New Drug Update

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1

Disclosure

I have no financial interests or relationships to disclose.

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2

Updated CDC Childhood Immunization Recommendations as of January 5, 2026

Immunizations Recommended for All Children:

- **The CDC will continue to recommend that all children are vaccinated against diphtheria, tetanus, acellular pertussis (whooping cough), Haemophilus influenzae type b (Hib), Pneumococcal conjugate, polio, measles, mumps, rubella, and human papillomavirus (HPV), for which there is international consensus, as well as varicella (chickenpox)**.
- **Recent scientific studies have shown that one dose of the HPV vaccine is as effective as two doses. The CDC is following the lead of several peer nation by recommending one instead of two doses of this vaccine.**
  - https://www.hhs.gov/press-room/fact-sheet-cdc-childhood-immunization-recommendations.html

3

Updated CDC Childhood Immunization Recommendations as of January 5, 2026

Immunizations Recommended for Certain High-Risk Groups or Populations:

- Like all medical products, vaccines and other immunizing agents have different risk-benefit profiles for different groups of people. Risk factors can include unusual exposure to the disease, underlying comorbidities, or the risk of disease transmission to others.
- **The immunizations recommended for certain high-risk groups or populations are for respiratory syncytial virus (RSV), hepatitis A, hepatitis B, dengue, meningococcal ACWY, and meningococcal B.**
  - https://www.hhs.gov/press-room/fact-sheet-cdc-childhood-immunization-recommendations.html

4

Updated CDC Childhood Immunization Recommendations as of January 5, 2026

Immunizations Based on Shared Clinical Decision-Making:

- It is not always possible for public health authorities to clearly define who will benefit from an immunization, who has the relevant risk factors, or who is at risk for exposure. Physicians and parents, who know the child, are then best equipped to decide based on individual characteristics.
- **The immunizations based on shared clinical decision-making are for rotavirus, COVID-19, influenza, meningococcal disease, hepatitis A, and hepatitis B.**
  - https://www.hhs.gov/press-room/fact-sheet-cdc-childhood-immunization-recommendations.html

5

Updated CDC Childhood Immunization Recommendations as of January 5, 2026

Insurance Coverage

- **All immunizations recommended by the CDC as of December 31, 2025, will continue to be fully covered by Affordable Care Act insurance plans and federal insurance programs, including Medicaid, the Children's Health Insurance Program, and the Vaccines for Children program. Families will not have to purchase them out of pocket.**
- This means that insurance will continue to cover more vaccines for children in the U.S. than in peer nations, where insurance generally only pays for recommended vaccines.
- **All childhood vaccines are still included in the Vaccine Injury Compensation Program (VICP), a program established by Congress nearly 40 years ago, said Richard H. Hughes IV, JD, MPH, who teaches vaccine law at George Washington University.**
  - https://www.hhs.gov/press-room/fact-sheet-cdc-childhood-immunization-recommendations.html

6

CMS Will No Longer Require States to Report Immunization Data Dec. 30, 2025

- **States will no longer have to report how many children they vaccinate to the Centers for Medicare and Medicaid Services (CMS), according to a Dec. 30 letter to state health officials.**
- In the letter, **CMS announced that the Child and Adult Core Set of Health Quality Measures for Medicaid and the Children's Health Insurance Program (CHIP) would no longer require states to report childhood immunization status, immunizations for adolescents, and prenatal immunization status.**
- https://www.medicaid.gov/federal-policy-guidance/downloads/sho25005.pdf

7

The American Academy of Pediatrics President Responds January 5, 2026

- **"Today's announcement by federal health officials to arbitrarily stop recommending numerous routine childhood immunizations is dangerous and unnecessary," said AAP President Andrew Racine, MD, PhD, FAAP, in a statement sent to media organizations. "The longstanding, evidence-based approach that has guided the U.S. immunization review and recommendation process remains the best way to keep children healthy and protect against health complications and hospitalizations."**
- "Said to be modeled in part after Denmark's approach, the new recommendations issued today by the U.S. Centers for Disease Control and Prevention no longer recommend routine immunization for many diseases with known impacts on America's children, such as hepatitis A and B, rotavirus, respiratory syncytial virus (RSV), flu, and meningococcal disease," added Racine. **"AAP continues to recommend that children be immunized against these diseases, and for good reason; thanks to widespread childhood immunizations, the United States has fewer pediatric hospitalizations and fewer children facing serious health challenges than we would without this community protection."**
  - Racine A. AAP Opposes Federal Health Officials' Unprecedented Move to Remove Universal Childhood Immunization Recommendations. American Academy of Pediatrics. https://www.aap.org/en/news-room/news-releases/aap/2025/aap-opposes-federal-health-officials-unprecedented-move-to-remove-universal-childhood-immunization-recommendations/

8

The Infectious Disease Society of America President Responds January 5, 2026

- **Infectious Diseases Society of America President Ronald G. Nahass, MD, said in a statement that the changes were reckless, hidden, and would ultimately negatively affect children.**
- **"Today's announcement that HHS is drastically altering the U.S. childhood vaccine schedule without a transparent process or clear scientific justification represents the latest reckless step in Secretary Kennedy's assault on the national vaccine infrastructure that has saved millions of lives. His actions put families and communities at risk and will make America sicker."**
- "Upending long-standing vaccine recommendations without transparent public review and engagement with external experts will undermine confidence in vaccines with the likely outcome of decreasing vaccination rates and increasing disease. Making these changes amid ongoing outbreaks of vaccine-preventable diseases shows a disregard for the real confusion families already face."
- "Disease prevalence differs country to country, and there has been demonstrated and ongoing need in the U.S. for the vaccines included in the childhood vaccine schedule. Most other high-income countries have universal health care and parental leave, both of which can support prevention and early care and contribute to lower disease prevalence."
- "It is irresponsible to haphazardly change vaccine recommendations without a solid scientific basis and transparent process. The commitment the U.S. has made to protecting children from vaccine-preventable illness and death must remain a top priority."
  - https://www.idse.net/Policy-Public-Health/Article/01-26/CDC-drops-childhood-shots-recommendations/79313

9

The American Medical Association Responds January 5, 2026

- **Sandra Adamson Fryhofer, M.D. Trustee, American Medical Association said "The American Medical Association is deeply concerned by recent changes to the childhood immunization schedule that affects the health and safety of millions of children. Vaccination policy has long been guided by a rigorous, transparent scientific process grounded in decades of evidence showing that vaccines are safe, effective, and lifesaving."**
- **"Changes of this magnitude require careful review, expert and public input, and clear scientific justification. That level of rigor and transparency was not part of this decision. When longstanding recommendations are altered without a robust, evidence-based process, it undermines public trust and puts children at unnecessary risk of preventable disease."**
- "The scientific evidence remains unchanged, and **the AMA supports continued access to childhood immunizations recommended by national medical specialty societies.** We urge federal health leaders to recommit to a transparent, evidence-based process that puts children's health and safety first and reflects the realities of our nation's disease burden."
  - https://www.ama-assn.org/press-center/ama-press-releases/ama-statement-changes-childhood-vaccine-schedule

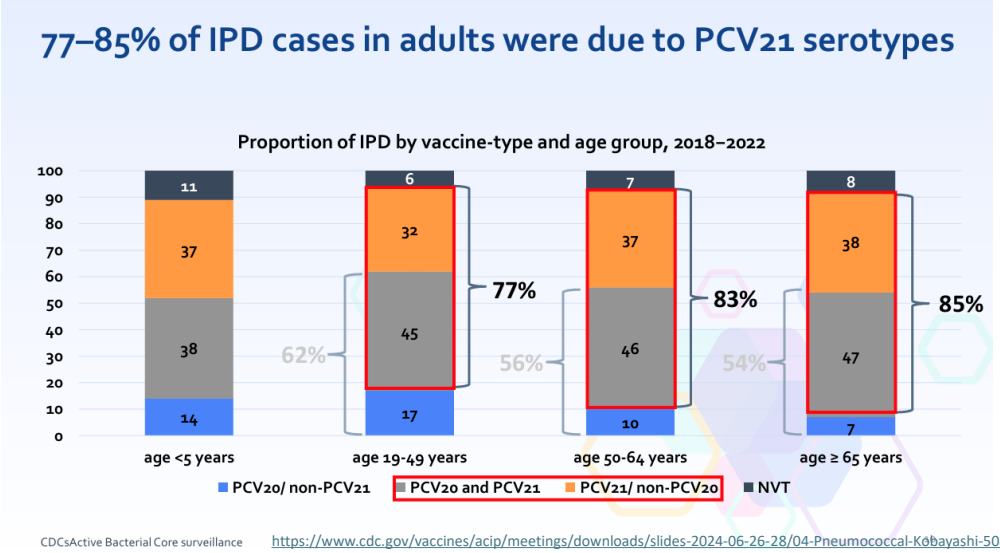
10

21-valent Pneumococcal Conjugate Vaccine (PCV-21) – Capvaxive by Merck

- **6-17-2024 the FDA approved pneumococcal 21-valent conjugate vaccine (PCV-21 vaccine) (Capvaxive) following priority review, and accelerated review, for the prevention of invasive pneumococcal disease (IPD) and pneumococcal pneumonia in adults ages 18 years and older. (Not currently recommended for children)**
- This is the **first pneumococcal vaccine that is specifically designed to protect against the serotypes that primarily infect older adults.** Data has shown that **the serotypes included in this vaccine are responsible for approximately 84% of IPD in adults aged 50 years and older.** The vaccine covers 21 serotypes, **including eight that are not targeted by any other available pneumococcal vaccines**, specifically serotypes 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B.

11

ACIP Working Group on PCV-21 in Adults



12

Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices

MMWR September 12, 2024 / 73(36);793–798

Adults ≥65 years old **New ≥ 50**
Complete pneumococcal vaccine schedules

CDC also recommended lowering the age for routine adult pneumococcal vaccination from 65 to 50 years old. CDC Oct 23, 2024

Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥1 year† → PPSV23¶
PPSV23 only at any age	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20 or PCV21	X ≥1 year† → PPSV23
PCV13 at any age & PPSV23 at <65 yrs	≥5 years → PCV20 or PCV21	X ≥5 years§ → PPSV23

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
¶ If PPSV23 is not available, PCV20 or PCV21 may be used
† Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF) leak
§ For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is ≥8 weeks since last PCV13 dose and ≥5 years since last PPSV23 dose; for others, the minimum interval for PPSV23 is ≥1 year since last PCV13 dose and ≥5 years since last PPSV23 dose

10/23/2024 Update: Removed the option to complete vaccine series with PPSV23 for PCV13-experienced adults

Shared clinical decision-making for those who already completed the series with PCV13 and PPSV23

Prior vaccines	Shared clinical decision-making option
Complete series: PCV13 at any age & **PPSV23** at ≥65 yrs	≥5 years → PCV20 or PCV21 — Together, with the patient, vaccine providers **may choose** to administer PCV20 or PCV21 to adults ≥65 years old who have already received PCV13 (but not PCV15, PCV20, or PCV21) at any age and PPSV23 at or after the age of 65 years old.

www.cdc.gov/pneumococcal/index.html

CDC U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

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Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices

MMWR September 12, 2024 / 73(36);793–798

Adults 19–64 years old with chronic health conditions
Complete pneumococcal vaccine schedules

New now age 19-49 years old 10/23/2024 Update

Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥1 year → PPSV23¶
PPSV23 only	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13† only	≥1 year → PCV20 or PCV21	X ≥1 year → PPSV23 — Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13† and PPSV23	**No vaccines** are recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 65 years old.	**New review recommendations at age 50**
Chronic health conditions	• Alcoholism • Chronic heart disease, including congestive heart failure and cardiomyopathies • Chronic liver disease	• Chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma • Cigarette smoking • Diabetes mellitus

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
¶ If PPSV23 is not available, PCV20 or PCV21 may be used
† Adults with chronic medical conditions were previously not recommended to receive PCV13

10/23/2024 Update: Removed the option to complete vaccine series with PPSV23 for PCV13-experienced adults

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Use of 21-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Recommendations of the Advisory Committee on Immunization Practices

MMWR September 12, 2024 / 73(36);793–798

Adults 19–64 years old with specified immunocompromising conditions
Complete pneumococcal vaccine schedules **New now age 19-49 years old 10/23/2024 Update**

Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥8 weeks → PPSV23†
PPSV23 only	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13 only	≥1 year → PCV20 or PCV21	X ≥8 weeks → PPSV23 → ≥5 years → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 1 dose of PPSV23	≥5 years → PCV20 or PCV21	X ≥5 years† → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 2 doses of PPSV23	≥5 years → PCV20 or PCV21	**No vaccines** recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
Immunocompromising conditions	• Chronic renal failure • Congenital or acquired asplenia • Congenital or acquired immunodeficiency§ • Generalized malignancy • HIV infection • Hodgkin disease • Iatrogenic immunosuppression¶ • Leukemia • Lymphoma • Multiple myeloma • Nephrotic syndrome • Sickle cell disease/other hemoglobinopathies • Solid organ transplant	

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
† If PPSV23 is not available, PCV20 or PCV21 may be used
† The minimum interval for PPSV23 is ≥8 weeks since last PCV13 dose and ≥5 years since last PPSV23 dose
§ Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease)
¶ Includes diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy

10/23/2024 Update: Removed the option to complete vaccine series with PPSV23 for PCV13-experienced adults

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Pneumococcal Vaccines: ACIP Meeting

Oct 23-24, 2024

- **National surveillance data show that PCV21 covers the serotypes that cause about 85% of IPD among adults age 65 and older, compared to about 54% for PCV20. However, among certain adult populations in the western United States (e.g., Alaska, Navajo Nation, Colorado, New Mexico, Oregon), 30% or more of IPD is due to serotype 4, which is included in PCV20, PCV15, and PPSV23, but not PCV21.** ACIP's current guidelines note that those caring for **groups disproportionately affected by serotype 4 may choose a serotype 4-containing product, which is among the reasons for not limiting this new recommendation to a single product.**
- **IPD surveillance from other geographic areas in the United States (e.g., midwestern, eastern, and southern regions) has not detected significant percentages of serotype 4.**
- This clinical guidance will be reviewed and updated as pneumococcal disease epidemiology evolves.
  - Weekly News from Immuninize.org Issue 1,781: October 23, 2024
  - MMWR | January 9, 2025 | Vol. 74 | No. 1

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PneumoRecs VaxAdvisor App for Vaccine Providers

- **PneumoRecs VaxAdvisor is a standalone application. It provides patient-specific guidance consistent with the immunization schedule recommended by the U.S. Advisory Committee on Immunization Practices** (ACIP). CDC releases guideline changes and enhancements to the app itself through app updates.
  - Download PneumoRecs VaxAdvisor on your mobile device:
  - iOS devices
  - Android devices
  - Use the web version
  - https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/app.html

17

Measles Cases in 2025 CDC

As of Dec. 31, 2025, a total of 2,144 measles cases were reported by 45 states, primarily Texas (803 cases), SC is second with 181 cases. In 2024 285 cases US.

Age

- Under 5 years: 537 (26%)
- 5-19 years: 865 (42%)
- 20+ years: 650 (31%)
- Age unknown: 13 (1%)

Vaccination Status

- **Unvaccinated or Unknown: 93%**
- **One MMR dose: 3%**
- **Two MMR doses: 4%**

11% of cases hospitalized (235 out of 2065), percent of Age Group

- **Under 5 years: 20% (105 of 537)**
- 5-19 years: 6% (53 of 865)
- 20+ years: 12% (77 of 650)
- Age unknown: 0% (0 of 13)

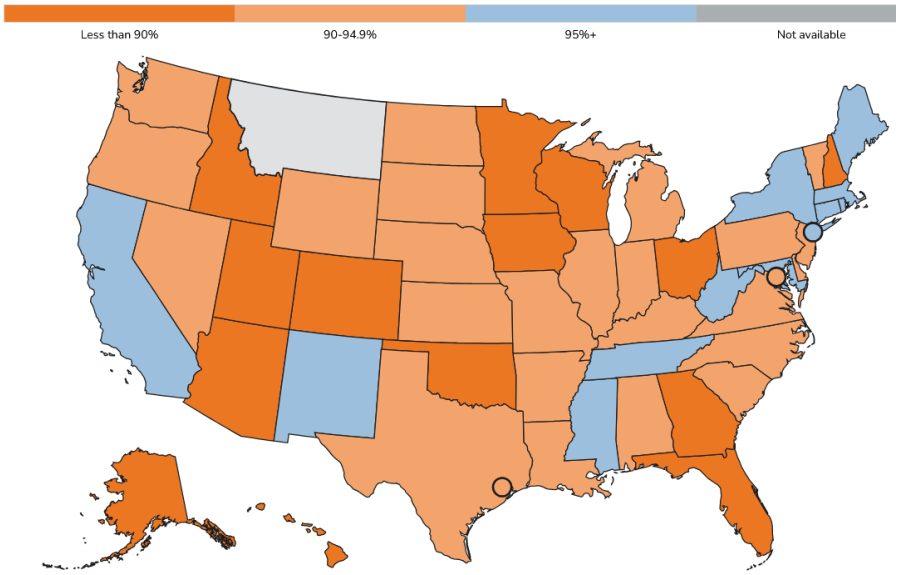
Deaths (related to Measles): 3 - 1 in a patient under 5 years, 1 in a school aged child and an additional death in an unvaccinated adult patient who tested positive for measles after death

https://www.cdc.gov/measles/data-research/index.html

18

MMR Vaccine Coverage for Kindergarteners

Percent Vaccinated **School Year 2023-2024**



Estimated Percent Vaccinated School Year 2023-2024

- Florida 88.1%
- Georgia 88.4%
- Kentucky 90%
- South Carolina 92.1%
- Louisiana 92.4%
- Arkansas 92.5%
- North Carolina 93.8%
- Virginia 94.2%
- Texas 94.3%
- Tennessee 95.1%
- Alabama 97.5%
- West Virginia 98.3%

NOTE: Heard Immunity for measles drops significantly when immunization rates fall below 95%

https://www.cdc.gov/measles/data-research/index.html

19

ACIP Recommends a Change in Schedule for MMR and MMRV Vaccines for Toddlers

- Sept. 19, 2025 The ACIP approved a resolution for the provision of immunization from measles, mumps, rubella, and varicella (chickenpox) through the Vaccines for Children Program. This vote creates consistency in coverage for all vaccine payment mechanisms, including other entitlement programs, following **ACIP's recommendation that toddlers through age three be immunized for varicella by standalone vaccination administered at the same time as the MMR vaccine, rather than the combination measles, mumps, rubella, and varicella (MMRV) vaccine.**
- **The CDC Immunization Safety Office's September 18 presentation to ACIP showed that healthy 12–23 months old toddlers have increased risk of febrile seizure seven to 10 days after MMRV vaccination compared to those given separate immunization for varicella and measles, mumps, and rubella (MMR). The MMRV vaccine doubles the risk of febrile seizures without conferring additional protection from varicella compared to standalone vaccination.**
  - https://www.hhs.gov/press-room/acip-recommends-covid19-vaccination-individual-decision-making.html

20

American Academy of Pediatrics Recommendations Sept. 18, 2025

- **The American Academy of Pediatrics (AAP) recommends the MMRV vaccine (Measles, Mumps, Rubella, and Varicella) as an option for children aged 12 months to 12 years, often preferred for children 4 years and older due to fewer injections, though it carries a slightly higher risk of fever/febrile seizures in younger toddlers (12-23 months) compared to separate MMR and varicella shots**, a point the AAP emphasizes parents discuss with their pediatrician for personalized decisions, supporting parental choice between the combined or separate vaccines.
  - **For Most: MMRV offers convenience (fewer shots) and is generally fine for ages 4+, says the AAP.**
  - **For Seizure-Prone Kids: Separate MMR and varicella vaccines are often recommended if a child has a personal or family history of seizures or immune issues.**
  - **https://www.aap.org/en/patient-care/measles/measles-vaccine/#:~:text=containing%20Vaccine%20Storage-,The%20AAP's%20Recommendations%20for%20Measles%20Vaccination,Prevention%20and%20Control%20Implementation%20page.**

21

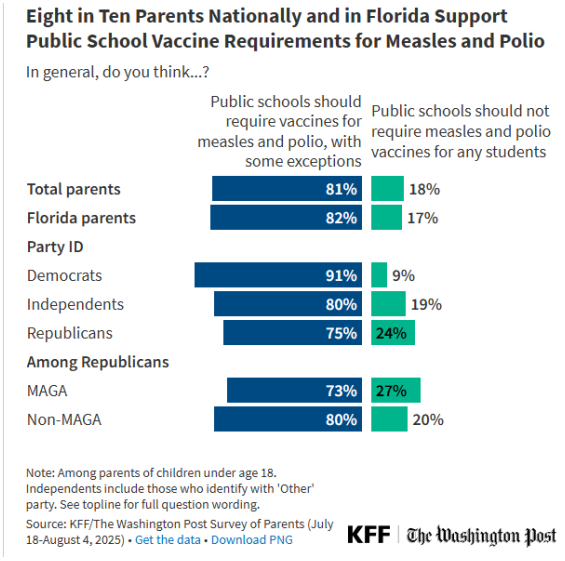
Whooping Cough/Pertussis Cases Are Increasing

- The **U.S. has tallied 27,871 cases of whooping cough thru mid Dec. in 2025, compared with 41,922 cases in the same period last year, the highest level in a decade** the CDC's data shows. The reports suggest that **at least 13 deaths have occurred in children this year.**
  - https://www.msn.com/en-us/health/diseases-and-conditions/deaths-from-this-entirely-preventable-disease-are-rising-as-cases-hit-almost-28-000-in-the-us/ar-AA1TpvQ5?ocid=BingNewsSerp
- The bacterial illness, formally known as pertussis, spreads easily and is especially dangerous for infants. People of any age can become ill from pertussis, which creates a thick mucus in the windpipe and makes it hard to breathe. But the disease is especially dangerous for infants, whose airways are smaller and more fragile. Children with pertussis may cough uncontrollably, stop breathing and turn blue; when they inhale through a narrowed windpipe, it makes a whooping sound — hence the name, Dr. Paul Offit said. The disease is sometimes called the "100 day cough" because illness can persist for months.
- To date, reports of antibiotic-resistant B. pertussis have been rare in the United States. However, resistance to macrolides, a class of antibiotics commonly used to treat pertussis, is becoming more common in certain countries (China and Peru).
  - https://www.cdc.gov/pertussis/php/surveillance/index.html

22

Most Parents Support Mandated Childhood Vaccination of School Aged Children

Sept 3,2025 Florida's Surgeon General announced that the state will end all vaccine mandates, including for school children, the first state in the nation to do so. Until now, all 50 states and D.C. had long-standing laws requiring children starting school to be vaccinated against diseases such as measles, mumps, and rubella (MMR) and polio at federally recommended ages. This move comes as **measles cases hit their highest levels since the disease was declared eliminated in the U.S. in 2000 (13 cases in US total), and amid rising exemption rates for school-age children.**



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Vaccine Exemptions for Sale?

Frontline Health Advocates is listed as a ministry/church, a Private Ministerial Assoc (P.M.A.), that provides medical vaccine exemptions for a $495 fee. The group was founded by William Lionberger, a chiropractor affiliated with America's Frontline Doctors.

https://frontlinehealthadvocates.com/

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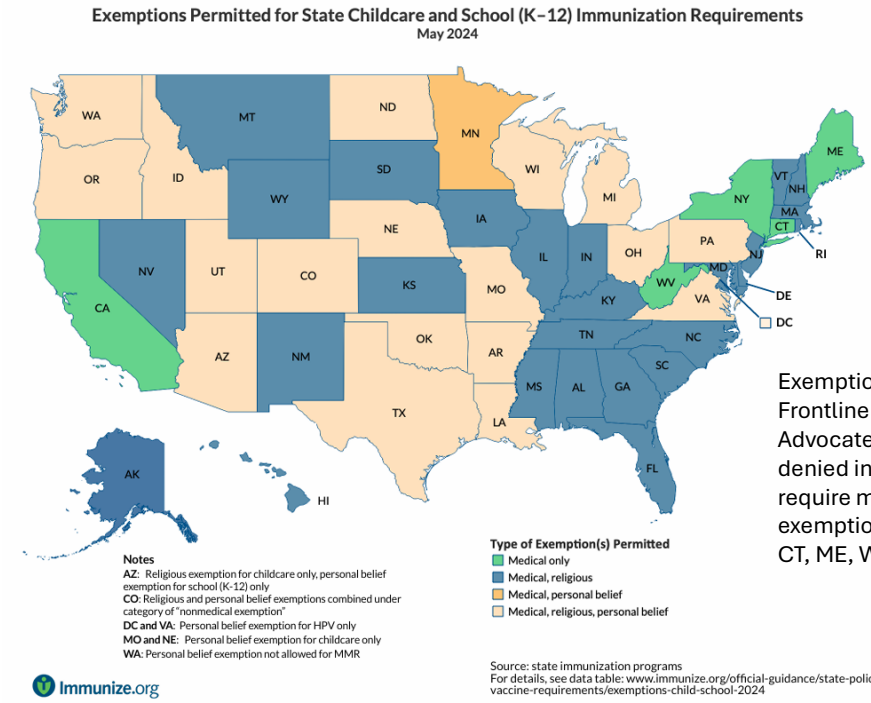

Exemptions filed by Frontline Health Advocates are typically denied in states that require medical exemptions only (CA, NY, CT, ME, WV).

25

Influenza Vaccine Composition for the 2025-2026 U.S. Influenza Season

- **March 13, 2025, the FDA convened a meeting of scientific and public health experts from the FDA, Centers for Disease Control and Prevention and Department of Defense to recommend the composition of the 2025-26 flu vaccines. (No ACIP) The recommendations are similar to the previous year's strain selection.**
  - **FDA recommends** that **the trivalent formulation of egg-based influenza vaccines** for the 2025-2026 U.S. influenza season contain the following:
    - an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
    - an A/Croatia/10136RV/2023 (H3N2)-like virus; and
    - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

    Growing the virus in eggs can result in genetic changes (egg adaptation) that makes the vaccine less effective than cell cultured versions.
  - **FDA recommends** that **the trivalent formulation of cell- or recombinant-based influenza vaccines** for the 2025-2026 U.S. influenza season contain the following:
    - an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
    - an A/District of Columbia/27/2023 (H3N2)-like virus; and
    - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.
      - https://www.fda.gov/vaccines-blood-biologics/influenza-vaccine-composition-2025-2026-us-influenza-season

26

CDC/ACIP Recommendations for the 2025-26 Influenza Vaccines

Updates to the Influenza Vaccination Recommendations: Four updates to the 2024–25 recommendations are presented in this report. These include three FDA-approved labeling changes and a new recommendation approved through discussion at the June 2025 ACIP meeting.

- In March 2025, FDA issued recommendations for the antigenic composition of 2025–26 U.S.-approved influenza vaccines.
- **In September 2024, FDA approved FluMist (LAIV3) for self-administration (for recipients aged 18 through 49 years) or administration by a caregiver aged ≥18 years (for children and adolescents aged 2 through 17 years). FluMist for self-administration or caregiver administration is anticipated to become available during the 2025–26 season**.
- **In March 2025, FDA expanded approval of Flublok (RIV3), previously approved for persons aged ≥18 years, to children and adolescents aged 9 through 17 years. Flublok is now approved for persons aged ≥9 years**.
- **On June 26, 2025, ACIP made a new recommendation that children aged ≤18 years, pregnant women, and all adults receive seasonal influenza vaccines only in single-dose formulations that are free of thimerosal as a preservative. (Multidose vials will no longer be available)**

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CDC/ACIP Recommendations for the 2025-26 Influenza Vaccines

- **Routine annual influenza vaccination is recommended for all persons aged ≥6 months who do not have contraindications.**
- **For most groups, vaccination should ideally be offered during September or October. Vaccination should continue throughout the season as long as influenza viruses are circulating.**
- **For most adults (particularly those aged ≥65 years) and during the first or second trimester of pregnancy, vaccination during July and August should be avoided unless there is concern that later vaccination might not be possible.**
  - MMWR 2025;74(32):500-507
- **Revised for 2026, now influenza vaccines for patients aged 6 mo to 18 y/o are listed as Shared Clinical Decision Making.**

28

CDC/ACIP Recommendations for the 2025-26 Influenza Vaccines

ACIP recommends that **adults aged ≥65 years preferentially receive any one of the following:**

- **High-dose inactivated influenza vaccine (HD-IIV3, Fluzone High-Dose),**
- **Recombinant influenza vaccine (RIV3, Flublok), or**
- **Adjuvanted inactivated influenza vaccine (aIIV3, Fluad).**
  - If none of these three vaccines is available at a vaccination opportunity, then any other age-appropriate influenza vaccine should be used.
  - **Data support greater potential benefit of high-dose inactivated, adjuvanted inactivated, or recombinant vaccines relative to standard-dose unadjuvanted IIVs in this age group, with the most data available for HD-IIV3; but comparisons of these vaccines with one another are limited.**
  - **Solid organ transplant recipients aged 18 through 64 years who are receiving immunosuppressive medication regimens may receive HD-IIV3 or aIIV3 as acceptable options.** MMWR 2025;74(32):500-507

29

Influenza Cases Increasing Significantly

- **Jan. 2, 2026** — The holiday season brought a massive spike in influenza cases across the U.S.
- **New data from the U.S. Centers for Disease Control and Prevention (CDC) indicate that the virus is spreading rapidly, with some regions reporting record numbers of infections and hospitalizations.**
- **At least 7.5 million people had been sickened by late December, resulting in at least 81,000 hospitalizations and 3,100 deaths, including eight pediatric deaths.**
  - https://www.cdc.gov/fluview/surveillance/2025-week-51.html

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COVID19 Vaccine ACIP Meeting 4-15-2025

- **Only 23% of adults and 13% of children received the 2024-2025 COVID vaccine, according to CDC data.**
- **Data presented by CDC officials at the meeting showed the waning severity of the coronavirus pandemic. For example, COVID-19 dropped from the third leading cause of death among U.S. adults in 2021 to the 12th spot in 2023. And hospitalization rates fell from a peak of about 500 per 100,000 population in 2020-2021 and 2021-2022 down to about 60 per 100,000 in the 2024-2025 season.**
- **From October 2024 to March 2025, children and adolescents comprised about 4% of COVID-related hospitalizations, with the highest rates among those younger than 6 months of age. More than half (59%) of those hospitalized had at least one underlying medical condition.**
- **A recent poll of the ACIP COVID-19 Work Group showing that 76% of its members supported a non-universal (risk-based) recommendation for the 2025-2026 respiratory virus season. A vote of the ACIP is scheduled for the June meeting. The ACIP does suggest that ~75% of adults have at least one risk factor for COVID-19.**
  - MEDPAGE Today April 16, 2025

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COVID-19 Vaccine, mRNA-mNEXSPIKE by Moderna

- **The nucleoside-modified mRNA in MNEXSPIKE is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the N-terminal domain (NTD) and receptor-binding domain (RBD) of the Spike (S) glycoprotein of SARSCoV-2**. The vaccine elicits an immune response which protects against COVID-19.
  - Each 0.2 mL dose of MNEXSPIKE (2025-2026 Formula) contains 10 mcg
- **The 2025-26 vaccine is FDA approved for adults 65 years of age and older, or 12 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19.**
- **Spikevax, the original Moderna mRNA COVID-19 vaccine, remains in production; it is licensed for use in persons ≥12 years old and is available under an Emergency Use Authorization (EUA) for children 6 months to 11 years old.**

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COVID-19 Vaccine, mRNA-mNEXSPIKE

Feature	mNEXSPIKE	Spikevax (Original/Current)
Dose (mRNA)	10 micrograms (mcg)	50 mcg (for ages 12+) or 25 mcg (ages 6-11)
Design	Codes for only specific, key domains (N-terminal and receptor-binding) of the spike protein	Codes for the entire spike protein of SARS-CoV-2
Targeted Response	More focused immune response due to targeted design	Elicits a broader, but less focused, immune response
Efficacy	Demonstrated numerically higher relative efficacy (rVE) against COVID-19 compared to Spikevax in clinical trials (e.g., 13.5% higher in adults 65+)	Effective, but the newer design shows potential for better protection
Storage	Can be refrigerated for up to 90 days; stable at room temperature for 24 hours	Can be refrigerated for up to 60 days; stable at room temperature for 12 hours

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COVID-19 Vaccine, mRNA-mNEXSPIKE

- Licensure of the new vaccine was based on the results of a **randomized, observer-blind noninferiority trial (available as a presentation) in 11,454 persons ≥12 years old who had previously received a primary series of a COVID-19 vaccine** (adults ≥18 years old had also received at least one booster dose). **Subjects received a single dose of mNEXSPIKE or Spikevax (both bivalent formulations targeting the original and BA.4/5 Omicron strains of SARS-CoV-2). After a median follow-up of 8 months, the incidence of COVID-19 occurring ≥2 weeks after immunization was 9.9% with mNEXSPIKE and 10.8% with Spikevax**; mNEXSPIKE met the prespecified criteria for **noninferiority to Spikevax (relative efficacy 9.3%** [95% CI -6.6% to 22.8%]). Results in **adults ≥65 years old were similar to those in the overall population (relative vaccine efficacy 13.5%** [95% CI -7.7% to 30.6%]). Seroresponse rates and geometric mean neutralizing antibody titer levels were higher with the new vaccine.
  - https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/02-Rizkalla-COVID-508.pdf

34

mRNA Vaccines and US Federal Funding

- **August 6, 2025, HHS Secretary Kennedy announced that he was withdrawing $500 million in funding and winding down development of mRNA vaccines including Covid-19 and the potential threat of H5N1 Avian influenza. (22 mRNA vaccine-related projects funded by BARDA).**
- **Rick Bright, PhD, a former director of the Biomedical Advanced Research and Development Authority (BARDA), the HHS agency that pulled its funding for mRNA vaccine projects, called it a "huge blow to our national security“**
- **Brett Giroir, MD, former HHS Assistant Secretary for Health under the first Trump administration, who served on the White House coronavirus task force, also called it a "dangerous decision that denies the data on mRNA vaccines. “He added that mRNA vaccines are "our best rapid response platform and there is no substitute for it.“**
- Tina Tan, MD, president of the Infectious Diseases Society of America, said in a statement that "halting promising research that is already underway wastes taxpayer dollars and prohibits the scientific progress.”
  - https://www.medpagetoday.com/washington-watch/washington-watch/116862

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ACIP Recommends COVID-19 Immunization Based on Individual Decision-making

- **Sept. 19, 2025** - The Centers for Disease Control and Prevention’s (CDC) Advisory Committee on Immunization Practices (ACIP) today **unanimously recommended that vaccination for COVID-19 be determined by individual decision-making. ACIP’s recommendation applies to all individuals six months and older. It includes an emphasis that the risk-benefit of vaccination in individuals under age 65 is most favorable for those who are at an increased risk for severe COVID-19 and lowest for individuals who are not at an increased risk,** according to the CDC list of COVID-19 risk factors.
  - **‘shared clinical decision-making’ guideline is a step down from the ACIP’s far more common, ‘routine’ recommendations for vaccines. It is used in situations where the committee wishes to highlight vaccination as an option for individuals (ie, may vaccinate) without actively encouraging it.**
  - https://www.hhs.gov/press-room/acip-recommends-covid19-vaccination-individual-decision-making.html

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Respiratory Syncytial Virus

- **RSV is the most frequent cause of lower respiratory tract illness in infants worldwide. In most parts of the U.S., RSV circulation is seasonal, typically starting during the fall and peaking in the winter.** The virus is especially common in children, and **most individuals can be expected to be infected with RSV by the time they reach two years of age.**
- RSV most often causes cold-like symptoms in infants and young children, it can also lead to serious LRTD such as pneumonia and bronchiolitis (swelling of the small airway passages in the lungs). In infants and children, the risk of RSV-associated LRTD is highest during the first year of life. **According to the Centers for Disease Control and Prevention, RSV is the leading cause of infant hospitalization in the U.S.**
  - https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants

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Respiratory Syncytial Virus Vaccine, Adjuvanted – Arexvy

- **May 3, 2023** - GSK announced that the US Food and Drug Administration (FDA) has **approved Arexvy (respiratory syncytial virus vaccine, adjuvanted) for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older. This is the first RSV vaccine for older adults to be approved anywhere in the world.**
- While GSK's vaccine has shown **efficacy of 82.6% in preventing RSV in year one and 94.1% efficacy in preventing severe disease**, those **figures drop to 77.3% and 84.6% in the second RSV season, respectively, with a median follow-up time of 14 months from administration.**
  - https://www.fiercepharma.com/pharma/cdc-advisory-panel-examines-gsk-pfizer-rsv-data-will-vote-afternoon-recommended-use

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Respiratory Syncytial Virus Unadjuvanted Bivalent Stabilized Prefusion F Protein Vaccine – Abrysvo by Pfizer

- **May 31, 2023, the FDA approved Pfizer's Respiratory Syncytial Virus unadjuvanted bivalent A and B strain stabilized prefusion F protein vaccine for the prevention of lower respiratory tract disease caused by RSV in individuals 60 years and older.**
- **Pfizer's vaccine has shown 66.7% efficacy in the first year against RSV, with 85.7% protection against severe disease. In the second season, at month 18, the efficacy numbers wane to 49% and 78.6%, respectively.**
  - Both companies plan to test a subset of trial participants with a booster dose after two years post initial administration.
- The CDC also provided a cost-effectiveness model for the two vaccines, which showed GSK's vaccine providing significantly more value—even when priced at $270 per dose compared to $200 for the Pfizer vaccine.
  - https://www.fiercepharma.com/pharma/cdc-advisory-panel-examines-gsk-pfizer-rsv-data-will-vote-afternoon-recommended-use

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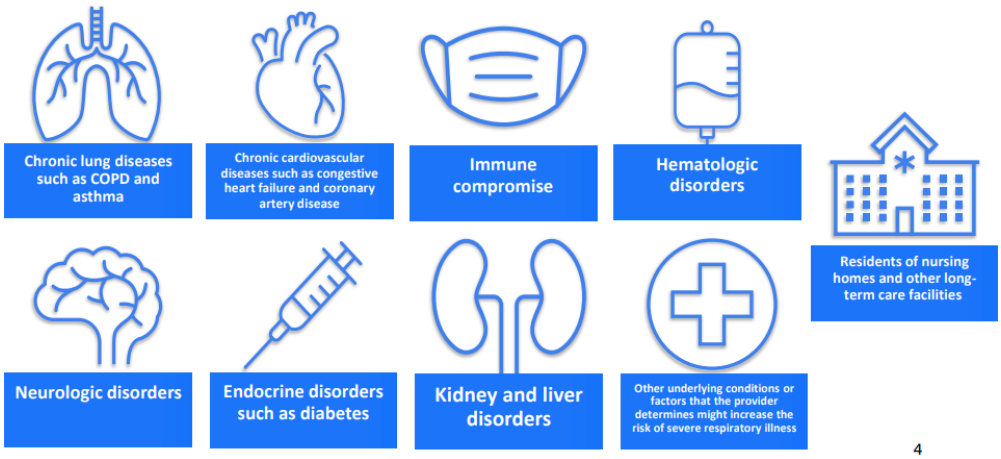
ACIP Meeting 6-21-2023

If shared clinical decision-making is recommended adults who may be at higher risk of RSV disease include persons with:



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https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/07-RSV-Adults-Britton-508.pdf

40

mRNA-based RSV Vaccine, Encoding the Stabilized RSV Prefusion F Glycoprotein- mRESVIA by Moderna

- **May 31, 2024, FDA approved MRESVIA is indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older.**
- Each 0.5 mL dose of MRESVIA contains 50 mcg of nucleoside modified mRNA encoding the RSV F glycoprotein.
- Data is from the **on-going Phase 2-3, 35,541 patient Conquer RSV Study.**
  - N Engl J Med 2023;389:2233-44.

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ACIP Meeting 6-26-2024

- **All adults ages 75 years and older should receive a single dose of any respiratory syncytial virus (RSV) vaccine, and adults ages 60 to 74 years who are at increased risk of severe RSV disease should receive a vaccine, according to a unanimous 11-0 vote** by the CDC's Advisory Committee on Immunization Practices (ACIP).
- Also, **people who have already received the RSV vaccine are not recommended to receive a booster, based on data that showed another dose did not improve outcomes.**
- **These recommendations supplant the current recommendation that adults ages 60 and older may receive RSV vaccination after engaging in shared clinical decision-making with their healthcare provider.**

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ACIP Meeting 4-16-2025

- **The CDC's Advisory Committee on Immunization Practices (ACIP) voted 14-0, with one abstention, on Wednesday to recommend that high-risk patients ages 50 to 59 be vaccinated for respiratory syncytial virus (RSV).**
- **Booster dose: the ACIP voted that "RSV vaccination is recommended as a single dose only. Persons who have already received RSV vaccination are NOT recommended to receive another dose.“**
  - MEDPAGE Today April 16,2025

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FDA Requires Guillain-Barré Syndrome (GBS) Warning in the Prescribing Information for RSV Vaccines Abrysvo and Arexvy

- **1/7/2025** The Prescribing Information for each vaccine has been revised to include the following language in the Warnings and Precautions section:
  - **Abrysvo- The results of a postmarketing observational study suggest an increased risk of Guillain-Barré syndrome (~9 cases/million doses) during the 42 days following vaccination with Abrysvo.**
  - **Arexvy- The results of a postmarketing observational study suggest an increased risk of Guillain-Barré syndrome (~7 cases/million doses) during the 42 days following vaccination with Arexvy.**
- GBS is a rare disorder in which the body’s immune system damages nerve cells, causing muscle weakness and sometimes paralysis.
  - https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-requires-guillain-barre-syndrome-gbs-warning-prescribing-information-rsv-vaccines-abrysvo-and?utm_medium=email&utm_source=govdelivery

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Respiratory Syncytial Virus Unadjuvanted Bivalent Stabilized Prefusion F Protein Vaccine – Abrysvo

- **August 21,2023 The FDA approved Abrysvo (Respiratory Syncytial Virus Vaccine), the first vaccine approved for use in pregnant individuals to prevent lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age**. Abrysvo is **approved for use at 32 through 36 weeks gestational age of pregnancy.** Abrysvo is administered as a single dose injection into the muscle.
- The application was **granted Priority Review status and Fast Track and Breakthrough Therapy designations.**
  - https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants

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Enhanced Placental Antibody Transfer Efficiency with Longer Interval Between Maternal Respiratory Syncytial Virus Vaccination and Birth

- **124 pregnant patients from Mass General or Mt Sinai who received the Abrysvo RSV vaccine and some of their infants were evaluated for level of RSV F antibodies.**
- **Maternal vaccination 2 to 3 weeks and 3 to 4 weeks prior to delivery was associated with significantly lower cord: maternal transfer ratios than were observed when vaccination occurred >5weeks prior to delivery (P=.03 for 2-3 weeks, P=.007 for 3-4weeks.**
- **Vaccine administration earlier in the approved 32 to 36 week window (at least 5 weeks prior to delivery) results in the highest transplacental transfer of maternal antibodies to the neonate.** These results should inform the counseling of pregnant individuals on optimal vaccination timing.
  - American Journal of Obstetrics & Gynecology 2024 published on-line https://www.ajog.org/article/S0002-9378(24)01125-6/fulltext

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Respiratory Syncytial Virus (RSV) Vaccine Administration Errors in Young Children and Pregnant People

- **The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) have received reports of the Pfizer (Abrsyvo) or GSK (Arexvy) RSV vaccines being administered in error to young children (25 reports in children <2 y/o). CDC and FDA have also received 128 reports of the GSK RSV vaccine (Arexvy) being administered in error to pregnant people.**
- **For infants and young children who are recommended to receive nirsevimab but received either the Pfizer (Abrysvo) or GSK (Arexvy) RSV vaccine in error, administer a dose of nirsevimab.**
- **For pregnant people who have received the GSK RSV vaccine (Arexvy) in error, do not give a dose of the Pfizer RSV vaccine (Abrysvo). Instead, the infant (if younger than 8 months) should receive nirsevimab during RSV season (October through March in most of the continental United States).**
  - COCA Now: CDC Clinician Outreach and Communication Activity January 22, 2024

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Suzetrigine – Journavx by Vertex Pharmaceuticals

January 30, 2025, the FDA approved suzetrigine (Journavx) 50 milligram oral tablets, a first-in-class non-opioid analgesic, to treat moderate to severe acute pain in adults.

- The application received Breakthrough Therapy, Fast Track and Priority Review designations by the FDA.
- The first new medication that works differently for pain in over 20 years. **Suzetrigine is a selective blocker of the NaV1.8 voltage-gated sodium channel,** compared to other known voltage-gated sodium channels (NaV1.1 through 1.9). **NaV1.8 is expressed in peripheral sensory neurons including dorsal root ganglion neurons, where its role is to transmit pain signals (action potentials). By selectively inhibiting NaV1.8 channels, suzetrigine inhibits transmission of pain signals to the spinal cord and brain.**
  - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

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Suzetrigine – Journavx

- **Voltage-gated sodium channel 1.8 (**NaV1.8) is a genetically and pharmacologically validated pain target that **is selectively expressed in peripheral pain-sensing neurons and not in the central nervous system (CNS).**
- **T ½ ~24 hours, metabolized by CYP3A4 to a less active metabolite M6-SUZ**
  - **Strong CYP3A4 inhibitors are contraindicated, and moderate inhibitors reduce dose of Suzetrigine. Strong Inducers are also contraindicated.**
  - **Effect of Food - Administration of 100 mg of suzetrigine (the first dose) with a meal resulted in decreased initial concentrations of suzetrigine and M6-SUZ in comparison to a fasted state and a delayed the Tmax to 5 hrs with food vs. 3 hrs fasting.**
  - No clinically significant differences in pharmacokinetics of suzetrigine and M6-SUZ were observed based on age (18-75 years), sex, body weight (44-126 kg), race, and renal impairment (eGFR ≥ 15 mL/min).
  - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

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Suzetrigine – Journavx

- The efficacy of suzetrigine in the treatment of moderate to severe acute pain in adults was established **in two randomized, double-blind, placebo and active-controlled trials of acute pain, one following full abdominoplasty (Trial 1) and the other following bunionectomy (Trial 2).**
  - In each trial, pain intensity was measured using a patient-reported 11-point numeric pain rating scale (NPRS), ranging from 0 no pain to 10 the worst pain imaginable. **Patients were eligible for study participation if they had moderate to severe pain on the verbal categorical rating system (VRS) and a pain score of ≥ 4 on the NPRS,** within 4 hours of the abdominoplasty completion (Trial 1) or during the 9-hour period after discontinuation of regional anesthesia following bunionectomy (Trial 2).
  - Once eligible, **patients were randomized to receive oral suzetrigine, placebo, or hydrocodone bitartrate/acetaminophen (HB/APAP) for a duration of 48 hours**. For the suzetrigine treatment regimen, patients received an initial loading dose of 100 mg, followed by 50 mg every 12 hours. For the HB/APAP-control regimen, patients received 5 mg/325 mg every 6 hours. **For both studies, 400 mg of ibuprofen every 6 hours, as needed for pain relief, was permitted as a rescue medication.**
    - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

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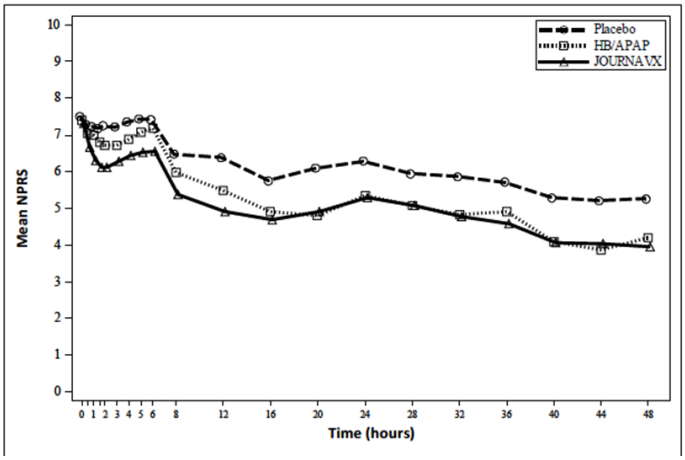
Suzetrigine – Journavx

- **1,118 adult patients with moderate to severe acute pain following a full abdominoplasty procedure** suzetrigine n = 447, placebo n = 223, and hydrocodone bitartrate/acetaminophen (HB/APAP) n = 448).
- The majority of patients were **female (98%),** and the **mean age was 42 years** (range: 18 to 69). The study population consisted of **70% White** participants, 27% Black or African American participants, 1% Asian participants, 0.8% Native Hawaiian or other Pacific Islander participants, 0.5% American Indian or Alaska Native participants, and 0.9% Other or Multiracial participants, among which 34% identified as Hispanic or Latino.
- The **mean pain score at baseline was 7.4 (range: 4 to 10).** All baseline characteristics, including NPRS, VRS, and BMI were generally balanced across treatment arms.
  - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

Figure 1: Mean Pain Intensity Over Time in Adults with Moderate to Severe Acute Pain Following Full Abdominoplasty (Trial 1)



In Trial 1, 89% of patients in the suzetrigine group completed the treatment period (compared to 75% of patients in the placebo group and 85% of patients in the HB/APAP group), **9% of patients in the suzetrigine group discontinued due to lack of efficacy (compared to 22% of patients in the placebo group and 13% of patients in the HB/APAP group).**

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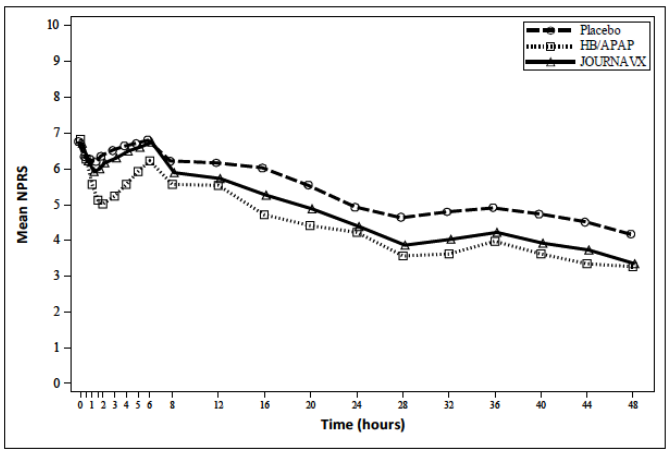
Suzetrigine – Journavx

- **1,073 adult patients with moderate to severe acute pain following bunionectomy** (suzetrigine n = 426, placebo n = 216, and HB/APAP n = 431).
- The majority of patients **were female (85%), and the mean age was 48 years** (range: 18 to 75). The study population consisted of **71% White** participants, 24% Black or African American participants, 2% Asian participants, 0.2% Native Hawaiian or other Pacific Islander participants, 1% American Indian or Alaska Native participants, and 1% Other or Multiracial participants, and 0.3% with race missing, among which 34% identified as Hispanic or Latino.
- **The mean pain score at baseline was 6.8** (range: 4 to 10). All baseline characteristics, including NPRS, VRS, and BMI were generally balanced across treatment arms.
  - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

Figure 2: Mean Pain Intensity Over Time in Adults with Moderate to Severe Acute Pain Following Bunionectomy (Trial 2)



In Trial 2, 87% of patients in the suzetrigine group completed the treatment period (compared to 82% of patients in the placebo group and 90% of patients in the HB/APAP group), and **12% of patients in the suzetrigine group discontinued due to lack of efficacy (compared to 16% of patients in the placebo group and 8% of patients in the HB/APAP group).**

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Suzetrigine – Journavx

eTable 7. Secondary Endpoints: Rescue Medication

	Abdominoplasty		Bunionectomy	
	Suzetrigine N = 447	Placebo N = 223	Suzetrigine N = 426	Placebo N = 216
Secondary Endpoint: Proportion of participants using rescue medication from 0 to 48 hours compared to placebo				
Participants using rescue medication from 0 to 48 hours, n (%)	362 (81.0)	196 (87.9)	364 (85.4)	185 (85.6)
Nominal *P* value vs. placebo	0.0237	--	0.9143	--
Secondary Endpoint: Total rescue medication usage from 0 to 48 hours compared to placebo				
Total rescue medication usage from 0 to 48 hours (mg), median	800.0	1200.0	800.0	800.0
Nominal *P* value vs. placebo[a]	0.0080	--	0.0205	--
Secondary Endpoint: Time to first use of rescue medication compared to placebo				
Time to first use of rescue medication (min), median (95% CI)	186 (158, 212)	115 (100, 132)	157 (145, 192)	185 (143, 210)
Nominal *P* value vs. placebo	<0.0001	--	0.8592	--

CI: confidence interval; **N**: number of participants in the analysis set; **n:** number of participants

Notes: Table includes participants who were randomized and received at least one dose of study drug. Participants were analyzed according to their randomized treatment. Rescue medication was ibuprofen (400 mg orally, every 6 hours as need).

Anesthesiology 2025; 142:1085–99

https://cdn-links.lww.com/permalink/aln/d/aln_2025_03_17_bozic_aln-d-24-01394_sdc1.pdf

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Suzetrigine – Journavx

Nausea and Vomiting: In **Trial 1**, the incidence of patients who experienced either nausea or vomiting was **20% in suzetrigine-treated patients, 33% in HB/APAP-treated patients, and 25% in placebo-treated patients.** In **Trial 2**, the incidence of patients who experienced either nausea or vomiting was **9% in suzetrigine-treated patients, 16% in HB/APAP-treated patients, and 12% in placebo-treated patients.**

Table 2: Adverse Reactions Reported in ≥1% of JOURNAVX-Treated Patients and Greater than Rate of Placebo in Two 48-hour Trials in Moderate to Severe Acute Pain (Trials 1 and 2, Pooled)

Adverse Reactions (Preferred Term)	Placebo (N = 438) n (%)	JOURNAVX (N = 874) n (%)	HB/APAP [a] (N = 879) n (%)
Pruritus	7 (1.6)	18 (2.1)	30 (3.4)
Muscle spasms	2 (0.5)	11 (1.3)	6 (0.7)
Increased blood creatine phosphokinase	2 (0.5)	10 (1.1)	7 (0.8)
Rash	2 (0.5)	10 (1.1)	6 (0.7)

[a] Patients received 5 mg/325 mg of oral hydrocodone bitartrate/acetaminophen (HB/APAP) every 6 hours.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

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Suzetrigine – Journavx

Dosage/Cost:

- **The recommended starting dose of suzetrigine is 100 mg (2 x 50 mg tabs) orally. Take the starting dose on an empty stomach at least 1 hour before or 2 hours after food to avoid delay in onset of action.** Clear liquids may be consumed during this time (e.g., water, apple juice, vegetable broth, tea, black coffee).
- **Starting 12 hours after the initial dose, take 50 mg of suzetrigine orally every 12 hours. Take these doses with or without food**.
  - Avoid food or drink containing grapefruit during treatment with suzetrigine.
- Use suzetrigine for the shortest duration, consistent with individual patient treatment goals. **Use of suzetrigine for the treatment of moderate to severe acute pain has not been studied beyond 14 days.**
- **Cost ~$15.50/50 mg tabs**
  - https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219209s000lbl.pdf

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Suzetrigine for Acute Pain: Effectiveness and Value ICER Final Report

Midwest CEPAC Votes

Table 3.8. Midwest CEPAC Votes on Comparative Clinical Effectiveness Questions

Question	Yes	No
Patient Population for all questions: Adult patients with Acute Pain that is not adequately controlled with non-systemic therapies (e.g., heat therapy, local anesthetic).		
For patients with acute pain, is the current evidence adequate to demonstrate that the net health benefit of suzetrigine in addition to non-systemic therapies (e.g., heat therapy, local anesthetic) is greater than that of non-systemic therapies alone?	7	7
For patients with acute pain, is the current evidence adequate to distinguish the net health benefit of suzetrigine from that of oral opioid analgesics (with or without acetaminophen), each in addition to non-systemic therapies?	2	12
For patients with acute pain, is the current evidence adequate to distinguish the net health benefit of suzetrigine from that of oral NSAIDs, each in addition to non-systemic therapies?	0	14

Suzetrigine for Acute Pain: Effectiveness and Value
Institute for Clinical and Economic Review Final Report March 31, 2025

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What's new in GINA 2025?

GINA Global Strategy for Asthma Management and Prevention

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EDITORIAL
GINA 2019

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel[1], J. Mark FitzGerald[2], Eric D. Bateman[3], Leonard B. Bacharier[4], Allan Becker[5], Guy Brusselle[6], Roland Buhl[7], Alvaro A. Cruz[8], Louise Fleming[9], Hiromasa Inoue[10], Fanny Wai-san Ko[11], Jerry A. Krishnan[12], Mark L. Levy[13], Jiangtao Lin[14], Søren E. Pedersen[15], Aziz Sheikh[16], Arzu Yorgancioglu[17] and Louis-Philippe Boulet[18]

Reddel et al. ERJ 2019; 53: 1901046

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Overuse of Short-acting B2-agonists in Asthma Is Associated with Increased Risk of Exacerbation and Mortality: A Nationwide Cohort Study of the Global SABINA Program

- Data from the **Swedish national registries, asthma patients aged 12–45 years with two or more collections of drugs for obstructive lung disease during 2006–2014 were included.** SABA overuse was defined as collection of more than two SABA canisters in a 1-year baseline period following inclusion. **SABA use was grouped into 3–5, 6–10 and ≥11 canisters per baseline-year.**
- The analysis included 365,324 asthma patients (mean age 27.6 years; 55% female); average follow-up was 85.4 months. 30% overused SABA, with 21% collecting 3–5 canisters per year, 7% collecting 6–10 canisters per year and 2% collecting ≥11 canisters per year. Increasing number of collected SABA canisters was associated with:
- **Increased risk of exacerbation, as follows. 3–5 canisters: hazard ratio (HR) 1.26** (95% CI 1.24–1.28); **6–10 canisters: 1.44** (1.41–1.46); **and ≥11 canisters: 1.77** (1.72–1.83), **compared to two or fewer canisters per year.**
- Higher SABA use was associated with incrementally **increased mortality risk (2564 deaths observed), as follows. 3–5 canisters: HR 1.26** (95% CI 1.14–1.39); **6–10 canisters 1.67** (1.49–1.87); and **≥11 canisters: 2.35** (2.02–2.72) **compared to two or fewer canisters per year.**
  - Eur Respir J 2020; 55: 1901872 [https://doi.org/10.1183/13993003.01872-2019]

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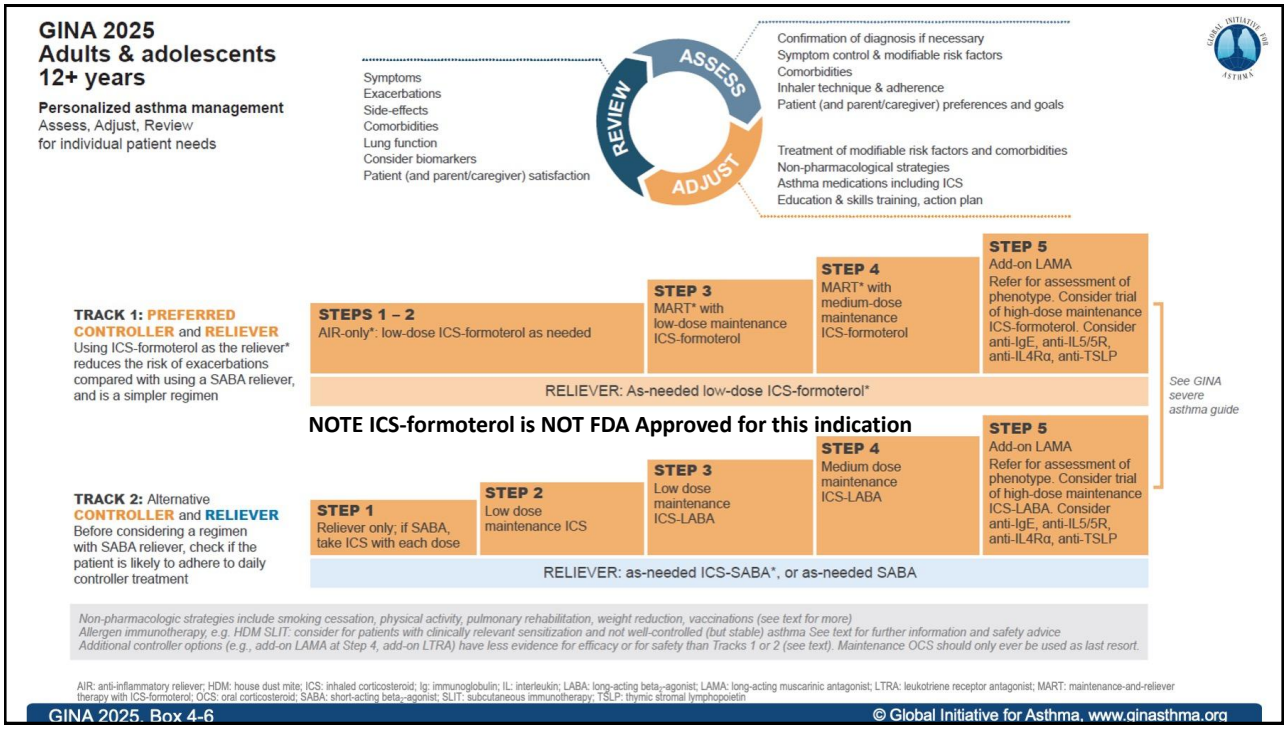

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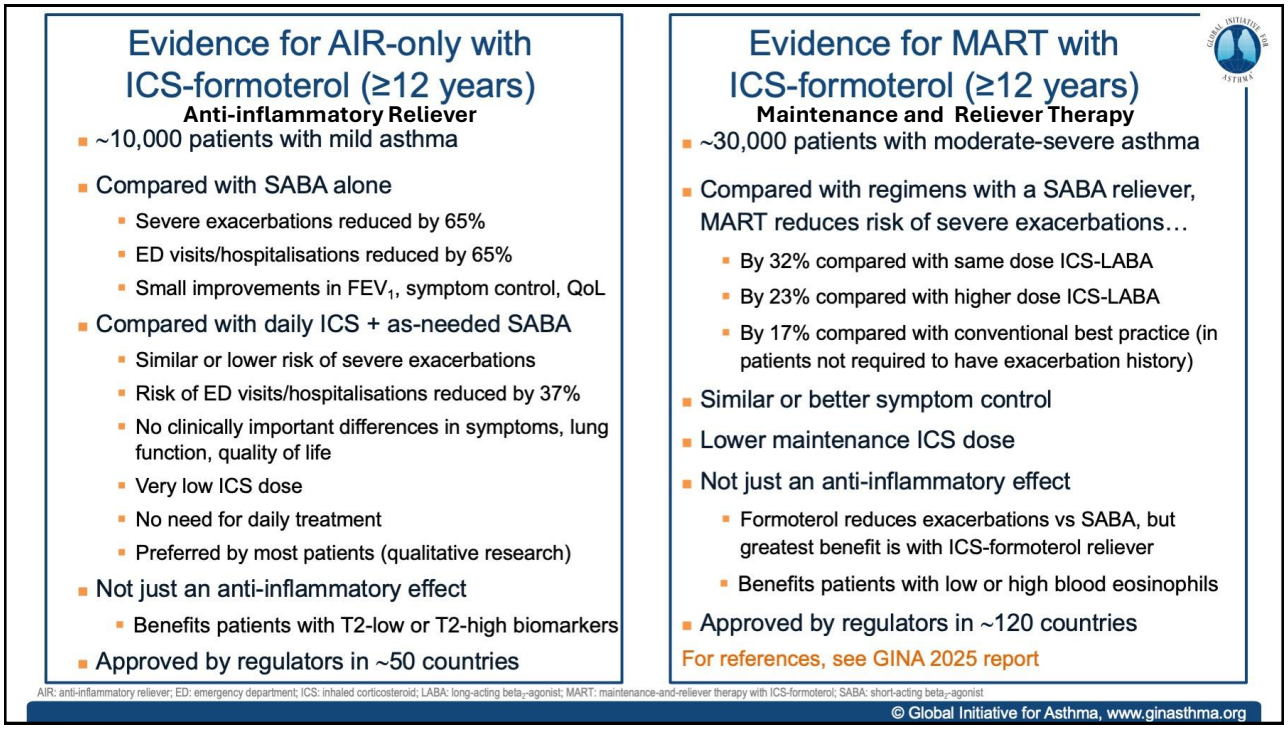

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Generic Symbicort - Breyna

- **On July 31, 2023, Viatris and Kindeva Drug Delivery announced the launch of Breyna (budesonide and formoterol fumarate dihydrate) inhalation aerosol, the first FDA-approved generic version of AstraZeneca's (AZ's) Symbicort**, an inhaled corticosteroid (ICS)/long-acting beta2-agonist (LABA) inhaler for the **treatment of asthma (ages 6 and older)** and chronic obstructive pulmonary disease (COPD). Breyna is **AB rated and shares the same indications as Symbicort.**
- **Breyna is available in the same 80 mcg/4.5 mcg and 160 mcg/4.5 mcg dosage strengths as Symbicort.**
- **Prasco launched an authorized generic (AG) version of Symbicort in January 2020.**
- **Cost: $98 -253.00 Breyna, Brand Symbicort ~$370 – 440.00**
- **Teva/Catalent are awaiting FDA approval as well.**

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Global Initiative for Chronic Obstructive Lung Disease

2025 REPORT

Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease

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2025 Teaching Slide Set

Initial Pharmacological Treatment

Figure 3.7

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	GROUP E: LABA + LAMA* *consider LABA+LAMA+ICS* if blood eos ≥ 300*	
0 or 1 moderate exacerbations (not leading to hospital admission)	GROUP A: A bronchodilator (mMRC 0-1, CAT < 10)	GROUP B: LABA + LAMA* (mMRC ≥ 2, CAT ≥ 10)

*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

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Bronchodilators in Stable COPD

Figure 3.19

2025 Teaching Slide Set

- Inhaled bronchodilators in COPD are central to symptom management and commonly given on a regular basis to prevent or reduce symptoms **(Evidence A)**
- Inhaled bronchodilators are recommended over oral bronchodilators **(Evidence A)**
- Regular and as-needed use of SABA or SAMA improves FEV1 and symptoms **(Evidence A)**
- Combinations of SABA and SAMA are superior compared to either medication alone in improving FEV1 and symptoms **(Evidence A)**
- LABAs and LAMAs are preferred over short-acting agents except for patients with only occasional dyspnea **(Evidence A)**, and for immediate relief of symptoms in patients already on long-acting bronchodilators for maintenance therapy
- LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates **(Evidence A)**
- LAMAs have a greater effect on exacerbation reduction compared with LABAs **(Evidence A)** and decrease hospitalizations **(Evidence B)**
- When initiating treatment with long acting bronchodilators the preferred choice is a combination of a LABA and a LAMA. In patients with persistent dyspnea on a single long-acting bronchodilator treatment should be escalated to two **(Evidence A)**.
- Combination treatment with a LABA and a LAMA increases FEV1 and reduces symptoms compared to monotherapy **(Evidence A)**
- Combination treatment with a LABA+LAMA reduces exacerbations compared to monotherapy **(Evidence B)**
- Combinations can be given as single inhaler or multiple inhaler treatment. Single inhaler therapy may be more convenient and effective than multiple inhalers
- Ensifentrine significantly improves lung function **(Evidence A)**, dyspnea **(Evidence A)** and health status **(Evidence B)**
- Theophylline exerts a small bronchodilator effect in stable COPD **(Evidence A)** and that is associated with modest symptomatic benefits **(Evidence B)**

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Factors to Consider when Initiating ICS Treatment

Figure 3.21

2025 Teaching Slide Set

Factors to consider when adding ICS to long-acting bronchodilators:

(note the scenario is different when considering ICS withdrawal)

STRONGLY FAVORS USE	History of hospitalization(s) for exacerbations of COPD[#]
	≥ 2 moderate exacerbations of COPD per year[#]
	Blood eosinophils ≥ 300 cells/μL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year[#]
	Blood eosinophils 100 to < 300 cells/μL
AGAINST USE	Repeated pneumonia events
	Blood eosinophils < 100 cells/μL
	History of mycobacterial infection

[#]despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.7 & 3.18 for recommendations); *note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

Adapted from & reproduced with permission of the © ERS 2019: *European Respiratory Journal 52 (6) 1801219; DOI: 10.1183/13993003.01219-2018 Published 13 December 2018*

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Anti-Inflammatory Therapy in Stable COPD

Figure 3.20

2025 Teaching Slide Set

Inhaled Corticosteroids	• Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease **(Evidence A)** • An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with exacerbations and moderate to very severe COPD **(Evidence A)** • We do not encourage the use of a LABA+ICS combination in COPD. If there is an indication for an ICS the combination LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice • Triple inhaled therapy of LABA+LAMA+ICS improves lung function, symptoms and health status, and reduces exacerbations, compared to LABA+ICS, LABA+LAMA or LAMA monotherapy **(Evidence A)**. Recent data suggesta beneficial effect of triple inhaled therapy versus fixed-dose LABA+LAMA combinations on mortality in symptomatic COPD patients with a history of frequent and/or severe exacerbations • If patients with COPD have features of asthma, treatment should always contain an ICS • Independent of ICS use, there is evidence that a blood eosinophil count < 2% increases the risk of pneumonia **(Evidence C)** • Combinations can be given as single or multiple inhaler therapy. Single inhaler therapy may be more convenient and effective than multiple inhalers
Oral Glucocorticoids	• Long-term use of oral glucocorticoids has numerous side effects **(Evidence A)** with no evidence of benefits **(Evidence C)**
PDE Inhibitors	• In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations: ▪ Roflumilast improves lung function and reduces moderate and severe exacerbations **(Evidence A)** • Ensifentrine improves lung function **(Evidence A)** but an effect on exacerbations has not been evaluated in patients at increased exacerbation risk

Daliresp
Ohtuvayre

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Triple Inhaled LABA/LAMA/ICS Therapy

Google Images 2-10-2024

Fluticasone furoate, umeclidinium, and vilanterol inhalation powder), for oral inhalation TRELEGY ELLIPTA ®
Once a day dosing
Cost: ~$630-735.00

Budesonide, glycopyrrolate, and formoterol fumarate inhalation aerosol **device BREZTRI AEROSPHERE®** -The inhaler device is bright yellow
-More accurate puff indicator means patients will know exactly how many doses they have left
-Upgraded cap designed to prevent unintended discharge of medicine
- **BID dosing**
Cost: ~$660-720.00

Google Images 2-10-2024

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Ensifentrine – Ohtuvayre by Verona Pharma

- **June 26, 2024 FDA approved ensifentrine (Ohtuvayre) a dual inhibitor of the phosphodiesterase 3 (PDE3) and phosphodiesterase 4 (PDE4) enzymes, combines bronchodilator and non-steroidal anti-inflammatory properties in one compound to treat COPD in adults including chronic bronchitis, emphysema, or both.**, Verona says, differentiating it from existing drug classes used to treat COPD.
- Phase III clinical trials (**ENHANCE-1 and ENHANCE-2**). **Patients** aged 40–80 years **with moderate to severe symptomatic COPD were enrolled.** 760 (ENHANCE-1)and 789 (ENHANCE-2) patients were randomized and **treated with nebulized twice-daily ensifentrine 3 mg or placebo**, (69% and 55% receiving concomitant long-acting muscarinic antagonists or long-acting b2-agonists with or without ICS, respectively).
  - Am J Respir Crit Care Med Vol 208, Iss 4, pp 406–416, Aug 15, 2023

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Ensifentrine – Ohtuvayre

- "**While the results of ENHANCE-1 and -2 are promising, there remains some uncertainty about the magnitude of overall benefit in patients receiving optimized modern inhaler therapies for COPD. We do not have significant concerns about harms with ensifentrine.** For these reasons, **we have high certainty that ensifentrine added to maintenance therapy, compared with maintenance therapy alone, results in at least a small net health benefit, and may result in substantial net health benefit ("B+")."**
- **Estimated cost ~ $3,000/month or $36,000/year (ICER benefit price benchmark ~$7,500-$12,700.00 per year)**
- **"The exclusion of patients on LAMA/LABA therapy or on triple inhaler therapy raises questions about the benefits of ensifentrine when added on to some of the most recommended regimens."**
  - Draft Report - Ensifentrine for Chronic Obstructive Pulmonary Disease Institute for Clinical and Economic Review, 4/10/2024
  - https://icer.org/wp-content/uploads/2024/04/COPD_Draft-Report_For-Publication_04102024.pdf

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New Dosage for Chlorthalidone – Hemiclor
by PRM Pharma

- The **FDA has approved a 12.5-mg tablet formulation of the thiazide-like diuretic chlorthalidone (HemiClor) for treatment of hypertension. Evidence-based SHEP and ALLHAT Trials**
- FDA approval of the 12.5-mg formulation was based on data from an **8-week double-blind trial in 1714 adults with hypertension who were randomized to receive one of six fixed-dose combinations of azilsartan medoxomil and chlorthalidone (Edarbyclor) or the individual components alone. Monotherapy with chlorthalidone 12.5 mg was similar in efficacy to the 25-mg dose with fewer adverse effects (hypokalemia.**
  - J Clin Hypertens (Greenwich) 2012; 14:284. doi:10.1111/j.1751-7176.2012.00616.x

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Chlorthalidone - Hemiclor

- 12.5 mg provided ≈ 80% of the BP-lowering effect observed at 25 mg over a 24-hr dosing interval:
- **Reduction in trough SBP ABPM after 8 weeks:**
  - **12.5 mg by 12.7 mmHg**
  - **25 mg by 15.9 mmHg**
- **Lower Incidence of Hypokalemia** (Hypokalemia occurred ≈ 5 times more frequently with chlorthalidone 25 mg than with 12.5 mg) Observed frequency after 8 weeks:
  - **25 mg – 11.9 %(19/160)**
  - **12.5 mg – 2.6 % (4/156)**
- **Cost: 12.5 mg tabs x 30 $35-50.00 vs. ~ $9-25.00 25 mg tabs x 30 generic**

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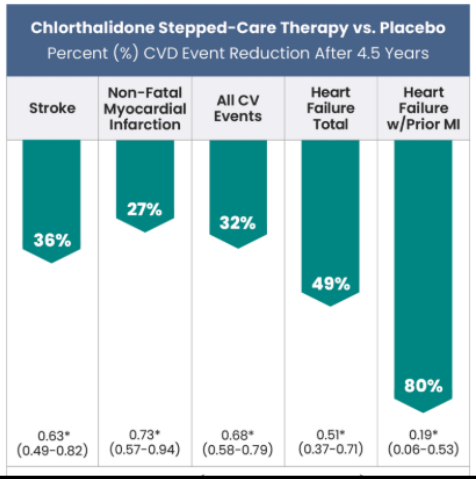
CV Outcomes with Chlorthalidone 12.5-25 mg Dose

SHEP Trial (JAMA 2000;284;(4):465-471)



ALLHAT Trial (JAMA. 2002; 288(23):2981-2997)

- After 4.9 years, stepped-care therapy initiated with 12.5mg chlorthalidone significantly reduced stoke, CV events and heart failure*
- **15% fewer strokes vs. lisinopril (p = 0.02)**
- **19% lower heart failure incidence vs. lisinopril (p < 0.001)**
- **38% lower heart failure incidence vs. amlodipine (p < 0.001)**
- **10% reduction in CV events vs. lisinopril (p < 0.001)**
- *There was no difference in the primary outcome (combined fatal CHD or nonfatal myocardial infarction) across treatment groups.

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Tradipitant – Nereus by Vanda Pharmaceuticals

- **Dec. 30, 2025 the U.S. Food and Drug Administration (FDA) has approved Nereus (tradipitant), an oral neurokinin-1 (NK-1) receptor antagonist, for the prevention of vomiting induced by motion. This approval marks the first new pharmacologic treatment in motion sickness in over four decades.**
- Today, **motion sickness remains prevalent** in civilian life, **with approximately 25–30% of adults —roughly 65–78 million people in the U.S.—experiencing symptoms during common travel modes** such as cars, planes, or boats. **Globally, up to one-third of individuals are highly susceptible. While most cases are mild, an estimated 5–15% of the population experiences severe, recurrent symptoms that can significantly impact quality of life.**
- **Motion sickness arises from a sensory conflict between visual, vestibular, and proprioceptive inputs, triggering the release of substance P and activation of NK-1 receptors in the central nervous system, leading to nausea and vomiting. Tradipitants mechanism of action—potent and selective antagonism of NK-1 receptors—directly addresses this pathway.**
  - https://www.drugs.com/newdrugs/fda-approves-nereus-tradipitant-prevention-motion-sickness-6709.html

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Tradipitant – Nereus

- **The efficacy of tradipitant is supported by data from three pivotal clinical trials—two Phase 3 real-world provocation studies conducted on boats (Motion Syros and Motion Serifos) and one additional supporting study—with participants who had documented histories of motion sickness.**
- **In Motion Syros (n=365), vomiting incidence was 18.3–19.5% with tradipitant versus 44.3% with placebo (p<0.0001).** Front Neurol. 2025 Mar 4;16:1550670. doi: 10.3389/fneur.2025.1550670.
- **In Motion Serifos (n=316), vomiting rates were 10.4–18.3% with tradipitant versus 37.7% with placebo (p≤0.0014), representing risk reductions of over 50–70%.** https://www.prnewswire.com/news-releases/vanda-pharmaceuticals-reports-positive-results-from-a-second-phase-iii-study-of-tradipitant-in-motion-sickness-302146315.html
- Across the pivotal program, tradipitant consistently demonstrated significant reductions in vomiting and a favorable safety profile consistent with acute use.

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Tradipitant – Nereus

- **In placebo-controlled clinical trials, somnolence (6%, 12%) and fatigue (6%, 8%) were adverse reactions reported in subjects who took a single dose of 85 mg or 170 mg tradipitant, respectively. Tradipitant may impair the mental and/or physical abilities required for driving a motor vehicle or operating heavy machinery. Concomitant use of other drugs that cause central nervous system depression and strong CYP3A4 inhibitors may increase this effect.** If concomitant use is unavoidable, warn patients against driving and other activities requiring complete mental alertness.
- **Nereus (tradipitant) is a neurokinin-1 receptor antagonist licensed by Vanda from Eli Lilly and Company.** Nereus is approved for the acute prevention of vomiting induced by motion in adults, and is **currently in clinical development for a variety of indications, including gastroparesis and the prevention of nausea and vomiting induced by GLP-1 receptor agonists.**

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Tradipitant – Nereus

- Recommended Dosage and Administration:
- **The recommended dosage of tradipitant - Nereus is 85 mg or 170 mg as a single oral dose.** Use the lowest effective dose. The safety of tradipitant for the prevention of vomiting induced by motion in adults for more than 90 doses has not been established in clinical trials.
- **Administer tradipitant orally approximately 60 minutes before an event expected to cause vomiting induced by motion.**
- The **maximum dosage in a 24-hour period is a single dose of 85 mg or 170 mg. (T1/2 ~34 hrs)**
- **Administer tradipitant on an empty stomach, at least 1 hour prior to or 2 hours after a full meal. (High fat meal delays Tmax by ~2 hrs)**
- Cost: **85 mg caps**, price has not yet been announced but it is expected to be expensive

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Etripamil - Cardamyst by Milestone Pharmaceuticals

- **Dec. 12, 2025 The FDA approved etripamil - Cardamyst a nasal spray, for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults. This approval marks the first time that more than two million Americans with PSVT will have a rapid-acting treatment option they can self-administer outside the emergency department or other healthcare setting.**
- **Etripamil is an L-type calcium influx inhibitor (slow channel blocker or calcium ion antagonist). Etripamil exerts its pharmacologic effect by modulating the influx of ionic calcium across the cell membrane of the AV nodal cells as well as arterial smooth muscles and contractile myocardial cells. By interrupting reentry at the AV node, etripamil can restore sinus rhythm in patients with PSVT.**

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Etripamil - Cardamyst

- The FDA approval of Cardamyst is supported by a clinical trial program based on safety data from **more than 1,800 participants and more than 2,000 episodes of PSVT. This includes the successful Phase 3 RAPID trial, a global, randomized, double-blind comparison of Cardamyst nasal spray (1 spray 35 mg in each nostril and may repeat x 1 after 10 minutes if needed 70 -140 mg vs. placebo (Lancet 2023; 402: 118–28).** In clinical studies**, participants using Cardamyst were two times more likely to convert symptomatic PSVT to sinus rhythm and did so more than three times faster compared with placebo.** The RAPID trial achieved its primary endpoint with **64% of those who self-administered Cardamyst (N=99) converting from supraventricular tachycardia (SVT) to sinus rhythm within 30 minutes compared to 31% on placebo (N=85) (HR = 2.62; p<0.001). At one hour, the benefit was demonstrated in 73% of participants.** In addition, significant reductions in time to conversion in those who took Cardamyst were evident early and durable, with a **median time to conversion of 17 minutes (95% CI: 13.4, 26.5) for those treated with Cardamyst vs. 54 minutes (95% CI: 38.7, 87.3) for those treated with placebo.**

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Etripamil - Cardamyst

- **Contraindicated in patients with:**
  - **Heart failure – New York Heart Association (NYHA) Class II to IV.**
  - **Wolff-Parkinson-White (WPW), Lown-Ganong-Levine (LGL) syndromes, or manifest pre-excitation (delta wave) on a 12-lead electrocardiogram (ECG).**
  - **Sick sinus syndrome without a permanent pacemaker.**
  - **Second degree atrioventricular (AV) Mobitz 2 block or higher degree of AV block.**
- **WARNINGS AND PRECAUTIONS**
  - **Syncope Related to Hemodynamic Effects - Because of effects on blood pressure, heart rate, and cardiac conduction, etripamil may cause dizziness and/or syncope, especially in patients with a history of syncope and high-grade AV block or sinus node dysfunction, or those with a history of syncope during an episode of SVT. In clinical trials, a small percentage of patients (0.4%) experienced clinically significant hypotension during test dosing prior to randomization, which precluded further participation in the study. Patients with a history of hypotensive episodes or those at increased risk for hemodynamic instability should be monitored appropriately when initiating etripamil.**
  - **Patients should be cautioned about these possible adverse effects and advised to administer Etripamil in a sitting position, and in a location where the risk of fall is minimal.**

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Etripamil - Cardamyst

- **Etripamil was safely administered to patients taking beta blockers or calcium channel blockers. In RAPID, 107 (42%) patients were on beta blockers and 81 (32%) patients were on calcium channel blockers.**
- **The majority of treatment-related adverse reactions reported in clinical studies with etripamil have been related to local reactions to, at, or near the nasal administration site, including the nose, throat, and eyes.** These local reactions **included nasal discomfort, nasal congestion, throat irritation, oropharyngeal pain, lacrimation, rhinorrhea, bleeding from the nose, upper-airway cough syndrome, and sneezing.**

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Etripamil - Cardamyst

- **Instructions for use:**
  - **Sit down** and remove the one nasal spray from the 2-dose container, **Insert the nasal spray device into the first nostril and push the plunger up to spray. Inhale normally and keep your head straight.** Completely release the plunger. **Remove the nasal spray device from the first nostril. Insert the same nasal spray device into the second nostril and spray right away. Stay seated and keep your head straight for 10 minutes. When medicine drips out, wipe your nose. Do not blow your nose for 10 minutes.** Throw away (discard) the device after use.
  - **If you continue to have symptoms after 10 minutes: Repeat by administering the second dose with the new device. If your symptoms have not improved within 20 minutes after your second dose, call your healthcare provider or get emergency medical help right away.**
  - **Do not use more than 2 etripamil - Cardamyst devices (140 mg) within a 24 hour period.**
  - **Cost: ~$1,700-3,400 per 2 doses GoodRx**

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Treatment of Atrioventricular Nodal Reentrant Tachycardia (AVNRT) Paroxysmal Superventricular Tachycardia (PSVT)

- **Atrioventricular nodal reentrant tachycardia (AVNRT) is the most common form of regular, sustained, paroxysmal supraventricular tachycardia (PSVT), accounting for nearly two-thirds of all PSVTs, and is more common in female patients.** AVNRT can present at any age; however, patients usually experience their first episode in adolescence or young adulthood**. In a series of 231 patients with AVNRT, the mean age of symptom onset was 32 years, with two-thirds of cases beginning after the age of 20. AVNRT usually occurs in patients with otherwise normal hearts;** however, it can occur in patients with structural heart disease.
- Patients with atrioventricular nodal reentrant tachycardia (AVNRT) often experience **symptoms such as palpitations (98 percent), dizziness or lightheadedness (78 percent), dyspnea (47 percent), or chest pain (38 percent); less commonly, they report fatigue (19 percent) and syncope (16 percent)**. Because of the paroxysmal nature of the arrhythmia, the **onset and termination of the symptoms are usually sudden.**
  - UpToDate accessed 1-4-2025

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Treatment of Atrioventricular Nodal Reentrant Tachycardia (AVNRT) Paroxysmal Superventricular Tachycardia (PSVT)

- **Stable patients — For stable patients with AVNRT (ie, those without hypotension, shock, decreased level of consciousness, or heart failure), we adhere to the following sequential approach to terminating the arrhythmia.**
- **Step 1: Valsalva maneuver** – As the initial treatment of AVNRT, we attempt one or more vagal maneuvers. We typically start with a standard Valsalva maneuver, followed by a modified Valsalva maneuver if the standard one is ineffective. Carotid sinus massage is another option. In a **standard Valsalva maneuver, the patient is placed in a supine or semirecumbent position and instructed to inhale normally, close their mouth, pinch their nose, and push their breath out against the closed mouth for 10 to 15 seconds.** The modified Valsalva maneuver consists of the standard Valsalva maneuver followed by supine positioning and passive leg raising.
  - In one **systematic review, which included 316 patients with a total of 965 episodes of AVNRT and AV reciprocating tachycardia (AVRT), the standard Valsalva maneuver successfully terminated 45 percent of supraventricular tachycardia (SVT) episodes and was more effective than carotid sinus massage.**
  - UpToDate accessed 1-4-2025

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Treatment of Atrioventricular Nodal Reentrant Tachycardia (AVNRT) Paroxysmal Superventricular Tachycardia (PSVT)

- **Step 2: Adenosine** – For patients with AVNRT that persists following vagal maneuvers, or in whom these maneuvers cannot be adequately performed, we suggest **IV adenosine rather than longer-acting AV nodal blockers.**
  - **In an observational study of 95 patients with AVNRT, adenosine terminated the arrhythmia in 86 percent of patients.**
- **Step 3: Beta blocker or calcium channel blocker** – If vagal maneuvers and adenosine are ineffective, or AVNRT recurs shortly after the arrhythmia was terminated, **we suggest administering IV nondihydropyridine calcium channel blockers (eg, verapamil, diltiazem) or IV beta blockers (eg, metoprolol, esmolol). We prefer these medications over cardioversion**, which requires that the patient receive moderate sedation by specially trained personnel in a monitored setting.
  - **Calcium channel blockers have been shown to terminate SVT (not specifically AVNRT) in 64 to 98 percent of patients, while data on the effectiveness of beta blockers are more limited.**
  - UpToDate accessed 1-4-2025

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Treatment of Atrioventricular Nodal Reentrant Tachycardia (AVNRT) Paroxysmal Superventricular Tachycardia (PSVT)

- **Patient-initiated treatment of recurrent AVNRT — For all patients with AVNRT, we develop a plan for patient-initiated treatment of arrhythmia recurrence in the outpatient setting.**
- **Valsalva maneuver (all patients)** — We instruct all patients with AVNRT to perform the standard Valsalva maneuver. Patients who have been educated on the proper performance of this maneuver are often able to terminate subsequent episodes of AVNRT on their own**. If the maneuver is successful, patients generally do not need to seek urgent medical attention.** However, patients should seek medical attention if the arrhythmia persists despite several attempts
- **Single dose of medication (select patients) — For patients who are having infrequent, well-tolerated episodes of AVNRT that are not terminated by the Valsalva maneuver, and who do not want catheter ablation or chronic suppressive medication, an alternative strategy is to take a single dose of an oral medication (eg, beta blocker, nondihydropyridine calcium channel blocker) or intranasal calcium channel blocker (etripamil) to terminate recurrent arrhythmia.** This approach may reduce the need for emergency department visits and help a patient avoid chronic medical therapy or catheter ablation.
- **In small studies in patients with supraventricular arrhythmias, single doses of an oral beta blocker or calcium channel blocker have been associated with rates of termination ranging from 60 to 90 percent.**
- **Etripamil (70 mg) is an intranasal medication that can be self-administered for the acute termination of paroxysmal supraventricular tachycardia (SVT).** The RAPID trial randomly assigned 692 adults with a history of paroxysmal SVT to self-administered etripamil or placebo. During 184 arrhythmia episodes, the rates of conversion were higher with etripamil than placebo (64 versus 31 percent; hazard ratio [HR] 2.62, 95% CI 1.66-4.15). In a subsequent open-label study in 1116 patients who self-treated 1054 episodes of SVT, 70.5 percent of patients converted to sinus rhythm (median time to conversion 18.3 minutes). Etripamil is safe and generally well tolerated. This drug received approval from the US Food and Drug Administration (FDA) in December of 2025. UpToDate accessed 1-4-2025

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New Drug Update

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