The Medical Letter®

on Drugs and Therapeutics

Volume 66 **October 14, 2024**

ISSUE No. 1713

IN THIS ISSUE

The Medical Letter®
on Drugs and Therapeutics

Volume 66 October 14, 2024

Take CME Exams

ISSUE No. 1713

IN THIS ISSUE

Capvaxive – A 21-Valent Pneumococcal Conjugate Vaccine

The FDA has licensed *Capvaxive* (PCV21; Merck), a 21-valent pneumococcal conjugate vaccine, for prevention of invasive pneumococcal disease (IPD) and pneumococcal pneumonia in adults. Four other pneumococcal vaccines are currently available in the US: *Prevnar 20* (PCV20), *Vaxneuvance* (PCV15), and *Prevnar 13* (PCV13) are conjugate vaccines licensed for use in persons ≥6 weeks old, and *Pneumovax 23* (PPSV23) is a pneumococcal polysaccharide vaccine licensed for use in persons ≥2 years old (see Table 1).[1]

Pronunciation and Abbreviation Key

Capvaxive: cap vacks' iv
IPD = invasive pneumococcal disease
PCV = pneumococcal conjugate vaccine
PPSV = pneumococcal polysaccharide vaccine

PNEUMOCOCCAL DISEASE — *Streptococcus pneumoniae* is a common cause of bacterial pneumonia. Adults ≥65 years old and persons with certain medical and immunocompromising conditions (see Figure 1 online) are at increased risk of developing IPD. In the US, vaccination against *S. pneumoniae* has substantially reduced the incidence of pneumococcal disease in children and adults.

THE NEW VACCINE — Like PCV13, PCV15, and PCV20, PCV21 contains capsular polysaccharide antigens conjugated to a protein carrier (nontoxic diphtheria CRM_{197} toxin). The 21 serotypes included in *Capvaxive* account for 85% of IPD cases in adults ≥65 years old; PCV20 includes serotypes that account for 54% of these cases. PCV21 includes 8 serotypes that are not included in any of the other currently available pneumococcal vaccines (see Table 2); these serotypes account for 30% of IPD cases in adults ≥65 years old. Some serotypes included in the other vaccines were excluded from PCV21 because they are no longer commonly associated with pneumococcal disease in adults.

Key Points: *Capvaxive*

- **Description:** A 21-valent pneumococcal conjugate vaccine (PCV21).
- **Indication:** Prevention of invasive pneumococcal disease and pneumococcal pneumonia in adults.
- **Coverage:** PCV21 includes serotypes that collectively account for 85% of IPD cases in adults ≥65 years old.
- **Adverse Effects:** Injection-site reactions, fatigue, headache, myalgia, and arthralgia.
- **Dosage:** Single 0.5-mL dose given by intramuscular injection.
- **Cost:** One dose costs $287.
- **Conclusion:** The CDC Advisory Committee on Immunization Practices (ACIP) recommends PCV21 as an option for adults when a PCV vaccine is recommended.

Capvaxive does not protect against serotype 4, which is included in other pneumococcal vaccines and is responsible for ≥30% of IPD cases in certain populations (i.e., adults <65 years old living in some western US regions who are homeless, have chronic lung disease or alcohol use disorder, smoke, or use injectable drugs).

CLINICAL STUDIES — FDA approval of *Capvaxive* was based on the results of 3 trials (STRIDE-3, STRIDE-5, and STRIDE-6; STRIDE-5 is unpublished) evaluating its immunogenicity in both vaccine-naive and previously vaccinated adults. In STRIDE-3 and STRIDE-6, immune responses elicited by PCV21 were noninferior to those

Table 1. Pneumococcal Conjugate Vaccines

Vaccine	Formulations	Usual Adult Dosage	Cost[1]
Prevnar 13 (PCV13; Pfizer)	0.5 mL susp in single-use prefilled syringes	0.5 mL x 1 dose	$211.10
Vaxneuvance (PCV15; Merck)	0.5 mL susp in single-use prefilled syringes	0.5 mL x 1 dose	215.30
Prevnar 20 (PCV20; Pfizer)	0.5 mL susp in single-use prefilled syringes	0.5 mL x 1 dose	232.20
Capvaxive (PCV21; Merck)	0.5 mL soln in single-use prefilled syringes	0.5 mL x 1 dose	287.00

soln = solution; susp = suspension

1. Approximate WAC for one dose. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/drug-pricing-policy.

elicited by PCV15, PCV20, and PPSV23 for all shared serotypes.[2,3]

In STRIDE-5 (summarized in the package insert), 1080 adults ≥50 years old were randomized to receive PCV21 with or 30 days after receiving a quadrivalent influenza vaccine. Immune responses elicited when the two vaccines were administered together were noninferior to those elicited when PCV21 was given 30 days after influenza vaccination for 20 of 21 pneumococcal serotypes (not serotype 23B) and for 3 of 4 influenza strains.

ADVERSE EFFECTS — Injection-site reactions (pain, swelling, and erythema), fatigue, headache, myalgia, and arthralgia were the most common adverse effects reported with *Capvaxive* in clinical trials. Adverse effects were similar when *Capvaxive* was administered alone or with a quadrivalent inactivated influenza vaccine. Like other conjugate vaccines, *Capvaxive* is contraindicated for use in persons with a severe allergy to diphtheria toxoid.

PREGNANCY — The American College of Obstetricians and Gynecologists (ACOG) recommends pneumococcal vaccination for pregnant women at increased risk of severe pneumococcal disease.[4] No adequate data are available on the use of PCV21 in pregnant women. No adverse developmental outcomes were observed in animal studies.

ACIP RECOMMENDATIONS — The CDC Advisory Committee on Immunization Practices (ACIP) recommends PCV21 as an option for adults who are candidates for pneumococcal vaccination.[5] Previously unvaccinated adults who are ≥65 years old or 19-64 years old with certain underlying medical conditions or other risk factors should receive a one-time dose of PCV21 or PCV20, or a dose of PCV15 followed ≥1 year later by PPSV23.

Table 2. Pneumococcal Vaccine Serotypes

Serotype	PCV13	PCV15	PCV20	PPSV23	PCV21
1	X	X	X	X	
3	X	X	X	X	X
4	X	X	X	X	
5	X	X	X	X	
6A	X	X	X		X
6B	X	X	X	X	
7F	X	X	X	X	X
9V	X	X	X	X	
14	X	X	X	X	
18C	X	X	X	X	
19A	X	X	X	X	X
19F	X	X	X	X	
23F	X	X	X	X	
22F		X	X	X	X
33F		X	X	X	X
8			X	X	X
10A			X	X	X
11A			X	X	X
12F			X	X	X
15B			X	X	X
2				X	
9N				X	X
17F				X	X
20				X	
15A					X
15C					X[1]
16F					X
20A					X
23A					X
23B					X
24F					X
31					X
35B					X

PCV13 = 13-valent conjugate vaccine *(Prevnar 13)*; PCV15 = 15-valent conjugate vaccine *(Vaxneuvance)*; PCV20 = 20-valent conjugate vaccine *(Prevnar 20)*; PPSV23 = 23-valent polysaccharide vaccine *(Pneumovax 23)*; PCV21 = 21-valent conjugate vaccine *(Capvaxive)*.

1. *Capvaxive* contains the de-*O*-acetylated polysaccharide of 15B, which induces immunogenicity to serotype 15C due to a similar molecular structure.

Specific recommendations for pneumococcal vaccination of adults based on vaccination status, age, and risk factors are available in Figures 1 and 2 (online).

DOSAGE AND ADMINISTRATION — *Capvaxive* is supplied in single-dose, prefilled syringes that should be stored in a refrigerator. It should be given intramuscularly as a single 0.5-mL dose.

CONCLUSION — The new 21-valent pneumococcal conjugate vaccine *Capvaxive* contains serotypes

that collectively account for 85% of invasive pneumococcal disease in older adults in the US, including 8 serotypes that are not included in other currently available pneumococcal vaccines. It is a recommended option for adults who are candidates for pneumococcal vaccination. ■

Additional Content Available Online

Figure 1: Pneumococcal Vaccine Recommendations for Adults 19-64 Years Old
http://medicalletter.org/TML-article-1713f
Figure 2: Pneumococcal Vaccine Recommendations for Adults ≥65 Years Old
http://medicalletter.org/TML-article-1713g

1. Two new pneumococcal vaccines – Prevnar 20 and Vaxneuvance. Med Lett Drugs Ther 2021; 63:188.
2. HL Platt et al. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. Lancet Infect Dis 2024 July 1 (epub).
3. P Scott et al. A phase 3 clinical study to evaluate the safety, tolerability, and immunogenicity of V116 in pneumococcal vaccine-experienced adults 50 years of age or older (Stride-6). Clin Infect Dis 2024 July 31 (epub).
4. American College of Obstetricians and Gynecologists. Maternal immunization. Practice advisory. October 2022. Available at: https://bit.ly/3ys9uyu. Accessed September 26, 2024.
5. M Kobayashi et al. Use of 21-valent pneumococcal conjugate vaccine among U.S. adults: recommendations of the Advisory Committee on Immunization Practices - United States, 2024. MMWR Morb Mortal Wkly Rep 2024; 73:793.

An Epinephrine Nasal Spray *(neffy)* for Anaphylaxis

Related article(s) since publication

The FDA has approved an epinephrine nasal spray (*neffy* – ARS Pharma) for emergency treatment of type 1 hypersensitivity reactions including anaphylaxis in patients who weigh ≥30 kg. It is the first noninjectable epinephrine product to be approved for this indication.

Pronunciation Key

neffy: neh' fee

INJECTABLE EPINEPHRINE — Multiple epinephrine auto-injector formulations are available for emergency treatment of anaphylaxis (see Table 1). *EpiPen* and its generics have been used effectively for years. A generic version of *Adrenaclick* (brand no longer manufactured) is similar to *EpiPen* in size and functionality. *AUVI-Q* provides visual signals and audio instructions, has an automatic needle retraction system, and appears to be more convenient to carry and easier to use than *EpiPen*.[1] Because of differences in device design and instructions for use, these auto-injectors are not interchangeable and pharmacists cannot substitute one for another.

Key Points: *neffy*

- **Description:** The first epinephrine nasal spray.
- **Indication:** Emergency treatment of type 1 hypersensitivity reactions including anaphylaxis in patients who weigh ≥30 kg.
- **Clinical Studies:** In studies in healthy subjects, the nasal spray appeared to be pharmacologically comparable to injectable epinephrine.
- **Adverse Effects:** Throat irritation, headache, nasal discomfort, a jittery sensation, tremor, and rhinorrhea can occur.
- **Dosage:** One 2-mg spray intranasally; the dose can be repeated 5 minutes later if symptoms do not improve.
- **Cost:** The wholesale acquisition cost of a package containing two single-use devices is $710; according to the manufacturer, the cost for most patients with commercial insurance will not exceed $25.
- **Conclusion:** The *neffy* nasal spray could be more convenient to use than injectable epinephrine for some individuals. It has not been studied in persons with underlying structural nasal conditions.

An epinephrine prefilled syringe *(Symjepi)* is also FDA-approved for emergency treatment of anaphylaxis. It requires the user to manually inject the needle and push down the plunger, which may be difficult for some patients, particularly children.[2]

Some injectable epinephrine products have not been consistently available in recent years; at press time, *EpiPen*, the generic version of *Adrenaclick,* and *Symjepi* were on back order with no estimated return date.[3]

THE NEW FORMULATION — Each *neffy* nasal spray device contains a single 2-mg dose of epinephrine and is about the size of a teabag; the product is supplied in packages containing two devices. The drug delivery system is the same as that used in several other FDA-approved nasal sprays, including naloxone *(Narcan)*. An absorption-enhancing agent *(Intravail)*, which is also used in nasal spray formulations of drugs such as sumatriptan *(Tosymra)* and diazepam *(Valtoco)*, increases epinephrine bioavailability.[4]

CLINICAL STUDIES — As with injectable epinephrine products for treatment of anaphylaxis, no efficacy trials were required for FDA approval of *neffy*. Approval was based on the results of five pharmacologic studies (summarized in the package insert) in a total of 175 healthy adults and 42 healthy children 8-17 years old who weighed ≥30 kg. Exposure to epinephrine and changes in blood pressure and pulse rate following a 2-mg dose of the nasal spray were comparable to those following a 0.3-mg IM dose, including in subjects with seasonal allergic rhinitis

Table 1. Some Epinephrine Products for Anaphylaxis[1]

Product	Usual Adult Dosage[2]	Cost[3]
Auto-Injectors		
EpiPen (Mylan) generic (Mylan,[4] Teva)	0.3 mg IM or SC	$608.60[5] 300.00[5]
generic (Amneal)[6]	0.3 mg IM or SC	300.00[7]
AUVI-Q (Kaléo)	0.3 mg IM or SC	621.90[8]
Syringe		
Symjepi (US Worldmeds)	0.3 mg IM or SC	250.00[9]
Nasal Spray		
neffy (ARS Pharma)	2 mg intranasally	710.00[10]

1. In patients who weigh ≥30 kg.
2. A second dose can be administered using a new device if needed.
3. Approximate WAC for two doses. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.
4. The Mylan product is an authorized generic drug.
5. Mylan provides free epinephrine auto-injectors to eligible uninsured or underinsured patients who are from families earning up to 400% of the federal poverty level (https://aspe.hhs.gov/poverty-guidelines). Manufacturer-issued coupons for *EpiPen* and its authorized generic are available for patients with commercial insurance.
6. Authorized generic of *Adrenaclick*, which has been discontinued.
7. Available at discounted prices at some pharmacies (at CVS pharmacies, the cash price is $110.00 for a package containing two auto-injectors).
8. Kaléo provides free *AUVI-Q* auto-injectors to eligible uninsured patients who are from families earning up to 250% of the federal poverty level (https://aspe.hhs.gov/poverty-guidelines). According to the manufacturer, the out-of-pocket cost should not exceed $35 for most patients with standard commercial insurance or $150 for patients with high-deductible commercial insurance.
9. A manufacturer-issued coupon card reduces the copay to $0 for commercially insured patients and reduces the cost by $100 for uninsured patients.
10. Wholesale acquisition cost according to the manufacturer. According to the manufacturer, the out-of-pocket cost should not exceed $25 for most patients with commercial insurance or $199 for those using coupons from discount sites such as GoodRx.

who underwent a nasal allergen challenge. The nasal spray has not been studied in persons with underlying structural nasal conditions, such as polyps or a history of nasal injury or surgery.

ADVERSE EFFECTS — The most common adverse effects of two doses of *neffy* in adults (incidence 7-19%) were throat irritation, headache, nasal discomfort, a jittery sensation, tremor, and rhinorrhea. Similar adverse effects were observed in children. The nasal spray solution contains sodium metabisulfite, which could cause a hypersensitivity reaction in patients with a sulfite allergy, but a history of sulfite sensitivity should not deter emergency use of the product.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of *neffy* is one 2-mg spray administered into one nostril. If symptoms do not improve after 5 minutes, a second spray may be administered into the same nostril using a new device. The devices should be stored at room temperature, but excursions up to 50° C (122° F) are permitted; injectable epinephrine formulations only permit excursions to 30° C (86° F). At temperatures below -15° C (5° F), the nasal spray solution freezes and the device does not deliver epinephrine. Like other epinephrine products, *neffy* should be replaced before its expiration date. The shelf life of *neffy* is 30 months, which is longer than injectable epinephrine products (generally 12-18 months).

According to the manufacturer, the out-of-pocket cost for two *neffy* nasal spray devices should not exceed $25 for most patients with commercial insurance or $199 for those using coupons from discount sites such as GoodRx.[5]

CONCLUSION — The *neffy* nasal spray offers a new, potentially more convenient route of epinephrine delivery for emergency treatment of anaphylaxis in adults and children who weigh ≥30 kg. Whether its effectiveness differs from that of injectable epinephrine remains to be determined. Until data on the efficacy of *neffy* become available, some expert clinicians are advising patients to also carry an injectable epinephrine product. *Neffy* has not been studied in patients with underlying structural nasal conditions, such as polyps or a history of injury or surgery. ■

1. Auvi-Q epinephrine auto-injector returns. Med Lett Drugs Ther 2017; 59:33.
2. An epinephrine prefilled syringe (Symjepi) for anaphylaxis. Med Lett Drugs Ther 2019; 61:25.
3. American Society of Health-System Pharmacists. Current drug shortages. Available at: https://bit.ly/3Qs7ETT. Accessed September 26, 2024.
4. AK Ellis et al. Development of neffy, an epinephrine nasal spray, for severe allergic reactions. Pharmaceutics 2024; 16:811.
5. ARS Pharma Press Release. ARS Pharmaceuticals receives FDA approval of neffy (epinephrine nasal spray), the first and only needle-free treatment for type I allergic reactions, including anaphylaxis. August 9, 2024. Available at: https://bit.ly/4cyySk4. Accessed September 26, 2024.

Vonoprazan *(Voquezna)* for Nonerosive GERD

The potassium-competitive acid blocker vonoprazan (*Voquezna* – Phathom), which was approved earlier for treatment of erosive esophagitis, has now been approved by the FDA for relief of heartburn associated with nonerosive gastroesophageal reflux disease (GERD) in adults.[1] Vonoprazan is also available copackaged with amoxicillin *(Voquezna Dual Pak)* and with amoxicillin and clarithromycin *(Voquezna Triple Pak)* for treatment of *Helicobacter pylori* infection.[2]

Pronunciation Key	
Vonoprazan: von oh' pra zan	***Voquezna*:** voe kwez' nah

GERD — Heartburn and regurgitation are the classic symptoms of GERD. Other symptoms may include chest pain and chronic cough. Drugs that suppress gastric acid are the standard treatment for GERD. Proton pump inhibitors (PPIs) are more effective than H_2-receptor antagonists (H2RAs) in relieving heartburn. Most patients will have a relapse of symptoms after stopping treatment; long-term maintenance treatment is often necessary.[3,4]

PHARMACOLOGY — Vonoprazan blocks the final step of acid secretion in the gastric parietal cell by competitively blocking potassium binding to hydrogen-potassium ATPase (the "proton pump"). Unlike PPIs, vonoprazan does not require activation by acid. Vonoprazan is more rapidly absorbed, has a longer half-life (~7 hours vs ~1-2 hours), and achieves a higher intragastric pH than PPIs.[5]

CLINICAL STUDIES — FDA approval of vonoprazan for the new indication was based on the results of a double-blind trial in 772 patients with nonerosive GERD who had heartburn on at least 4 of 7 days prior to randomization. Patients were randomized to receive vonoprazan 10 or 20 mg or placebo once daily for 4 weeks. After 4 weeks, patients taking placebo were rerandomized to receive vonoprazan 10 or 20 mg for an additional 20 weeks; those already taking vonoprazan continued taking their original dose. The percentage of heartburn-free days through week 4, the primary endpoint, was statistically significantly greater with both doses of vonoprazan than with placebo (44.8% with 10 mg and 44.4% with 20 mg vs 27.7%). The mean percentage of heartburn-free days during the 20-week extension period with vonoprazan was 61-63%.[6]

In a trial in 483 patients in Japan with nonerosive GERD who were randomized to receive vonoprazan 10 mg or placebo once daily for 4 weeks, the percentage of heartburn-free days, the primary endpoint, was not significantly greater with vonoprazan compared to placebo (72.6% vs 61.5%).[7]

No trials directly comparing vonoprazan to PPIs or H2RAs for treatment of nonerosive GERD are available.

ADVERSE EFFECTS — In the pivotal clinical trial, the most common adverse effects (frequency ≥2%) of vonoprazan were abdominal pain, constipation, diarrhea, nausea, and urinary tract infection. As with PPIs, *Clostridioides difficile* infection, acute tubulointerstitial nephritis, bone fractures, and severe cutaneous adverse reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis can occur with use of vonoprazan. Vitamin B12 deficiency and hypomagnesemia have also been reported. Hyperplasia of the gastric mucosa and gastric hyperplastic polyps with chronic bleeding have been reported with long-term use of vonoprazan in patients with erosive esophagitis.[8]

Key Points: Vonoprazan *(Voquezna)*

- **Description:** Oral potassium-competitive acid blocker.
- **Indication:** Relief of heartburn associated with nonerosive GERD in adults.
- **Efficacy:** Vonoprazan was associated with more heartburn-free days compared to placebo in one 4-week trial.
- **Adverse Effects:** GI adverse effects and urinary tract infection were most common.
- **Drug Interactions:** Vonoprazan may interact with drugs that induce CYP3A4, are substrates of CYP2C19, or require gastric acid for absorption.
- **Dosage:** 10 mg orally once daily.
- **Cost:** A 28-day supply costs $606.
- **Conclusion:** Until more long-term safety data become available, other acid-suppressing drugs are preferred.

DRUG INTERACTIONS — Vonoprazan can decrease serum concentrations of drugs that require gastric acidity for absorption, such as the antiretroviral drugs rilpivirine and atazanavir. Vonoprazan is a CYP3A4 substrate; use with strong or moderate CYP3A4 inducers can decrease serum concentrations of vonoprazan and should be avoided. Vonoprazan is an inhibitor of CYP2C19; it may increase serum concentrations of CYP2C19 substrates and can reduce the antiplatelet effect of clopidogrel, which is converted to its active form by CYP2C19.[9]

PREGNANCY AND LACTATION — No adequate data are available on vonoprazan use in pregnant women. In animal studies, liver lesions and increased stomach weight were reported in rats that had gestational or lactational exposure to vonoprazan. Vonoprazan and its metabolites are present in rat milk. No data are available on the presence of vonoprazan in breast milk or its effects on the breastfed infant or milk production. Breastfeeding is not recommended during treatment with the drug.

DOSAGE, ADMINISTRATION, AND COST — *Voquezna* is supplied in 10- and 20-mg tablets. The recommended dosage for relief of heartburn

associated with nonerosive GERD is 10 mg once daily for 4 weeks. The tablets should be swallowed whole; they should not be chewed or crushed. The wholesale acquisition cost (WAC) for a 28-day supply of *Voquezna* is $606.[10]

CONCLUSION — The potassium-competitive acid blocker vonoprazan *(Voquezna)* reduced heartburn significantly in patients with nonerosive GERD in one 4-week placebo-controlled trial, but not in a second trial. Data on its long-term safety are lacking. Older, less expensive acid-suppressing drugs should be tried first. ■

1. Vonoprazan (Voquezna) for erosive esophagitis. Med Lett Drugs Ther 2023; 65:203.
2. Two vonoprazan combinations (Voquezna) for H. pylori. Med Lett Drugs Ther 2022; 64:169.
3. PO Katz et al. ACG clinical guideline for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol 2022; 117:27.
4. Drugs for GERD and peptic ulcer disease. Med Lett Drugs Ther 2022; 64:49.
5. DY Graham and MP Dore. Update on the use of vonoprazan: a competitive acid blocker. Gastroenterology 2018; 154:462.
6. L Laine et al. Vonoprazan is efficacious for treatment of heartburn in non-erosive reflux disease: a randomized trial. Clin Gastroenterol Hepatol 2024 May 14 (epub).
7. Y Kinoshita et al. Efficacy and safety of vonoprazan in patients with nonerosive gastroesophageal reflux disease: a randomized, placebo-controlled, phase 3 study. Clin Transl Gastroenterol 2019; 10:e00101.
8. C Goto et al. Long-term vonoprazan administration causes gastric fundic gland-type hyperplastic polyps and chronic bleeding. Clin J Gastroenterol 2023; 16:159.
9. Inhibitors and inducers of CYP enzymes and P-glycoprotein and other transporters. Med Lett Drugs Ther 2023 January 25 (epub). Available at: www.medicalletter.org/downloads/CYP_PGP_Tables.pdf.
10. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.

A New RSV Vaccine *(mResvia)* for Adults ≥60 Years Old

The FDA has licensed *mResvia* (Moderna), an mRNA respiratory syncytial virus (RSV) vaccine, for prevention of lower respiratory tract disease (LRTD) caused by RSV in adults ≥60 years old. It is the first mRNA vaccine to be licensed in the US for this indication. Two recombinant RSV vaccines, *Arexvy* and *Abrysvo*, are also available for prevention of RSV LRTD.[1] *Arexvy* is approved for use in adults ≥50 years old.[2] *Abrysvo* is approved for use in adults ≥60 years old and in pregnant women to prevent RSV LRTD in their infants.

Pronunciation and Abbreviation Key

mResvia: em res vee uh
RSV = respiratory syncytial virus
LRTD = lower respiratory tract disease

Key Points: *mResvia*

- **Description:** An mRNA respiratory syncytial virus (RSV) vaccine encoding a stabilized prefusion form of the RSV fusion (F) glycoprotein.
- **Indication:** FDA-approved for prevention of lower respiratory tract disease (LRTD) caused by RSV in adults ≥60 years old.
- **Efficacy:** A single dose has prevented RSV LRTD in adults ≥60 years old compared to placebo. One dose of *mResvia* appears to be less effective over two RSV seasons than one dose of a recombinant RSV vaccine (*Arexvy* or *Abrysvo*).
- **Adverse Effects:** Most common are injection-site pain, axillary swelling or tenderness, fatigue, headache, myalgia, arthralgia, and chills.
- **Dosage:** A single 50 mcg/0.5 mL IM dose.
- **Cost:** The wholesale acquisition cost for one dose is $290.
- **Conclusion:** The CDC Advisory Committee on Immunization Practices (ACIP) recommends a single dose of any available RSV vaccine for all adults ≥75 years old and for those 60-74 years old at increased risk of severe RSV disease.

RSV DISEASE — RSV typically causes a mild upper respiratory tract infection in adults, but older adults, particularly those with underlying health conditions, have an increased risk of RSV-associated hospitalization. RSV epidemics in the Northern Hemisphere typically occur between October and April, peaking in December or January.

EFFICACY OF RECOMBINANT VACCINES — Both *Arexvy* and *Abrysvo* have been shown to reduce the incidence of RSV LRTD in adults ≥60 years old.[1] A case-control analysis of patients ≥60 years old hospitalized for acute respiratory illness found that vaccination with a recombinant RSV vaccine was about 75% effective against RSV-associated hospitalization during the first season of use.[3] Use of *Abrysvo* in pregnant women reduced the incidence of medically-attended RSV LRTD in their infants during one RSV season.[1]

Table 1. RSV Vaccines

Vaccine	Dose/Schedule	Cost[1]
Arexvy (GSK)	120 mcg/0.5 mL IM once	$294.00
Abrysvo (Pfizer)	120 mcg/0.5 mL IM once	295.00
mResvia (Moderna)	50 mcg/0.5 mL IM once	290.00

1. Approximate WAC for one dose. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.

THE NEW VACCINE — *mResvia* is a lipid nanoparticle-encapsulated, mRNA-based vaccine. It encodes a stabilized prefusion form of the RSV fusion (F) glycoprotein derived from an RSV A strain. The RSV prefusion F glycoprotein mediates viral fusion and host-cell entry and elicits neutralizing antibodies. The same antigen is used in *Arexvy* and *Abrysvo*.

CLINICAL STUDIES — FDA approval of *mResvia* was based on the preliminary results of an ongoing observer-blinded trial (ConquerRSV) in 35,064 adults ≥60 years old who were randomized to receive a single dose of *mResvia* or placebo. The vaccine was effective, compared to placebo, in preventing a first episode of RSV LRTD (see Table 2). Vaccine efficacy against RSV-associated acute respiratory disease was 68.4%; efficacy against RSV A was higher than that against RSV B (78.5% vs 51.7%).[4]

Table 2. Efficacy of *mResvia* in Adults ≥60 Years Old[1]

	RSV LRTD (≥2 signs/symptoms)[2]	RSV LRTD (≥3 signs/symptoms)[2]
Median follow-up 3.7 months	78.7%	80.9%
Median follow-up 8.6 months	62.5%	61.1%

RSV LRTD = respiratory syncytial virus-associated lower respiratory tract disease

1. E Wilson et al. N Engl J Med 2023; 389:2233; R Das. ACIP presentation slides: June 26-28, 2024 meeting.
2. Vaccine efficacy (based on hazard ratio, *mResvia* vs placebo) for prevention of a first episode of RSV LRTD with ≥2 lower respiratory signs/symptoms or ≥3 lower respiratory signs/symptoms starting 14 days after vaccination.

A follow-up report found that a single dose of *mResvia* was ~50% effective in preventing RSV LRTD over 18 months in adults ≥60 years old.[5] Higher efficacy rates against RSV LRTD over two RSV seasons have been reported following a single dose of *Arexvy* or *Abrysvo* (67.7% over 23.3 months with *Arexvy* and 81.5% over 16.4 months with *Abrysvo*).[6,7]

ADVERSE EFFECTS — In the ConquerRSV trial, the most common local adverse effects reported within 7 days of *mResvia* vaccination were injection-site pain (55.9%) and axillary swelling or tenderness (15.2%). Systemic adverse effects included fatigue (30.8%), headache (26.7%), myalgia (25.6%), arthralgia (21.7%), and chills (11.6%). More cases of urticaria were reported with *mResvia* than with placebo within 28 days after administration (15 vs 5). One participant in the *mResvia* group developed facial paralysis 4 days after vaccination. Atrial fibrillation and Guillain-Barré syndrome (GBS) were reported following administration of *Arexvy* or *Abrysvo* in clinical trials. Vaccine-related cardiac arrhythmias and GBS were not reported in clinical trials with *mResvia*.[5]

Table 3. Risk Factors for Severe RSV Disease

- Chronic medical conditions (e.g., pulmonary, cardiac, renal)
- Moderate or severe immune compromise
- Frailty
- Severe obesity (body mass index >40 kg/m^2)
- Residence in a nursing home or other long-term care facility

ACIP RECOMMENDATIONS — The CDC Advisory Committee on Immunization Practices (ACIP) has updated its recommendations for use of RSV vaccines in older adults. A single dose of an RSV vaccine is now recommended for all adults ≥75 years old and for those 60-74 years old at increased risk of severe RSV disease (see Table 3).[8] For optimal protection, the vaccine should be given before the onset of the RSV season. Administration of an RSV vaccine and other adult vaccines during the same visit is considered acceptable, but local or systemic reactogenicity could increase.[9]

DOSAGE AND ADMINISTRATION — The *mResvia* vaccine is supplied as a frozen suspension in prefilled syringes containing a single 50 mcg/0.5 mL IM dose. The syringe can be thawed in the refrigerator for 60 minutes and should stand at room temperature for 10-20 minutes before administration. A syringe that is thawed at room temperature is ready to be administered after 45 minutes.

CONCLUSION — A single dose of *mResvia*, the first mRNA respiratory syncytial virus (RSV) vaccine, was effective in preventing RSV-associated lower respiratory tract disease during one RSV season in adults ≥60 years old. Follow-up data suggest that one dose of *mResvia* may offer less protection over two RSV seasons than one dose of *Arexvy* or *Abrysvo*, the recombinant RSV vaccines available in the US. The CDC Advisory Committee on Immunization Practices recommends a single dose of any available RSV vaccine for all adults ≥75 years old and for those 60-74 years old at increased risk of severe RSV disease. ■

1. Two vaccines (Arexvy and Abrysvo) for prevention of RSV disease. Med Lett Drugs Ther 2023; 65:155.
2. In brief: RSV vaccine (Arexvy) for ages 50-59. Med Lett Drugs Ther 2024; 66:113.
3. D Surie et al. RSV vaccine effectiveness against hospitalization among US adults 60 years and older. JAMA 2024 Sep 4 (epub).
4. E Wilson et al. Efficacy and safety of an mRNA-based RSV preF vaccine in older adults. N Engl J Med 2023; 389:2233.
5. R Das. Update on Moderna's RSV vaccine, mResvia (mRNA-1345), in adults ≥60 years of age. ACIP presentation slides: June 26-28, 2024 meeting. Available at: https://bit.ly/4ciO7hH. Accessed September 26, 2024.

6. I Munjal. RSVpreF adult clinical development update. ACIP presentation slides: June 26-28, 2024 meeting. Available at: https://bit.ly/4ciO7hH. Accessed September 26, 2024.
7. S Gerber. Arexvy (adjuvanted RSVPreF3) 2-year update. ACIP presentation slides: June 26-28, 2024 meeting. Available at: https://bit.ly/4ciO7hH. Accessed September 26, 2024.
8. A Britton et al. Use of respiratory syncytial virus vaccines in adults aged ≥60 years: updated recommendations of the Advisory Committee on Immunization Practices – United States, 2024. MMWR Morb Mortal Wkly Rep 2024; 73:696.
9. CDC. Vaccines and immunizations. Healthcare providers: RSV vaccination for adults 60 years of age and over. July 3, 2024. Available at: https://bit.ly/3yC0A1n. Accessed September 26, 2024.

IN BRIEF

New Warning for Fezolinetant *(Veozah)*

The FDA has required a new warning in the label of the oral selective neurokinin 3 (NK3) receptor antagonist fezolinetant *(Veozah)* about the risk of hepatoxicity.[1,2] The label of fezolinetant, which was approved by the FDA in 2023 for treatment of moderate to severe vasomotor symptoms due to menopause, already contained a warning about hepatic transaminase elevations associated with use of the drug.

The new warning was based on a single post-marketing case of acute mixed hepatocellular cholestatic drug-induced liver injury. The patient presented with fatigue, nausea, itching, jaundice, light-colored stools, dark urine, and elevated hepatic enzyme and total bilirubin levels within 40 days of starting fezolinetant.

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin levels should be checked before starting fezolinetant, monthly for the first 3 months, and at 6 and 9 months after starting the drug. Fezolinetant should not be started if ALT or AST concentrations are ≥2 times the upper limit of normal (ULN) or if total bilirubin is elevated. The drug should be stopped if transaminase levels are >5 times the ULN or if transaminase levels are >3 times the ULN and total bilirubin level is >2 times the ULN. ■

1. FDA Drug Safety Communication. FDA adds warning about rare occurrence of serious liver injury with use of Veozah (fezolinetant) for hot flashes due to menopause. Stop medicine if signs and symptoms of liver injury occur. September 12, 2024. Available at: https://bit.ly/4ghd4MK. Accessed September 26, 2024.
2. Fezolinetant (Veozah) for menopausal vasomotor symptoms. Med Lett Drugs Ther 2023; 65:97.

Additional Content Available Online

Addendum: Effectiveness of mRNA COVID-19 Vaccines
http://medicalletter.org/TML-article-1713h
In Brief: Afamitresgene Autoleucel *(Tecelra)* for Synovial Sarcoma
http://medicalletter.org/TML-article-1713i
Erzofri — Another Once-Monthly Paliperidone Formulation
http://medicalletter.org/TML-article-1713j

Coming Soon

- Drugs for Hepatitis C
- Extended-Release Carbidopa/Levodopa *(Crexont)* for Parkinson's Disease
- *Eroxon* OTC Topical Gel for Erectile Dysfunction
- *FluMist* Influenza Vaccine for Self-Administration

The Medical Letter Is Available On-the-Go!

Did you know you can access your Medical Letter subscription online and on your mobile device?

To access online, go to: www.medicalletter.org and log in (or register if it's your first time). To get The Medical Letter on your mobile device, download our app from the App Store (for iPhone/iPad) and log in with your username and password (must register online first).

Don't wait for the next issue to come in the mail. Access the latest information and earn CME credit anywhere, anytime!

Subscription Services

Address:
The Medical Letter, Inc.
145 Huguenot St. Ste. 312
New Rochelle, NY 10801-7537
www.medicalletter.org

Customer Service:
Call: 800-211-2769 or 914-235-0500
Fax: 914-632-1733
E-mail: custserv@medicalletter.org

Permissions:
To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org

Subscriptions (US):
1 year - $159; $65 per year for students, interns, residents, and fellows in the US and Canada.
Reprints - $45 per issue or article

Site License Inquiries:
E-mail: SubQuote@medicalletter.org
Call: 800-211-2769
Special rates available for bulk subscriptions.

Get Connected:

Copyright 2024. ISSN 1523-2859

The Medical Letter®

Continuing Medical Education Program

medicalletter.org/cme-program

Earn up to 52 Credits per Year for Free

Choose CME from The Medical Letter in the format that's right for you!

- **Free Individual Activities – Free to active subscribers of *The Medical Letter*. Answer 10 questions per issue and submit answers online. Earn 2 credits/activity. A score of 70% or greater is required to pass.**
- **Comprehensive Activity – Available online or in print to Medical Letter subscribers, this 130 question exam enables you to earn 26 credits immediately upon successful completion of the post-activity. A score of 70% or greater is required to pass. Comprehensive activities allow you to learn at your own pace in the comfort of your home or office. Comprehensive activities are offered every January and July enabling you to earn up to 52 credits per year. $79.50/activity.**
- **Paid Individual Activity – Available to nonsubscribers. Answer 10 questions per issue and submit answers online. Earn 2 credits/activity. $15/activity. A score of 70% or greater is required to pass.**

ACCREDITATION INFORMATION:

ACCME: The Medical Letter is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Medical Letter designates this enduring material for a maximum of 2 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ABIM MOC: Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit. Your participation information will be shared with ABIM through PARS.

ABS CC: Successful completion of this activity enables the learner to earn credit toward the CME requirement of the American Board of Surgery's Continuous Certification program. It is the CME activity provider's responsibility to submit learner completion information to ACCME for the purpose of granting ABS credit.

AAFP: The AAFP has reviewed The Medical Letter Continuing Medical Education Program, and deemed it acceptable for AAFP credit. Term of approval is from 01/01/2024 to 12/31/2024. Physicians should claim only the credit commensurate with the extent of their participation in the activity. This session (Issue 1713) is approved for 2.00 Enduring Materials, Self-Study AAFP Prescribed Credit(s).

AAPA: This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. This activity is designated for 2 AAPA Category 1 CME credits. Approval is valid from 10/3/2024 to 10/3/2025. PAs should only claim credit commensurate with the extent of their participation. AAPA reference number: CME-2010618.

ACPE: The Medical Letter is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This exam is acceptable for 2.0 hours of knowledge-based continuing education credit (0.2 CEU).

AOA: This activity, being ACCME (AMA) accredited, is acceptable for Category 2-B credit by the **American Osteopathic Association (AOA)**.

The **American Nurses Credentialing Center (ANCC)** and the **American Academy of Nurse Practitioners (AANP)** accept *AMA PRA Category 1 Credit™* from organizations accredited by the ACCME.

Physicians in Canada: Members of The College of Family Physicians of Canada are eligible to receive Mainpro-M1 credits (equivalent to AAFP Prescribed credits) as per our reciprocal agreement with the American Academy of Family Physicians.

MISSION:

The mission of The Medical Letter's Continuing Medical Education (CME) Program is to support the professional development of healthcare providers including physicians, nurse practitioners, pharmacists, and physician associates by providing independent, unbiased drug information and treatment recommendations that are free of industry influence. The content of the educational activities primarily includes comparative reviews of pharmacologic treatment for common conditions and unbiased reviews of newly FDA-approved drugs that focus on their pharmacology, efficacy in clinical trials, dosage and administration, adverse effects, and drug interactions. The Medical Letter delivers educational content in the form of self-study material.

The expected outcome of the CME program is to increase the participant's knowledge about, or apply knowledge into practice after assimilating, information presented in materials contained in The Medical Letter.

The Medical Letter will strive to continually improve the CME program through periodic assessment of the program and activities. The Medical Letter aims to be a leader in supporting the professional development of healthcare providers by providing continuing medical education that is unbiased and free of pharmaceutical industry influence. The Medical Letter does not sell advertising or receive any commercial support.

GOAL:

Through this program, The Medical Letter expects to provide the healthcare community with unbiased, reliable, and timely educational content that they will use to make independent and informed therapeutic choices in their practice.

DISCLOSURE:

Principal Faculty for this Activity:

Mark Abramowicz, M.D., President has disclosed no relevant financial relationships
Jean-Marie Pflomm, Pharm.D., Editor in Chief has disclosed no relevant financial relationships

In addition to the Principal Faculty above, the following have also contributed to this activity:
Michael P. Viscusi, Pharm.D., Associate Editor has disclosed no relevant financial relationships.
Brinda M. Shah, Pharm.D., Consulting Editor has disclosed no relevant financial relationships.
Cynthia Covey has disclosed no relevant financial relationships.
Amy Faucard, MLS, Associate Editor has disclosed no relevant financial relationships.

LEARNING OBJECTIVES FOR THIS ACTIVITY:

Activity participants will read and assimilate unbiased reviews of FDA-approved and off-label uses of drugs and other treatment modalities. Activity participants will be able to select and prescribe, or confirm the appropriateness of the prescribed usage of, the drugs and other therapeutic modalities discussed in *The Medical Letter* with specific attention to clinical trials, pathophysiology, dosage and administration, drug metabolism and interactions, and patient management. Activity participants will make independent and informed therapeutic choices in their practice.

Upon completion of this activity, the participant will be able to:

1. Review the efficacy and safety of *Capvaxive*, a 21-valent pneumococcal conjugate vaccine, for prevention of invasive pneumococcal disease and pneumococcal pneumonia in adults.
2. Review the efficacy and safety of inhaled epinephrine *(neffy)* for emergency treatment of type 1 hypersensitivity reactions including anaphylaxis.
3. Review the efficacy and safety of vonoprazan *(Voquezna)* for treatment of heartburn associated with nonerosive gastroesophageal reflux disease (GERD).
4. Review the efficacy and safety of *mResvia*, an mRNA respiratory syncytial virus (RSV) vaccine, for prevention of lower respiratory tract disease caused by RSV in adults ≥60 years old.

CREDIT:

Participants who complete this activity and achieve a score of 70% or higher on the post-activity exam will be awarded 2 credits.
Have any questions? Call us at 800-211-2769 or 914-235-0500 or e-mail us at: custserv@medicalletter.org

Questions on next page

The Medical Letter®

Online Continuing Medical Education

DO NOT FAX OR MAIL THIS PAGE

To earn credit, go to: medicalletter.org/CMEstatus

Note: The participant should read the post-activity questions prior to beginning the activity. After careful review of the text, tables, and cited references, the participant should take time to reflect on how the newly acquired knowledge will be applied to clinical practice, affect patient care, and improve outcomes.

Issue 1713 Post-Activity Questions

(Correspond to questions #71-80 in Comprehensive Activity #91, available January 2025)

***Capvaxive* – A 21-Valent Pneumococcal Conjugate Vaccine**

1. The 8 serotypes included in PCV21 *(Capvaxive)* that are not included in other available pneumococcal vaccines account for what percentage of invasive pneumococcal disease cases in adults ≥65 years old?
   a. 10%
   b. 20%
   c. 30%
   d. 50%

2. The serotypes included in PCV20 *(Prevnar 20)* account for what percentage of invasive pneumococcal disease cases in adults ≥65 years old?
   a. 27%
   b. 39%
   c. 54%
   d. 78%

3. PCV21 does not protect against serotype:
   a. 4
   b. 19A
   c. 22F
   d. 15B

Epinephrine Nasal Spray *(neffy)* for Anaphylaxis

4. Epinephrine nasal spray *(neffy)* is FDA-approved for use in:
   a. adults only
   b. children ≤12 years old only
   c. all persons ≥6 months old
   d. all persons who weigh ≥30 kg

5. FDA approval of epinephrine nasal spray *(neffy)* was based on the results of:
   a. clinical trials in adults with anaphylaxis
   b. clinical trials in patients with urticaria
   c. pharmacologic studies in healthy subjects showing it is comparable to injectable epinephrine
   d. all of the above

Vonoprazan *(Voquezna)* for Nonerosive GERD

6. Vonoprazan:
   a. requires activation by acid
   b. has a shorter half-life than PPIs
   c. achieves a higher intragastric pH than PPIs
   d. all of the above

7. In the pivotal double-blind trial in patients with nonerosive GERD, the percentage of heartburn-free days through week 4 with use of vonoprazan 10 mg once daily was about:
   a. 30%
   b. 45%
   c. 60%
   d. 75%

8. Which of the following can occur with use of vonoprazan?
   a. GI adverse effects
   b. *Clostridioides difficile* infection
   c. acute tubulointerstitial nephritis
   d. all of the above

9. Which of the following statements about vonoprazan is correct?
   a. it can decrease serum concentrations of drugs that require gastric acidity for absorption
   b. it can reduce the antiplatelet effect of clopidogrel
   c. strong CYP3A4 inducers can reduce its serum concentrations
   d. all of the above

A New RSV Vaccine *(mResvia)* for Adults ≥60 Years Old

10. The mRNA RSV vaccine *mResvia*:
    a. appears to provide better protection against RSV A than RSV B
    b. has not been associated with cardiac arrythmias in clinical trials
    c. is a recommended option for RSV vaccination in all adults ≥75 years old and in those 60-74 years old at increased risk of severe RSV disease
    d. all of the above

ACPE UPN: Per Issue Exam: 0379-0000-24-713-H01-P; Release: October 3, 2024, Expire: October 2, 2025
Comprehensive Exam 91: 0379-0000-25-091-H01-P; Release: January 2025, Expire: January 2026

Successful completion of the post-test is required to earn AAPA Category 1 CME credit. Successful completion is defined as a cumulative score of at least 70 percent correct.