Respiratory Syncytial Virus Vaccine (ABRYSVO)
Mini-Monograph
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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; TBD=to be determined; VANF=VA National Formulary; GBS=Guillain-Barre syndrome

FDA Approval	**Description/MOA**	ABRYSVO is a prefusion RSV vaccine (containing RSV preF A and RSV preF B antigens) which works by inducing an immune response against RSV
	Indication(s) Under Review	Prevention of lower respiratory tract disease caused by respiratory syncytial virus in individuals 60 years of age and older. Approved by FDA on 5/31/23.
	Dosage Form(s)	Supplied as a single-dose vial of lyophilized antigen and a prefilled syringe with Sterile Water Diluent for intramuscular injection (0.5 mL)

Clinical Evidence	**Study/Design**	One large phase 3 trial (**RENOIR)** in patients ≥ 60 years of age who received ABRYSVO (n=17,197) or placebo (n=17,186). **Primary endpoints were vaccine efficacy (VE) for RSV-LRTD* with 2 or with 3 symptoms comparing IR/1000 PY with vaccine vs. placebo at least 14 days after vaccination.** Other endpoints included medically-attended RSV-LRTD, hospitalization and death Smaller supportive trials assessed immunogenicity, safety and immune persistence and impact of concomitant flu vaccine on safety and immunogenicity.
	Population	**RENOIR** enrolled immunocompetent patients (healthy or with stable chronic conditions) aged ≥60 years. End stage renal disease, unstable cardiac disease and conditions associated with risk of prolonged bleeding were excluded.
	Demographics	Mean age 68 years; male (50%); race (78% white, 13% black) Participants followed for 1 full season and 1 partial 2nd season (Northern hemisphere only) with mean of 12 months of follow-up per patient. 52% had at least 1 comorbidity (most common tobacco, 52%, diabetes, 19%, asthma, 9%, COPD, 6%)
	Intervention	Single intramuscular dose vs. placebo (0.5 mL)
	Results	ABRYSVO reduced risk of developing RSV-associated LRTD with ≥ 3 symptoms by 89% for season 1 (2 vs. 18 cases) and 79% during a partial season 2 (3 vs. 14 cases). **Overall VE of 84% over 1.5 seasons after a single dose (5 vs. 32 cases) [95% CI 60, 95]** Significant benefit also shown in subgroups (≥ 65 yrs., ≥ 70 yrs., those with ≥ 1 comorbidity) **VE for medically attended RSV-LRTD was 81%** over 1.5 seasons after a single dose **Only 4 hospitalizations due to RSV** (vaccine 1, placebo 3) (non-significant result) Co-administration with influenza vaccine met non-inferiority criteria, although titers were somewhat lower and clinical significance of this is unknown
	Limitations	Low number of cases, short follow-up to assess immune-persistence in subsequent years Low number of patients at highest risk for RSV complications and low numbers of hospitalizations during trial. Efficacy in higher risk patients unknown
	Summary	A single dose of ABRYSVO 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.

**RSV-LRTD: at least 2 or 3 signs or symptoms (cough, wheezing, sputum production, shortness of breath or tachypnea) lasting > 1 day with PCR confirmed RSV. CDC uses 3 signs/symptoms for comparison to efficacy endpoints.*

Safety	**Boxed Warnings**	None
	Contraindications	History of severe allergic reaction to ABRYSVO or any component of the product
	Warnings/ Precautions	Prevention and management of allergic reactions, syncope (after administration) Those who are immunocompromised may have a diminished response
	Adverse reactions (AE)	**Solicited AEs in RENOIR (ABRYSVO vs. placebo):** • **Injection site pain (11% vs. 6%)** • Fatigue (16% vs. 14%) • Myalgia (10% vs. 8%) • Headache (13% vs. 12%) • Arthralgia (8% vs. 7%) **Severe reactogenicity events (Grade 3) in 1% of vaccine vs. 0.7% of control subjects** Serious AEs (SAEs) in 4% of each group Three inflammatory neurologic events within 42 days of vaccination: • 1 case of Guillain-Barre syndrome (GBS) 14 days post vaccination • 1 case of Miller Fisher syndrome (GBS variant) 10 days after vaccination and • 1 worsening of pre-existing undifferentiated polyneuropathy at 21 days post-vaccination Numerical imbalance in atrial fibrillation was noted within 30 days postvaccination (10 vs. 4 cases), which will be monitored post-marketing

Drug and Alternatives	Formulary status	Clinical Guidance	Other Considerations
RSV vaccine, adjuvanted (ABRYSVO)	F	FDA approved for patients aged 60 years and older as a single dose ACIP recommended those ≥ 60 years of age may receive a single dose based on shared decision making between patient and provider	Data only through mid-season 2
RSV vaccine, adjuvanted (AREXVY)	F	FDA approved for patients aged 60 years and older as a single dose ACIP recommended those ≥ 60 years of age may receive a single dose based on shared decision making between patient and provider	Adverse events may be higher than ABRYSVO, possibly due to adjuvant Lack of data regarding consequences of 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.
- ABRYSVO 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 1 full and a 2nd partial season 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.

- Another RSV vaccine, AREXVY, by GlaxoSmithKline was also FDA approved in 2023. ACIP does not distinguish between products in their recommendations.

References

1. Respiratory syncytial virus vaccine, adjuvanted (ABRYSVO) [prescribing information]. Pfizer: May 2023
2. FDA summary basis for regulatory action, ABRYSVO. 5/3/23. Accessed 8/23/23.
3. ACIP Meeting materials: June 2023. Accessed 8/23/23.
4. Walsh EE, Marc G, Zareba AM, et al. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. *NEJM* 2023;388:1465
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: ABRYSVO for prevention of RSV. https://www.cdc.gov/vaccines/acip/recs/grade/GSK-Adjuvanted-RSVPreF3-adults-etr.html
7. Evidence to recommendation tables for RSV vaccines in older adults: ACIP Evidence to Recommendations for Use of Pfizer Bivalent RSVpreF Vaccine (ABRSYVO) in Older Adults | CDC