

# Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY)

## Mini-Monograph

Aug 2023

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

Abbreviations: MOA=mechanism of action; RSV=respiratory syncytial virus; n=number of patients; IR/1000PY=Incidence rate per 1000 person years; RSV-LRTD= RSV confirmed lower respiratory tract infection; HD=high dose; TBD=to be determined; VANF=VA National Formulary; GBS=Guillain-Barre syndrome

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| <b>FDA Approval</b> | <b>Description/MOA</b>            | AREXVY is a prefusion-F RSV vaccine (recombinant RSV surface protein F stabilized in a prefusion conformation with an AS01 <sub>E</sub> adjuvant) which works by inducing an immune response against RSV. |
|                     | <b>Indication(s) Under Review</b> | Prevention of lower respiratory tract disease caused by respiratory syncytial virus in individuals 60 years of age and older. Approved by FDA on 5/23/23.   |
|                     | <b>Dosage Form(s)</b>             | Supplied as a single-dose vial of lyophilized antigen with a vial of adjuvant suspension for intramuscular injection (0.5 mL)   |

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| <b>Clinical Evidence</b> | <b>Study/Design</b> | One large phase 3 trial (AReSVi-006) in patients ≥ 60 years of age who received AREXVY (n=12,467) or placebo (n=12,499). <b>Primary endpoint was vaccine efficacy (VE) by comparing IR/1000 PY of RSV-LRTD in vaccine vs. placebo recipients at least 14 days after vaccination.</b> Other endpoints included medically-attended RSV-LRTD, hospitalization and death<br>Smaller supportive trials assessed immunogenicity, safety and immune persistence and to assess impact of concomitant influenza vaccine on safety and immunogenicity.  |
|                          | <b>Population</b>   | AReSVi-006 enrolled immunocompetent patients aged 60 years or over. Patients with pre-existing chronic conditions could be enrolled provided they were medically stable. Immunocompromised patients were excluded.  |
|                          | <b>Demographics</b> | Median age 70 years; male (48%); race (79% white, 9% black, 8% Asian).<br>Participants followed for 2 full RSV seasons (mean 15 months follow-up per patient)<br><br>39% had at least 1 comorbidity (cardiorespiratory 20% [COPD, asthma, other chronic respiratory disease or chronic heart failure], endocrine/metabolic 26% [DM, liver or kidney disease]). 66% of patients classified as low/medium risk.   |
|                          | <b>Intervention</b> | Single intramuscular dose vs. placebo (0.5 mL)  |
|                          | <b>Results</b>      | AREXVY reduced risk of developing RSV-LRTD by 83% in season 1 (7 vs. 40 cases), and 56% during season 2 (20 vs. 91 cases). <b>Overall VE over 2 seasons of 75% with a single dose (30 vs. 139 cases) [95% CI 60, 85].</b> Revaccination at 12 months did not confer additional protection over a single dose.<br><br>Significant benefit also shown in subgroups (≥ 65 yrs., ≥ 70 yrs., those with ≥ 1 comorbidity)<br><br><b>Vaccine efficacy 78% against medically attended RSV-LRTD over 2 seasons (12 vs. 63 cases). Only 6 hospitalizations due to RSV (vaccine 1, placebo 5) (non-significant difference)</b><br><br>Co-administration with influenza vaccine met non-inferiority criteria, although titers were somewhat lower and clinical significance of this is unknown. No data coadministration with other vaccines. |
|                          | <b>Limitations</b>  | Low number of cases, short follow-up to assess immune-persistence in subsequent years.<br><br>Low number of patients at highest risk for RSV complications (no immunocompromise) and few hospitalizations. Efficacy in higher-risk patients is unknown.   |
|                          | <b>Summary</b>      | A single dose of AREXVY provided moderate to high efficacy in reducing RSV-LRTD (and medically attended) but benefit on hospitalization or death or benefit in highest risk populations are unknown.  |

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| <b>Safety</b> | <b>Boxed Warnings</b>         | None  |
|               | <b>Contraindications</b>      | History of severe allergic reaction to AREXVY or any component of the product   |
|               | <b>Warnings/Precautions</b>   | Appropriate treatment available for management of possible anaphylactic reactions or syncope<br>Immunocompromised persons may have a diminished response.   |
|               | <b>Adverse reactions (AE)</b> | <p><b>Solicited AEs in AReSVi-006 safety subset (AREXVY vs. placebo):</b></p> <ul style="list-style-type: none"> <li>• <b>Injection site pain (61% vs. 9%)</b></li> <li>• <b>Fatigue (34% vs. 16%)</b></li> <li>• <b>Myalgia (29% vs. 8%)</b></li> <li>• <b>Headache (27% vs. 13%)</b></li> <li>• <b>Arthralgia (18% vs. 6%)</b></li> </ul> <p><b>Severe reactogenicity events (Grade 3) 3.8% of AREXVY vs. 0.9% of placebo subjects</b><br/> Serious AEs (SAEs) 4% of each group.<br/> Across all GSK trials safety database, 3 cases of inflammatory neurologic events occurred</p> <ul style="list-style-type: none"> <li>• 1 case of GBS 9 days after AREXVY (related to vaccination)</li> <li>• 2 cases of ADEM (transverse myelitis or acute disseminated encephalomyelitis) 7 and 22 days after AREXVY, 1 of which was fatal, although other possible causes noted. Both occurred with coadministration of influenza vaccines (open label phase 3 trial)</li> </ul> <p>Numeric imbalance in atrial fibrillation within 30 days postvaccination (10 vs. 4 cases)<br/> Trend towards higher reactogenicity when co-administered with high-dose or adjuvanted influenza vaccine</p> |

| <b>Drug and Alternatives</b>      | <b>Formulary status</b> | <b>Clinical Guidance</b>   | <b>Other Considerations</b>  |
|-----------------------------------|-------------------------|--|--|
| RSV vaccine, adjuvanted (ABRYSVO) | F                       | FDA approved for ≥ 60 years and older as a single dose<br><br>ACIP recommendation: those ≥ 60 years of age may receive a single dose based on shared clinical decision making between patient and provider | Data only through mid-season 2   |
| RSV vaccine, adjuvanted (AREXVY)  | F                       | FDA approved for ≥ 60 years and older as a single dose<br><br>ACIP recommended those ≥ 60 years of age may receive a single dose based on shared clinical decision making between patient and provider     | Adverse events may be higher than ABRYSVO, possibly due to adjuvant<br><br>Limited data regarding on co-administration with other adjuvanted or reactogenic vaccines |

## Conclusions/Projected Place in Therapy

- RSV is associated with an estimated 60,000-160,000 hospitalizations and 6,000-10,000 deaths each year in adults aged 65 years and older. Certain conditions increase the risk for severe disease and hospitalization
- AREXVY demonstrated moderate to high efficacy reducing the incidence of RSV-LRTD and medically attended RSV-LRTD in adults aged 60 years or older; clinical trials thus far have not been powered to show a difference in RSV requiring hospitalization or death. In addition, those at highest risk (multiple comorbidities, immunocompromised, frail) were not included or underrepresented in the phase 3 trial, so efficacy in those populations is unclear.
- **In June of 2023, the ACIP voted to recommend that adults ≥ 60 years may receive a single dose of an RSV vaccine, using shared clinical decision making.** ACIP noted the vaccine had moderate to high efficacy over 2 full seasons with an acceptable safety profile but felt more evidence from post-marketing surveillance was needed for potential immune-

mediated diseases (such as Guillain-Barre) and atrial fibrillation. More data is needed in the highest risk patients, more data on hospitalization and death, and durability of response over multiple seasons.

- Unlike routine recommendations, those based on SDCM do not target all persons in a particular age or risk group.
- The decision to vaccinate should be based on a discussion between health care provider and patient, which may be guided by the individual's risk for disease and their characteristics, values and preferences; the provider's clinical discretion; and the characteristics of the vaccine.
- As part of this discussion, the risk for severe RSV disease should be considered. Those most likely to benefit include those with chronic medical conditions such as;
  - Chronic lung disease (asthma or COPD)
  - Cardiovascular disease (such as CHF or coronary artery disease)
  - Moderate/severe immunocompromise
  - Diabetes mellitus
  - Neurologic or neuromuscular condition
  - Kidney or liver disease
  - Hematologic disorders
  - Other factors include
    - Residence in a nursing home or other long-term care facility
    - Frailty
    - Advanced age
    - Other underlying conditions that a healthcare provider determines might increase severe RSV risk
- ACIP recommends that co-administration with other adult vaccines during the same visit is ACCEPTABLE but note data is only available for administration with flu vaccines, and administering with other vaccines might increase local or systemic reactogenicity.
  - *Of note, the recombinant zoster vaccine contains the same adjuvant as AREXVY which might increase local and systemic adverse events, which are already considerable with both vaccines individually.* Other vaccines with adjuvants include adjuvanted influenza vaccine and HEPLISAV-B
- Another RSV vaccine, ABRYVO, by Pfizer was also FDA approved in 2023. ACIP does not distinguish between products in their recommendations.

## References

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1. Respiratory syncytial virus vaccine, adjuvanted (AREXVY) [prescribing information]. GlaxoSmithKline: May 2023
2. FDA summary basis for regulatory action, AREXVY. 5/3/23. Accessed 8/26/23.
3. [GSK ACIP Presentation 6/21/2023](#). Accessed 8/29/23.
4. Papi A, Ison MG, Langley JM, et al. Respiratory syncytial virus prefusion F protein vaccine in older adults. *NEJM* 2023;388:595
5. Melgar M, Britton A, Roper L, et al. Use of respiratory syncytial virus vaccines in older adults: Recommendations of the Advisory Committee on Immunization Practices – United States, 2023. *MMWR* 2023;72(29):793-801.
6. ACIP GRADE tables: AREXVY for prevention of RSV. [Grading of Recommendations, Assessment, Development, and Evaluation \(GRADE\): GSK RSVPreF3 Vaccine \(AREXVY\) | CDC](#)
7. Evidence to recommendation tables for RSV vaccines in older adults: [ACIP Evidence to Recommendations for Use of GSK Adjuvanted RSVPreF3 Vaccine \(AREXVY\) in Adults Ages 60 and Older | CDC](#)

