▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION

AREXVY (Recombinant Respiratory Syncytial Virus pre-fusion F protein) powder and suspension for suspension for injection

1 NAME OF THE MEDICINE

Recombinant Respiratory Syncytial Virus pre-fusion F protein (RSVPreF3) ($AS01_E$ adjuvanted vaccine)

2 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 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* saponin (QS-21) (25 micrograms) and 3-O-desacyl-4'-monophosphoryl lipid A (MPL) from *Salmonella minnesota* (25 micrograms).

List of excipients with known effect

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Powder and suspension for suspension for injection.

The powder is white.

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

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

AREXVY is indicated for active immunisation of individuals 60 years and older for the prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV).

The use of this vaccine should be in accordance with official recommendations.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage:

AREXVY is administered as a single dose of 0.5 mL.

The need for revaccination has 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.

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.

AREXVY is for single use in one patient only. Discard any residue.

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

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substances or to any component of the vaccine (see Sections 2 QUALITATIVE AND QUANTITATIVE COMPOSITION and 6.1 LIST OF EXCIPIENTS)

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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. However, 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.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures 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 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.

Use in the elderly

There are no special precautions for use in the elderly.

Paediatric use

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

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Use with other vaccines

AREXVY can be given concomitantly with inactivated unadjuvanted seasonal influenza vaccine (Flu Quadrivalent containing a combined total of 60 micrograms Hemagglutinin (HA) per dose). There was no evidence of interference in the immune response to the antigens contained in the co-administered vaccines (see Section 5.1 PHARMACODYNAMIC PROPERTIES, Clinical trials). For adverse effects, please see Section 4.8 ADVERSE EFFECTS - Safety Data from RSV OA=ADJ-007.

Data are currently not available for concomitant administration with other vaccines.

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on 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.

Use in pregnancy

(Pregnancy Category B2)

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 3557 pregnant women in a single clinical study, an increase in preterm births was observed compared to placebo.

In a reproductive and developmental toxicity study, female rats were administered $AS01_B$ adjuvant alone by intramuscular injection 28 and 14 days prior to mating, on gestation days 3, 8, 11, and 15, and on lactation Day 7. The total dose was similar to the dose of $AS01_E$ in AREXVY. No adverse effects on preweaning development up to post-natal day 25 were observed. There was no vaccine related fetal malformations or variations.

In another reproductive and developmental toxicity study, female rabbits were administered the $AS01_B$ adjuvant by intramuscular injection 28 and 14 days prior to mating, on gestation days 3, 11, 16, and 24, and on lactation Day 7. The total dose was 2 times the dose of $AS01_E$ in AREXVY. $AS01_B$ produced no adverse effects on embryofetal or pre- and post-natal survival, growth or development of the offspring up to day 35 of age.

Use in lactation

There are no data on the excretion of AREXVY in human or animal milk. AREXVY is not recommended in breastfeeding/lactating women.

4.7 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. However, some of the effects mentioned under Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS) (e.g. fatigue) may temporarily affect the ability to drive or use machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical trial data

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	rhinorrhoea
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

Safety Data from RSV OA=ADJ-006:

Solicited Adverse Reactions: A subset of study participants (solicited safety set) was monitored for solicited adverse reactions using standardised paper diary cards during the 4 days (i.e., day of vaccination and the next 3 days) following a dose of AREXVY or 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 frequencies 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 and who completed their diary.

[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, 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.

Serious Adverse Events: In RSV OA=ADJ-006, participants were monitored for all serious adverse events (SAEs) that occurred 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%).

Deaths: From vaccination through the first analysis of the ongoing RSV OA=ADJ-006, 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, 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.

Safety Data from RSV OA=ADJ-007:

In the open-label Phase III RSV OA=ADJ-007 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) either concomitantly at Day 1 (N = 442), or 1 dose of Flu Quadrivalent at Day 1 followed by a dose of AREXVY 1 month later (N = 443).

The reported frequencies of specific solicited local (administration site) and systemic adverse reactions are presented in Table 2.

Table 2: 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 upon either concomitant or separate administration of AREXVY with Flu Quadrivalent vaccine

	AREXVY + Flu Quadrivalent concomitant administration %		Flu Quadrivalent + AREXVY one month apart %	
Local Adverse Reactions	Flu Quadrivalent N = 438	AREXVY N = 438	Flu Quadrivalent N = 438	AREXVY N = 419
Pain, Any[a]	28.3	47.9	20.5	39.1
Pain, Grade 3[a]	0.9	2.7	0	1.4
Erythema, >20 mm	1.1	4.1	0.5	2.1
Erythema, >100 mm	0	0	0	0
Swelling, >20 mm	1.4	3.2	0.7	1.0
Swelling, >100 mm	0	0	0	0
Systemic Adverse Reactions	N = 438		N = 438	N = 419
Fatigue, Any[b]	22.4		12.8	17.9
Fatigue, Grade 3[b]	0.9		0.5	1.0
Myalgia, Any[b]	22.1		9.4	19.6
Myalgia, Grade 3[b]	0.7		0	1.2
Headache, Any[b]	21.7		12.8	16.2
Headache, Grade 3[b]	0.5		0.5	1.0
Arthralgia, Any[b]	16.2		4.8	11.2
Arthralgia, Grade 3[b]	0.7		0	0.7
Fever, ≥38.0°C/100.4°F[c]	2.5		0.7	1.0
Fever, >39.0°C/102.2°F[c]	0.7		0	0.2

N = number of participants with documented dose.

[a] 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).

[b] 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).

[c] Temperature taken by any route (oral, axillary, or tympanic).

Serious Adverse Events Reported from Other Studies

Study RSV OA=ADJ-004 (NCT04732871): One case of Guillain-Barré syndrome beginning 9 days after AREXVY vaccination was reported in a participant enrolled in a study site in Japan.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Insufficient data are available.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

The RSVPreF3 antigen in AREXVY is derived from the laboratory-adapted RSV-A A2 strain, stabilised in the pre-fusion conformation of the naturally occurring F protein for which both RSV-A and B subtypes share high amino acid sequence homology. 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 induce 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. 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 antibody responses. 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.

Clinical trials

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 dyspneoa (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.

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 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 84.6% (95% CI [32.1, 98.3]) and 80.9% (95% CI [49.4, 94.3]), respectively.

Table 3. Efficacy Analysis: First RSV-associated LRTD Overall, by Age, co-morbidity and subtypes 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	82.6 (57.9, 94.1)
60-69 years	6963	4	1.0	6979	21	5.5	81.0 (43.6, 95.3)
70-79 years	4487	1	0.4	4487	16	6.5	93.8 (60.2, 99.9)
Participants with at least 1 comorbidity of interest	4937	1	0.4	4861	18	6.6	94.6 (65.9, 99.9)
RSV-A	12466	2	0.3	12494	13	1.9	84.6 (32.1, 98.3)
RSV-B	12466	5	0.7	12494	26	3.8	80.9 (49.4, 94.3)

[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 84.4% (95% CI: [46.9, 97.0]) 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 (2 cases among participants who received AREXVY and 3 cases among participants who received placebo).

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 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 94.1 % (95% CI [62.4, 99.9]) 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 71.7% (95% CI [56.2, 82.3]).

Table 4: Efficacy Analysis: Severe RSV-associated LRTD 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	
Severe RSV-associated LRTD	12466	1	0.1	12494	17	2.5	94.1 (62.4-99.9)

[a]CI = Confidence Interval (95%). Two-sided exact CI for vaccine efficacy is derived based on Poisson model adjusted by age categories and regions.

N = Number of participants included in each group

n = Number of participants having first occurrence of severe RSV-confirmed LRTD occurring from Day 15 post vaccination

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 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 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).

There was no evidence for interference in the immune response to any of the antigens contained in both co-administered vaccines. 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 neutralising 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.

Currently no clinical data is available on coadministration of AREXVY with other vaccines.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

AREXVY was not tested for genotoxicity.

Carcinogenicity

AREXVY was not tested for carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Powder (RSVPreF3 antigen):

Trehalose dihydrate

Polysorbate 80

Monobasic potassium phosphate

Dibasic potassium phosphate

Suspension ($AS01_E$ Adjuvant System):

Dioleoylphosphatidylcholine

Cholesterol

Sodium chloride

Dibasic sodium phosphate

Monobasic potassium phosphate

Water for injections

6.2 INCOMPATIBILITIES

This medicinal product must not be mixed with other medicinal products.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

For shelf-life after reconstitution of the medicinal product, see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Use and Handling.

6.4 SPECIAL PRECAUTIONS FOR 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 Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Use and Handling.

6.5 NATURE AND CONTENTS OF CONTAINER

AREXVY is presented as:

- 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.

Not all strengths, dose forms, pack sizes, container types may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Not relevant to vaccines.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

Level 4, 436 Johnston Street,

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9 DATE OF FIRST APPROVAL

14 January 2024

10 DATE OF REVISION

N/A

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
N/A	New Product Information

Version 1.0