Arexvy

Recombinant Respiratory Syncytial Virus Pre-Fusion F Protein 120 mcg

Powder for suspension for injection

QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 mL) contains 120 micrograms of RSVPreF3[1] antigen adjuvanted with $AS01_E$[2].

[1]Respiratory Syncytial Virus (RSV) glycoprotein F stabilised 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 immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in:

- adults 60 years of age and older
- adults 50 through 59 years of age who are at increased risk for RSV disease

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

Dosage and Administration

Posology

Arexvy is administered as a single dose of 0.5 mL.

The need for revaccination with a subsequent dose has not been established.

Paediatric population

The safety and efficacy of ***Arexvy*** in children have not been established.
No data are available.

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

Traceability

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

Prior to immunization

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. Close observation for at least 15 minutes is recommended following vaccination.

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 precautions are in place to avoid injury from faints.

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 intramuscular administration to these individuals.

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

Excipients
This medicinal product contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium-free'.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Interactions
Use with other vaccines
Arexvy can be given concomitantly with inactivated seasonal influenza vaccines (standard dose unadjuvanted, high dose unadjuvanted, or standard dose adjuvanted).

The safety profile of ***Arexvy*** when co-administered with inactivated seasonal influenza vaccines was comparable to when ***Arexvy*** was administered alone. For immunogenicity data, 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.

Concomitant administration of ***Arexvy*** with other vaccines has not been studied.

Pregnancy and Lactation
Fertility
There are no data on the effects of ***Arexvy*** on human fertility.

Animal studies do not indicate direct or indirect harmful effects with respect to fertility in females.

Pregnancy
There are no data from the use of ***Arexvy*** in pregnant women. ***Arexvy*** is not recommended during pregnancy.

After administration of an investigational unadjuvanted RSVPreF3 vaccine to 3,557 pregnant women in a single clinical study, an increase in preterm births was observed compared to placebo. Currently no conclusion on a causal relationship between administration of unadjuvanted RSVPreF3 and preterm birth can be drawn.

Results from animal studies do not indicate direct or indirect harmful effects with respect to development and reproductive toxicity.

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.

Arexvy has a minor influence on the ability to drive and use machines. Some of the effects mentioned under section "*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 pooled analysis of data generated in two placebo-controlled Phase III clinical study (conducted in Europe, North America, Asia and Southern Hemisphere) in adults ≥60, and 50 through 59 years of age in which 12,467 adults received one dose of ***Arexvy*** and 12,499 received placebo with a follow-up period of approximately 12 months.

In study participants 60 years of age and older, the most commonly reported adverse reactions were injection site pain (61%), fatigue (34%), myalgia (29%), headache (28%), and arthralgia (18%). These adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination.

Most other adverse reactions were uncommon and similarly reported between the study groups.

In study participants 50 through 59 years of age (769 participants, including 386 participants with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease), a higher incidence of injection site pain (76%), fatigue (40%), myalgia (36%), headache (32%), and arthralgia (23%) was observed, compared with those 60 years of age and older (381 participants) in the same study. However, the duration severity of these events were comparable across age groups in the study.

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
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

Adverse events should be reported to GSK Indonesia via website https://gsk.public.reportum.com and Pusat Farmakovigilans/MESO Nasional Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif Badan Pengawas Obat dan Makanan.
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

Overdose
Insufficient data are available.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamics
ATC code
Pharmacotherapeutics group: Vaccines, other viral vaccines, ATC code: J07BX05.

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 neutralising titers. In addition, RSVPreF3 formulated with $AS01_E$ can elicit specific binding antibodies directed to site Ø, a highly neutralising 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 for up to 3 RSV seasons in RSV OA=ADJ-006, a Phase III, randomized, placebo-controlled, observer-blind clinical study conducted in 17 countries from Northern and Southern Hemispheres.

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.

The primary efficacy analysis set over the first RSV season included 24,960 participants who received 1 dose of ***Arexvy*** (N=12,466) or placebo (N=12,494).

Pre-Season 2, participants who received ***Arexvy*** were re-randomized to receive placebo (n=4,991) or a second dose of ***Arexvy*** (n=4,966). Participants who received placebo before Season 1 received a second dose of placebo before Season 2. The participants were followed up to the end of the third RSV season (median follow-up time 30.6 months).

The median age of participants was 69 years (range: 59 to 102 years), with approximately 74% over 65 years of age, approximately 44% over 70 years of age and approximately 8% over 80 years of age. Approximately 52% were female. 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). Among participants in the modified Exposed Set for the analysis of efficacy over 2 and over 3 RSV seasons, demographic and baseline characteristics were similar to those in the modified Exposed Set for the analysis of efficacy over the first RSV season.

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).

Confirmed RSV cases were determined by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) on nasopharyngeal swab during all ARI episodes. ARI was defined by the presence of at least 2 respiratory symptoms/signs for at least 24 hours (nasal congestion, sore throat, lower respiratory symptoms/signs, as described below), 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.

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/rhonchi, 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.

Severe RSV-associated LRTD was defined as qRT-PCR confirmed RSV-associated LRTD with at least 2 lower respiratory signs, or preventing normal, everyday activities or requiring supportive therapy.

Efficacy against RSV-associated LRTD over the first RSV season
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.

Compared with placebo, ***Arexvy*** significantly reduced the risk of developing RSV-associated LRTD by 82.6% (96.95% CI: [57.9, 94.1]) in participants 60 years of age and older, which met the pre-specified success criterion for the primary study objective (Table 1). 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 and RSV B-associated LRTD was 84.6% (95% CI [32.1, 98.3]) and 80.9% (95% CI [49.4, 94.3]), respectively.

Table 1: Efficacy analysis over the first RSV season: First RSV-associated LRTD overall, by age and co-morbidity subgroups in RSV OAD=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]	12,466	7	1.0	12,494	40	5.8	82.6 [57.9; 94.1]
60-69 years	6,963	4	1.0	6,979	21	5.5	81.0 [43.6; 95.3]
70-79 years	4,487	1	0.4	4,487	16	6.5	93.8 [60.2; 99.9]
≥80 years	1,016	2	3.6	1,028	3	5.4	Cannot be reliably estimated[c]
Participants with at least 1 comorbidity of interest	4,937	1	0.4	4,861	18	6.6	94.6 [65.9; 99.9]

[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%.
[c]Due to the low number of cases accrued in this age group.
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 84.4% (95% CI: [46.9, 97.0]) in participants 70 years of age and older.

Compared with placebo, ***Arexvy*** significantly reduced the risk of developing RSV- associated LRTD in pre-frail participants by 92.9% (95% CI [53.4, 99.8]). The vaccine efficacy in the frail subgroup (189 participants in ***Arexvy*** vs 177 participants in placebo) cannot be reliably estimated due to the low number of total cases accrued (2 cases).

Efficacy against severe RSV-associated LRTD and RSV-associated ARI over the first RSV season
Compared with placebo, ***Arexvy*** significantly reduced the risk of developing severe RSV-associated LRTD by 94.1 % (95% CI [62.4, 99.9]) in participants 60 years of age and older. 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 (oxygen supplementation).

Arexvy significantly reduced the risk of developing confirmed RSV-associated ARI in adults ≥60 years of age by 71.7% (95% CI [56.2, 82.3]).

Patient Reported Outcome over the first RSV season
Arexvy was assessed vs. placebo in the RSV OA=ADJ-006 study to quantify the reduction in intensity of respiratory symptoms using a patient reported outcome measure, the FLU-PRO questionnaire. In participants with an RSV-confirmed ARI episode who completed the FLU-PRO questionnaire, ***Arexvy*** significantly reduced the intensity of lower respiratory tract symptoms of RSV by a clinically meaningful difference vs. placebo as assessed by the maximum FLU-PRO Chest score (scale range 0-4) over the first 7 days of the episode (Mean [standard deviation] of 1.32 [1.02] in the ***Arexvy*** group vs 1.90 [0.93] in the placebo group).

Efficacy against RSV-associated LRTD over 2 RSV seasons and over 3 RSV seasons
Participants 60 years of age and older who received 1 dose of ***Arexvy*** or placebo were followed over 3 RSV seasons (up to the end of the second and third seasons in the Northern Hemisphere), with a median follow-up time of 17.8 months, over 2 RSV seasons and 30.6 months over 3 RSV seasons. The vaccine efficacy against RSV-associated LRTD over 2 RSV seasons was 67.2% (97.5% CI [48.2, 80.0]) and over 3 RSV seasons was 62.9% (97.5% CI [46.7, 74.8]).

The vaccine efficacy against RSV A-associated LRTD and RSV B-associated LRTD over 3 RSV seasons was 69.8% (97.5% CI [42.2, 85.7]) and 58.6% (97.5% CI [35.9, 74.1]), respectively.

The vaccine efficacy analyses by age subgroup and for participants with at least one comorbidity of interest are presented in Table 2.

Table 2. Efficacy analyses over two RSV seasons and over three RSV seasons: First RSV-associated LRTD overall, by age and co-morbidity subgroups in RSV OA=ADJ-006 (modified Exposed Set)

Subgroup	AREXVY[a]			Placebo			% Efficacy[c] (CI)[d]
	N[b]	n	Incidence Rate per 1,000 Person-Years	N[b]	n	Incidence Rate per 1,000 Person-Years	
Over 2 RSV seasons							
Overall (≥60 years)	12,469	30	2.0	12,498	139	8.0	67.2 (48.2, 80.0)
60 to 69 years	6,963	17	2.1	6,981	74	7.7	65.4 (40.4, 80.9)
70 to 79 years	4,489	9	1.7	4,489	55	8.8	74.9 (48.4, 89.2)
≥80 years	1,017	4	3.5	1,028	10	7.2	Cannot be reliably estimated[e]

Participants with at least 1 comorbidity of interest	4,983	16	2.7	4,919	72	10.6	66.7 (41.8, 82.0)
Over 3 RSV seasons							
Overall (≥60 years)	12,468	48	2.4	12,498	215	7.9	62.9 (46.7, 74.8)
60 to 69 years	6,962	28	2.5	6,981	117	7.6	60.3 (39.5, 74.8)
70 to 79 years	4,489	15	2.1	4,489	85	8.6	70.6 (48.4, 84.3)
≥80 years	1,017	5	3.3	1,028	13	6.0	Cannot be reliably estimated[e]
Participants with at least 1 comorbidity of interest	5,014	25	3.2	4,951	116	10.8	64.7 (45.1, 78.1)

[a]Participants who received a second dose of ***Arexvy*** did not contribute to these efficacy analyses after receipt of Dose 2.

[b]Several analyses were performed resulting in a different number of participants included in each analysis due to new or updated information obtained for some participants.

[c]VE(%) Poisson method – adjusted by age, region, and season for overall (≥60 years) and participants with at least 1 comorbidity of interest and adjusted by region and season for analysis by age category.

[d]CI=Confidence Interval (97.5% for the overall ≥60 years and 95% for all subgroup analyses).

[e]Due to the low number of cases accrued in this age group.

Two-sided exact CI for vaccine efficacy is derived based on Poisson model adjusted by age categories, regions and season.

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.

Subgroup analyses of RSV-associated LRTD vaccine efficacy over 2 RSV seasons and 3 RSV seasons showed similar efficacy point estimates. In participants 70 years of age and older, over 2 RSV seasons and over 3 RSV seasons, the vaccine efficacy against RSV-associated LRTD was 69.3% (95% CI [43.4, 84.6]).

The vaccine efficacy against severe RSV-associated LRTD over 2 RSV seasons was 78.8% (95% CI [52.6, 92.0]) in participants 60 years of age and older (7 cases in the ***Arexvy*** group and 48 cases in the placebo group, amongst which 1 case in the ***Arexvy*** group and 5 cases in the placebo group required supportive therapy [oxygen supplementation and positive airway pressure]). The vaccine efficacy against severe RSV-associated LRTD over 3 RSV seasons was 67.4% (95% CI [42.4, 82.7]) in participants 60 years of age and older (15 cases in the ***Arexvy*** group and 75 cases in the placebo group, amongst which 2 cases in the ***Arexvy*** group and 5 cases in the placebo group required supportive therapy [oxygen supplementation and positive airway pressure]).

Efficacy against RSV-associated LRTD over the second RSV season and over the third RSV season

The vaccine efficacy against RSV-associated LRTD over the second RSV season with median follow-up of 6.3 months was 56.1% (95% CI [28.2, 74.4]) in participants 60 years of age and older (20 cases in the ***Arexvy*** group and 91 cases in placebo group).

The vaccine efficacy against RSV-associated LRTD over the third RSV season with median follow-up of 7.0 months was 48.0% (95% CI [8.7, 72.0]) in participants 60 years of age and older (16 cases in the ***Arexvy*** group and 61 cases in the placebo group).

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.

Adults 60 years and older

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 increase of the RSV-A and RSV-B neutralising titers compared to pre-vaccination were 10.5-fold (95% CI [9.9, 11.2]) and 7.8-fold (95% CI [7.4, 8.3]) at 1-month post-vaccination, 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 [25th, 75th]) of the RSVPreF3-specific CD4+ T-cells (per million of CD4+ T cells) was 1,339.0 (829.0, 2,136.0) 1-month post-vaccination and 666.0 (428.0, 1,049.5) 6-months post-vaccination as compared to 191.0 (71.0, 365.0) pre-vaccination.

Immunogenicity in adults 50 through 59 years of age at increased risk for RSV disease

The non-inferiority of the immune response to ***Arexvy*** in adults 50 through 59 years of age compared to adults 60 years of age and older, where vaccine efficacy against RSV-associated LRTD was demonstrated, was evaluated in a Phase III, observer-blind, randomised, placebo-controlled study.

Cohort 1 consisted of participants 50 through 59 years of age separated in 2 sub-cohorts (Adults-AIR and Adults-non-AIR) according to their medical history. Adults-AIR (adults at increased risk) sub-cohort consisted of participants with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease (***Arexvy***, N=386; placebo, N=191) such as chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney or liver disease. Adults-non-AIR sub-cohort consisted of participants without pre-defined, stable, chronic medical conditions (***Arexvy***, N=383; placebo, N=192). Cohort 2 (OA; older adults) consisted of participants 60 years of age and older (Arexvy, N=381).

The primary immunogenicity objectives were to demonstrate non-inferiority of the humoral immune response (in terms of RSV-A and RSV-B neutralising titers) following the administration of ***Arexvy*** at 1-month post-vaccination in participants 50 through 59 years of age with and without pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease, compared to participants 60 years of age and older.

Table 3. Summary of adjusted GMT and SRR values, and adjusted GMT ratios and SRR differences in terms of RSV-A and RSV-B neutralising titers (ED60) in adults 60 years of age and older (OA) relative to adults 50 through 59 years of age with (Adults-AIR) and without (Adults- non-AIR) pre-defined, stable, chronic medical conditions[a] leading to an increased risk for RSV disease – Per Protocol Set

RSV-A neutralising titers (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio (95% CI)[b]**	**SRR (%) (95% CI)**	**SRR difference (95% CI)[c]**
OA	**7 440.1 (6 768.4, 8 178.5)**	**0.8 (0.7, 1.0)**	**80.4 (75.8, 84.5)**	**(-12.1, -0.9)**
Adults-AIR	**8 922.7 (8 118.2, 9 806.9)**		**86.9 (82.8, 90.3)**	
OA	**7 492.6 (6 819.1, 8 232.7)**	**1.0 (0.8, 1.1)**	**80.4 (75.8, 84.5)**	**-2.4 (-8.3, 3.5)**
Adults-non-AIR	**7 893.5 (7 167.5, 8 692.9)**		**82.8 (78.3, 86.8)**	
RSV-B neutralising titers (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio[b]**	**SRR (95% CI)**	**SRR difference[c]**
OA	**8 062.8 (7 395.9, 8 789.9)**	**0.8 (95% CI [0.7, 0.9])**	**74.5 (69.5, 79.0)**	**-7.2 (95% CI [-13.3, -0.9])**
Adults- AIR	**10 054.7 (9 225.4, 10 958.7)**		**81.6 (77.1, 85.6)**	
OA	**8 058.2 (7 373.1, 8 807.0)**	**0.9 (97.5% CI [0.8, 1.0])**	**74.5 (69.5, 79.0)**	**-3.7 (97.5% CI [-11.1, 3.7])**
Adults-non-AIR	**9 009.5 (8 226.8, 9 866.6)**		**78.2 (73.3, 82.6)**	

[a]Pre-defined, stable, chronic medical conditions such as chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney or liver disease.
[b,c]The prespecified criteria for non-inferiority of the immune responses were defined as the 2-sided 95% or 97.5% CI upper limits (UL) on the adjusted GMT ratios (OA over Adults-AIR or Adults-non-AIR) ≤ 1.5 and the UL of the 2-sided 95% or 97.5% CI on the SRR difference (OA minus Adults-AIR or Adults-non-AIR) ≤ 10% in participants 60 years of age and older (OA) relative to participants 50 through 59 years of age with (Adults-AIR) or without (Adults-non-AIR) pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease
ED60: Estimated dilution 60; CI=Confidence interval; GMT=Geometric mean titer; SRR=Seroresponse rate

The non-inferiority criteria of the immune responses for the RSV-A and RSV-B neutralising titers were met. The efficacy of ***Arexvy***, in adults 50 through 59 years of age at increased risk for RSV disease, can be inferred following comparison of the immune response in adults 50 through 59 years of age with the immune response in adults 60 years of age and older in whom vaccine efficacy was demonstrated.

Immunogenicity following concomitant vaccination
In three open-label Phase III clinical studies, participants were randomized to receive 1 dose of ***Arexvy*** administered either concomitantly at Day 1 or separately (1 month apart) with inactivated seasonal quadrivalent influenza vaccine (standard dose unadjuvanted, adults ≥60 years of age, N=885; high dose unadjuvanted, adults ≥65 years of age, N=1,029; or standard dose adjuvanted, adults ≥65 years of age, N=1,045). The prespecified criteria for non-inferiority of the immune responses were defined as the 2-sided 95% confidence interval UL on the group GMT ratios ≤1.50 for the RSV-A neutralising titers and haemagglutinin inhibition titers against each of the Flu strains, in the separate administration versus co-administration groups.

There was no evidence of interference in the immune response to RSV-A or any of the four Flu antigens when ***Arexvy*** was co-administered with standard dose unadjuvanted or high dose unadjuvanted seasonal influenza vaccines.

Upon co-administration of ***Arexvy*** with standard dose adjuvanted seasonal influenza vaccine, there was no evidence of clinically relevant interference in the immune response to RSV-A or any of the four Flu antigens. The UL of the GMT ratio was ≤1.50 for RSV-A and three out of four Flu strains. For Flu A/H3N2, the UL of the GMT ratio was 1.53.

Immune responses for the RSV-B neutralising titers were comparable in the separate administration versus co-administration groups in all three studies.

Pharmacokinetic
Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical Studies
See *Pharmacodynamic Effects*.

Non-Clinical Information
Non-clinical data reveal no special hazard 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 a 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.

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 the 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.

Presentations
Box, 1 vial of powder injection RSVPreF3 Antigen (1 dose) + 1 vial of suspension injection $AS01_E$ Adjuvant @ 0,5 mL Reg. No. DKI2476704144A1

HARUS DENGAN RESEP DOKTER

Manufactured by:
GlaxoSmithKline Biologicals s.a.
20, Avenue Fleming – 1300 Wavre
Belgium

Released by :
GlaxoSmithKline Biologicals s.a.
89, rue de l'Institut - 1330 Rixensart
Belgium

Imported by:
PT Glaxo Wellcome Indonesia
Jakarta, Indonesia

Version number	: 04
Reference	: EMEA/H/C/006054 + Arexvy: EPAR – Product Information (last updated:09/10/2024) and GDS07/IPI06 (30 September 2024)
Date of local revision	: 24 Mar 2025

PACKAGE LEAFLET: INFORMASI UNTUK PASIEN

Arexvy

Recombinant Respiratory Syncytial Virus Pre-Fusion F Protein 120 mcg

Serbuk untuk suspensi injeksi

Baca Leaflet Ini Dengan Saksama Sebelum Anda Mendapatkan Vaksin Ini.
- Simpan leaflet ini. Anda mungkin butuh untuk membacanya lagi
- Jika Anda memiliki pertanyaan lebih lanjut, Anda dapat menghubungi dokter atau apoteker Anda
- Vaksin ini diresepkan untuk Anda. Jangan diberikan untuk orang lain
- Jika ada kejadian ikutan pasca imunisasi (KIPI) yang menjadi serius atau jika Anda mengalami KIPI yang tidak tercantum pada leaflet ini, harap hubungi dokter atau apoteker Anda

Pada Leaflet Ini:

1. Apakah *Arexvy* Itu dan Digunakan untuk Apa

Arexvy adalah vaksin yang digunakan untuk melindungi orang dewasa 60 tahun ke atas terhadap virus yang disebut 'Respiratory Syncytial Virus' (RSV).

Arexvy juga membantu melindungi terhadap RSV pada orang dewasa 50 hingga 59 tahun yang berisiko tinggi terkena penyakit RSV.

RSV adalah virus pernapasan yang menyebar dengan sangat mudah.
- RSV dapat menyebabkan penyakit saluran pernapasan bagian bawah – infeksi paru-paru dan bagian tubuh lainnya yang membantu Anda bernapas.

Infeksi RSV dapat terjadi pada usia berapapun, dan biasanya menyebabkan gejala ringan seperti pilek pada orang dewasa. Tetapi dapat juga:
- Menyebabkan penyakit pernapasan yang lebih serius pada bayi dan orang dewasa yang lebih tua.
- Memperburuk beberapa penyakit, seperti penyakit pernapasan jangka panjang atau penyakit jantung.

Bagaimana ***Arexvy*** bekerja
Arexvy membantu pertahanan alami tubuh Anda dengan membentuk antibodi dan sel darah putih khusus. Ini melindungi Anda dari RSV.
Arexvy tidak mengandung virus, sehingga tidak dapat menyebabkan infeksi.

2. Apa yang Perlu Anda Ketahui Sebelum Mendapatkan *Arexvy*

Jangan gunakan *Arexvy*
- Jika Anda memiliki reaksi alergi terhadap zat aktif atau bahan lain dalam vaksin ini (tercantum pada *Bagian 5)*.

Jangan gunakan ***Arexvy*** jika salah satu dari hal tersebut di atas terjadi pada Anda. Jika Anda tidak yakin, konsultasikan dengan dokter atau apoteker Anda.

Peringatan dan tindakan pencegahan
Konsultasikan dengan dokter atau apoteker Anda sebelum menerima ***Arexvy***:
- Jika Anda pernah mengalami reaksi alergi berat setelah penyuntikan vaksin lain

- Jika Anda mengalami infeksi berat dengan panas tinggi (demam). Jika ini terjadi, vaksinasi dapat ditunda sampai keadaan membaik. Infeksi ringan seperti pilek seharusnya tidak menjadi masalah, namun demikian konsultasikan dengan dokter Anda terlebih dahulu
- Jika Anda mengalami masalah pendarahan atau mudah mengalami memar
- Jika Anda pingsan dengan suntikan sebelumnya. Pingsan dapat terjadi sebelum atau sesudah suntikan.

Jika salah satu dari hal di atas berlaku untuk Anda (atau Anda tidak yakin), konsultasikan dengan dokter atau apoteker Anda sebelum Anda diberikan ***Arexvy.***

Seperti semua vaksin, ***Arexvy*** mungkin tidak sepenuhnya melindungi semua orang yang divaksinasi.

Obat Lain dan *Arexvy*
Beritahu dokter atau apoteker Anda jika:
- Anda sedang atau baru saja menggunakan obat lain, termasuk obat yang didapatkan tanpa resep
- Anda baru saja menerima vaksin lain.

Arexvy dapat diberikan bersamaan dengan vaksin flu.
Jika ***Arexvy*** diberikan bersamaan dengan vaksin suntik lainnya, direkomendasikan untuk disuntikkan pada tempat suntikan yang berbeda, yang berarti lengan yang berbeda untuk setiap suntikan.

Kehamilan dan menyusui
Jika Anda sedang hamil atau menyusui, atau Anda kemungkinan hamil atau berencana untuk mempunyai anak, konsultasikan dengan dokter atau apoteker Anda sebelum Anda diberikan vaksin ini.
Arexvy tidak direkomendasikan diberikan selama kehamilan atau menyusui.

Mengemudi dan menggunakan mesin
Beberapa efek yang disebutkan pada bagian 4. “Kemungkinan Kejadian Ikutan Pasca Imunisasi (KIPI)” dapat mempengaruhi kemampuan mengemudi atau menggunakan mesin untuk sementara. Jangan mengemudi atau menggunakan mesin jika Anda merasa kurang sehat.

***Arexvy* mengandung natrium dan kalium**
Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per dosis, artinya ‘bebas natrium’
Obat ini mengandung kurang dari 1 mmol kalium (39 mg) per dosis, artinya ‘bebas kalium’.

3. Bagaimana Cara Pemberian *Arexvy*

Arexvy diberikan sebagai suntikan dosis tunggal 0,5 mL ke dalam otot, biasanya lengan atas.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan vaksin ini, tanyakan kepada dokter atau apoteker Anda.

4. Kemungkinan Kejadian Ikutan Pasca Imunisasi (KIPI)

Seperti obat-obatan lain, ***Arexvy*** dapat menyebabkan KIPI, walaupun tidak semua orang akan mengalami KIPI.

Berikut KIPI yang mungkin terjadi setelah menggunakan ***Arexvy***:

Sangat umum (ini dapat terjadi lebih dari 1 dalam 10 dosis vaksin):
- rasa sakit di tempat suntikan
- merasa lelah (*fatigue*)
- sakit kepala
- nyeri otot (*myalgia*)
- nyeri sendi (*arthralgia*)
- kemerahan pada tempat suntikan diberikan

Umum (ini dapat terjadi hingga 1 dari 10 dosis vaksin):
- bengkak pada tempat suntikan diberikan
- demam
- menggigil
- hidung berlendir/meler

Tidak umum (ini dapat terjadi hingga 1 dari 100 dosis vaksin)
- gatal pada tempat suntikan
- nyeri
- merasa tidak enak badan (malaise)
- pembesaran kelenjar getah bening, atau pembengkakan kelenjar di leher, ketiak atau selangkangan (lymphadenopathy)
- reaksi alergi seperti ruam
- merasa mual (nausea)
- sakit perut

Beri tahu dokter atau apoteker Anda jika Anda mengalami KIPI yang tercantum di atas. Sebagian besar KIPI ini memiliki intensitas ringan hingga sedang dan tidak bertahan lama.

Jika KIPI menjadi serius, atau jika Anda melihat terdapat KIPI yang tidak tercantum dalam leaflet ini, segera konsultasikan pada dokter atau apoteker Anda.

Laporkan Kejadian Tidak Diinginkan (KTD) ke GSK Indonesia melalui situs web https://gsk.public.reportum.com.

5. Cara Penyimpanan *Arexvy*
- Simpan dalam lemari es (2°C - 8°C).
- Jangan dibekukan.
- Simpan dalam kemasan asli untuk melindungi dari cahaya.

6. Informasi Lain
Apa kandungan *Arexvy*
Zat aktif:
Setelah rekonstruksi, 1 dosis (0,5 mL) mengandung:

RSVPreF3[1] antigen[2,3]	120 micrograms

[1]*Respiratory Syncytial Virus recombinant glycoprotein F stabilised in the pre-fusion conformation = RSVPreF3*
[2]*RSVPreF3 produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology*
[3]adjuvan AS01$_E$ mengandung:

Plant extract Quillaja saponaria Molina, fraction 21 (QS-21)	25 micrograms
3-O-desacyl-4'-monophosphoryl lipid A (MPL) from Salmonella minnesota	25 micrograms

RSVPreF3 adalah protein yang ada dalam *Respiratory Syncytial* Virus. Protein ini tidak menular.

Adjuvan digunakan untuk meningkatkan respon tubuh terhadap vaksin.

Bahan lain:
- **Serbuk (RSVPreF3 antigen):** *trehalose dihydrate, polysorbate 80 (E 433), potassium dihydrogen phosphate (E 340), dipotassium phosphate (E 340)*
- **Suspensi:** *dioleoyl phosphatidylcholine (E 322), cholesterol, sodium chloride, disodium phosphate anhydrous (E 339), potassium dihydrogen phosphate (E 340) and water for injection.*

Lihat bagian 2 "***Arexvy*** mengandung natrium dan kalium".

Bagaimana bentuk dari *Arexvy* dan isi kemasan
- Serbuk dan suspensi untuk suspensi injeksi.
- Serbuk berwarna putih.
- Suspensi *opalescent*, tidak berwarna hingga cairan kecoklatan pucat.

Kemasan ***Arexvy*** terdiri dari:
- Serbuk (RSVPreF3 antigen) untuk 1 dosis dalam vial
- Suspensi (adjuvan AS01$_E$) untuk 1 dosis dalam vial

HARUS DENGAN RESEP DOKTER

Diproduksi oleh:

GlaxoSmithKline Biologicals s.a.
20, Avenue Fleming – 1300
Wavre, Belgia.

Dirilis oleh:
GlaxoSmithKline Biologicals s.a.
89, rue de l'Institut – 1330
Rixensart, Belgia.

Diimpor oleh:
PT Glaxo Wellcome Indonesia
Jakarta, Indonesia.

Dus, 1 vial serbuk injeksi RSVPreF3 Antigen (1 dosis) + 1 vial suspensi injeksi AS01$_E$ Adjuvant @ 0,5 mL Reg. No. DKI2476704144A1

Version number	: 04
Reference	:EMEA/H/C/006054 + Arexvy: EPAR – Product Information (last updated:09/10/2024) and GDS07/IPI06 (30 September 2024)
Date of local revision	: 24 Mar 2025