
Overall (≥60 years)[b]	12466	7	1.0	12494	40	5.8	82.58 (57.89, 94.08)
60-69 years	6963	4	1.0	6979	21	5.5	80.96 (43.56, 95.25)
70-79 years	4487	1	0.4	4487	16	6.5	93.81 (60.15, 99.85)
Participants with at least 1 comorbidity of interest	4937	1	0.4	4861	18	6.6	94.61 (65.88, 99.87)

[a] CI = Confidence Interval (96.95% for the overall (≥60 years) and 95% for all subgroup analyses). Two-sided exact CI for vaccine efficacy is derived based on Poisson model adjusted by age categories and regions.
[b] Primary confirmatory objective with pre-specified success criterion of lower limit of the 2-sided CI for vaccine efficacy above 20%
N = Number of participants included in each group
n = Number of participants having first occurrence of RSV-confirmed LRTD occurring from Day 15 post vaccination

Compared with placebo, Arexvy significantly reduced the risk of developing RSV-associated LRTD by 84.37% (95% CI: [46.91, 97.04]) in participants 70 years of age and older. The vaccine efficacy in the subgroup of participants 80 years of age and older (1016 participants in Arexvy vs. 1028 participants in placebo) cannot be concluded due to the low number of total cases accrued (5 cases).

Compared with placebo, Arexvy significantly reduced the risk of developing RSV-associated LRTD in pre-frail participants by 92.92% (95% CI [53.44, 99.83]). The vaccine efficacy in the frail subgroup (189 participants in Arexvy vs. 177 participants in placebo) cannot be concluded due to the low number of total cases accrued (2 cases).

Efficacy Against Severe RSV-associated LRTD and RSV-associated ARI

In study RSV-OA=ADJ-006, severe RSV-associated LRTD was defined as RT-PCR confirmed RSV-associated LRTD with at least 2 lower respiratory signs, or as an RT-PCR confirmed RSV-associated LRTD episode assessed as 'severe' by the investigator. One case of severe RSV-associated LRTD in the Arexvy group and 17 cases in the placebo group were reported, amongst which 2 cases required supportive therapy. Compared with placebo, Arexvy significantly reduced the risk of developing severe RSV-associated LRTD by 94.10 % (95% CI [62.37, 99.86]) in participants 60 years of age and older.

Acute respiratory illness (ARI) was defined by the presence of at least 2 respiratory symptoms/signs for at least 24 hours, or at least 1 respiratory symptom/sign + 1 systemic symptom/sign (fever or feverishness, fatigue, body aches, headache, decreased appetite) for at least 24 hours. Arexvy significantly reduced the risk of developing confirmed RSV-associated ARI in adults ≥ 60 years of age by 71.71% (95% CI [56.23, 82.27]).

Immunogenicity of Arexvy

An immunological correlate of protection has not been established; therefore the level of immune response that provides protection against RSV-associated LRTD is unknown.

The immune responses to Arexvy were evaluated in a Phase III immunogenicity and safety study RSV-OA=ADJ-004 in adults 60 years and older. Functional humoral immune responses post-vaccination compared to pre-vaccination were evaluated with results from 940 participants for RSV-A and 941 participants for RSV-B for month 1 vs. pre-vaccination, and 928 participants for RSV-A and 929 participants for RSV-B at month 6 vs. pre-vaccination. The cell-mediated immune responses were evaluated with results from 471 participants at pre-vaccination, 410 at month 1 and 440 at month 6.

Arexvy elicited RSV-specific humoral and cellular immune responses. The geometric mean RSV-A and RSV-B neutralizing titers 1 month post-immunisation were 10.5-fold (95% CI [9.9, 11.2]) and 7.8-fold (95% CI [7.4, 8.3]), respectively, and 4.4-fold (95% CI [4.2, 4.6]) and 3.5-fold (95% CI [3.4, 3.7]) at 6 months post-vaccination, respectively. The median frequency (percentile [25^{th}, 75^{th}]) of the RSVPreF3-specific CD4+ T-cells (per million of CD4+ T cells) was 1339.0 (829.0, 2136.0) 1 month post-vaccination and 666.0 (428.0, 1049.5) 6 months post-vaccination as compared to 191.0 (71.0, 365.0) pre-vaccination.

Immunogenicity following concomitant vaccination

In an open-label Phase III clinical study, participants 60 years of age and older received 1 dose of Arexvy and inactivated unadjuvanted seasonal influenza vaccine (Flu Quadrivalent containing a combined total of 60 micrograms Hemagglutinin (HA) per dose) at month 0 (N = 442), or 1 dose of Flu Quadrivalent at month 0 followed by a dose of Arexvy at month 1 (N = 443).

The criteria for non-inferiority of the immune responses in the control versus co-administration group were met as the 2-sided 95% confidence interval upper limits on the group geometric mean titer ratios were below 1.50 for the RSV-A neutralizing antibodies and haemagglutinin inhibition antibodies against the strains Flu A/Hong Kong/H3N2, Flu A/Victoria/H1N1, Flu B/Phuket/Yamagata, and Flu B/Washington/Victoria. However, numerically lower RSV A and B neutralizing titres and numerically lower influenza A and B haemagglutination inhibition titres were observed when Arexvy and inactivated seasonal influenza vaccine were co-administered than when they were administered separately. The clinical relevance of this finding is unknown.

Pharmacokinetics

Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical studies

See *Pharmacodynamic Effects*.

Non-Clinical Information

Non-clinical data reveal no special hazards for humans based on general safety studies.

PHARMACEUTICAL INFORMATION

List of Excipients

Powder (RSVPreF3 antigen):

Trehalose dihydrate
Polysorbate 80
Potassium dihydrogen phosphate
Dipotassium phosphate

Suspension (AS01$_E$ Adjuvant System):

Dioleoyl phosphatidylcholine
Cholesterol
Sodium chloride
Disodium phosphate, anhydrous
Potassium dihydrogen phosphate
Water for injections

Shelf Life

The expiry date is indicated on the packaging.

Storage

Store in a refrigerator (2 °C – 8 °C).

Do not freeze. Discard if the vial has been frozen.

Store in the original package in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see *Use and Handling*.

The storage conditions are detailed on the packaging.

Nature and Contents of Container

- Powder for 1 dose in a vial (type I glass) with stopper (butyl rubber).
- Suspension for 1 dose in a vial (type I glass) with a stopper (butyl rubber).

Arexvy is available in a pack size of 1 vial of powder plus 1 vial of suspension or in a pack size of 10 vials of powder plus 10 vials of suspension.

Incompatibilities

Arexvy must not be mixed with other medicinal products.

Use and Handling

The powder and suspension should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, do not reconstitute the vaccine.

How to prepare Arexvy:

Arexvy must be reconstituted prior to administration.

1. Withdraw the entire contents of the vial containing the suspension into a syringe.
2. Add the entire contents of the syringe into the vial containing the powder.
3. Gently swirl until the powder is completely dissolved.

The reconstituted vaccine is an opalescent, colourless to pale brownish liquid.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, do not administer the vaccine.

After reconstitution, the vaccine should be used promptly; if not possible, the vaccine should be stored in the refrigerator (2°C – 8°C) or at room temperature up to 25°C. If not used within 4 hours it should be discarded.

Before administration:

1. Withdraw 0.5 mL of the reconstituted vaccine into the syringe.
2. Change the needle so that you are using a new needle.

Administer the vaccine intramuscularly.

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

Not all presentations are available in every country.

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