swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report
Extension of therapeutic indication

Arexvy

International non-proprietary name:	respiratory syncytial virus (RSV) prefusion F protein
Pharmaceutical form:	powder and suspension for suspension for injection
Dosage strength(s):	120 micrograms / 0.5 mL
Route(s) of administration:	intramuscular
Marketing authorisation holder:	GlaxoSmithKline AG
Marketing authorisation no.:	69310
Decision and decision date:	extension of therapeutic indication approved on 16 September 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
GMT	Geometric mean titre
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
LRTD	Lower respiratory tract disease
LRTI	Lower respiratory tract infection
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
SRR	Seroresponse rate
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
URTI	Upper respiratory tract infection

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Arexvy is indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 18 years of age and older.
The official vaccination recommendations on the appropriate use should be observed.

2.2.2 Approved indication

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;
- adults 18 to 59 years of age with an increased risk for an RSV-associated LRTD.

The official vaccination recommendations on the appropriate use should be observed.

2.2.3 Requested dosage

Summary of the requested standard dosage:

No change to the dosage recommendation was requested with the application for extension of indication.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	3 November 2025
Formal control completed	13 November 2025
List of Questions (LoQ)	3 March 2026
Response to LoQ	9 April 2026
Preliminary decision	9 June 2026
Response to preliminary decision	7 August 2026
Final decision	16 September 2026
Decision	approval

3 Medical context

The human respiratory syncytial virus (RSV) causes acute respiratory tract illness in persons of all ages. The clinical manifestations vary with age and health status. Natural infection with RSV does not lead to long-term immunity, and recurrent infections can occur in both children and adults.
In addition to premature infants and infants under 6 months of age, older adults and subjects with immunosuppression or underlying chronic medical conditions are at risk for severe lower respiratory tract infection (LRTI).
Healthy adults are infected with RSV repeatedly throughout their lives, as immunity is not long-lasting, and typically have symptoms restricted to the upper respiratory tract.
Treatment of RSV-associated respiratory disease is limited to supportive measures.

Swiss national recommendations propose RSV vaccination for all subjects 75 years and above and for subjects between 60 and 74 years of age with higher risk of severe RSV disease (including immunodeficiencies, chronic underlying diseases, and patients living in long-term care facilities). Additionally, vaccination is recommended for subjects between 18 and 59 years of age with severe immune deficiency or other underlying conditions with very high risk for severe RSV disease.

At the time of this submission, two other RSV vaccines – Abrysvo and mRESVIA – were available in Switzerland in addition to Arexvy.
Abrysvo is an RSV prefusion F (preF) A and preF B recombinant vaccine (non-adjuvanted) approved for the passive immunisation of infants against RSV LRTI through maternal immunisation and the active immunisation against RSV LRTI in adults 60 years and above and adults 18-59 years of age at high risk for RSV disease.
mRESVIA is an mRNA vaccine coding preF A and is approved for active immunisation of adults 18 years and older; it has a similar indication to Abrysvo.

4 Nonclinical aspects

The applicant did not submit new nonclinical studies to support the requested extension of the indication. This was considered acceptable. Based on the ERA, the extension of the indication will not be associated with a significant risk for the environment.

5 Clinical aspects

Efficacy data in the requested population were not available.

One clinical study was submitted in support of this indication extension for adults 18-49 years of age. Study RSV OA=ADJ-025 was a phase 3, open-label, uncontrolled, non-randomised, multi-centre study with the aim of demonstrating non-inferior immune response in younger adults aged 18-49 years with underlying medical conditions relative to older adults ≥60 years of age, for whom vaccine efficacy has been established.

The study met its primary objectives by demonstrating that the immunogenicity in adults 18-49 years of age at increased risk for RSV disease was non-inferior to that observed in adults ≥60 years of age in terms of neutralising antibody titres (geometric mean titre [GMT] ratio upper limit ≤1.5 and seroresponse rates (SRR difference upper limit ≤10%) for both RSV-A and RSV-B at 1-month post-vaccination. Vaccine efficacy against RSV-confirmed lower respiratory tract disease (LRTD) was demonstrated in adults ≥60 years of age in the phase 3 study RSV OA=ADJ-006 (which was the pivotal study for the initial marketing authorisation); vaccine effectiveness can be inferred for the younger at-risk population.

The at-risk adults aged 18-49 years enrolled in the study had stable, chronic medical conditions (mostly cardiac disorders, diabetes mellitus, and asthma). Immunosuppressed subjects were excluded; data in adults with very high risk for severe RSV disease were therefore not available.

The secondary endpoints at 6 months post-vaccination showed a decrease in the immune response in terms of RSV-A and B neutralising titres in both the younger and older adult cohorts. However, the neutralisation titres remained above baseline. Subgroup analyses by age at vaccination in the age groups 18-49, 60-69, and ≥70 years showed that the immune response at 1 month post-vaccination in terms of GMT and SRR tends to decrease with increase in age, which is a common finding for vaccines and is acceptable.

The initially proposed indication was broader than the studied population of younger adults at risk in study RSV-OA=ADJ-025. Immunogenicity data directly supporting the requested indication were not available in healthy younger adults. Further, the benefit-risk ratio of Arexvy in healthy young adults differs from that in at-risk adults due to the following issues: Clinical efficacy in the elderly was demonstrated for the prevention of LRTD. However, this cannot be directly inferred for the general younger adult population, as in healthy younger adults, RSV mostly causes upper respiratory tract infection (URTI). RSV in healthy adults usually presents as an URTI with mild to moderate symptoms; due to the smaller risk of severe disease, the medical need is therefore lower than for at-risk subjects and the elderly. It is acknowledged that morbidity is not negligible in this age group but lower than for influenza or SARS-CoV-2 infections, even though the exact incidence of RSV disease in this age group is not well known.

Additionally, similarly to other vaccines, the use of Arexvy carries some potential risks. (The safety profile of Arexvy includes Guillain-Barré syndrome, which was observed in the post-marketing setting.)

Therefore, the indication was restricted to adults with increased risk of an RSV-induced LRTI.

As an additional indication extension within the present application, the applicant requested removal of the at-risk restriction for adults 50-59 years of age. This request was supported by additional immunogenicity analyses from study RSV-OA=ADJ-018, which formed the basis for the initial approval in at-risk adults 50-59 years of age.

In support of the proposed extension to adults 50-59 years of age irrespective of risk status, non-inferior immunogenicity was demonstrated in a subcohort of healthy adults 50-59 years of age compared with older adults, based on the same non-inferiority criteria as discussed above. Immune responses, as measured by neutralising antibody titres at 6 months post-vaccination, were also comparable between the groups.

Given that the above-mentioned limitations affecting the benefit-risk ratio in the younger healthy adult population also apply to adults aged 50-59 years without risk factors, the request to remove the at-risk restriction for the already approved population of adults aged 50-59 years was not accepted.

Arexvy was more reactogenic in the younger at-risk vs the older adult population. A higher rate of solicited events (injection site pain, myalgia, fatigue, headache, and arthralgia) was reported in the younger at-risk adult group compared to the older adult group. The median duration and severity of these events was, however, comparable across the age groups.

The percentage of participants with unsolicited adverse events (AEs) considered related to study intervention by the investigator was higher in the younger at-risk adult group than in the older adult group (8.7% vs 3.0%). This was mainly driven by the higher percentage of participants with general disorders and administration site conditions (4.1% and 1.9%, respectively) and gastrointestinal disorders (2.2% and 0.2%, respectively).

There were no deaths or related serious adverse events, or events of neurological demyelinating disease in the study.

Based on the safety results of RSV OA=ADJ-025, Arexvy had an acceptable reactogenicity and safety profile in at-risk adults 18-49 years of age. The safety profile in this group was overall consistent with the known safety profile of Arexvy.

The higher reactogenicity in younger age groups is not unexpected for vaccines and is adequately reflected in the Information for healthcare professionals.

5.1 Final clinical benefit-risk assessment

Non-inferior immunogenicity was demonstrated in participants aged 18-49 years at increased risk for RSV disease compared with older adults aged ≥60 years. Consequently, the efficacy of the vaccine in younger adults at increased risk is inferred from the efficacy previously established in the older adult population.
No new safety concerns were identified. As generally observed in vaccine studies, the reactogenicity in the younger population was higher than in the elderly.
The benefit-risk ratio of Arexvy in adults 18-49 years of age at increased risk for RSV LRTD was considered positive.

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Arexvy was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo-pro.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

Arexvy

Respiratory Syncytial Virus (RSV) vaccine (recombinant, adjuvanted)

Composition

Active substances

Respiratory syncytial virus (RSV) pre-fusion protein F (RSVPreF3 antigen), produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cells.

Excipients

*Powder (*RSVPreF3 antigen*):* trehalose dihydrate, polysorbate 80, potassium dihydrogen phosphate, dipotassium phosphate.
Suspension (*$AS01_E$ adjuvant):* purified *Quillaja* saponin (QS-21), 3-*O*-desacyl-4'-monophosphoryl lipid A (MPL), dioleoyl phosphatidylcholine, cholesterol, sodium chloride, disodium phosphate anhydrous, potassium dihydrogen phosphate, water for injections.
After reconstitution, one vaccine dose contains 1.78 mg sodium and 0.35 mg potassium.

Pharmaceutical form and active substance quantity per unit

Powder and suspension for suspension for injection (i.m.).
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 $AS01_E$ 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.

Indications/Uses

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;
- adults 18 to 59 years of age with an increased risk for an RSV-associated LRTD.

The official vaccination recommendations on the appropriate use should be observed.

Dosage/Administration

Consideration should be given to the official vaccination recommendations for the immunisation schedules.

To ensure traceability of biotechnological medicinal products, it is recommended that the trade name and batch number be documented for each treatment.

Usual dosage

Arexvy is administered as a single dose of 0.5 mL.

Children and adolescents

The safety and efficacy of Arexvy in children and adolescents younger than 18 years of age have not been established. No data is available. Arexvy is not authorised for use in the paediatric population.

Mode of administration

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

For instructions on reconstitution of the medicinal product before administration, see “Instructions for handling” section.

Contraindications

Hypersensitivity to the active substances or to any of the other components of the vaccine (see “Composition” and “Pharmaceutical form and active substance quantity per unit”).

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.

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 in 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.

Guillain-Barré syndrome

The results of a post-marketing observational study in individuals aged 65 years or older suggest an increased risk of Guillain-Barré syndrome within 42 days of vaccination with Arexvy (see " Undesirable effects " section).

Limitations of the clinical data

Studies on the clinical efficacy and safety of Arexvy have been conducted in adults 60 years of age and older.

The effectiveness of Arexvy in adults between 50 and 59 years of age at an increased risk for RSV disease can be inferred on the basis of an immune response comparable to that in adults 60 years of age and older, for whom the efficacy of the vaccine has been proven.

Excipients

This medicinal product contains less than 1 mmol of sodium (23 mg) per vaccine dose, i.e. it is almost “sodium-free”.

This medicinal product contains potassium, but less than 1 mmol (39 mg) per vaccine dose, i.e. it is almost “potassium-free”.

Interactions

Use with other vaccines

Arexvy can be administered concomitantly with inactivated seasonal influenza vaccines (standard-dose unadjuvanted, high-dose unadjuvanted, or standard-dose adjuvanted) or with a herpes zoster vaccine (recombinant, adjuvanted).

The safety profile of Arexvy when co-administered with inactivated seasonal influenza vaccines was comparable to when Arexvy was administered alone.

The safety profile of Arexvy when administered concomitantly with a herpes zoster vaccine (recombinant, adjuvanted) was comparable to the sequential administration of the vaccines.

Immunogenicity following concomitant administration with influenza vaccines

In three open-label Phase III clinical studies, the participants were randomised and received 1 dose of Arexvy either concomitantly on Day 1 or separately (1 month later) with an inactivated seasonal quadrivalent influenza vaccine (standard-dose unadjuvanted, adults ≥60 years of age; high-dose unadjuvanted, adults ≥65 years of age; or standard-dose adjuvanted, adults ≥65 years of age).
In the case of concomitant administration of Arexvy with a standard-dose adjuvanted seasonal influenza vaccine, there were no indications of any clinically relevant impairment of the immune response to RSV-A or any of the four influenza antigens. The immune response triggered by flu A/H3N2 did not, however, meet the predefined criteria for non-inferiority (the upper limit (UL) of the 95% CI for the GMT ratio was 1.53, so was above the predefined limit of ≤1.5).
The RSV-B neutralisation titres were comparable across all three studies for both separate and concomitant administration.
In the case of concomitant administration of Arexvy and seasonal inactivated influenza vaccines, numerically lower RSV-A and RSV-B neutralising antibody titres and numerically lower influenza A and B haemagglutination inhibition antibody titres were observed compared with separate administration. However, this was not observed consistently across all studies. The clinical relevance of these observations is not known.
Immunogenicity following concomitant administration with a herpes zoster vaccine (recombinant, adjuvanted)
In an open-label Phase III clinical study, participants 50 years of age and older were randomised into two groups. In the first group (N = 265), on Day 1, participants received a dose of herpes zoster vaccine and a dose of Arexvy, followed by a second dose of herpes zoster vaccine on Day 61. In the second group (N = 265), participants received a dose of herpes zoster vaccine on Day 1 and on Day 61, and a dose of Arexvy on Day 31. The prespecified criteria for non-inferiority of the immune responses were defined as the UL of the 2-sided 95% CI of the GMT ratios of the separate versus co-administration groups ≤ 1.50 for the RSV-A and RSV-B neutralizing titers, and a GMC ratio ≤ 1.50 for anti-gE antibody concentrations.
The non-inferiority criteria of the immune responses were met when the two vaccines were administered concomitantly.
If Arexvy is to be given at the same time as another injectable vaccine, the vaccines should always be injected at different sites.
Currently, there are no available data on the concomitant administration of Arexvy with other vaccine.

Pregnancy, lactation

Pregnancy

There are no data from clinical trials on the use of Arexvy in pregnant women. The administration of Arexvy during pregnancy is not recommended.

After administration of an investigational unadjuvanted RSVPreF3 vaccine to 3,557 pregnant women in a single clinical trial, an increase in preterm births was observed compared to placebo.
Results from animal studies with an investigational unadjuvanted RSVPreF3 vaccine and results with Arexvy do not indicate direct or indirect reproductive toxicity (see “Preclinical data”).

Lactation

To date, there are no data on the excretion of Arexvy in human or animal milk. The administration of Arexvy is not recommended in breast-feeding women.

Fertility

There are no data on the effects of Arexvy on human fertility.
Animal studies do not indicate any direct or indirect harmful effects on female fertility.

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.

Undesirable effects

In a placebo-controlled Phase III clinical study (RSV OA=ADJ-006), participants 60 years of age and older received either one dose of Arexvy (N = 12 469) or placebo (N = 12 503), with a follow-up period of approximately 12 months. The most commonly reported adverse reactions were injection site pain (61%), fatigue (34%), myalgia (29%), headache (28%), and arthralgia (18%).
In a placebo-controlled phase III clinical study (RSV OA=ADJ-018), 769 participants 50 through 59 years of age received one dose of Arexvy. The most commonly reported adverse reactions were injection site pain (76%), fatigue (40%), myalgia (36%), headache (32%), and arthralgia (23%).
In an open-label phase III clinical study (RSV OA=ADJ-025), 1,029 participants 18 through 49 years of age received one dose of Arexvy. The most commonly reported adverse reactions were injection site pain (76%), fatigue (60%), myalgia (60%), headache (44%), and arthralgia (28%).
In these two studies, there was a higher incidence of injection site pain, fatigue, myalgia, headache, and arthralgia in participants 18 through 49 years of age and 50 through 59 years of age compared with those 60 years of age and older. However, the median duration and severity of these events were comparable across age groups.
The safety profile presented in the table below is based on a pooled analysis of data from phase III clinical studies (RSV OA=ADJ-006, -018 and -025) conducted in Europe, North America, Asia and Southern hemisphere in adults 18 years of age and older, and on post-marketing experience.
Adverse drug reactions are listed below by MedDRA system organ class and by frequency according to the following convention: “very common” (≥1/10), “common” (≥1/100, <1/10), “uncommon” (≥1/1,000, <1/100), “rare” (≥1/10,000, <1/1,000), “very rare” (<1/10,000).

System Organ Class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
Immune system disorders	Uncommon	Hypersensitivity reactions (such as rash)
Nervous system disorders	Very common	Headache (32%)
	Very rare	Guillain-Barré syndrome*
Respiratory, thoracic, and mediastinal disorders	Common	Rhinorrhea
Gastrointestinal disorders	Uncommon	Nausea, abdominal pain, vomiting
Musculoskeletal and connective tissue disorders	Very common	Myalgia (40%), arthralgia (22%)
General disorders and administration site conditions	Very common	Injection site pain (68%), fatigue (42%)
	Common	Injection site erythema, injection site swelling, fever, chills
	Uncommon	Injection site pruritus
		Pain, malaise
	Not known	Necrosis at the injection site**

* Undesirable effect from the post-marketing phase

** Undesirable effect from spontaneous reports

In Study RSV OA=ADJ-006 (NCT04886596), within 30 days of vaccination, atrial fibrillation was reported in 10 subjects who received Arexvy and 4 subjects who received placebo (of which 7 events in the Arexvy arm and 1 event in the placebo arm were serious); the onset of symptoms ranged from 1 to 30 days post-vaccination. The information currently available on the atrial fibrillation is insufficient to determine a causal relationship to the vaccine. Within 6 months of vaccination, serious events of atrial fibrillation were reported in 13 subjects who received Arexvy and 15 subjects who received placebo.

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 one participant enrolled at a study site in Japan.

In an observational study after the market launch in the USA, an increased risk of Guillain-Barré syndrome was observed in individuals aged 65 years and over in the first 42 days after vaccination with Arexvy (estimated 7 additional cases per million doses administered). However, due to the study design, a causal relationship cannot be considered proven with certainty.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

Insufficient data are available.

Properties/Effects

ATC code

J07BX05

Mechanism of action

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.

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.

Pharmacodynamics

Clinical efficacy

The efficacy of Arexvy against RSV-associated LRTD in adults aged 60 years and older was evaluated over up to 3 RSV seasons in the Phase III, randomised, placebo-controlled, observer-blind clinical study (RSV OA=ADJ-006) conducted in 17 countries in the Northern and Southern Hemispheres.

The primary population for the efficacy analysis (referred to as the modified exposed set) consisted of adults aged 60 years and older who received at least one dose of Arexvy or placebo and had not reported confirmed RSV-associated acute respiratory illness (ARI) prior to Day 15 after vaccination.

The primary efficacy analysis set for the first RSV season included 24,960 participants who received one dose of Arexvy (N = 12,466) or placebo (N = 12,494) and were followed for the development of RSV-associated LRTD for up to 10 months (median of 6.7 months).

Prior to Season 2, participants receiving Arexvy were re-randomised to placebo (N = 4,991) or a second dose of Arexvy (N = 4,966). Participants who received placebo prior to Season 1 received a second dose of placebo prior to Season 2. Participants were followed through the end of the third RSV season (median follow-up time of 30.6 months).

The median age of participants was 69 years (range: 59 to 102 years), with around 74% over 65 years, around 44% over 70 years and around 8% over 80 years. About 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 endocrine/metabolic conditions (diabetes, advanced liver or renal disease).

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

Confirmed cases of RSV were determined by quantitative reverse transcription polymerase chain reaction (qRT-PCR) on nasopharyngeal swabs. 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 at least 3 lower respiratory symptoms for at least 24 hours. Lower respiratory tract symptoms included: new or increased sputum, new or increased cough, new or increased dyspnoea (shortness of breath). Lower respiratory signs included: new or increased wheezing, crackles, respiratory rate ≥20 respirations/min, low or decreased oxygen saturation (O_2 saturation <95% and ≤90% if baseline is <95%) or need for oxygen supplementation.

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 RSV-B-associated LRTD during the first season.

Compared with placebo, Arexvy significantly reduced the risk of RSV-associated LRTD by 82.6% (96.95% CI: [57.9-94.1]) in participants 60 years of age and older, who met the pre-specified success criterion for the primary study objective (Table 1). Vaccine efficacy against RSV-LRTD was observed over the median follow-up period of 6.7 months.

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 1: Efficacy analysis over the first RSV season: first RSV-associated LRTD overall and by age and comorbidity subgroups in study 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]	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	[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 overall analysis [≥ 60 years] and 95% for all subgroup analyses). Two-sided exact CI for vaccine efficacy was derived based on a Poisson model adjusted by age categories and regions.

[b]Primary confirmatory objective with a pre-specified success criterion of a lower limit of the two-sided CI for vaccine efficacy above 20%.

[c]Cannot be conclusively assessed due to the small number of cases occurring 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 in participants aged 70 years and older by 84.4% (95% CI: [46.9-97.0]).

Compared with placebo, Arexvy significantly reduced the risk of 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 conclusively assessed due to the low number of total cases accrued (2 cases).

Amongst 18 RSV-associated LRTD cases with at least 2 lower respiratory signs or preventing everyday activities, 4 cases of severe RSV-associated LRTD requiring oxygen supplementation occurred in the placebo group, while there were none in the RSVPreF3 group.

Efficacy against RSV-associated LRTD over 2 RSV seasons and over 3 RSV seasons

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

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.

Vaccine efficacy against RSV-associated LRTD was similar in the subgroup of participants with at least one significant comorbidity.

A second dose of vaccine administered 12 months after the first dose provided no additional efficacy benefit.

Table 2: Efficacy analyses over two and three RSV seasons in study 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							
Total (≥ 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	[e]
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	[e]

[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 for some participants.

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

[d]CI = confidence interval (97.5% for overall analysis ≥ 60 years and 95% for all subgroup analyses).

[e]Cannot be conclusively assessed due to the low number of cases occurring in this age group. Two-sided exact CI for vaccine efficacy was derived based on a Poisson model adjusted by age categories, regions and seasons.

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.

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

Vaccine efficacy against RSV-associated LRTD over the second RSV season with a median follow-up period 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 the placebo group).

Vaccine efficacy against RSV-associated LRTD over the third RSV season with a median follow-up period 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

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 of age and over

The immune responses to Arexvy were evaluated in Phase III immunogenicity and safety study RSV OA=ADJ-004 in adults 60 years of age and older. The 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 neutralizing 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 [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.

Adults 18 through 59 years of age with an increased risk for RSV disease

The non-inferiority of the immune response to Arexvy in adults 18 through 59 years of age compared to adults 60 years of age and older, for whom the vaccine efficacy against RSV-associated LRTD was demonstrated, was evaluated in two studies, a Phase III, observer-blind, randomised, placebo-controlled study (RSV OA=ADJ-018) and, a Phase III, open-label study (RSV OA=ADJ-025).
In the RSV OA=ADJ-018 study, Cohort 1 consisted of participants 50 through 59 years of age separated in 2 sub-cohorts according to their medical history. Sub-cohort 1 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. Sub-cohort 2 consisted of participants without pre-defined, stable, chronic medical conditions (Arexvy, N=383; placebo, N=192). Cohort 2 consisted of participants 60 years of age and older (Arexvy, N=381).
The RSV OA=ADJ-025 study consisted of participants 18 through 49 years of age with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease such as chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney or liver disease, or neurological or neuromuscular disease (total N=1,029; 426 of whom were part of the immunogenicity subset), and participants 60 years of age and older (N=429). All study participants received one dose of Arexvy.
The primary immunogenicity objective was to demonstrate non-inferiority of the humoral immune response (in terms of RSV-A and RSV-B neutralizing titers) following the administration of Arexvy at 1-month post-vaccination in participants 50 to 59 years of age with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease, and participants 18 through 49 years of age

with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease, compared to participants 60 years of age and older.

The prespecified criteria for non-inferiority of the immune responses were defined as the 2-sided (95%) CI upper limits (UL) on the group geometric mean titre (GMT) ratios ≤ 1.50 and the UL of the 2-sided (95%) CIs on the Seroresponse Rate (SRR) difference ≤ 10% for the RSV-A and RSV-B neutralizing titers in both studies.

The non-inferiority criteria of the immune responses for the RSV-A and RSV-B neutralizing titers were met in both age groups. The efficacy of Arexvy, in adults 18 through 59 years of age, can be inferred from vaccine efficacy demonstrated in adults 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 titres (ED60) in adults 60 years of age and older (OA) compared to adults 50 through 59 years of age with (Adults-AIR) pre-defined, stable, chronic medical conditions[a] leading to an increased risk for RSV disease - *Per Protocol Set*

RSV-A-neutralizing antibody titers (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio (95% CI)[b]**	**SRR (%) (95% CI)**	**SRR difference (95% CI)[c]**
OA (N=342) (≥ 60 years)	7440.1 (6768.4; 8178.5)	0.8 (0.7; 1.0)	80.4 (75.8; 84.5)	-6.5 (-12.1; -0.9)
Adults-AIR (N=343) (50-59 years)	8922.7 (8118.2; 9806.9)		86.9 (82.8; 90.3)	
RSV-B-neutralizing antibody titers (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio (95% CI)[b]**	**SRR (95% CI)**	**SRR difference (95% CI)[c]**
OA (N=342) (≥ 60 years)	8062.8 (7395.9; 8789.9)	0.8 (0.7; 0.9)	74.5 (69.5; 79.0)	-7.2 (-13.3; -0.9)
Adults-AIR (N=343) (50-59 years)	10,054.7 (9225.4; 10,958.7)		81.6 (77.1; 85.6)	

[a] Predefined, stable, chronic medical conditions such as chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney or liver disease.

[b,c] The predefined criteria for non-inferiority of immune responses were defined as the two-sided 95% CI upper limits for the adjusted GMT ratios (OA over Adults-AIR) ≤1.5 and the upper limits for the two-sided 95% CI for the SRR difference (OA minus Adults-AIR) ≤10% for participants 60 years of age and older (OA) compared with participants between 50 and 59 years of age with predefined, stable, chronic medical conditions associated with an increased risk for RSV disease (Adults-AIR).

ED60: estimated dilution 60; CI = confidence interval; GMT = geometric mean titer; SRR = seroresponse rate

Table 4: Summary of adjusted GMT and SRR values, and adjusted GMT ratios and SRR differences in terms of RSV-A and RSV-B neutralising titres (ED60) in adults 60 years of age and older (OA) compared to adults 18 through 49 years of age with pre-defined, stable, chronic medical conditions[a] leading to an increased risk for RSV disease (Adults-AIR) - *Per Protocol Set*

RSV-A neutralising titres (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio (95% CI)** [b]	**SRR (%) (95% CI)**	**SRR difference (95% CI)** [c]
OA (N=417) (≥ 60 years)	8 591.5 (7 902.7, 9 340.3)	0.72 (0.64, 0.81)	77.7 (73.4, 81.6)	-9.4 (-14.6, -4.1)
Adults-AIR (N=394) (18-49 years)	11 914.6 (10 933.2, 12 984.2)		87.1 (83.3, 90.2)	
RSV-B neutralising titres (ED60)				
	Adjusted GMT (95% CI)	**Adjusted GMT ratio (95% CI)** [b]	**SRR (95% CI)**	**SRR difference (95% CI)** [c]
OA (N=417) (≥ 60 years)	9 087.6 (8 372.1, 9 864.2)	0.73 (0.65, 0.82)	77.2 (72.9, 81.2)	-10.1 (-15.3, -4.8)
Adults-AIR (N=394) (18-49 years)	12 503.4 (11 490.5, 13 605.4)		87.3 (83.6, 90.4)	

[a] Pre-defined, stable, chronic medical conditions such as chronic pulmonary disease, chronic cardiovascular disease, diabetes, chronic kidney or liver disease, or neurological or neuromuscular disease.

[b,c] The prespecified criteria for non-inferiority of the immune responses were defined as the 2-sided 95% CI upper limits (UL) on the adjusted GMT ratios (OA over Adults-AIR) ≤ 1.5 and the UL of the 2-sided 95% CI on the SRR difference (OA minus Adults-AIR) ≤ 10% in participants 60 years of age and older (OA) relative to participants 18 through 49 years of age with pre-defined, stable, chronic medical conditions leading to an increased risk for RSV disease (Adults-AIR).

ED60: Estimated dilution 60; CI = Confidence interval; GMT = Geometric mean titre; SRR = Seroresponse rate

Pharmacokinetics

An evaluation of pharmacokinetic properties is not required for vaccines.

Absorption

Not applicable.

Distribution

Not applicable.

Metabolism

Not applicable.

Elimination

Not applicable.

Preclinical data

Non-clinical data reveals no special hazards for humans based on conventional safety studies.
Reproductive and developmental studies with an unadjuvanted RSVPreF3 vaccine as well as results from a study with Arexvy in rabbits did not reveal any vaccine-related effects on female fertility, gestation or embryo-foetal or offspring development.

Other information

Incompatibilities

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

Shelf life

Do not use this medicine after the expiry date ("EXP") stated on the pack.
For shelf life after reconstitution of the medicinal product, see “Instructions for handling” section.

Special precautions for storage

Store in the refrigerator (2-8°C) in the original packaging to protect from light and keep out of the reach of children. Do not freeze. Discard if the vial has been frozen.
For storage conditions after reconstitution of the medicinal product, see “Instructions for handling” section.

Instructions for 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.

<u>How to prepare Arexvy:</u>

Arexvy must be reconstituted prior to administration.
1. Withdraw the entire contents of the vial containing the suspension into a syringe with a suitable needle (21G to 25G).
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 this is not possible, the vaccine should be stored in the refrigerator (2-8°C) or at room temperature up to 25°C. If the vaccine is 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 national requirements.

Authorisation number

69310 (Swissmedic)

Packs

Pack with 1 vial with powder and 1 vial with suspension (B)
Pack with 10 vials with powder and 10 vials with suspension (B)

Marketing authorisation holder

GlaxoSmithKline AG, 6340 Baar

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