RSVpreF (Abrysvo®)[4]

Classification

RSV Vaccine

Pharmacology

Active Immunization: ABRYSVO induces an immune response against RSVpreF that protects against lower respiratory tract disease caused by RSV.

Passive Immunization: Antibodies to RSV antigens from individuals vaccinated in pregnancy are transferred transplacentally to protect infants younger than 6 months of age against LRTD and severe LRTD caused by RSV.

Indication

Immunization of pregnant individuals: Immunization of pregnant individuals at 32-36 weeks gestational age for the prevention of RSV-LRTD and severe RSV-LRTD in infants from birth through 6 months of age.

Immunization of individuals ≥ 60-year-old: Active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in individuals 60 years of age and older.

Dosage/Administration

A single 0.5 mL intramuscular injection. There are currently no recommendations for repeat vaccination.

Supplied as two vials, a lyophilized antigen component (a sterile white powder) that is to be reconstituted and an accompanying prefilled syringe containing sterile water diluent component. A Vial adapter is included to assist with reconstitution.

Use in Special Populations

Pregnancy: A voluntary pregnancy exposure registry has been established that collects data from either patients or providers for patients that have been exposed to Abrysvo while pregnant. 1-800-616-3791 to enroll in or obtain information about the registry.

Study 1 enrolled 7,358 pregnant individuals who were randomized 1:1 and received Abrysvo or placebo. This revealed no evidence for vaccine-associated increase in the risk of congenital anomalies or fetal deaths.

Study 2 evaluated 115 pregnant individuals who received Abrysvo and 117 who received placebo. A numerical imbalance in preterm births in Abrysvo recipients was observed compared to placebo recipients in these two clinical studies.

Abrysvo has not been studied in pregnant individuals less than 24 weeks gestational age, and those at increased risk for preterm birth.

Lactation: It is unknown whether Abrysvo is secreted in human milk, no data is available to assess the effects of Abrysvo on breastfed infants or on milk production/excretion. Provider discretion should be used when evaluating the decision to breastfeed post-vaccination.

Pediatric Use: The safety and effectiveness of Abrysvo to prevent RSV LRTD and severe RSV LRTD in infants born to individuals vaccinated at younger than 10 years of age have not been established.

The safety and effectiveness of Abrysvo to prevent RSV LRTD in non-pregnant individuals younger than 18 years of age via active immunization have not been established.

Geriatric Use: Approved for use in individuals 60 years of age and older.

Contraindication

Do not administer ABRYSVO to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of ABRYSVO.

Component list

- RSV stabilized prefusion F proteins
- Tromethamine
- Tromethamine hydrochloride
- Sucrose
- Mannitol
- Polysorbate 80
- Sodium chloride

Precautions

Potential risk of preterm birth: There is currently insufficient evidence to establish or exclude a causal relationship between preterm birth and Abrysvo

administration. There was an observed numerical imbalance of preterm births towards Abrysvo when compared to placebo. To avoid any potential risk of preterm birth, administration of Abrysvo is limited to individuals at 32 and through 36 weeks gestational age.

Preventing and managing allergic vaccine reactions: It is recommended that appropriate medical supervision and treatment be available to manage possible anaphylactic reactions following administration of Abrysvo.

Syncope: It is recommended to take appropriate measures to avoid injury from fainting due to possible risk of Syncope in association with the administration of injectable vaccines.

Altered immunocompetence: In immunocompromised persons Abrysvo may produce a diminished immune response.

Limitations of vaccine effectiveness: After vaccination, Abrysvo may not protect all vaccine recipients.

Adverse Effects

In pregnant individuals, the most commonly reported (≥10%) adverse reactions were pain at the injection site (40.6%), headache (31.0%), muscle pain (26.5%), and nausea (20.0%). Most of the serious adverse events in maternal participants were related to pregnancy complications and occurred after the 1-month period following vaccination.

In Study 1, 3,682 pregnant individuals received Abrysvo and 3,676 received placebo at 24 through 36 weeks' gestation. The infant safety population included 3,568 and 3,558 infants born to individuals in the Abrysvo or placebo group, respectively. Among the infants born to individuals in the Abrysvo group and in the placebo group, 202 (5.7%) and 169 (4.7%), respectively, had adverse events of preterm birth and 180 (5.0%) and 220 (6.2%), respectively, had reported congenital malformations or anomalies. There were 10 (0.3%) fetal deaths in the Abrysvo group and 8 (0.2%) in the placebo group.

Table 3 Select Pregnancy-related Serious Adverse Events in Study 1 in Pregnant Individuals Occurring at any Time Following Vaccination[a]

Serious Adverse Reaction	ABRYSVO N=3,682 n (%)	95% CI	Placebo N=3,675 n (%)	95% CI
All Maternal SAEs	598 (16.2)	(15.1, 17.5)	558 (15.2)	(14.0, 16.4)
Pre-eclampsia	68 (1.8)	(1.4, 2.3)	53 (1.4)	(1.1, 1.9)
Gestational hypertension	41 (1.1)	(0.8, 1.5)	38 (1.0)	(0.7, 1.4)
Premature rupture of membranes	15 (0.4)	(0.2, 0.7)	16 (0.4)	(0.2, 0.7)
Preterm premature rupture of membranes	15 (0.4)	(0.2, 0.7)	10 (0.3)	(0.1, 0.5)
Hypertension	13 (0.4)	(0.2, 0.6)	6 (0.2)	(0.1, 0.4)
Maternal death[b]	1 (<0.1)	(0.0, 0.2)	0	(0.0, 0.1)
Fetal Death[c]	10 (0.3)	(0.1, 0.5)	8 (0.2)	(0.1, 0.4)

[a] Includes all SAEs from vaccination to 6 months post-delivery (up to approximately 10 months, depending on the gestational age at the time of vaccination). In Study 1, eclampsia occurred in 5 participants (3 in the ABRYSVO group and 2 in the placebo group) and HELLP syndrome occurred in 5 participants (2 in the ABRYSVO group and 3 in the placebo group).

[b] There was one maternal death in the ABRYSVO group due to postpartum hemorrhage that was not likely to be associated with vaccination.

[c] A total of 18 intrauterine deaths were reported for the index pregnancy: 10 intrauterine deaths in the ABRYSVO group (0.3%) and 8 intrauterine deaths in the placebo group (0.2%). The intrauterine deaths represented various clinical conditions and presentations resulting in fetal demise without clear evidence of a common pathophysiology.

(The above table is from the Abrysvo package insert)

In individuals 60 years of age and older, the most commonly reported (≥10%) adverse reactions were fatigue (15.5%), headache (12.8%), pain at the injection site (10.5%), and muscle pain (10.1%). Within 30 days after vaccination, atrial fibrillation was reported in 10 vaccine recipients and 4 placebo recipients (of which 4 in the Abrysvo group and 3 in the placebo group were serious adverse events); the onset of symptoms was 18 to 30 days post vaccination. The currently available information on atrial fibrillation is insufficient to determine a causal relationship to the vaccine. In Study 3, Severe Adverse Events were reported by 2.3% of participants in both the Abrysvo and placebo groups. Three participants in the Abrysvo group had SAEs which were assessed as possibly related to study vaccination: Guillain-Barre Syndrome reported 7 days after vaccination, Miller Fisher Syndrome reported 8 days after vaccination, and hypersensitivity reported 8 hours after vaccination.

Monitoring

Immediate supervision after administration of the vaccination is recommended due to potential risk of allergic vaccine reactions and syncope. Any adverse events believed to have resulted from Abrysvo should be reported to the Vaccine Adverse Event Reporting System.

Interactions

Immunosuppressant agents: Immunosuppressant agents may diminish the immunological response to Abrysvo.

Tdap: Abrysvo may diminish the therapeutic effect of Tdap vaccination when administered together. Specifically, concentrations of acellular pertussis antigens (pertussis toxin [PT], filamentous hemagglutinin (FHA), and pertactin [PRN]) were lower when Abrysvo was administered concomitantly with Tdap compared to Tdap alone.

Efficacy

In pregnant individuals 32-36 weeks of gestational age: It was found that Vaccine Efficacy results met the statistical criterion for success which was defined as a lower bound confidence interval >20% for reducing severe RSV-LRTD. This result held true through all points assessed to 180 days. Statistical criterion for success were not met for reducing RSV-LRTD but clinically meaningful efficacy was observed after 90 days.

Table 6 Vaccine Efficacy of ABRYSVO Against Severe LRTD Caused by RSV - Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals (Study 1)[a]

Time Period	ABRYSVO Number of Cases N=3,495[b]	PLACEBO Number of Cases N=3,480[b]	VE (%) (CI)[c]
90 days	6	33	81.8 (40.6, 96.3)
120 days	12	46	73.9 (45.6, 88.8)
150 days	16	55	70.9 (44.5, 85.9)
180 days	19	62	69.4 (44.3, 84.1)

CI - confidence interval; N – number of participants; RSV – respiratory syncytial virus; VE - vaccine efficacy
[a] The prespecified success criterion was met for this endpoint evaluation
[b] Evaluable efficacy population
[c] 99.5% CI at 90 days; 97.58% CI at later intervals

Table 7 Vaccine Efficacy of ABRYSVO Against LRTD Caused by RSV - Infants From Birth Through 6 Months of Age by Active Immunization of Pregnant Individuals (Study 1)[a]

Time Period	ABRYSVO Number of Cases N=3,495[b]	PLACEBO Number of Cases N=3,480[b]	VE (%) (CI)[c]
90 days	24	56	57.1 (14.7, 79.8)
120 days	35	81	56.8 (31.2, 73.5)
150 days	47	99	52.5 (28.7, 68.9)
180 days	57	117	51.3 (29.4, 66.8)

CI - confidence interval; N – number of participants; RSV – respiratory syncytial virus; VE - vaccine efficacy
[a] The prespecified success criterion (a CI lower bound >20%) was not met for this endpoint evaluation at 90 days
[b] Evaluable efficacy population
[c] 99.5% CI at 90 days; 97.58% CI at later intervals

(The above table is from the Abrysvo package insert)

In individuals ≥ 60-year-old: Participants were randomized (1:1) to receive Abrysvo (n=17,197) or placebo (n=17,186). Randomization was stratified by age, 60-69 years (n=21,499, 63%), 70-79 years (n=10,948, 32%), and ≥80 years (n=1,934, 6%). Healthy adults and adults with stable chronic diseases were included. Among enrolled participants 15% had stable chronic cardiopulmonary conditions such as chronic obstructive pulmonary disease (COPD), asthma, or congestive heart failure (CHF).

Vaccine efficacy (VE), against RSV-LRTD, defined as the relative risk reduction of first episode of RSV-LRTD in the Abrysvo group compared to the placebo group in the first RSV season, was assessed. Pre-specified success criteria were met for prevention of RSV-LRTD with ≥2 symptoms and prevention of RSV-LRTD with ≥3 symptoms.

The median duration of follow-up for efficacy was 7 months. Participants are planned to be followed for up to two RSV seasons, approximately 25 months.

Table 11 Vaccine Efficacy of ABRYSVO Against RSV-LRTD - Individuals 60 years of Age and Older (Study 3)[a]

Efficacy Endpoint	ABRYSVO N=16,306[b] n	Placebo N=16,308[b] n	VE (%) (96.66% CI)
First episode of RSV-associated lower respiratory tract disease with ≥2 symptoms	11	33	66.7 (28.8, 85.8)
First episode of RSV-associated lower respiratory tract disease with ≥3 symptoms	2	14	85.7 (32.0, 98.7)

CI – confidence interval; N – number of participants; n = number of cases; RSV – respiratory syncytial virus; VE – vaccine efficacy (VE based on case count ratio is calculated as 1-(P/[1-P]), where P is the number of RSVpreF cases divided by the total number of cases)

[a] NCT05035212

[b] Evaluable efficacy population

(The above table is from the Abrysvo package insert)

Dosage Forms/Cost (AWP)

IM, Single dose vial to be reconstituted with supplied diluent and vial adapter as a kit. Supplied in cartons of 1, 5, and 10 kits.

Pricing from Morris and Dickson: $354.00/dose

Safety Considerations

Look Alike-Sound Alike: Arexvy (RSVPreF3)

Summary/Conclusion

Abrysvo is FDA approved for prevention of RSV-LRTD in adults ≥ 60-year-old and immunization of pregnant individuals for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age. The data from the clinical trials is robust and targets an appropriate population for RSV-LRTD and would be applicable to numerous state hospital patients with the indication for adults ≥ 60-year-old as well as a potentially useful extra indication of immunization of pregnant individuals in the 32-36 week gestational period. The side effect profile is favorable and is one of two new novel vaccinations against RSV-LRTD. A potential downside is the increased price when compared to Arexvy.

Recommendation

Add both Arexvy and Abrysvo to the formulary. The prevention of RSV-LRTD in the State Hospital system would prove majorly beneficial. Despite Arexvy's more limited target population it would still be beneficial to have a secondary, cheaper, option should Abrysvo encounter supply issues or the additional indication of vaccination in pregnant individuals at 32-36 weeks gestational age is not needed.

Arexvy vs Abrysvo at a Glance

Medication	**Arexvy (RSVPreF3)**	**Abrysvo (RSVpreF)**
Cost	$336.00/dose[1]	$354.00/dose[2]
Population	≥ 60-year-old[3]	≥ 60-year-old and pregnant individuals at 32-36 weeks gestational age[4]
Route and form	IM, single dose vial to be reconstituted[3]	IM, single dose vial to be reconstituted[4]
Storage	2-8°C[3]	2-8°C[4]
Effectiveness	82.6% efficacy in reducing the risk of developing RSV-LRTD in patients ≥ 60-year-old.[3]	76.5% Vaccine Efficacy against severe RSV-LRTED in Infants from birth through 6 months of age.[4] 85.7% vaccine effectiveness in preventing RSV-LRTD with ≥3 symptoms in patients ≥ 60-year-old.[4]

References

1. Morris & Dickson. (12/18/2023) Arexvy product information. https://www.mdwebportal.net/mdwp/ProductInfo.aspx?id=%20J5eMCrNe8yLXTHzzCMKFwwXYXrRzJneHeUdXauNfCsw=&item=296996
2. Morris & Dickson. (12/18/2023) Abrysvo product information. https://www.mdwebportal.net/mdwp/ProductInfo.aspx?id=%20J5eMCrNe8yLXTHzzCMKFwwXYXrRzJneHeUdXauNfCsw=&item=296566
3. Arexvy (RSVpreF3) [package insert]. Durham, NC: GlaxoSmithKline Biologicals; 2023
4. Abrysvo (RSVPreF) [package insert]. New York, NY: Pfizer Inc; 2023

Date: 12/18/2023
Prepared by: Tyler Stromberg PharmD
Reviewed by: Kasey Leggette Peña, PharmD, BCPP