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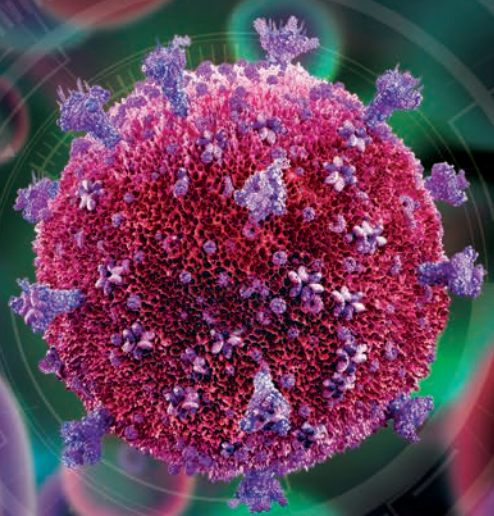
QUARTERLY
SUMMER 2026 VACCINES

# Next-Gen Vaccines

## More Targeted Ways to Fight Disease



Preparing for RSV Season:
ARE YOUR PATIENTS VACCINATED?

Cancer Vaccines:
TREATMENT AND PREVENTION

VACCINES ON THE HORIZON FOR Opioid Overdose

SOLVING THE CRISIS OF THE Opioid Epidemic

UPDATE ON Mast Cell Activation Syndrome

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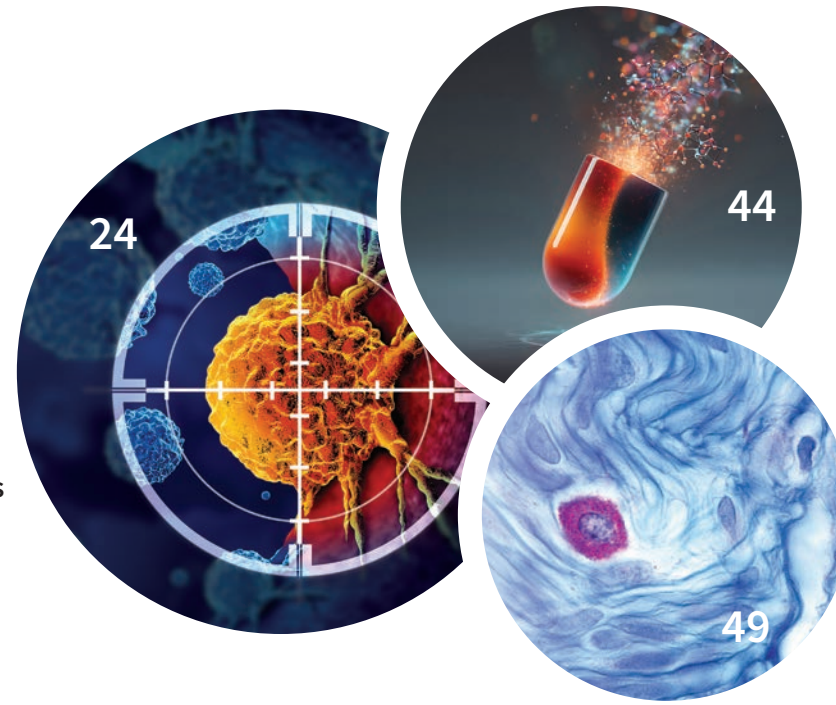


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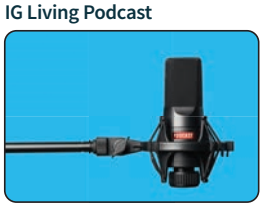

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# Expanding Role of Vaccines Beyond Traditional Use

**TODAY, THERE** is a broader shift in medicine: one in which vaccines are no longer limited to preventing infectious diseases, but are increasingly being designed as tools to address many different types of health challenges. Traditionally, vaccines worked by preparing the immune system to fight off viruses or bacteria before infection occurred. Now, scientists are expanding that same principle to help the body recognize and respond to much more complex threats. This shift reflects a deeper understanding of the immune system and shows how vaccine technology is evolving into a powerful, flexible approach for not only prevention, but also treatment and long-term disease management.

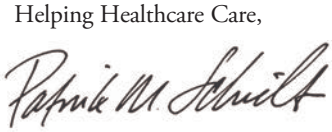
In this issue, we begin with a look at the traditional approach in our article "Preparing for RSV Season with Vaccinations" (p.18), which is especially important since we know vaccination rates remain lower than ideal even as we enter the season when virus rates spiral. We highlight who is most at risk, how the virus spreads and how timing of vaccination or antibody protection is critical due to seasonal and geographic differences. We also outline available options, including maternal vaccines, infant monoclonal antibodies and adult vaccines, while stressing the key role healthcare providers play in improving uptake through education, reminders and communication.

Building on decades of progress in vaccines that harness the immune system, our article "Advancements in Cancer Vaccines" (p.24) explores how these vaccines are emerging as a powerful next step in cancer immunotherapy. We take a look at preventive vaccines, such as those targeting cancer-causing viruses, as well as therapeutic vaccines designed to treat existing cancers, including highly personalized approaches using mRNA and tumor-specific neoantigens. Clearly, advances in genomics, artificial intelligence and vaccine technology are accelerating this field, yet challenges like cost, complexity and tumor resistance remain. Nevertheless, cancer vaccines have the potential to make cancer treatment more precise, personalized and effective in the future.

Even newer vaccines are being explored as a novel tool to prevent overdose and treat opioid use disorder. Despite existing prevention efforts, medications and public health initiatives, opioid-related deaths remain high, prompting researchers to pursue new solutions. Our article "Opioid Overdose: Are Vaccines the Answer?" (p.28) highlights the extensive research efforts, early clinical trials and promising preclinical results showing these vaccines can block opioid effects and reduce overdose risk. Although still experimental and facing development challenges, opioid vaccines could become a valuable addition to current treatments in the future.

As always, we hope you enjoy the additional articles in this issue of *BioSupply Trends Quarterly*, and find them both relevant and helpful to your practice.

Helping Healthcare Care,



Patrick M. Schmidt
Publisher

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Our mission is to serve as the industry's leading resource for timely, newsworthy and critical information impacting the biopharmaceuticals marketplace, while providing readers with useful tips, trends, perspectives and leading indicators on the topics pertinent to their business.

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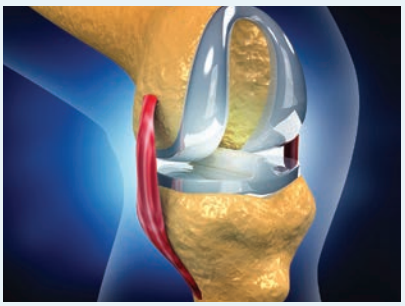
## CMS Proposes to Lower Costs for Hip, Knee and Ankle Replacements

Medicare beneficiaries undergoing knee, hip and ankle replacements, among the most frequent surgeries for people with Medicare, could soon experience more coordinated care and lower costs under a new Centers for Medicare and Medicaid Services (CMS) proposal. CMS is looking to implement these improvements by expanding the Comprehensive Care for Joint Replacement (CJR) Model nationwide through the Hospital Inpatient Prospective Payment System and Long-Term Care Hospital Prospective Payment System proposed rule.



Based on evaluation of the CJR Model, the CJR-X Model would create strong incentives for hospitals to coordinate care more effectively, avoid unnecessary services like avoidable re-hospitalization and emergency care, and focus on delivering the best outcomes for patients. It would specifically encourage better communication with post-acute care providers to support recovery. Beginning Oct. 1, 2027, CJR-X would be required for most hospitals, making it the first mandatory, nationwide test of an episode-based payment model. ❖

CMS to Improve Patient Care Experience and Lower Costs for Hip, Knee, and Ankle Replacements. Centers for Medicare and Medicaid Services press release, April 10, 2026. Accessed at www.cms.gov/newsroom/press-releases/cms-improve-patient-care-experience-lower-costs-hip-knee-ankle-replacements.

## New CMS Proposal to Speed up Patient Access to Drugs

The Centers for Medicare and Medicaid Services (CMS) is proposing changes to reduce long waiting periods for drugs, reducing barriers to timely access to critical treatments. The Interoperability Standards and Prior Authorization for Drugs proposed rule would advance sweeping reforms to modernize prior authorization for drugs by establishing clear decision deadlines for impacted payers — no later than 24 hours for urgent requests and 72 hours for standard requests — and increasing transparency through full disclosure of claims denials and appeals outcomes.

The rule would expand electronic prior authorization requirements to include drugs, aligning processes across Medicare Advantage, Medicaid, the Children's Health Insurance Program, Qualified Health Plans (QHP) issuers on the Federally-facilitated Exchanges and Small Group Market QHPs on the Federally-facilitated Small Business Health Options Program. Impacted payers would also be required to publicly report prior authorization metrics for drugs, including approval and denial rates, appeal outcomes and decision timeframes.

In addition, plans would report Application Programming Interface usage metrics to CMS, allowing the agency to monitor adoption and performance of electronic systems. These measures would give patients, providers and policymakers clearer insight into how consistently and efficiently prior authorization requests are handled. Public reporting would increase accountability and make it easier to compare how plans handle prior authorization decisions.

The rule also proposes adopting Fast Healthcare Interoperability Resources-based standards to replace the outdated X12N 278 transaction standard currently used by a minority of health plans. This would enable real-time electronic workflows — including streamlined submission of clinical documentation — reducing administrative burden and improving speed and accuracy. ❖

CMS Proposes Major Reforms to Speed Up Patient Access to Drugs, Increase Transparency, and Reduce Administrative Burden. Centers for Medicare and Medicaid Services press release, April 10, 2026. Accessed at www.cms.gov/newsroom/press-releases/cms-proposes-major-reforms-speed-up-patient-access-drugs-increase-transparency-reduce-administrative.

## CMS Launches First Wave of HealthTech Ecosystem Tools

During the Centers for Medicare and Medicaid Services (CMS) HealthTech Ecosystem Live! First Wave Launch event, which brought together CMS infrastructure, a new Medicare App Library and an initial set of patient-facing applications, a decision was made to move the nation beyond clipboards, fax machines and repetitive paperwork into a seamless, digital-first era.

Since calling on industry last year to help build a modern digital health ecosystem, more than 700 organizations have pledged support. That commitment has now evolved into real-world progress by hundreds of companies.

CMS highlighted tools from more than 50 companies, many of which are already accessible or will be available to the public soon. These efforts represent the first real-world implementation of a connected digital health ecosystem, where patients can access, share and use their health information through trusted applications.

As part of the event, interoperable digital tools were introduced intended to streamline care and improve the patient experience. Highlights included:

- Digital data access and check-in ("Kill the Clipboard"), allowing patients to securely share information with a simple scan on their phone.
- Personalized health applications, offering tailored guidance on nutrition, wellness and chronic disease management — extending care beyond clinic walls. ❖

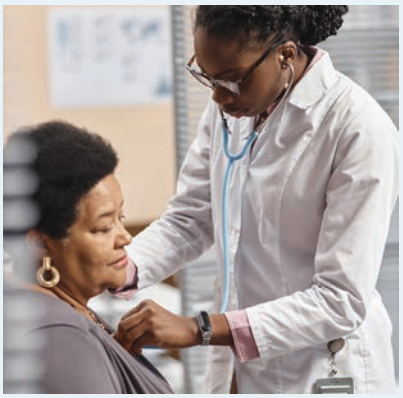
CMS Launches First Wave of HealthTech Ecosystem Tools, Fast-Tracking a Fully Digital, Patient-Centered Health System. Centers for Medicare and Medicaid Services press release, April 9, 2026. Accessed at www.cms.gov/newsroom/press-releases/cms-launches-first-wave-healthtech-ecosystem-tools-fast-tracking-fully-digital-patient-centered.

## New Healthcare Advisory Committee Created to Improve Patient Care

The U.S. Department of Health and Human Services (HHS) and the Centers for Medicare and Medicaid Services (CMS) announced the members of the Healthcare Advisory Committee, a new federal advisory body comprised of leaders from across the healthcare system to provide expert advice on improving, strengthening and modernizing U.S. healthcare. The committee will advise on ways to improve how care is financed and delivered across Medicare, Medicaid, the Children's Health Insurance Program and the Health Insurance Marketplace.

The following individuals, selected through a competitive review process that drew more than 400 nominations nationwide, will serve on the Healthcare Advisory Committee: Robert Bessler, MD, Kimberly Brandt, JD (ex officio), Sebastian Caliri, Stephanie Carlton (ex officio), David Carmouche, MD, Elizabeth M. Fago, Clive K. Fields, MD, William J. Gassen, JD, Jenni Gudapati, PhD, Valerie D. Huhn, Dennis Laraway, Dan Liljenquist, JD, Andrew Lynch, Ursel J. McElroy, Kyu Rhee, MD, Tony Robbins, Russ Thomas and Linda Thomas-Hemak, MD.

The committee will provide non-binding recommendations to inform federal healthcare policy and program administration. Over its term, it will focus on: 1) developing actionable policy solutions to prevent and better manage chronic disease; 2) advancing accountability for safety and outcomes while reducing unnecessary administrative burden; 3) expanding the use of real-time data to support a higher quality of care, speed up claims processing and improve quality measurement; 4) enhancing care



for vulnerable populations, including those served by Medicaid; and 5) strengthening Medicare Advantage sustainability, including modernizing risk adjustment and quality measurement.

More information can be found at www.cms.gov/priorities/healthcare-advisory-committee/overview. ❖

HHS and CMS Announce Healthcare Advisory Committee Members to Improve Patient Care and Modernize the U.S. Healthcare System. U.S. Department of Health and Human Services press release, March 27, 2026. Accessed at www.hhs.gov/press-room/hhs-cms-announce-healthcare-advisory-committee-members-improve-patient-care.html.

# Impacts of IRA's 3rd Release: Drug Pricing in a Radically Different Market!

By Bonnie Kirschenbaum, MS, FASHP, FCSHP

**COUPLING THE** drug pricing component of the Inflation Reduction Act (IRA) of 2022 with other rule changes affecting several sites of care in the healthcare environment will help you understand and prepare for upcoming changes.

The IRA initiated some of the most significant changes to U.S. prescription drug pricing regulations. Since then, there have been multiple other models and rules that have continued to change or address drug pricing. To recap the provisions of the IRA: The price negotiation program lowers prescription drug costs for seniors by empowering Medicare to negotiate the cost of prescription drugs and aims to target the most costly drugs in the program. The federal government will directly regulate the price of prescription drugs in Medicare, indirectly limit the ability of drug manufacturers to increase wholesale prices and make major changes to the Medicare Part D prescription drug benefit. Medicare Parts B and D gain negotiation powers that apply to the price of a limited number of drugs with no generic or biosimilar competition. Additionally, the Act ended a 19-year-old ban on Medicare negotiating the price of prescription medicines with manufacturers that began in 2003 when they were prohibited from directly negotiating Part D drug prices.

A significant additional benefit of the IRA requires all Medicare Part D plans to cover each of the drugs selected for price negotiation, including all dosages and forms, when negotiated prices take effect. This expands beneficiaries' access to such drugs.

*2022 (Oct. 1):* Initially, Medicare Part B-qualifying biosimilars were paid at average sales price (ASP) plus eight percent of the reference add-on rather than ASP plus six percent to encourage the use of biosimilars with competition, as well as to lower costs for and improve patient access to these products. Medicare Part D drug rebates were altered in this first 12-month period if their prices for certain Part D drugs increased faster than the rate of inflation over the 12-month period.

*2023:* Cost-sharing began for insulin to ensure those enrolled in a Medicare prescription drug plan wouldn't pay more than $35 out of pocket for a month's supply of each insulin they use that is covered by their Medicare prescription drug plan and dispensed at a pharmacy or through a mail-order pharmacy. Medicare Part B drug rebates from the manufacturers were required if prices for certain Part B drugs increased faster than the rate of inflation. Most notably, the first 10 Medicare Part D drugs selected for the Drug Price Negotiation Program were announced with maximum fair prices (MFP) to be subsequently negotiated and become effective in 2026.

*2024:* The elimination of the five percent cost-sharing in the catastrophic phase of Medicare Part D kicked in after enrollees reached $7,050 in out-of-pocket costs for covered drugs. (2025 caps to patients' Part D out-of-pocket costs are $2,000.) Drug Price Negotiation Program prices were published revealing the MFP negotiated for the first 10 selected Medicare Part D drugs effective 2026. (We've reached that milestone!)

*2025:* The out-of-pocket Part D limit fell to not more than $2,000 for prescription drugs that may be paid in monthly increments. A Manufacturer Medicare Part D Discount Program replaced the coverage gap discount program and applies to both the initial coverage and catastrophic phases. The next negotiation cohort of 15 more Medicare Part D drugs were announced with MFPs that go into effect in 2027.

*2026:* This is the first year beneficiaries are seeing the negotiating results with the cycle for adding an ever-increasing number of products continuing each year. This first round of price negotiations cut the price of 10 of the most commonly used medications in Medicare by at least 40 percent. The negotiated prices for the first 10 drugs that went into effect on Jan. 1 are expected to save Medicare beneficiaries an estimated $1.5 billion. The key components of the IRA are now fully underway: The Medicare Part D redesign is done, the Medicare Prescription Payment Plan is set and the Drug Price Negotiation Program is effective for 2026. These reforms impact the broader healthcare ecosystem and its key players across the industry, including the pharmacies that service their patients. Eligible patients filling prescriptions for the 10 eligible drugs will pay no more than the MFP. If the pharmacy paid more to acquire the product, it is eligible for a rebate from the manufacturer through the Medicare Transaction Facilitator that is administered by the Centers for Medicare and Medicaid Services (CMS).

*2027 and beyond:* At this point in the cycle, Part B drugs are added to the cohort of products subject to MFP negotiation. This will lead to 15 more Medicare Part B or Part D drugs up for price negotiation that will be announced when their MFPs become effective in 2028 and 20 more the next year with the cycle continuing. Medicare's Part D prescription drug insurance program covers ambulatory care medications and, for the first time, Medicare's Part B program covers outpatient care such as that provided in infusion centers. This list — along with the common Medicare-covered conditions they treat (and recent one-year Medicare costs associated with them) — includes:[1]

- Dulaglutide: type 2 diabetes ($4.9 billion)
- Bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy): HIV ($3.9 billion)
- Abatacept (Orencia): rheumatoid arthritis and psoriatic arthritis ($2.5 billion)
- Secukinumab (Cosentyx): plaque psoriasis, psoriatic arthritis and ankylosing spondylitis ($2.3 billion)
- Apalutamide (Erleada): prostate cancer ($1.9 billion)
- Ribociclib (Kisqali): breast cancer ($1.6 billion)
- Vedolizumab (Entyvio): ulcerative colitis and Crohn's disease ($1.5 billion)
- Abemaciclib (Verzenio): breast cancer ($1.4 billion)
- Botulinum toxin: chronic migraine, overactive bladder, spasticity and other movement disorders ($1.1 billion)
- Lenvatinib (Lenvima): kidney cancer ($1.1 billion)
- Omalizumab (Xolair): asthma, chronic hives and nasal polyps ($1.1 billion)
- Brexpiprazole (Rexulti): major depressive disorder, schizophrenia and agitation in Alzheimer's dementia ($1.1 billion)
- Tofacitinib (Xeljanz): rheumatoid arthritis, psoriatic arthritis and ulcerative colitis ($1 billion)
- Umeclidinium/vilanterol (Anoro Ellipta): chronic obstructive pulmonary disease ($813 million)
- Certolizumab pegol (Cimzia): Crohn's disease, rheumatoid arthritis and psoriatic arthritis ($787 million)

Both the Outpatient Prospective Payment System and the Physician Fee Service (PFS) rules set the coverage and administration of Medicare Part B. CMS continues to explore or implement change that affects outpatient use of drugs and biologics. Here are the most impactful to watch for in the upcoming proposed rules for 2027 and beyond:

Drug Price Negotiation Program MFP units will be included in and, thus, will lower ASP (this begins in 2028 when the first Part B drugs are eligible for MFP). CMS clarified that MFP units should be included in the calculation of ASP given their inclusion in the calculation of Best Price under Medicaid. Inclusion of MFP units in ASP is likely to drive ASP prices lower. For each selected drug, CMS will publish an MFP-based payment limit instead of the ASP-based payment limit in the quarterly pricing files starting with Initial Price Applicability Year 2028 when the MFP is live for Part B. As a result, there will no longer be a published ASP-based payment limit for a selected drug while it is subject to an MFP. Spillover effect into the commercial market is expected. This change will have a downstream impact on commercial payers that tie their reimbursement rates to Part B payment rates published in the Part B payment file. Expect lower add-on payments since they'll be calculated as six percent of MFP instead of six percent of ASP.

The Inpatient-Only price list is shrinking to allow procedures by outpatient providers. This enables outpatient providers, such as ambulatory surgery centers, to be paid for a wider array of services. "CMS believes that the evolving nature of the practice of medicine allows more procedures to be performed on an outpatient basis with a shorter recovery time."

According to the Ambulatory Surgery Center Association, "This policy allows for these services to be paid by Medicare in the hospital outpatient setting when determined to be clinically appropriate, giving physicians greater flexibility in determining the most appropriate site of service. The new policy has the potential to improve access to care, and to reduce federal spending because inpatient care tends to be costlier. The elimination of the Inpatient-Only list provides Medicare beneficiaries the ability to work with their surgeon to best determine the appropriate site of care." ❖

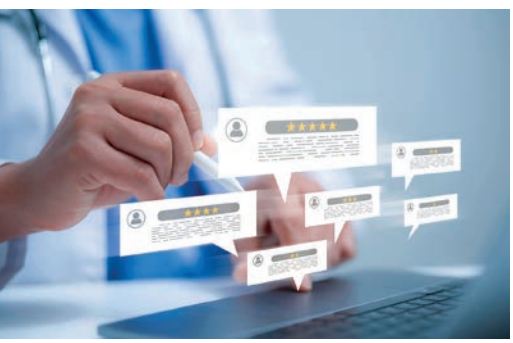
## Reference

1. Frieden, J. Botox, Trulicity, and 13 Other Drugs Selected for Medicare Price Negotiations. Medpage Today. Accessed at www.medpagetoday.com/publichealthpolicy/medicare/119619.

**BONNIE KIRSCHENBAUM**, MS, FASHP, FCSHP, is a freelance healthcare consultant with senior management experience in both the pharmaceutical industry and the pharmacy section of large corporate healthcare organizations and teaching hospitals. She has an interest in reimbursement issues and in using technology to solve them. Kirschenbaum is a recognized industry leader in forging effective alliances among hospitals, physicians, pharmaceutical companies and distributors and has written and spoken extensively in these areas.

# Medical Practice Marketing Strategies: Five Ways to Put Your Practice on the Map

By Rachel Maier, MS



**IF YOUR** medical practice relies on word-of-mouth referrals, it may be time to update your marketing strategy. A 2024 Pew Research Center report found that 77 percent of patients research providers online before booking an appointment.[1] In fact, the 2025 Local Consumer Review Survey by BrightLocal showed that 42 percent of patients consider online reviews just as important as personal recommendations.[2] While direct referrals won't ever be obsolete, today's patients rely on input from total strangers. Instead of primarily asking friends and family for recommendations, they increasingly turn to online communities for suggestions and opinions about healthcare providers; they want to know who to see and who to avoid.

Patients even turn to Internet search engines such as Google, Bing, Yahoo and even AI-powered platforms such as ChatGPT to find healthcare providers in the area; once they find your name, they search for information about you and decide whether to make an appointment based on what they find. If patients were to look for you online today, would they find you? And if they did, what would they think about you?

Here are five strategies to help your practice stand out.

## Claim Your Name Online

When you search for your practice name online, does it show up with the correct information? If not, it's time to add or verify your business profile on platforms like Google so your patients can find you. Doing so allows you to control how your business information appears online. This small step can literally put your practice on the map. Your business profile gives Google the information it needs to point patients to you. (See business.google.com to add your business to Google.)

Once your practice is claimed online, platforms will display your name, address, phone number, hours of operation, website, photos and reviews. The more robust your presence, the more information they get about you. If they can't find you or get a bad first impression, they're less likely to book an appointment with you. A simple Internet search is often a patient's first encounter with you, so it's important to make a good impression.

## Paint Your Digital Front Door

How long has it been since you looked at your own website? Is it time for a fresh coat of digital paint? Just like your brick-and-mortar building needs maintenance to stay up to date and inviting, your online presence needs maintenance and updates, too. Consider what impression your website gives patients: Is it attractive, professional and inviting? Is it easy to navigate? Does it clearly communicate who you are, what you do and why patients should pick you rather than a competing practice across town? Can patients navigate your site quickly and efficiently, and can they find your contact information in a snap?

Revamping your website can be as simple as a light revision or as in-depth as a major overhaul. No matter how awesome your marketing efforts may be, if you don't have a solid online presence, you're far less likely to grow your practice.

## Implement and Optimize SEO

Once your information is online, patients need to find it. That's where SEO comes in. SEO stands for "search engine optimization," and it helps your practice appear higher in a list of Internet search results. According to Net One Click, a marketing agency specializing in small and mid-sized medical practices, most patients begin their healthcare search on Google, and the top three map results get the most clicks.[3]

When you implement SEO, you give search engines the information they need to find your practice, and when done correctly, it ranks higher in search results, meaning it will (ideally) be within the first several business listings. SEO involves developing a well-structured website and clear, descriptive page titles with relevant content that includes keywords, helping search engines understand who you are,

what you offer and how you can help patients. It not only sends more traffic to your website but also establishes your practice as a trusted leader in your field.

You can implement SEO yourself, but you may opt to hire an expert to help. Many marketing firms specialize in SEO for medical practices; their expertise may be worth the expense, especially as AI reshapes how people find answers online.

## Stay Engaged on Social Media

Traditional word-of-mouth referrals aren't enough to increase your patient load. Today, you've got to make sure your practice is positioned for digital recommendations and reviews, which are known as electronic word-of-mouth (or "eWOM"). Patients may share information about their experience at your clinic via user-generated content and may well tag your practice in the process. Don't miss out on the opportunity to leverage social proof to your benefit: People may mimic the medical decisions of other people when they see someone post about it. Plus, social media gives you an opportunity to engage with patients directly by creating videos of your own, answering relevant questions, creating polls and helping to distribute accurate, relevant information that potential patients are curious about.

It might be worth asking what your social media presence says about you and your practice. Is original content regularly uploaded and shared to platforms such as Facebook, Instagram and X? And if so, is it information your patients and potential patients care about? What you post can build trust and enhance your reputation.

## Leverage Positive Patient Reviews

Eighty-one percent of patients read patient reviews online before choosing a healthcare provider.[4] Reviews help patients decide whether a doctor offers the level of expertise and/or patient care they need or expect. According to BrightLocal, patients expect higher star ratings and increasingly give their business to entities with a 4.5+ star rating.[2]

How do you encourage satisfied patients to leave positive reviews of your practice? Make it a natural extension of their experience, and patients will come to expect it as part of the patient experience.

- Ask: Train front-desk staff to ask patients about their experience, and ask them to share it online.
- Make it easy: Post QR codes or direct links to online reviews on Google, Yelp or Healthgrades in your waiting room, or print them on patients' after-visit summaries.
- Follow up: Send automated requests via an email or text message with a warm message and direct links to Google, Yelp or Healthgrades 24 to 48 hours after their visit.
- Share patient success stories online: Patient testimonials can reassure nervous patients and help them take the next step of booking an appointment.
- Feature positive reviews online: Highlighting positive reviews from other patients tells others that leaving reviews is a normal part of the patient experience.

It's important to note that the Federal Trade Commission prohibits payment in exchange for reviews, and the Health Information Portability and Accountability Act (HIPAA) requires that patients' personal information remain private.

## When in Doubt, Hire Experts

There are many simple steps you can take on your own to make your practice stand out, but it may be worthwhile to bring in experts to manage your marketing efforts (and allow you to focus on patient care). And, marketing firms specializing in healthcare are adept at navigating privacy laws and creating a marketing plan that is HIPAA-compliant, ethical and empathetic.

Whether your in-house team needs help bolstering your online presence or your practice needs a full-fledged agency to develop a comprehensive marketing strategy, a simple Internet search for "medical marketing agencies" is a great way to get started. You might also check out Position Results' list of the top 11 best medical marketing companies in the U.S. (positionresults.com/best-medical-marketing-companies) to help you find the right marketing partner to help your practice. ❖

**If patients were to look for you online today, would they find you?**

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**RACHEL MAIER**, MS, is a Kansas City-based freelance writer and editor.

Research

## Pain-Relieving Drug with Minimal Addictive Properties Discovered

Researchers at the National Institutes of Health (NIH) have identified a novel, highly potent opioid that shows potential as a therapy for both pain and opioid use disorder without causing respiratory depression, tolerance or other indicators of potential for addiction in humans.

In the study, the researchers investigated formulations of an understudied class of synthetic opioid compounds, known as nitazenes (shelved in the 1950s due to excessive potency), which selectively engage mu-opioid receptors, primary targets for opioid drugs in the brain and peripheral nervous system. "Our goal was to study the profile, or pharmacology, of these drugs," said Michael Michaelides, PhD, senior author and NIH's National Institute on Drug Abuse investigator. "We wanted to decrease the potency and create a potential therapeutic. What we discovered exceeded our expectations."

Initially, research focused on a chemical formulation called FNZ that could be administered to rats and tagged with a radioisotope for positron emission tomography, which enables tracking of the drug in real time throughout the rat brain. They discovered that FNZ entered the brain only briefly, for approximately five to 10 minutes, yet pain relief, known as analgesia, persisted for at least two hours. Knowing that nitazenes can have active metabolites, or byproducts, an investigation of whether an FNZ metabolite might be responsible for the prolonged effect revealed DFNZ, another opioid dubbed a "superagonist" for its extremely high efficacy at the mu-opioid receptor. Whereas FNZ carries serious risks, including depressed breathing and high potential for addiction, DFNZ doesn't cause these effects.

At preclinical therapeutic doses, DFNZ produced a moderate and sustained increase in brain oxygen rather than depressing respiration. Repeated doses of the drug did not result in tolerance, drug dependency or meaningful withdrawal effects. Among 14 classic opioid withdrawal symptoms, the researchers only observed irritability, as measured by vocalization, when handling DFNZ-treated rats. They also found that while it does produce some rewarding effect, when the drug was replaced with saline, animals stopped the drug-seeking behavior, which is in contrast with other opioids.

According to the researchers, findings challenge the prevailing view that high-efficacy mu-opioid receptor drugs are unsuitable for development as safe analgesics, and should be explored for use in treatment for opioid use disorder and may be preferable to current opioid agonist medications, which have an associated risk of causing respiratory depression.

The research team is planning to pursue additional preclinical studies to support an application for regulatory approval to conduct studies of DFNZ in humans. ❖

NIH Researchers Discover Pain-Relieving Drug with Minimal Addictive Properties. National Institutes of Health press release, April 1, 2026. Accessed at www.nih.gov/news-events/news-releases/nih-researchers-discover-pain-relieving-drug-minimal-addictive-properties.

Research

## High-Dose Flu Vaccine Significantly Lowers Risk of Developing Alzheimer's

In a study at the University of Texas Health Science Center at Houston (UTHealth), researchers found that adults 65 and older who received a high-dose influenza vaccine had a significantly lower risk of developing Alzheimer's disease compared to those who received the standard dose.

In the retrospective cohort study, researchers led by a team at the McGovern Medical School at UTHealth analyzed health data from roughly 165,000 older adults who received either a high-dose or standard-dose influenza vaccine. They found that the high-dose flu vaccine reduced the risk of Alzheimer's disease in those 65 and older by nearly 55 percent over a roughly two-year period.

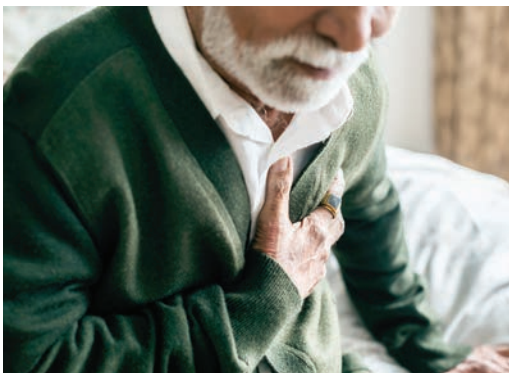
According to the researchers, the findings add to a growing body of evidence linking vaccination, and

possibly immune system activity, to reduced dementia risk. ❖

Bergeson, L. High-Dose Flu Vaccine Tied to Lower Alzheimer's Risk in Older Adults. University of Michigan CIDRAP, April 2, 2026. Accessed at www.cidrap.umn.edu/influenza-vaccines/high-dose-flu-vaccine-tied-lower-alzheimer-s-risk-older-adults.

Research

## Flu Vaccine, Even with Infection, Reduces Risk of Heart Attack and Stroke



A new study shows that influenza vaccination may help protect against heart attack and stroke even when it does not prevent people from getting the flu.

In the study, researchers at the Statens Serum Institut in Copenhagen analyzed data from a Danish health registry from the 2015-16 to 2023-24 flu seasons to identify adults aged 40 years and older who experienced a first-time hospitalization for acute myocardial infarction (AMI) or stroke within a year of laboratory-confirmed flu infection. Of the 1,221 identified adults, 610 were vaccinated and 621 were not.

They found that AMI risk increased roughly five-fold, and stroke risk rose about three-fold in the first week after flu infection compared with other time periods. But flu vaccination appeared to significantly reduce that risk. In fact, findings showed the risk of heart attack or stroke was reduced by half in participants who had received a flu vaccine compared with unvaccinated participants. ❖

Croci, R, Young, JJ, Emborg, H-D, et al. Influenza Vaccination Attenuates Acute Myocardial Infarction and Stroke Risk Following Influenza Infection: A Register-Based, Self-Controlled Case Series Study, Denmark, 2014 to 2025. *Eurosurveillance*, Volume 31, Issue 13, April 2, 2026. Accessed at www.eurosurveillance.org/content/10.2807/1560-7917.ES.2026.31.13.2500706.

Medicines

## FDA Approves Drug to Treat Hunter Syndrome

The U.S. Food and Drug Administration (FDA) approved Avlayah (tividenofusp alfa-eknm) to treat certain individuals with Hunter syndrome (Mucopolysaccharidosis type II or MPS II). Avlayah, an intravenous infusion given once weekly, is approved to treat neurologic manifestations of Hunter syndrome when the medication is started in presymptomatic or symptomatic pediatric patients weighing at least 5 kg prior to advanced neurologic impairment.


Hunter syndrome is a rare inherited lysosomal disorder in which sugar molecules called glycosaminoglycans build up within the cells' lysosomes. This substrate accumulation affects physical and mental development by causing abnormalities in the skeleton, heart, respiratory system, brain and other organs.

Approval is based on results from a Phase I/II multi-cohort, single-arm, open-label trial that enrolled 47 pediatric patients with Hunter syndrome aged 3 months to 13 years. In the trial, Avlayah significantly reduced cerebrospinal fluid heparan sulfate (CSF HS), a type of glycosaminoglycan. The 44 patients with measurements at week 24 had a 91 percent average decrease from baseline in CSF HS; the minimum and maximum percent change in CSF HS from baseline were 72 percent and 98 percent, respectively. At baseline, no patients had CSF HS levels below the upper limit of normal (ULN); at week 24, 93 percent of Avlayah-treated patients with CSF measurements had CSF HS levels below the ULN. Avlayah's labeling includes a boxed warning for allergic reactions, including anaphylaxis.

"Avlayah is the first product approved to address neurologic complications of Hunter syndrome, a very rare and often severe X-linked disorder in children, affecting about 500 people in the U.S., almost exclusively males," said Acting Center for Drug Evaluation and Reserch Director Tracy Beth Hoeg, MD, PhD. "The drug's application holder, Denali Therapeutics, is now conducting a randomized clinical trial that is more than 95 percent enrolled to evaluate the clinical benefit of this product. In the meantime, families with young children with Hunter syndrome will have access to a product that may favorably alter the course of the disease at the crucial time in life when there is the greatest potential for benefit." ❖

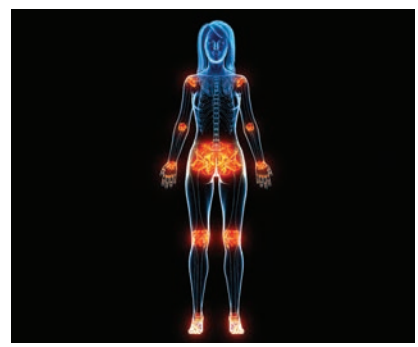
FDA Approves Drug to Treat Neurologic Manifestations of Hunter Syndrome. U.S. Food and Drug Administration press release, March 25, 2026. Accessed at www.fda.gov/news-events/press-announcements/fda-approves-drug-treat-neurologic-manifestations-hunter-syndrome.

Research

## Study Finds Connection with Inflammation in Autoimmune Diseases and Cancer Risk

In a recent study, a group of researchers reported that patients diagnosed with immune-mediated inflammatory disease (IMID) face a high risk of cancer in the first year after diagnosis; however, that risk gradually declines as inflammation decreases with treatment.

In this first nationwide Italian study, led by Antonio Giordano, MD, PhD, at the Sbarro Health Research Organization, evidence was collected over five years and included more than 356,000 patients. The team monitored patients with IMID from their initial diagnosis through follow-up, finding the reduction in cancer risk correlated with decreasing inflammation



rather than treatment effects alone. They also observed that patients with non-inflammatory diagnoses, such as diffuse connective tissue diseases, did not show the same early elevated cancer risk.

"The evidence that risk peaks early after diagnosis suggests that chronic inflammation, rather than just treatment, drives oncogenesis," said Daniela Marotto Puo, MD, of Azienda Socio-Sanitaria Locale della Gallura. "These findings are crucial for implementing standardized, age-stratified cancer surveillance protocols within our clinical practice. Ultimately, this work supports early, aggressive anti-inflammatory strategies as a potential means to mitigate long-term malignancy risks." ❖

Sbarro Health Research Organization (SHRO). Cancer Risk Rises with Autoimmune Disorders but Drops After Anti-Inflammatory Therapy, a Study Finds. Medical Xpress, March 31, 2026. Accessed at www.medicalxpress.com/news/2026-03-cancer-autoimmune-disorders-anti-inflammatory.html.

Medicines

## FDA Approves Gene Therapy for Rare Immune Disorder

The U.S. Food and Drug Administration (FDA) has approved Kresladi (marnetegragene autotemcel), the first gene therapy for the treatment of severe leukocyte adhesion deficiency type I (LAD-I). Kresladi is indicated for the treatment of pediatric patients with severe LAD-I due to biallelic variants in ITGB2 without an available human leukocyte antigen (HLA)-matched sibling donor for allogeneic hematopoietic stem cell transplant.

Kresladi consists of the patient's own hematopoietic (blood) stem cells (HSCs), which are genetically modified to introduce functional copies of the ITGB2 gene. Following conditioning, a single dose of Kresladi is infused intravenously to address the underlying cause of severe LAD-I by restoring CD18 and CD11a cell surface expression in white blood cells, including neutrophils.

Approval was based on an open-label, single-arm, multicenter study based on increases in neutrophil CD18 and CD11a cell surface expression (disease-specific biomarkers indicative of improved immune activity) at month 12 with sustained effect through month 24 post-infusion. Increases in neutrophil CD18 and CD11a cell surface expression reflected improved function of a protein complex of the two biomarkers on the surface of neutrophils, which is used as a surrogate endpoint that is reasonably likely to predict clinical benefit in LAD-I for accelerated approval. The clinical benefit of Kresladi will be confirmed in patients with severe LAD-I through post-marketing requirements. The most common side effects identified in the clinical study included anemia, low platelet and white blood cell counts, mouth sores, upper respiratory infections, viral infections, fever, febrile neutropenia, nausea, vomiting, skin infection, rash, vascular device-related infection and increased liver enzymes.

"Kresladi offers a potentially transformative treatment option that targets the root cause (pathophysiology) of this serious condition. Our office and FDA remain committed to advancing innovative gene therapies for rare pediatric diseases and making them available to patients as quickly as possible via accelerated approval pathway supported by use of novel surrogate endpoints," said Megha Kaushal MD, MS, acting deputy director of FDA's Center for Biologics Evaluation and Research Office of Therapeutic Products and pediatric hematologist. "For children with severe LAD-I and their families, this treatment allows them to participate in day-to-day activities and hopefully experience a better quality of life." ❖

FDA Approves First Gene Therapy for Severe Leukocyte Adhesion Deficiency Type I. U.S. Food and Drug Administration news release, March 26, 2026. Accessed at www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-severe-leukocyte-adhesion-deficiency-type-i.

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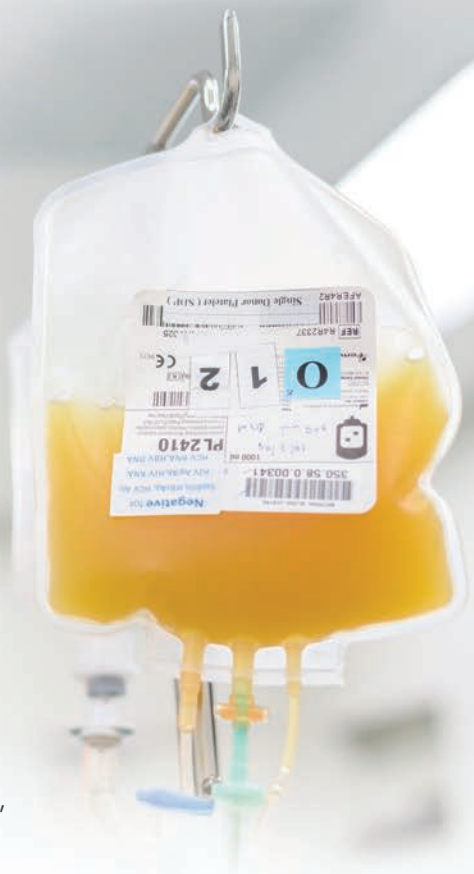

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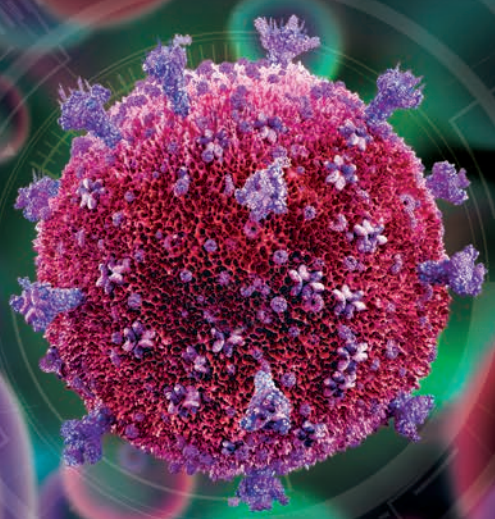
# Preparing for RSV Season with Vaccinations

This action plan for providers can help to ensure patients receive vaccinations against this virus that results in thousands of hospitalizations and sometimes death.

By Amy Scanlin, MS



**DEPENDING ON** geographic location, it is likely time to prepare for the upcoming respiratory syncytial virus (RSV) season. This common respiratory virus can lead to serious illness, particularly in infants and older adults, but this risk can be reduced by ensuring vaccines reach at-risk populations when they need them.

RSV leads to upwards of 6.5 million outpatient visits, 350,000 hospitalizations and 23,000 deaths annually in the U.S., according to the Centers for Disease Control and Prevention (CDC). It is the leading cause of hospitalization in infants. An additional 180,000 hospitalizations and 10,000 deaths are also possible in patients over age 50 with underlying health complications such as weakened immune systems.[1]

RSV can be highly contagious, with signs and symptoms of illness appearing four to six days after infection and contagion lasting three to eight days, or up to eight weeks in the case of immunocompromised patients.[1] In mild cases, symptoms of RSV are similar to the common cold, but in severe cases, it can spread to the lower respiratory tract and cause pneumonia or bronchiolitis. Since RSV lowers one's immunity, infection may also increase the risk of getting COVID-19, and if infections occur together, the severity of COVID-19 is worsened.

Some studies show that an annual RSV vaccine can be 90 percent effective in protecting against infant hospitalizations and 70 percent effective at preventing hospitalizations in older adults.[2] Yet, despite the scientific success of RSV vaccines, uptake is lower than preferred, and one of the main reasons could be that doctors may not be recommending it.

Creating a culture of immunization prior to the start of each RSV season is the most effective way to increase vaccine coverage rates. This culture includes reminder systems, patient education and open communication regarding the risk-benefit analysis of receiving the vaccine.

## Who Is Most at Risk?

Infants younger than six months old, and premature infants in particular, are most at risk of severe complications from RSV. Estimates suggest most children will have had RSV at least once by age 2 years. In healthy children, symptoms of RSV are usually mild and only require self-care until the patient feels well again. But, it is worth noting that there may be a link between severe RSV during childhood and a chance of developing asthma later in life.

Severe RSV infections pose a risk to adults ages 50 to 74 who have underlying medical conditions such as cardiopulmonary disease and weakened immune systems. Individuals over 75 years old, particularly those living in nursing homes, are at much greater risk. In fact, some suspect RSV is likely underdiagnosed in older adults with severe respiratory illnesses, and may be twice as likely in patients with chronic obstructive pulmonary disease (COPD). The risks for this older age group include myocardial infarctions, exacerbation of asthma and COPD symptoms, bronchospasms and pneumonia, particularly for those in nursing homes.[1]

**Immunizations are a patient's best defense against RSV, particularly in those who have high-risk conditions.**

## Seasonality and Geographic Variability

RSV season typically runs from November through March in most of the U.S. with peak season in December and January. However, that season may shorten or lengthen based on seasonality and circulation patterns. For instance, circulation in tropical climates like southern Florida, Hawaii, Puerto Rico and the Virgin Islands differ from those traditionally seen in the mainland U.S. Likewise, circulation patterns in Alaska are less predictable, and the duration of peak virus season is longer than the national average.

Therefore, the timing of RSV monoclonal antibodies in infants or vaccine administration in pregnant women and older adults is important. Sometimes, public health authorities may broadly elect to revise clinical and public health guidance regarding ideal timing. Similarly, providers must use clinical judgment for individual patients with travel plans to areas of increased RSV activity or when their return occurs outside of the ideal window of infant antibody delivery.[3]

## Who Is Vaccine-Eligible?

CDC recommends doctors give monoclonal antibodies to all infants under 8 months if their mother did not receive an RSV vaccine during pregnancy. In most cases, infants born after 14 days of maternal vaccination will not need administration of an RSV antibody. However, in rare circumstances, doctors may administer an RSV antibody to infants whose mothers did receive the RSV vaccine. These circumstances might include certain maternal medical conditions or if infants have undergone cardiopulmonary or other procedures

that might have led to a loss of maternal antibodies. The administration of infant monoclonal antibodies should occur between October and March in most of the U.S., or within babies' first week of life if born between October and March.[3]

Pregnant women may receive a maternal RSV vaccine in the months of September through January when they are between 32 and 36 weeks' gestation to protect their unborn child against severe RSV complications.[3]

## Effective two-way patient communication is the clearest, best path to achieving vaccination goals.

It is sometimes recommended that children aged 8 to 19 months receive an RSV antibody shortly before or as early as possible during their second RSV season. These instances include children who are severely immune compromised, have chronic lung disease, were born prematurely and required medical support at any time during the six months preceding the start of RSV season, have cystic fibrosis and are American Indian or Alaska Native. Additionally, if the mother did not receive the RSV vaccine during pregnancy, if her RSV vaccine status is unknown or if her baby was born within 14 days of her receiving the RSV vaccine, antibodies may be warranted. It is not advised to give RSV antibodies to children older than 8 months who are not at increased risk of severe RSV infection. Additionally, RSV antibodies are also not recommended for children 20 months or older.[3]

CDC recommends adults 60 to 74 years with increased risk for severe RSV and all adults over the age of 75 get an RSV vaccine between September and January.[2]

### Infant RSV Monoclonal Antibodies

One of two methods protects babies against severe RSV infections: Either their mother received a vaccine during pregnancy, or the administration of two U.S. Food and Drug Administration (FDA)-approved monoclonal antibody products for infants. The antibody products, nirsevimab (Beyfortus, approved in 2023) and clesrovimab (ENFLONSIA, approved in 2025), come in prefilled injectable syringes. Both are recommended for infants younger than 8 months when entering their first RSV season.[3]

Once children reach 8 months or they are entering their second RSV season, only nirsevimab has received FDA approval. Nirsevimab may be administered through age 19 months. Clesrovimab does not have FDA approval for administration in children older than 8 months of age or those entering their second RSV season.[3]

It is permissible to administer infant RSV antibodies and routine childhood vaccines in the same visit, with no necessary interval between infant RSV antibodies and live vaccines. However, in accordance with CDC General Best Practices, children who are acutely ill should usually wait to receive an infant RSV antibody.[3]

Infant monoclonal antibodies, unlike vaccines, do not activate the immune system. Therefore, they work best in the weeks after being administered and stay effective for around five months during the period when children are most susceptible to a severe infection.

The side effects of RSV monoclonal antibodies are generally mild and include swelling, redness or pain at the injection site that usually resolves quickly. Hypersensitivity reactions are uncommon; however, in February 2024, FDA updated the package insert for nirsevimab to include rare cases of hypersensitivity reactions post-licensure. These findings did not affect a determination of the product's overall risk-benefit at the October 2024 CDC Advisory Committee on Immunization Practices meeting.[4]

### Maternal RSV Vaccine

Pfizer's Abrysvo vaccine protects mothers-to-be against severe RSV when administered between 32 and 36 weeks of gestational age. Approved for use in pregnant women in 2023, Abrysvo is the only RSV vaccine approved and recommended for use by pregnant women. Babies delivered more than 14 days from their mother's RSV vaccination are protected from severe forms of RSV, and they will likely not need further antibody delivery in their first year.[4]

It is worth noting that Moderna manufactures a vaccine licensed for adults ages 18 to 59 who are at increased risk of severe RSV. However, Moderna's vaccine has not been approved for administration in pregnant women.[4]

Side effects of Abrysvo in pregnant women include discomfort at the injection site, headache, muscle pain and nausea. While serious adverse events balanced between vaccinated and placebo groups in clinical trials, the vaccine group saw a slight, not statistically significant, rise in preterm births and pre-eclampsia. Because of these potential risks, FDA has only approved Pfizer's Abrysvo no sooner than 32 weeks. CDC and FDA continue to monitor safety to ensure the benefits

of vaccination outweigh risks and will update any safety information accordingly.[4]

## Adult RSV Vaccines

Three vaccines are FDA-approved to protect adults from severe RSV infections.

Pfizer's Abrysvo may be used in adults aged 18 to 59 who are at risk of severe forms of RSV and in older adults over age 60.

GSK's Arexvy was approved in 2023 for those aged 50 to 59 who are at an increased risk of RSV and for adults over the age of 60.

Moderna's mResvia was approved in 2024 for adults 60 years of age and older. In 2025, FDA also licensed mResvia for adults age 18 to 59 who are at severe risk of RSV infections. Neither Abrysvo, Arexvy nor mResvia has been approved for use in infants or young children, and only Abrysvo is approved for use in pregnant women.[4]

Common side effects for each of the RSV vaccines in non-pregnant adults include pain at the administration site, headaches, muscle pain and fatigue. Individuals receiving Pfizer's Abrysvo may also experience nausea.[4]

The risk of severe vaccine reactions such as Guillain-Barré syndrome (GBS) increases as one ages. At an October 2024 Advisory Committee on Immunization Practices meeting, FDA presented updated post-licensure safety monitoring data for GSK and Pfizer vaccines focusing on confirmed GBS cases. Moderna's vaccine, with less time on the market, does not yet have post-licensure safety data available.

The data showed a small number of patients 60 years and older who received GSK's Arexvy and Pfizer's Abrysvo vaccines developed serious neurological conditions such as GBS (the results were statistically significant for the GSK vaccine but not statistically significant for the Pfizer vaccine), and FDA estimated the risk of GBS to be on the order of 10 excess cases per one million vaccinated adults 60 or older. Ongoing monitoring of all vaccines continues, and any necessary safety data will be udpated accordingly.[4]

## The Pink Book: Immunization Strategies for Healthcare Practices and Providers

CDC recommends healthcare providers develop an immunization quality improvement plan that increases vaccine uptake per guidelines laid out in The National Vaccine Advisory Committee Standards for child and adolescent immunization practices. These quality improvement programs are an excellent way to measure outcomes in improving vaccine coverage and to reduce disparities.

Appointing an immunization coordinator to act as the point person for all things immunization is an effective way to cross-coordinate the immunization needs of patients and the clinic, including proper storage and handling of the products themselves.

Daily reminder lists housed in electronic health records can be set up for each patient who will be seen in the clinic and who is vaccine-eligible. These lists will not only notify medical personnel at each encounter when a vaccine is due or past due, but they enable open and honest conversations so patients can freely ask questions and discuss concerns.

Clinics may also elect to initiate standing orders so that non-physician medical personnel who are trained to deliver vaccines correctly may do so. That training includes screening for contraindications and monitoring for post-vaccination adverse events. If patients agree to be vaccinated, physicians should consider giving the vaccine in the same office visit, then record the shot in the state's Immunization Information Systems database so an accurate and up-to-date record is available for all the patients' providers.

Participation in the Vaccines for Children (VFC) program reduces the financial burden of vaccine administration for low-income patients. It also reduces upfront costs, since vaccines delivered under the VFC program are not charged to the clinic.

## Achieving Vaccination Goals

Effective two-way patient communication is the clearest, best path to achieving vaccination goals. Medical personnel should be ready to discuss tailored reasons the RSV vaccine might be right for patients, and address patient questions and concerns. Medical personnel must document patients' decisions should they not wish to be vaccinated, and the reason for which may be optionally recorded in their records.

Even if patients decline, decisions may change over time along with their medical needs. Each appointment is an opportunity to educate and inform so patients understand the importance of vaccines.

RSV season is nearly here. Will your patients be ready? ❖

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**AMY SCANLIN,** MS, is a freelance writer and editor specializing in medical and fitness topics.

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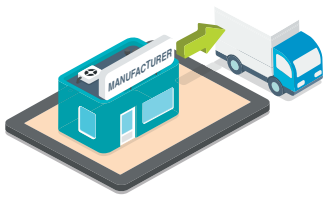


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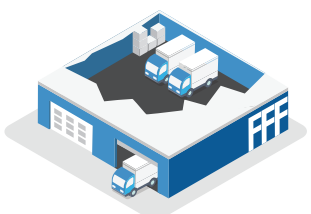

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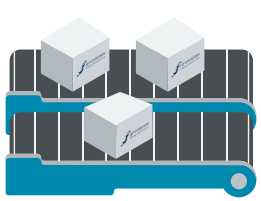

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In compliance with U.S. Drug Supply Chain Security Act (DSCSA) requirements, every product shipped from FFF is accompanied by a packing slip that includes information regarding the manufacturer and presentation, as well as the three T's: Transaction Information, Transaction History, and Transaction Statement.

## 8 TRACKING

To meet DSCSA requirements, FFF provides product traceability information on all packing slips. In addition, Lot-Track® electronically captures and permanently stores each product lot number, matched to customer information, for every vial of drug we supply.

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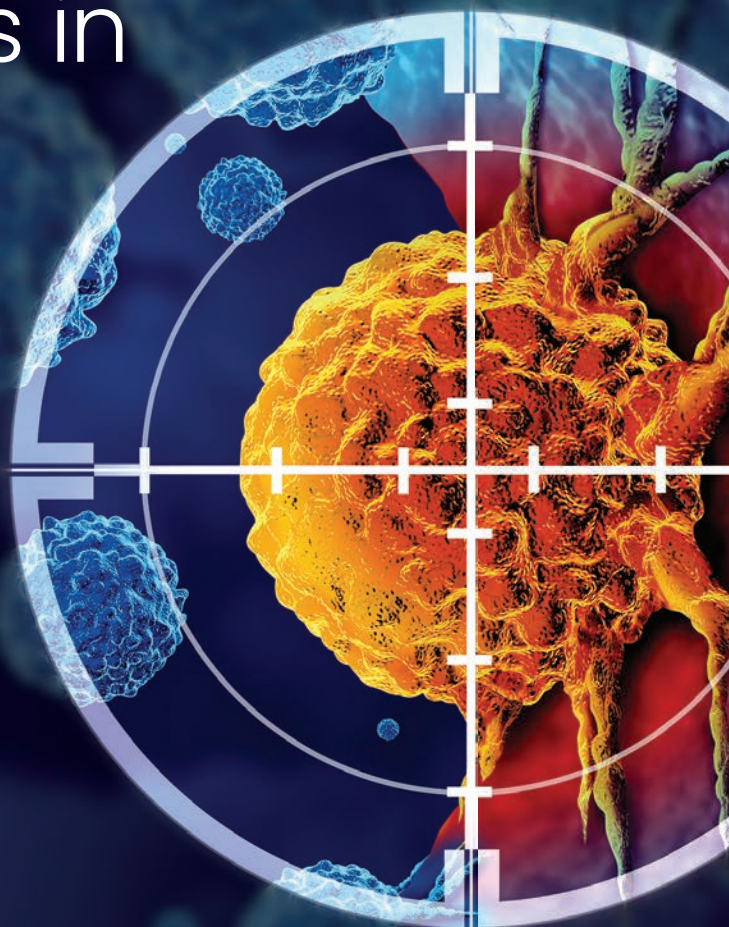
# Advancements in Cancer Vaccines

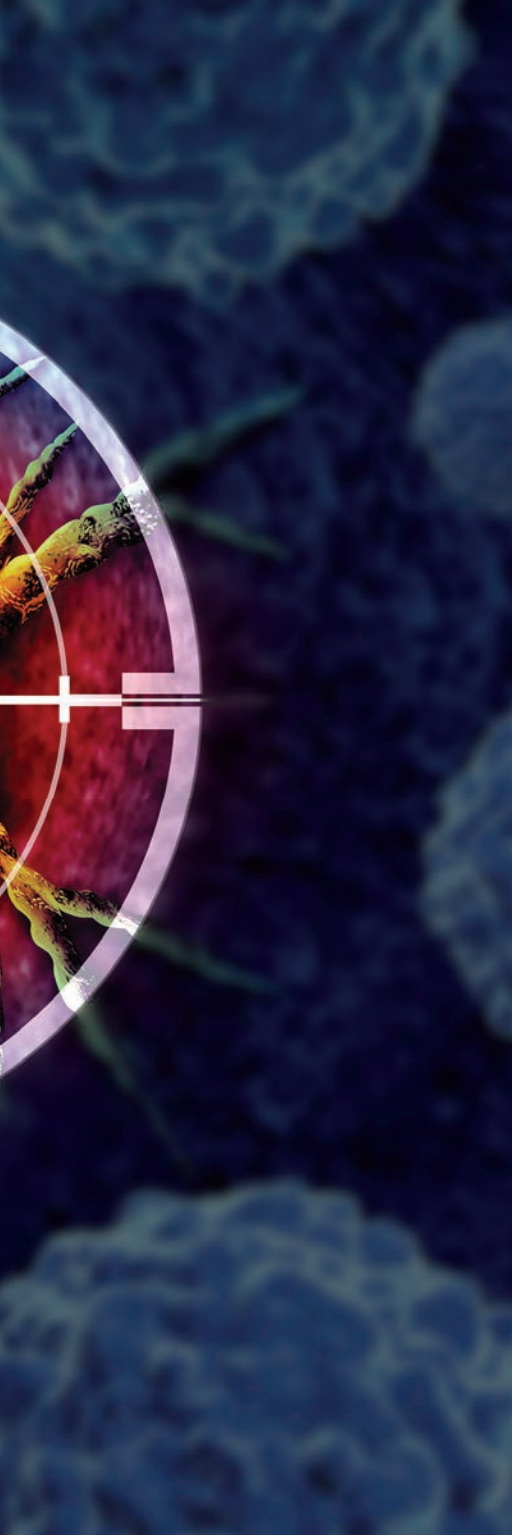
Emerging innovations are transforming cancer vaccines, positioning them as a promising pillar of future therapies capable of more precise and personalized treatment.

By Trudie Mitschang



**CANCER IMMUNOTHERAPY** has transformed the treatment landscape for many malignancies over the past two decades. Therapies that harness the immune system, including checkpoint inhibitors, monoclonal antibodies and adoptive cellular therapies, have improved survival rates in diseases once considered refractory to treatment. These treatments work by enhancing the body's natural ability to detect and destroy malignant cells, shifting oncology away from approaches that rely on chemotherapy or radiation alone.

Even with these advances, many tumors continue to evade immune detection or develop resistance to immunotherapy. As a result, researchers are increasingly exploring strategies that can more precisely train the immune system to recognize cancer cells as foreign



and mount durable responses against them. Among the most promising of these approaches are cancer vaccines. Cancer vaccines aim to stimulate immune responses against tumor cells by presenting tumor-associated antigens or tumor-specific neoantigens to the immune system. Unlike traditional vaccines designed to prevent infectious diseases, cancer vaccines may be used either prophylactically by preventing infection-related cancers, or therapeutically to treat existing malignancies.[1]

In recent years, advances in genomic sequencing, computational biology and messenger RNA (mRNA) technology have accelerated progress in the field of cancer vaccines. In fact, personalized cancer vaccines designed to target patient-specific tumor mutations are now entering late-stage clinical trials, with early results suggesting meaningful improvements in recurrence-free survival when used alongside immune checkpoint inhibitors.[2]

"Current immunotherapies successfully treat 20 percent of the deadliest cancers by unleashing the power of cancer-killing T cells," said Elizabeth Jaffee, MD, deputy director of the Johns Hopkins Kimmel Cancer Center. "Vaccines have the potential to increase the success of these immunotherapies in the other 80 percent of deadly cancers by creating cancer-killing T cells. The last decade of scientific discoveries has propelled vaccines toward becoming the next generation of successful immunotherapies for cancer treatment and prevention."[3]

## Understanding the Mechanisms of Cancer Vaccines

Cancer vaccines are broadly categorized into two groups: preventive vaccines that reduce cancer risk, and therapeutic vaccines that are designed to treat established disease.

Preventive cancer vaccines represent one of the most successful applications of immunization in oncology. These vaccines target infectious pathogens known to drive malignant transformation, thereby reducing the incidence of virus-associated cancers. The most widely utilized example is the human papillomavirus (HPV) vaccine, which protects against viral strains responsible for the majority of cervical cancers, as well as a substantial proportion of anal, oropharyngeal, penile and other anogenital malignancies.[4] Widespread HPV vaccination programs have led to marked reductions in infection rates and precancerous cervical lesions among vaccinated populations. In fact, population-level studies demonstrate that countries with high HPV vaccine uptake have observed reductions of up to 90 percent in HPV infections among vaccinated individuals.[5] These findings underscore the substantial potential of vaccination programs to prevent cancer before it develops.

Therapeutic cancer vaccines are designed to treat established malignancies by stimulating immune responses against tumor-associated antigens or neoantigens expressed by cancer cells. In contrast to preventive vaccines, which aim to avert disease onset, these approaches seek to mobilize the immune system to recognize and eliminate existing tumors. One of the earliest and most well-characterized examples is sipuleucel-T, a dendritic cell-based immunotherapy approved for the treatment of metastatic castration-resistant prostate cancer.[1] In this treatment approach, peripheral blood mononuclear cells are collected from the patient via leukapheresis and exposed to a fusion protein containing a prostate tumor antigen. The activated antigen-presenting cells are then reinfused, where they stimulate a T-cell-mediated immune response directed against prostate cancer cells.

Clinical trials demonstrated that sipuleucel-T improved overall survival by approximately four months compared with placebo in men with advanced prostate cancer.[6] Although the survival

rate benefit was modest, these findings provided important proof-of-concept that therapeutic cancer vaccines can yield clinically positive outcomes.

**In recent years, advances in genomic sequencing, computational biology and messenger RNA (mRNA) technology have accelerated progress in the field of cancer vaccines.**

Together, these cancer vaccine approaches illustrate how immunization strategies can be adapted to different points along the disease continuum, from risk reduction to active disease management. Ongoing advances in antigen selection, vaccine platforms and immune modulation continue to refine their effectiveness and expand their potential clinical applications.

## mRNA Vaccines and the Future of Precision Oncology

mRNA technology has emerged as a leading platform for next-generation cancer vaccines. Rather than delivering tumor antigens directly, mRNA vaccines encode genetic instructions that prompt host cells to produce tumor antigens internally, triggering immune activation. One of the key advantages is that mRNA vaccines can be rapidly designed, manufactured and modified to encode multiple tumor antigens simultaneously. The success of mRNA vaccine platforms during the COVID-19 pandemic demonstrated their scalability and safety in large populations.

One of the most advanced programs involving a personalized neoantigen vaccine is the mRNA-4157/V940, a novel mRNA-based personalized cancer vaccine that encodes up to 34 patient-specific tumor neoantigens. In addition to encoding the target antigens, mRNA vaccines also provide adjuvant properties that amplify the immune response. A randomized KEYNOTE-942 trial assessed the efficacy of the vaccine in prolonging recurrence-free survival (RFS) in patients with resected, stages IIIB/IIIC/IIID and IV melanoma, when given in combination with pembrolizumab, the standard-of-care adjuvant therapy in this patient population. Patients were randomly assigned to receive mRNA-4157/V940 in combination with pembrolizumab or pembrolizumab alone. The vaccine was administered every three weeks for a total of nine doses, and pembrolizumab was given every three weeks for up to 18 cycles. According to the 18-month primary trial analysis, there was a 44 percent reduction in the risk of recurrence or death in patients who received both mRNA-4157/V940 and pembrolizumab, compared to those who only received pembrolizumab.[2]

"For many patients with stage III/IV melanoma, there is a significant risk of recurrence following surgery. As such, demonstrating the longer-term potential of intismeran autogene and pembrolizumab to reduce the risk of recurrence for certain patients with melanoma is a meaningful milestone," said Marjorie Green, MD, senior vice president and head of oncology, global clinical development, Merck Research Laboratories.[7]

These results represent some of the first randomized clinical evidence supporting the use of personalized mRNA cancer vaccines in oncology and have prompted additional Phase III trials evaluating the approach in melanoma and other malignancies.

## Emerging Non-mRNA Cancer Vaccine Platforms

Neoantigen vaccines have emerged as a central component of precision oncology. Leveraging next-generation sequencing technologies, researchers can identify somatic mutations unique to an individual patient's tumor. The data is then analyzed using computational algorithms to predict which mutated proteins are most likely to elicit a strong and clinically meaningful immune response. Once prioritized, these neoantigens are incorporated into personalized vaccine constructs encoding tumor-specific sequences. Upon administration, the vaccine induces T-cell responses directed against cancer cells expressing these mutations, enabling highly targeted immune-mediated tumor destruction.[8]

This approach addresses several limitations associated with earlier vaccine strategies. Because neoantigens are not expressed in normal tissues, they represent highly specific immune targets, thereby minimizing the risk of off-target toxicity while enhancing antitumor specificity. Clinical investigation of neoantigen-based vaccines is rapidly expanding across a range of malignancies, including melanoma, lung cancer, pancreatic cancer and renal cell carcinoma. Early-phase studies have demonstrated the ability of these vaccines to generate robust, polyclonal T-cell responses capable of recognizing multiple tumor-specific mutations simultaneously, supporting their potential as a versatile and adaptable therapeutic platform.

In parallel, dendritic cell-based vaccines represent another important non-mRNA cancer treatment strategy. Dendritic cells are central to immune activation, functioning as professional antigen-presenting cells that initiate and regulate T-cell responses. Therapeutic approaches in this category involve isolating dendritic cells from the patient, loading them ex vivo with tumor-associated antigens and reinfusing them to stimulate a targeted immune response. While sipuleucel-T remains the most established example of a dendritic cell vaccine, similar platforms are under active investigation in glioblastoma (brain cancer), melanoma and other solid tumors.[9] Across numerous clinical trials in glioblastoma, dendritic cell vaccines have shown encouraging potential to extend patient survival. These results suggest that personalized, dendritic cell-based approaches may help overcome the highly immunosuppressive tumor microenvironment characteristic of brain tumors.[10]

Promising as they are, dendritic cell-based therapies face hurdles in broader implementation due to the complexity of individualized cell collection and processing. Researchers are therefore focused on streamlining production, improving scalability and reducing costs to make these therapies more widely accessible.

## Assessing the Role of AI

Personalized cancer vaccines are designed to train patients' immune systems to target their unique tumors. Developing them requires fine-tuning at every stage — from selecting neoantigens to engineering mRNA sequences and designing delivery systems. Artificial intelligence (AI) is now accelerating each step, making vaccines both faster to develop and more effective.

Deep learning models, including convolutional and recurrent neural networks and transformers, can predict how peptides bind to MHC molecules and how T cells will recognize them. Generative models optimize genetic sequences, while multitask frameworks integrate complex biological data to improve neoantigen selection and vaccine yield. Early results suggest these approaches outperform traditional methods, identifying targets more accurately and efficiently.

AI also enables truly personalized formulations. By analyzing a patient's genomic, proteomic and immunological profile, models can predict which delivery strategies and adjuvant combinations will work best. For instance, patients with high inflammation might benefit from gentler formulations, while those with immunosuppressive tumors may require stronger adjuvants. This patient-specific tailoring helps ensure vaccines elicit the strongest possible immune response, overcoming challenges that have long limited cancer vaccine effectiveness.[11]

## Addressing the Challenges Ahead

Cancer vaccines still face significant hurdles before becoming standard in clinical care. Biological challenges include tumor immune evasion and heterogeneity, which can limit how effectively a vaccine stimulates an antitumor response. Technical obstacles arise from the complexity of designing, manufacturing and delivering highly personalized therapies in a timely and cost-effective manner. Regulatory considerations also remain a moving target, as traditional frameworks must adapt to accommodate vaccines tailored to individual patients while maintaining rigorous standards for safety, quality and efficacy.[12]

Despite these challenges, progress is accelerating. Advances in mRNA platforms, genomic sequencing and tumor immunology — supported by AI-driven insights — are enabling highly personalized vaccines that can target patient-specific mutations with remarkable precision. The future likely involves combining vaccines with checkpoint inhibitors, targeted therapies and other immunomodulators to boost efficacy and overcome tumor resistance.

As these strategies are refined and validated in larger trials, cancer vaccines have the potential to transform oncology, making treatment more precise, durable and tailored to each patient. ❖

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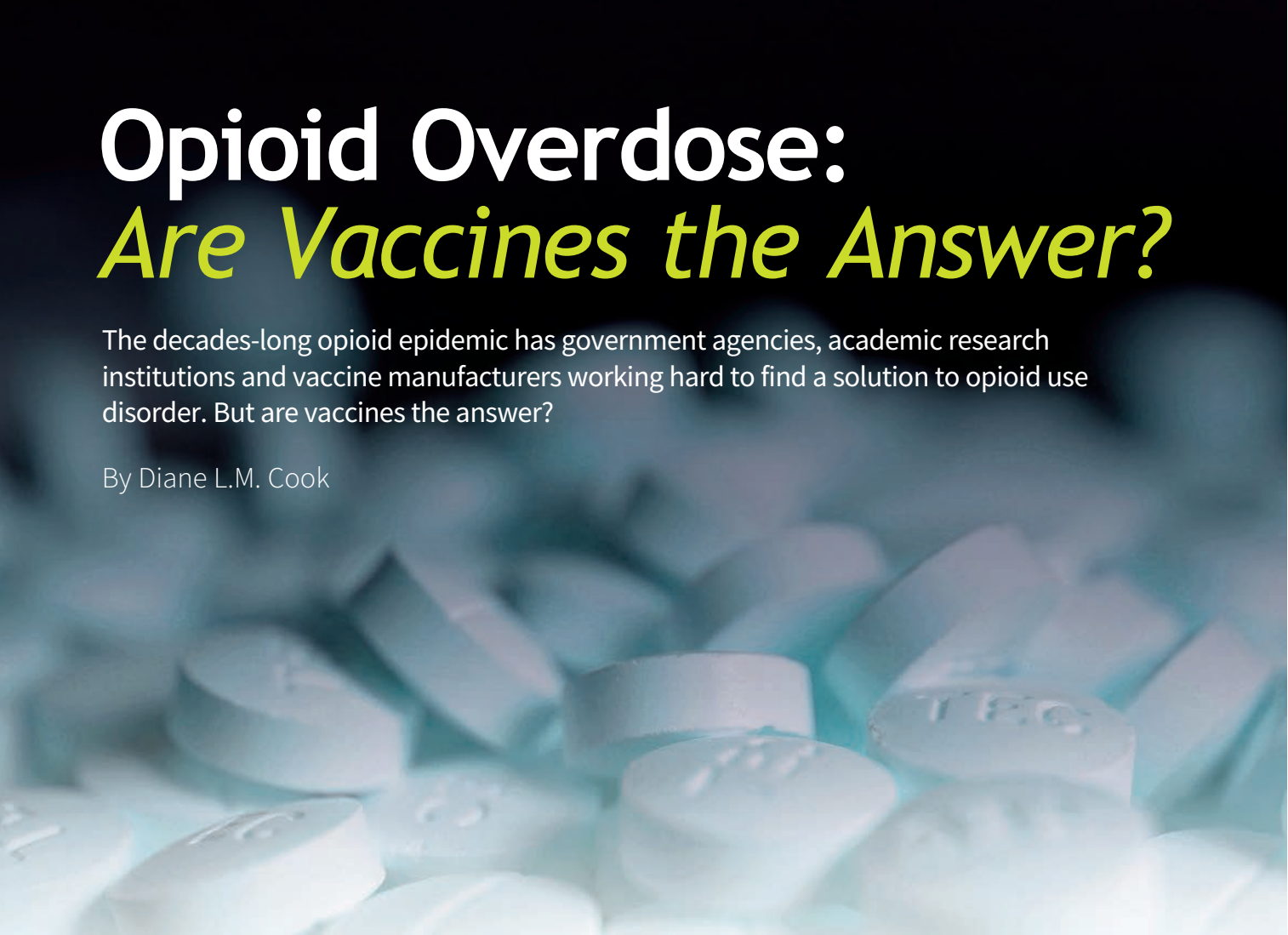
# Opioid Overdose: *Are Vaccines the Answer?*

The decades-long opioid epidemic has government agencies, academic research institutions and vaccine manufacturers working hard to find a solution to opioid use disorder. But are vaccines the answer?

By Diane L.M. Cook



**SINCE THE 1990S**, when the first wave of opioid overdose deaths began with an increase in prescribing opioids, the number of people with opioid use disorder (OUD) has increased at an alarming rate. The Centers for Disease Control and Prevention (CDC) reported that 806,000 lives were lost to opioid overdoses between 1999 and 2023 from prescription and non-prescription opioids.[1]

Based on this shockingly high number of opioid overdose deaths, CDC and the U.S. Food and Drug Administration (FDA) recently launched a number of initiatives that aim to prevent, as well as treat, persons with OUD and help reduce the number of opioid overdose deaths.

## Opioid Overdose Prevention

In May 2024, FDA launched Prescribe with Confidence, an educational campaign designed to provide primary care providers with resources, education and support when prescribing medication to treat patients with OUD. The goal is to increase the number of primary care providers who can recognize OUD and prescribe medication to treat it by helping them understand how to diagnose OUD and work with their patients to design an individualized treatment plan.[2]

FDA's Overdose Prevention Framework, announced in 2021, contains four priorities: 1) support primary prevention by eliminating unnecessary initial prescription drug exposure and inappropriate prolonged prescribing; 2) encourage harm reduction through innovation and education; 3) advance development of evidence-based treatments for substance use disorders; and 4) protect the public from unapproved, diverted or counterfeit drugs presenting overdose risks.[3]

In 2023, CDC announced its Overdose Data to Action (OD2A), a cooperative agreement that provides funding to 90 health departments under state and local programs to reduce drug overdoses: "This cooperative agreement supports jurisdictions in implementing prevention activities and in collecting accurate, comprehensive and timely data on nonfatal and fatal overdoses and in using those data to enhance programmatic and surveillance efforts. OD2A focuses on understanding and tracking the complex and changing nature of the drug overdose crisis by seamlessly integrating data and prevention strategies."

CDC also supports the Drug-Free Communities (DFC) program: "The DFC program has been a central component of our nation's youth substance use prevention strategy, and it provides funding and support to community coalitions to prevent and

reduce youth substance use."[4]

However, even after FDA approved three opioid medications for medication-assisted treatment (buprenorphine, methadone and naltrexone) for OUD and two overdose reversal medications (naloxone and nalmefene) to reverse active overdoses, opioid overdose deaths still average in the tens of thousands of deaths per year.

And, although CDC reported opioid overdose deaths decreased almost 27 percent in 2024,[5] the consensus among the population and in the medical community is that something more needs to be done to continue to dramatically reduce the number of opioid overdose deaths.

Therefore, in 2024, Elissa Weitzman, ScD, MSc, director of research for Boston Children's Hospital's Division of Addiction Medicine, conducted an interview study to explore the acceptability of a fentanyl vaccine to prevent opioid overdose deaths. The study showed many participants, including parents who had lost their children to overdose and adolescents at risk for overdose, were enthusiastic about a potential fentanyl vaccine. However, based on the interviews, Dr. Weitzman said, "One size is not going to fit all."[6]

## How Opioids and Opioid Vaccines Work

According to the Government Accountability Office's (GAO) spotlight on opioid vaccines, the vaccines are designed to block opioids, specifically fentanyl and heroin, from crossing the blood-brain-barrier (BBB), thereby preventing addiction and other negative effects.

Specifically, opioid vaccines are designed to trigger an immune response to chemical structures in opioid molecules. Opioid-specific antibodies stick to opioid molecules in the bloodstream, forming a unit that is too large to enter the central nervous system. By not crossing the BBB, the opioid molecule is not able to cause addiction or overdose death and is eventually excreted from the body.

"Opioid vaccines could offer advantages over current treatment options," said GAO. "[They] could be useful for at-risk individuals, patients in drug recovery programs and first responders who might accidentally come into contact with deadly opioids that can be absorbed through the skin."[7]

## Academic Research Institutions and Vaccine Manufacturers

For the past decade, several academic research institutions and vaccine manufacturers have partnered to develop an opioid vaccine. Yet, because adjuvants in opioid vaccines bind an opioid and select analogs in circulation, adjuvants are needed to increase the quantity and quality of the anti-drug antibody response in people with opioid addictions. As such, adjuvants, haptens, conjugates and delivery systems will need to be carefully evaluated in clinical trials.

**The Centers for Disease Control and Prevention reported that 806,000 lives were lost to opioid overdoses between 1999 and 2023 from prescription and non-prescription opioids.**

*University of Houston/ARMR Sciences, Inc.* The University of Houston (UH), in collaboration with Tulane University School of Medicine (that developed the adjuvant), is conducting research for a potential fentanyl vaccine candidate. Having been funded by the Department of Defense since 2016, preclinical studies have been completed, and clinical trials are currently underway.

Colin N. Haile, MD, PhD, research associate professor in the Gibson Addiction Research Laboratory at UH, said, "The adjuvant in this vaccine is a genetically modified non-infectious enterotoxin derived from *Escherichia coli* and cholera toxin, named dmLT. This adjuvant has been in 15 human clinical trials in combination with other vaccines, one of which was conducted in infants, with minimal to no side effects across studies. As well, this vaccine uses the carrier protein CRM197, which is currently in vaccines on the market."

In 2021, the results of a study to evaluate adjuvant and delivery strategies for conjugate antigen vaccination with fentanyl-based haptens showed "that dmLT or LTA1 adjuvant, as well as mucosal delivery, may be attractive strategies for improving the efficacy of vaccines against SUD [substance use disorder]."[8]

Although the oral version of this vaccine is still in development, Dr. Haile said, "The results of our 2021 study showed that the oral and intranasal formulations of our vaccine were more efficacious than administering the vaccine intramuscular."

According to the results of a preclinical study conducted in 2022, the "anti-FEN (fentanyl) vaccine conjugate in combination with the adjuvant dmLT produced significant amounts of anti-FEN antibodies that were associated

with complete blockade of FEN-induced analgesia in the tail flick and hotplate tests, rate-disrupting effects on schedule-controlled responding, and physiological effects. … Vaccination also significantly reduced FEN entry into the brain, and anti-FEN antibodies targeted FEN with no cross-reactions to other opioids."[9]

According to Dr. Haile, the results of the efficacy study of this vaccine in rodents were also successful: "This vaccine did not cause any adverse side effects in the immunized rats in the preclinical trial. The results also showed the vaccine blocked 92 to 98 percent of fentanyl from entering the animal's brain, and protection lasted 20 weeks, which might translate to up to a year of protection in humans.

**For the past decade, several academic research institutions and vaccine manufacturers have partnered to develop an opioid vaccine.**

"We have now tested our anti-fentanyl vaccine in hundreds, maybe thousands, of rodents in many different analgesic and behavioral paradigms. We recently finished experiments where we combined the vaccine with methadone and naltrexone, and it showed 100 percent blockage of fentanyl-induced analgesia and decreases in $O_2$ saturation and heart rate in our overdose model. We also showed the vaccine blocks fentanyl-induced reinstatement of drug-seeking behavior in animals self-administering fentanyl."

The results of the toxicology testing that were conducted in April 2025 were also successful, said Dr. Haile: "The results of the toxicology testing were excellent. We administered 20 times the dose we're going to administer to humans with no toxicity or adverse effects."

ARMR Sciences, Inc. (formerly Ovax Inc.), a biodefense company that develops preventive countermeasures to protect against bioweapons, has partnered with UH to develop this fentanyl vaccine candidate. Named ARMR100, the vaccine is in development for military and first responders with potential application for OUD patients.

Collin Gage, founder and CEO of ARMR, said, "ARMR's Phase I/II trial is scheduled to begin in the first quarter of 2026 and will enroll approximately 40 healthy adults at the Centre for Human Drug Research in the Netherlands. This will be the first time an anti-fentanyl vaccine has been tested in humans.

"The first part of the trial will evaluate the vaccine's safety and determine the best dosage. Volunteers will receive a series of two administrations in varying doses, and researchers will measure their blood antibody levels. In the second part of the trial, a small group of participants will receive a medical dose of fentanyl so that investigators can study how well the vaccine blocks its effects. We anticipate results of this trial in the first half of 2027."

Although the efficacy of this vaccine is currently unknown, it is anticipated that the two-shot regimen — potentially eventually a single dose — would protect humans for approximately a year, with the possibility of annual booster shots.

*University of Montana (UM)/Inimmune Corp./University of Washington (UW)/ Columbia University.* With $33.4 million in funding from the National Institutes of Health's Helping to End Addiction Long-term initiative, UM, in collaboration with Inimmune Corp., UW and Columbia University, began research in 2020 on a heroin and fentanyl vaccine that would protect persons with OUD and those at risk of accidental overdose.

"It [this funding] will allow us to advance lead opioid vaccine candidates to Phase I human clinical trials and better understand the safety and efficacy of our vaccine adjuvants, which early research has shown will be needed to increase the quantity and quality of the anti-drug antibody response in people with opioid addictions," said Jay Evans, PhD, director of the Center for Translational Medicine at UW.[10]

Inimmune Corp. is a biotechnology company that develops innovative immunotherapeutics, vaccine adjuvants and vaccines. Its lead vaccine candidate uses its own adjuvant INI-4001 in combination with a fentanyl hapten conjugated to a carrier protein, CRM-197. The inclusion of INI-4001 increases critical antibody titers, increasing the likelihood of protection in humans.

"Inimmune is a proud supporter of this groundbreaking, anti-fentanyl vaccine to combat one of the worst human-created epidemics in history," said David Burkhart, PhD, chief executive officer at Inimmune Corp. "This vaccine could save tens of thousands of lives every year and provide relief to families around the world who live in fear of fentanyl overdose of loved ones."

The results of one preclinical study showed that "the addition of the synthetic TLR7/8 [adjuvant] agonist INI-4001 to our lead anti-fentanyl vaccine significantly increased antigen-specific antibody titers, which led to increases in vaccine efficacy after drug challenge in multiple animal species, drug doses and administration paradigms," Dr. Burkhart added.[11]

In addition, he noted that the results of another preclinical study showed "the use of a synthetic TLR7/8 adjuvant, INI-4001, in combination with alum significantly and preferentially increased F1-specific IgG2a antibody titers and significantly increased average polyclonal antibody avidity [the total, accumulated binding strength of a multivalent antibody to a multivalent antigen] for the fentanyl hapten compared to F1-CRM and F1-CRM plus alum."[12]

"GLP toxicology studies have been completed for both the heroin and fentanyl vaccine candidates and are supportive for advancing these vaccine candidates to human clinical trials," said Dr. Evans. "The IND for the heroin vaccine has been submitted to the FDA. All IND enabling studies — efficacy, toxicology and GMP manufacturing — are also complete to support the fentanyl vaccine."

Inimmune and UW have completed the process development and scale-up manufacturing of GMP to produce the volumes and quality of vaccine products necessary for the Phase I clinical trials for both opioid vaccines. Inimmune will manufacture the vaccines for the clinical trials.

UM has also partnered with Marco Pravetoni, PhD, at UW whose research team designs haptens and drug conjugate vaccines that can elicit the production of antibodies against target opioids.

The Phase I clinical trial for the heroin vaccine is in the recruiting stage. This trial is being conducted at Columbia University and will include a drug challenge to evaluate its safety and efficacy. The trial will involve gradual dose escalation, and patients will be followed to evaluate how long the antibodies against the opioid will last.

However, Dr. Evans said, "The Phase I clinical trial for the fentanyl vaccine has been delayed due to recent HHS/NIH budget cuts and administration changes, but the team is hopeful this important vaccine program can secure the necessary funding in 2026 to advance the fentanyl vaccine to Phase I clinical trials."

*Boston Children's Hospital's (BCH) Precision Vaccines Program (PVP).* Based in the Department of Pediatrics at BCH, the PVP is an academic research program developing the next generation of vaccines tailored to vulnerable populations.

BCH-PVP is working in collaboration with UH and Inimmune to develop a fentanyl vaccine. The goals of this five-year project, currently on extension until 2027, are to identify adjuvants that would boost immune responses to the vaccine in this age group and to explore how opioids themselves affect immune responses.

The PVP applies precision medicine principles to vaccinology, thereby optimizing vaccines specific to vulnerable populations. Since 2019, the PVP has received almost $15 million from The Heal Initiative to work on its vaccine, and by the end of contract, will have received approximately $20 million.

Specifically, BCH-PVP is developing a novel adjuvant — PVP-037 — and a novel antigen — Oxeth-2 — that comprise an adjuvanted fentanyl vaccine. This fentanyl vaccine is comprised of a fentanyl hapten, a fentanyl-like molecule linked to CRM protein (CRM-197) and PVP-037 small molecule (TLR7/8 agonist adjuvant). These formulations are being tested in humans in in vitro assays and in rodents. Inimmune will manufacture the vaccine for clinical trials.

Preclinical trials testing different adjuvants in animal models began in 2023 and are expected to be complete in 2026. To date, the results of these studies show the adjuvanted vaccine demonstrates robust induction of antibodies that can block fentanyl's actions in animals. BCH-PVP hopes to publish data from this study soon.

"We believe youth and young adults — whether they have an OUD or not — will benefit from a fentanyl vaccine by reducing the risk of life-threatening overdose, which is currently a leading cause of death in this age group," said Ofer Levy, MD, PhD, director of the PVP-BCH.

*New York State Psychiatric Institute.* The New York State Psychiatric Institute, in partnership with Columbia University and UW, is currently enrolling 45 participants who have an OUD for its first-in-human, multi-site, oxycodone clinical trial. This study will evaluate the safety, degree of antibody production and preliminary efficacy.

Headed by Sandra D. Comer, PhD, professor of clinical neurobiology in the division on SUD and the Department of Psychiatry at Columbia University, the proposed study is designed as a Phase Ia/Ib clinical trial for an oxycodone Oxy(Gly)4-sKLH conjugate vaccine, adsorbed, which has been developed by Dr. Pravetoni and his team.

Healthy adults, aged 18 to 59 years, who meet DSM-5 criteria for OUD but are not seeking treatment for their drug use and are physically dependent on opioids, are being recruited. This study employs a between-groups, placebo-controlled design: two active vaccine doses and one placebo.

The primary completion of the study (last patient-last visit) is estimated to be at the end of 2026 with the full study results estimated to be available at the end of the first quarter in 2027.[14]

*CounterX Therapeutics, Inc.* Founded in 2025, CounterX Therapeutics, Inc., is a biotechnology company that develops high-affinity monoclonal antibody therapies and vaccines to address OUD and opioid overdose. The company is

currently researching two monoclonal antibodies (mAb) and two opioid vaccines.

CTRX-101, a mAb, was designed to bind fentanyl and its potent analogs in the circulation, block distribution to the brain and blunt its life-threatening effects. This mAb is differentiated because it binds directly to fentanyl and sequesters it in the bloodstream and does not interact with mu-opioid receptors in the brain like other available products that treat OUD.

CTRX-101 is a long-acting, once monthly, subcutaneous injectable therapeutic that is not an opioid or a controlled substance. It has been well-tolerated in preclinical models with no serious adverse events when used in combination with other OUD medications. And, it is not expected to cause opioid withdrawal and may be safe when used in combination with other OUD medications.

involving fentanyl and its analogs.

CounterX is also developing two opioid vaccines: CTRX-1001, a fentanyl vaccine for the prevention of accidental overdose in high-risk patients, and CTRX-2001, a heroin vaccine for OUD. These vaccines have reached IND (heroin vaccine) and a near IND completion (fentanyl vaccine).

In animal models, the vaccines provide protection against either fentanyl or heroin-induced pharmacological effects, including respiratory depression, bradycardia and drug self-administration, a preclinical model of OUD. They have also shown safety in various animal models.

"A fentanyl vaccine or mAb could provide a safety net for those patients diagnosed with an OUD, as well as those accidentally exposed to drug mixtures or counterfeit pills containing lethal doses of fentanyl or other related compounds. A vaccine or a mAb can really save lives,"

**Researchers hope an opioid vaccine might be available within the next three to five years, depending on the results of their clinical trials and FDA approvals.**

"Conducted in a translational preclinical model, the study demonstrates that administration of the CTRX-101 effectively restores normal breathing following fentanyl overdose," a recent study reported.[14] The company anticipates starting a Phase I clinical trial of CTRX-101 in 2026.

CTRX-201 is a next-generation mAb targeting fentanyl and its analogs that displays better safety, broader binding and a prolonged half-life, which will allow dosing every three months, thereby affording long-acting protection against overdose and active treatment of OUDs said Dr. Pravetoni.

CounterX has recently completed a licensing agreement with UM and UW, which secured intellectual property rights related to anti-opioid vaccines, antibodies and the CounterXCL discovery platform. This deal will strengthen the company's position on advancing its lead candidate into clinical trials.

## What the Future Holds for Opioid Vaccines

Opioid vaccines are still in the experimental phase with some vaccines currently in the preclinical to early-stage clinical trial phase. Researchers hope an opioid vaccine might be available within the next three to five years, depending on the results of their clinical trials and FDA approvals. Most trials so far have shown very promising results in animals that an opioid vaccine can significantly reduce fentanyl-driven behaviors and blunt its addictive and lethal effects. However, once opioid vaccines become available on the market, they will still need to be used with current OUD treatments. ❖

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Efforts to save the lives of those who overdose from opioids are forging ahead, but the problem will remain until the flow of opioids laced with fentanyl is stopped.

By Rachel Maier, MS

**THE EUPHORIC**, pain-blocking properties of opioids — a class of drugs made from, or made to mimic, compounds found in opium poppy plants — offer the promise of effective pain relief. At their best, they ease pain; at their worst, they ruin lives.

Opioids are extremely addictive, and it's easy to take too much. Since the late 1990s, some one million people have died due to opioid overdose on American soil, and the number continues to grow.[1] According to a Dec. 16, 2024, U.S. Drug Enforcement Agency (DEA) press release, 69 percent of the more than 107,440 drug-related deaths in 2023 involved fentanyl. DEA estimates more than 200 American lives are lost everyday to fentanyl overdose.[2]

But numbers aren't overdosing on opioids: *People* are. Many of them are routine users of stimulants such as cocaine and methamphetamine who accidentally overdose due to fentanyl that has been added to the drugs to amplify their effects. Others struggle with opioid use disorder (OUD); they are often people with chronic pain who have developed a dependence on their prescription opioid medications and accidentally take more than their body can handle. Still others are people who misuse opioids by taking pills prescribed to someone else. Increasingly, young people are dying after taking just one pill, typically a counterfeit version of a prescription pill such as Percocet or Xanax that was laced with fatal amounts of fentanyl. Even toddlers have become victims by inadvertently ingesting fentanyl.

Americans from every walk of life are falling prey to lethal doses of these dangerous narcotics. "All Americans across the U.S., coast to coast, and every community in between have been harmed by fentanyl," said DEA Administrator Anne Milgram in a statement on National Fentanyl Awareness Day in 2024.[3] They are our coworkers, neighbors, family and friends — people we know and love. In fact, a recent study published in

*JAMA Health Forum* showed more than a third of the U.S. population knows someone who died of a drug overdose. And while the study did not specify the overdose resulted from opioids, we know opioids have been involved in most drug overdoses for the past 20 years.[1]

The opioid epidemic is a complicated crisis, one without an easy off ramp, but a multifaceted, coordinated response effort is underway. Government agencies, nonprofit groups and innovative business solutions are joining forces with an all-hands-on-deck attitude to confront the crisis, support recovery and ultimately save lives.

## Understanding the Problem

The good news: Deaths involving opioid overdose are down. In May 2025, a Centers for Disease Control and Prevention (CDC) news release reported provisional data from CDC's National Center for Health Statistics that indicated deaths involving opioids decreased in 2024, dropping from an estimated 83,140 deaths in 2023 to 54,743 deaths in 2024.[4]

The bad news: Deaths involving opioid overdose remain critically high. According to DEA, illicit fentanyl is driving the disaster. Small doses of this highly potent, powerful opioid are fatal, and the market is monstrously flooded with it. In 2024, DEA seized more than 60 million fentanyl-laced fake pills containing nearly 8,000 pounds of fentanyl powder, representing more than 196 million deadly doses,[5] but there is no accounting for how much more was successfully trafficked into the U.S.

Fentanyl is an FDA-approved synthetic opioid used for pain relief that is 100 times more potent than morphine and 50 times more potent than heroin.[6] When used appropriately and under the supervision of a licensed medical professional, fentanyl has a legitimate medical use. However, illicit fentanyl — fentanyl manufactured outside of the U.S. and then smuggled across the border and sold illegally on American soil — poses a critical risk to the health and safety of its users.

According to DEA's National Drug Threat Assessment of 2024, the Sinaloa and Jalisco drug cartels are at the heart of the crisis. Their global supply chain networks rely on countries such as China to supply precursor chemicals and pill presses the cartels then use to make counterfeit versions of legitimate pills such as OxyContin, Percocet and Xanax.[7] Cartels smuggle the drugs into the U.S. and sell them to unsuspecting people, some wishing to circumvent opioid medication limits, some who want to buy prescriptions at a lower price — and none who suspect what they are buying contains enough fentanyl to kill them. These fake pills are sold on bogus online pharmacies or via a social media black market without a prescription and at lower prices.[7] The situation is exceedingly dangerous: DEA laboratory testing revealed six out of 10 fentanyl-laced fake prescription pills tested in 2022 contain a potentially lethal dose of fentanyl.[8] Cartels also mix deadly amounts of fentanyl into stimulants such as cocaine and methamphetamine to amplify their effects, and then sell them to recreational drug users who are also dying from opioid overdose. The problem is much larger than counterfeit pills.

**The opioid epidemic is a complicated crisis, one without an easy off ramp, but a multifaceted, coordinated response effort is underway.**

According to Scott Fishman, MD, director of the University of California, Davis, Center for Advancing Pain Relief, the opioid crisis didn't emerge overnight; it started nearly 30 years ago, after legal opioids became routinely prescribed when another American health crisis — chronic pain — emerged in the mid-1990s. In 2001, a Joint Commission program set pain as the fifth vital sign; in addition to assessing body temperature, blood pressure, pulse and respiratory rate, clinicians began asking patients to rate their pain on a numeric scale, with one being mild pain and 10 being the worst pain possible.[9]

Clinicians were trained to prescribe pain medication because they were not equipped to understand it or treat it appropriately. "Without this knowledge, and confronted with limited time, as well as mounting pressure for patient satisfaction, limited insurance coverage for non-opioid options, inaccurate data on opioid safety, and influences from drug companies, many clinicians reached for the easiest available treatment: opioids," wrote Scott Fishman, MD, in a 2021 article in *Pain Medicine*.[9] Pain wasn't treated; it was relieved. Between 2006 and 2012, 76 billion oxycodone and hydrocodone pills were dispersed, largely prescribed at high doses for long durations — a practice we now know is high-risk and associated with opioid abuse.[10]

The effort was well-intentioned but counterproductive: Addressing pain with opioids ignited a firestorm of addiction to them — what CDC describes as the

first wave of the opioid crisis. Opioid use disorder (OUD) became prevalent among patients prescribed legal opioid medicines; the powerful painkillers are highly addictive, and even the most controlled use of them often hooks patients and puts them at risk for accidental overdose.

Laws to limit the dosage and duration of opioids physicians could prescribe were passed in 2016; the hope was that restrictions would ameliorate misuse and addiction, and ultimately save lives. The opposite happened. Dependence raged, so patients looked for narcotics elsewhere. Many turned to heroin, an illegal opioid drug made from morphine. We know what happened next: a second wave of the opioid crisis marked by more misuse, addiction and overdose. Once illicit synthetic fentanyl flooded the market, the third wave began and people began unintentionally ingesting lethal amounts of fentanyl they didn't know were there.[11]

**Whereas opioid overdoses typically occur when people knowingly ingest opioids but inadvertently take too much (as in patients who take prescription opioids to control pain), fentanyl poisoning occurs when someone accidentally ingests a lethal amount of fentanyl, usually when they take a counterfeit pill laced with lethal amounts of the powerful narcotic.**

## Fentanyl Poisoning

Whereas opioid overdoses typically occur when people knowingly ingest opioids but inadvertently take too much (as in patients who take prescription opioids to control pain), fentanyl poisoning occurs when someone accidentally ingests a lethal amount of fentanyl, usually when they take a counterfeit pill laced with lethal amounts of the powerful narcotic. Even very small amounts of fentanyl — just two milligrams — can kill. According to DEA, fentanyl is the deadliest drug threat facing the U.S.[8]

And it's no wonder: Fentanyl is showing up in places people do not expect to find it.

But counterfeit versions of legal prescription medications are increasingly easy to get via the dark web and social media, where pills are inexpensive and unregulated. People suffering from chronic pain or OUD use these online outlets for easy access to legal medications such as Vicodin, OxyContin and Percocet, and many high school and college students seek out "study drugs," stimulants such as Adderall or Ritalin, believing they will help improve academic performance,[12] or benzodiazepines such as Xanax or Valium, thinking they will help them deal with anxiety.[13]

Pills obtained through illegitimate sources are often counterfeit and usually contain fentanyl. The fake pills might contain the same active ingredient as the real thing, but they might not; and if they do, it may be in different quantities. There is no quality control and no guarantee the drugs are safe. In fact, while fentanyl can be detected in them, there is no way to determine whether it is a lethal amount.[14] All it takes is one pill containing too much fentanyl to kill.

According to Get Smart About Drugs, a DEA resource for parents, educators and caregivers, fentanyl overdose is the leading cause of death for Americans age 18 to 45.[15] And, according to a 2024 UCLA Health article, an average of 22 adolescents ages 14 to 18 died each week in 2022 from drug overdoses.[16]

Even younger children are at risk of fentanyl poisoning when drug paraphernalia or everyday objects contaminated with opioids are within reach.

A 2-year-old boy in Grass Valley, Calif., who got his hands on drug paraphernalia in his own home was hospitalized for a suspected fentanyl overdose. According to a Nevada County Sheriff's office (NCSO) media release, emergency services received a distraught phone call on Dec. 10, 2024, reporting the toddler was overdosing on fentanyl. Emergency personnel found the child unresponsive and not breathing; they gave him multiple doses of naloxone, which revived him. Notably, NCSO officials found narcotics and drug paraphernalia in plain view at the toddler's home, some of which appeared to be fentanyl and methamphetamine along with pipes and syringes. "It should be noted many of these items could be easily accessed by a child and some were found on the floor," an agency spokesman said.[17]

A 1-year-old boy died on May 22, 2024, after ingesting a lethal amount of fentanyl. He was found unresponsive at Melville J. Courson Park and tragically never woke up.[18] Yet another 1-year-old child suffered a fentanyl poisoning at a park in New Britain, Conn., on July 14,

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2024. The boy had picked up a piece of plastic contaminated with opioids; he was revived and lived. Assistant Child Advocate Brendan Burke issued a stark warning: This could happen to any child, any time. "It could be any park, any public space, it could be anywhere because people are using drugs everywhere," Burke said. "Any time a child has access to that kind of paraphernalia and puts it in their mouth, it's a life-threatening event."[19]

## Action and Awareness

Addressing the opioid crisis remains a work in progress. The problem is too big for any one agency to tackle on its own, but federal and state government agencies, public health associations and community-based organizations are taking action to protect the American people, prosecute drug dealers and provide rescue and recovery support. With so many initiatives at the federal and state level, as well as in the private sector, it is impossible to list them all here. However, the response comes down to five major goals:

- *Stop the flow of fentanyl*. One aim is to cut fentanyl off at the source and prevent it from entering the nation. It's a big job, but U.S. Customs and Border Protection (CBP), an agency of the Department of Homeland Security, intercepts and seizes illegal drugs at the border every day. For example, CBP officers at the San Ysidro Port of Entry discovered and seized more than 25 pounds of fentanyl powder and nearly 60 pounds of cocaine when they searched the truck of a 59-year-old man seeking entry to the U.S. from Mexico on Nov. 19, 2024. "San Ysidro officers continue to exhibit unparalleled vigilance and expertise in successfully detecting narcotics that were meticulously concealed in non-factory metal compartments within the vehicle," said Mariza Marin, port director of the San Ysidro Port of Entry. "This incident showcases our dedication to protect our nation and communities from dangerous drugs and organizations intending to cause harm."[20]
- *Disrupt criminal drug networks and bring dealers to justice.* DEA, an agency of the U.S. Department of Justice, targets global criminal networks responsible for the flow of fentanyl into the U.S., with the ultimate objective of destroying the entire criminal enterprise.[21] DEA works with law enforcement at home and abroad to track down drug distributors and bring them to justice. "It's in everyone's best interest to make sure we not only cut off the source, but also arrest as many as we can up the supply chain leadership," said Assistant Special Agent in Charge Colin Dickey, lead of DEA enforcement operations in eastern Missouri.[21]

Lengthy, in-depth investigations into overdose deaths involving fentanyl link distributors to victims. Current federal drug statutes stipulate a 20-year mandatory minimum if death or serious bodily injury results from the use of the drugs, but there is an increasing push for harsher sentences.[22] "These are not overdoses. These are murders," Orange County District Attorney Todd Spitzer emphasized. "These dealers are essentially handing a loaded gun to unsuspecting victims knowing that they will probably die, and they don't care."[23]

The Felony Murder for Deadly Fentanyl Distribution Act of 2023 was introduced to Congress on Feb. 9, 2023; it would make the distribution of fentanyl resulting in death a first-degree murder.[24] As of this writing, the bill has been referred to the Committee on the Judiciary, but has not been passed. However, the HALT Fentanyl Act was signed into law by President Donald J. Trump on July 16, 2025. The bill permanently classifies fentanyl-related substances as Schedule I drugs under the Controlled Substances Act; schedule I drugs are substances with a high potential for abuse and indicates potential risks and harm associated with their use. According to President Trump, the legislation is "delivering another defeat for the savage drug smugglers and criminals and the cartels."[25]

- *Raising public awareness.* DEA issues ongoing public safety alerts warning Americans that counterfeit drugs are not safe or smart. It also launched the One Pill Can Kill campaign, which speaks out about the dangers of purchasing pills on social media and the deceptive marketing practices of drug cartels that pass off counterfeit pills as legitimate prescriptions.[26] The campaign provides social media graphics, images, sample posts, hashtags such as #onepillcankill and informative resources to educate parents and kids.

At the state level, governors have taken

**At the state level, governors have taken emergency action to combat the crisis and created similar campaigns to inform citizens about the dangers of fentanyl, and the first spouses have been instrumental in raising awareness.**

emergency action to combat the crisis and created similar campaigns to inform citizens about the dangers of fentanyl, and the first spouses have been instrumental in raising awareness. Led by Virginia First Lady Suzanne Youngkin and New Jersey First Lady Tammy Murphy, the first spouses have worked with the National Governors Association to arrange a briefing for state governors' staff members and the first spouses to hear from some of the nation's leading experts about national campaigns addressing the opioid epidemic, including the Ad Council, a non-profit organization that launched the Youth Fentanyl Awareness campaign. The first spouses were instrumental in establishing Aug. 21 as National Fentanyl Prevention and Awareness Day and Aug. 31 as International Overdose Awareness Day. "We hope to ensure that every family has the resources and information needed to protect their children from this deadly threat," said Youngkin.[27]

• *Improving OUD resources and support.* The Substance Abuse and Mental Health Services Administration (SAMHSA), a part of the U.S. Department of Health and Human Services (HHS), provides resources and practical support for people struggling with opioid addiction and OUD. SAMHSA awarded $8.1 billion in State Opioid Response grants and $307.5 million in Tribal Opioid Response grants to help fund state and tribal prevention, harm reduction, treatment and recovery support services for OUD and other concurrent substance use disorders.[28] SAMHSA also runs the National Helpline (1-800-662-HELP) and launched FindTreatment.gov, a confidential and anonymous resource that helps people seeking treatment for substance use disorders find health facilities, healthcare centers, practitioners who prescribe buprenorphine (a medication often prescribed to those in


OUD recovery) and opioid treatment providers, along with information about payment assistance.

• *Increasing access to naloxone.* Naloxone (generic for Narcan) is a medicine approved by FDA that quickly reverses an opioid overdose. Getting it into the hands of those who are at the highest risk of opioid overdose remains a challenge due to cost and stigma. In 2023, FDA approved the first over-the-counter (OTC) naloxone nasal spray,[29] OTC Narcan Nasal Spray, which is now available at pharmacies nationwide for less than $50.[28] Some naloxone products still require a prescription. FDA continues to recommend anyone taking opioid medication, knows someone taking opioid medication, taking medications to treat OUD, people who are at higher risk of opioid overdose due to recreational drug use or use of benzodiazepines and caregivers of people at risk for opioid overdose to carry naloxone. "We want naloxone in the hands of friends, family members and caregivers of people taking opioids," said Marta Sokolowska, PhD, FDA deputy center director for substance use and behavioral health.[30] To help reach that goal, most states have "standing orders" that allows other formulations of naloxone to be obtained without a prescription directly from pharmacists. Non-profit groups such as Harbor Path and NEXT Distro are also working to provide naloxone to high-risk individuals for free.

Naloxone is accessible — but getting people to use it remains a hurdle. Overdose education and naloxone distribution (OEND) programs help: They train people on how to recognize an overdose, administer naloxone and make naloxone available in communities. But OEND programs target bystanders, not people who use opioids, and programs vary from state to state.

## A Rapid Response Is Essential

Despite all the efforts to warn the public about the dangers of fentanyl and cut fentanyl off at the source, opioid overdose and fentanyl poisoning still happens, and fast intervention is necessary to save lives.

Opioids affect the part of the brain that regulates breathing; during an overdose event, breathing slows and can even stop. Naloxone is the best shot for survival when someone overdoses. This lifesaving medicine is an opioid antagonist: It attaches to opioid receptors, reverses and blocks the effect of opioids and quickly restores regular breathing.[31] Effects last 30 to 40 minutes, so multiple doses may be necessary.

Co-prescribing naloxone with prescription opioid medications remains an ongoing strategy to preemptively place naloxone where it may be needed before it is needed. Many stakeholders support co-prescribing naloxone, including CDC and SAMHSA, state departments of health, the World Health Organization and many advocacy groups such as the American Medical Association (AMA). "If it were not for naloxone, it is likely that many thousands more would be dead from an opioid-related overdose," said Patrice A. Harris, MD, chair of the AMA Opioid Task Force. "We know

that naloxone — by itself — will not reverse the nation's opioid epidemic, but it is a critical component that saves lives and provides a second chance."[32] The AMA Opioid Task Force encourages physicians to co-prescribe naloxone when clinically appropriate and advises them to consider whether the patient has a history of taking high doses of opioids or a concomitant benzodiazepine; has a history of substance use disorder; has an underlying mental health condition; has a medical condition such as respiratory disease that may make him or her more susceptible to opioid overdose; or is in a position to help someone else at risk for an opioid overdose.[33]

According to CDC, someone else was nearby in more than 40 percent of overdose deaths: "Having naloxone available allows bystanders to help a fatal overdose and save lives."[34] A study published in *Drug and Alcohol Dependence Reports* also showed that when naloxone is put in the hands of the community, they will use it. Expanding access and availability of naloxone in communities is among the most impactful interventions in decreasing opioid overdose deaths, but state distribution rates of naloxone do not meet community need.[34] A 2021 modeling study that set a saturation benchmark of naloxone available at 80 percent of witnessed overdoses found nearly every state in the U.S. was undersaturated with naloxone.[35]

## Reduce Stigma, Save Lives

Rooting out the problem is one thing; rescuing victims is another. But regardless of whether fentanyl poisoning was incidental or accidental, the stigma attached to it minimizes the perceived danger. People think, "I'm not an addict," "It won't happen to me" or "My kid knows better," and these assumptions cost lives. Fentanyl is everywhere. The toddlers who overdosed at daycare and on a public playground are proof that addiction isn't the only reason for the public health fiasco.[36] Efforts to crush the criminal drug circuit, raise awareness, bolster OUD recovery resources and increase access to naloxone will certainly help save lives, but until the flow of fentanyl stops, people from all walks of life remain at risk.

"We've got to get over the stigma associated with drug use," Davis added. "Fentanyl is a game-changer, and we are in a public safety crisis because of it. It impacts all races, genders and people across the socio-economic spectrum. We'll keep arresting the criminals and reducing the supply of this man-made health hazard, but to reduce the demand, it's going to take all of us to bring down these overdose deaths."[21] ❖

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**RACHEL MAIER**, MS, is a Kansas City-based freelance writer and editor.

ODRESCUE™

**Empowering Communities Against Opioid Overdose**


# Discover How ODRescue Puts Life-Saving Resources Within Arm's Reach

**Easy to Integrate:**
ODRescue integrates life-saving preparedness into your unique environment.

**Naloxone Locator Map:**
Quickly find naloxone nearest you and empower your community with the tools to act.

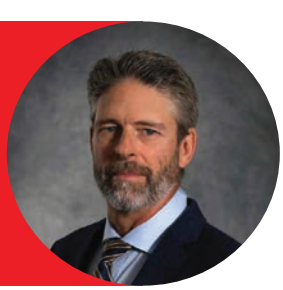
**Location Awareness:**
Get real-time visibility of ODRescue locations for fast access and response.

**Product Management:**
Automatically track expiration dates and usage to ensure you're always prepared.

**Reporting Use:**
Record naloxone responses to find high-risk areas and support communities in need.

## LET'S CONNECT!

**Mark Wojciechowski**
**Business Development Manager**
MWojciechowski@ODRescue.com | 951.383.5760



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# Naloxone in the Right Place at the Right Time: *The Mission Behind ODRescue*


By Ronale Tucker Rhodes, MS

**THE U.S. REMAINS** in a high-severity phase of the opioid epidemic, now dominated by counterfeit pills and drugs such as heroin, cocaine and methamphetamine laced with lethal amounts of illicit fentanyl. And, while there is more awareness and expanded efforts to combat this crisis, overdose deaths are still at or near record levels.

So, what is the answer? Naloxone (often known by the brand name Narcan) is a rapid-acting, non-addictive, U.S. Food and Drug Administration-approved drug used to reverse opioid overdoses by knocking opioids off brain receptors. It acts as an opioid antagonist, restoring normal breathing in minutes, and is available as a nasal spray or injection, often over-the-counter. Naloxone is highly accessible, yet getting it into the hands of people to use it remains a hurdle.

## ODRescue to the Rescue

FFF Enterprises, Inc., is on a mission to change that. The goal: To alter the course of overdose fatalities in the country through ODRescue, a new initiative ensuring the tools needed for lifesaving overdose prevention are in the right place at the right time. ODRescue Boxes are designed to equip people in the community with tools needed to respond to an overdose situation anywhere, from schools and libraries to airports and stadiums. The Boxes mount on walls in high-traffic, high-visibility areas, much like AED cabinets or fire extinguishers. They are equipped with a CPR mask, a one-way valve with filter, nitrile gloves, an antiseptic wipe and enough space for two boxes of naloxone. Its bold, clear design allows bystanders to quickly and confidently help someone experiencing an overdose. Simple illustrations of overdose symptoms are shown on the front cover, and a QR code with a link to training videos appears on the back cover. When the box is opened, emergency services are immediately and automatically notified.

What differentiates the ODRescue Box is that it makes the lifesaving medicine more accessible than simply storing it in a first aid kit or medical cabinet. According to Mark Wojciechowski, business development manager at ODRescue, it is built for visibility, access and readiness. "Unlike naloxone stored in a cabinet — often hidden or inaccessible — the box is clearly marked and strategically placed for immediate use," explains Wojciechowski. "It also supports proper storage and tracks expiration, and some models can trigger alarms and alerts when accessed. This turns naloxone from a passive supply into an active part of emergency response."

The ODRescue platform also addresses one of the biggest gaps in overdose response: knowing where naloxone is when it's needed. "Even in communities where naloxone is widely distributed, it's often not easily discoverable in real time," says Wojciechowski. "ODRescue comes with a locator that creates a shared, community-driven map of publicly accessible naloxone, which empowers bystanders — who are often the true first responders — to act quickly. It also helps organizations contribute to a broader safety network by making their resources visible and accessible beyond their own walls. In effect, it connects isolated points of access into a coordinated system."

What's more, the technology brings two critical improvements: immediate response coordination and better data. "On the response side, alerts notify designated personnel when a box is accessed, reducing response time and increasing the likelihood of a successful intervention," explains Wojciechowski. "On the data side, usage and reporting tools provide insight into when and where interventions are happening. This helps organizations and public health leaders move beyond assumptions and make informed decisions about placement, training and resource allocation."

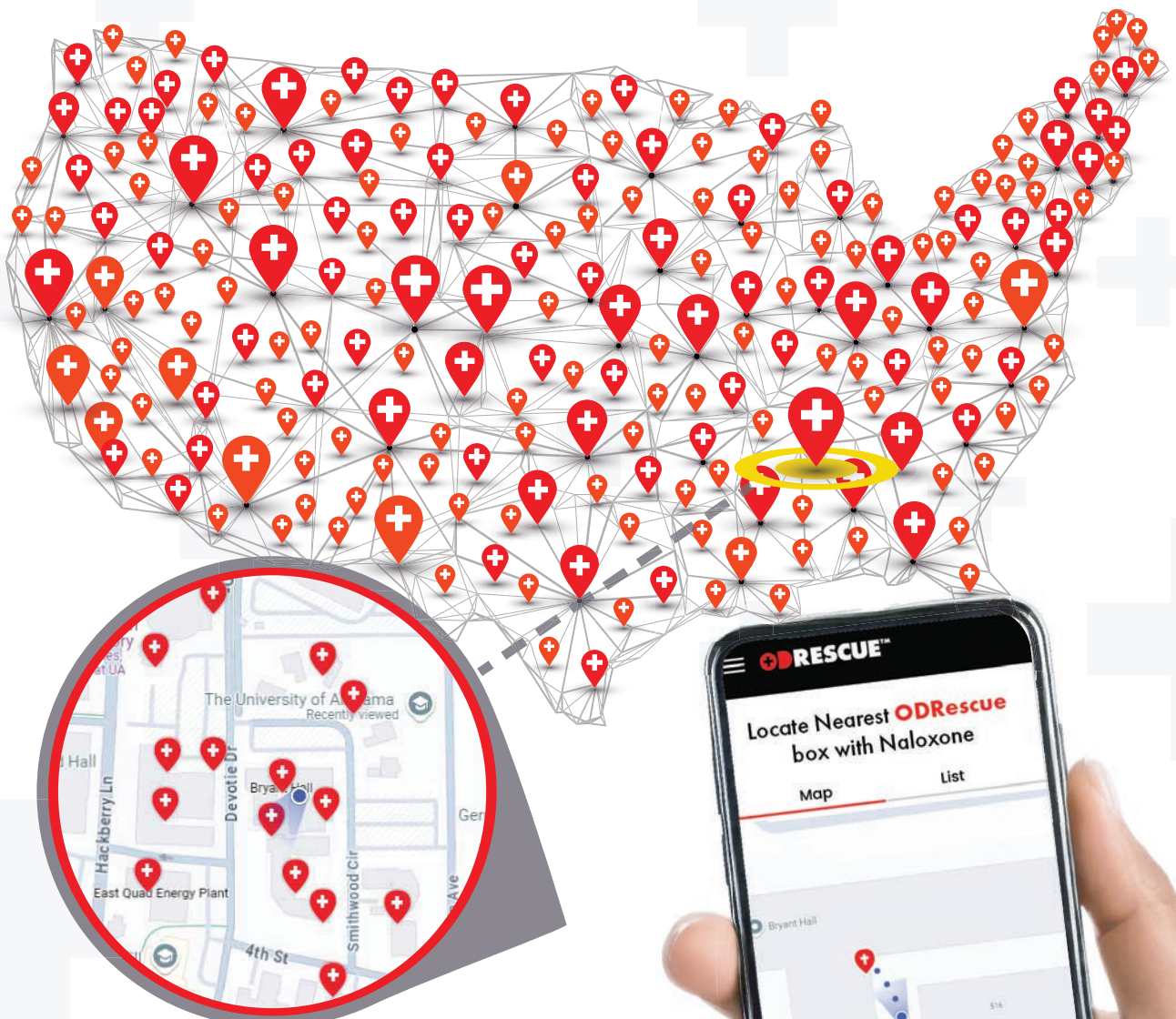
## A Proactive vs. Reactive Approach to Saving Lives

The ultimate goal: to shift overdose response from a reactive, fragmented effort to a proactive, standardized part of public safety, similar to AEDs for cardiac emergencies. "We hope that in five to 10 years, naloxone will not only be widely available, but also visible, normalized and integrated into everyday environments — schools, workplaces, hospitality settings and public spaces," says Wojciechowski. "Access alone is not enough — preparedness is what saves lives. ODRescue is about making naloxone part of a reliable, community-wide response network — one that empowers everyday people to act, supports organizations with better tools and provides the data needed to improve outcomes over time." ❖

**RONALE TUCKER RHODES**, MS, is a the senior editor-in chief of *BioSupply Trends Quarterly*.

# ODRESCUE™ Naloxone Locator Map

A FREE, interactive map pinpoints where naloxone is located, helping individuals, organizations, and agencies quickly connect communities with life-saving medication.

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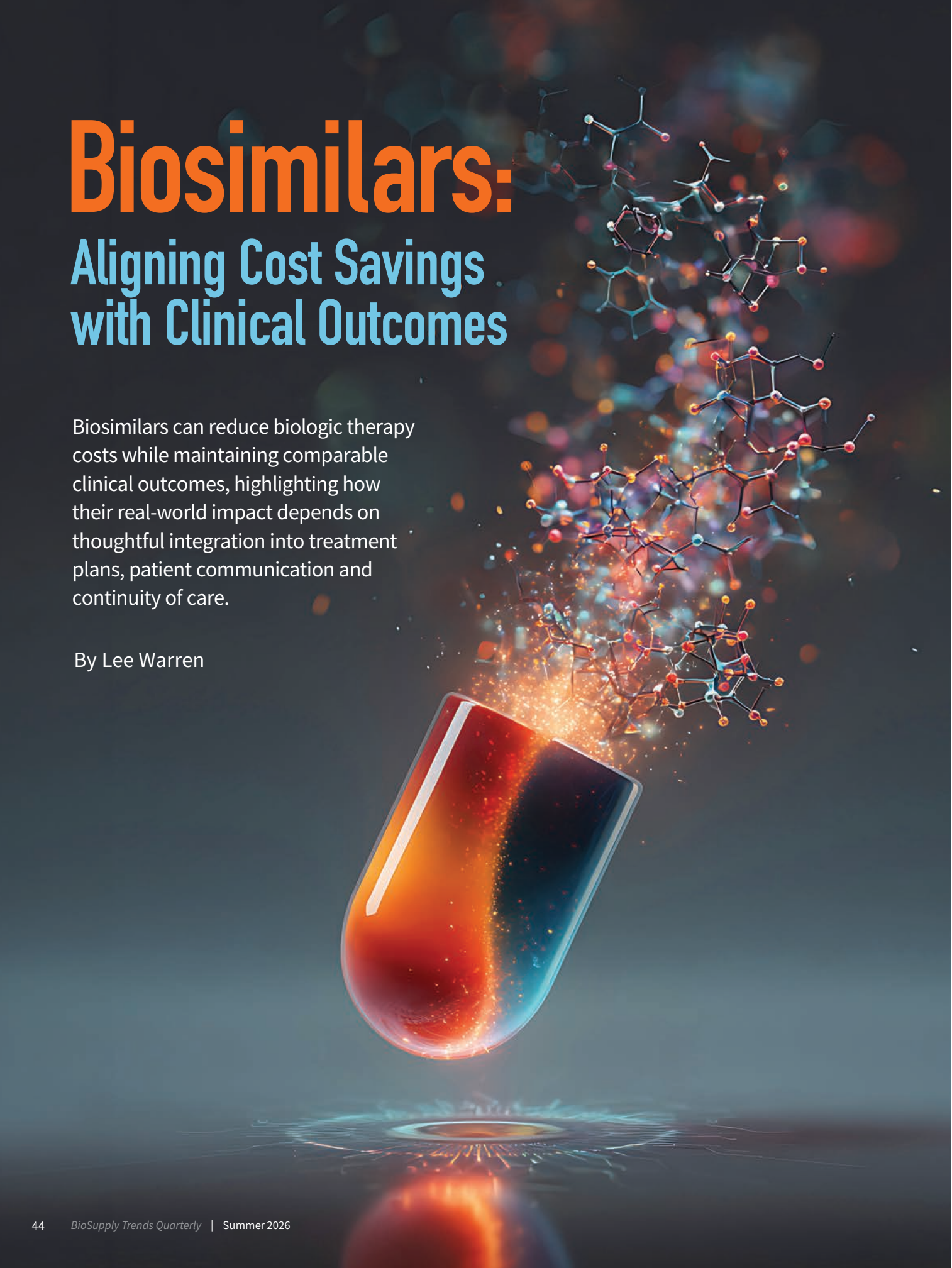
# Biosimilars:

## Aligning Cost Savings with Clinical Outcomes

Biosimilars can reduce biologic therapy costs while maintaining comparable clinical outcomes, highlighting how their real-world impact depends on thoughtful integration into treatment plans, patient communication and continuity of care.

By Lee Warren



**BIOSIMILARS HAVE** moved from mere theoretical cost-saving alternatives to everyday clinical realities as biologic patents have expired, formularies were adopted and increased payer pressure was applied to reduce specialty drug spending. The economic rationale is well-established, but do those savings result in patients receiving equally effective care in real-world situations? In practice, the answer often depends on whether those cost savings make it easier for patients to start and stay on treatment without disruption.

A patient requiring biologic therapy who previously faced high out-of-pocket costs may be more likely to initiate and continue treatment when a lower-cost biosimilar is available. However, these gains may not extend to patients who are already stable on their current biologic therapy. In those cases, switching to a lower-cost alternative due to insurance or formulary requirements may introduce uncertainty or disrupt continuity of care, potentially offsetting those gains.

These dynamics are not limited to a single condition or patient scenario. Across therapeutic areas — including oncology, gastroenterology and rheumatology — biosimilars are increasingly used both when treatment is started and throughout ongoing care. As their use expands, clinicians are encountering a range of outcomes shaped not only by clinical equivalence but also by how these therapies are introduced, maintained or substituted within existing treatment plans.

A growing body of clinical and real-world evidence has begun to clarify these outcomes, demonstrating comparable efficacy, safety and immunogenicity across major therapeutic areas, as well as supporting the safe use of biosimilars in appropriately selected patients.

## Clinical Outcomes

Across multiple studies and post-marketing analyses, biosimilars have demonstrated comparable efficacy, safety and immunogenicity to their reference biologics, with no clinically meaningful differences observed in the conditions for which they are approved — a requirement of the U.S. Food and Drug Administration. This consistency has been a key factor in supporting their broader integration into clinical practice.

A systematic review of 90 studies involving 14,225 patients across multiple diseases found no consistent differences in efficacy, safety or immunogenicity.[1] A randomized, double-blind NOR-SWITCH trial of 482 patients in the *New England Journal of Medicine* found no significant difference in disease worsening between reference infliximab and its biosimilar (CT-P13),[2] supporting the safety of switching in appropriately selected patients.

Importantly, this evidence extends across major therapeutic areas, including oncology, rheumatology and gastroenterology, with biosimilars demonstrating consistent clinical performance in both patients starting treatment for the first time and those who have been previously treated.

Switching between a reference biologic and a biosimilar has also been examined in multiple clinical and real-world settings. Across these studies, transitions have not been associated with meaningful changes in efficacy, safety or immunogenicity in appropriately selected patients. While ongoing monitoring remains important, the available evidence suggests biosimilars can be used safely in both initiation and switching scenarios within routine clinical practice.[3]

Real-world studies and patient registry data have further supported these findings, demonstrating sustained efficacy and safety of biosimilars in routine clinical use across diverse patient populations.

## Cost Savings

Biosimilars offer a clear cost advantage over originator biologics, with lower acquisition prices driven by increased market competition following patent expiration. While the degree of price reduction varies by product and market, these differences can be substantial, particularly in high-cost therapeutic areas.

Biosimilars are typically 15 to 30 percent cheaper at launch, with deeper discounts over time as competition increases. Even so, these therapies remain costly. Insurance coverage generally offsets a significant portion of the expense, but patients are often responsible for coinsurance or deductible-based payments tied to the drug's price. As a result, even a 15 to 30 percent reduction in price can translate into meaningful decreases in out-of-pocket spending, particularly for patients requiring long-term biologic therapy.

**Biosimilars are typically 15 to 30 percent cheaper at launch, with deeper discounts over time as competition increases.**

For example, a patient with rheumatoid arthritis who previously delayed starting a biologic due to annual treatment costs exceeding $50,000 may be able to begin therapy sooner when a lower-cost

biosimilar becomes available. Improved formulary positioning in some cases may also reduce access barriers, allowing treatment to begin earlier and continue more consistently.

A similar dynamic can be seen in oncology, where the cost of biologic therapies can be substantial. A patient receiving treatment for HER2-positive breast cancer may require ongoing therapy with a monoclonal antibody. When a lower-cost biosimilar is available, reduced financial burden and improved formulary access may allow treatment to proceed without delay or interruption, which is critical for maintaining therapeutic effectiveness.

Beyond acquisition cost, the use of biosimilars has been associated with reductions in total cost of care for both health systems and patients. Lower drug spending can reduce overall treatment costs and give health systems greater flexibility in how resources are used. In practice, this may include expanding access to biologic therapies or easing treatment restrictions, with some resources redirected to other areas of care.

While manufacturer-sponsored assistance programs and nonprofit support may help reduce costs for some patients, access to these resources varies and does not eliminate financial barriers entirely.

Even so, reductions in drug costs can still have meaningful clinical implications for patients. Lower out-of-pocket costs may reduce financial barriers to treatment initiation and support greater adherence over time.

For example, patients treated with a biosimilar infliximab have been shown to pay approximately 12 percent less out of pocket compared to those receiving the reference biologic. As biosimilars improve affordability and availability, their use has also been associated with greater treatment uptake and persistence in real-world settings. In chronic conditions requiring long-term biologic therapy, this can support more consistent treatment and reduce the likelihood of interruptions in care.

## Impact on Patient Care

Beyond cost considerations, biosimilars influence how patients engage with treatment over time. Adherence is not solely a function of affordability, but also of patient confidence in the therapy being prescribed. Patients who understand their treatment plan and feel comfortable with changes — particularly when transitioning from a reference biologic — are more likely to remain consistent with therapy. Clear communication from physicians and care teams plays a critical role in maintaining that confidence.

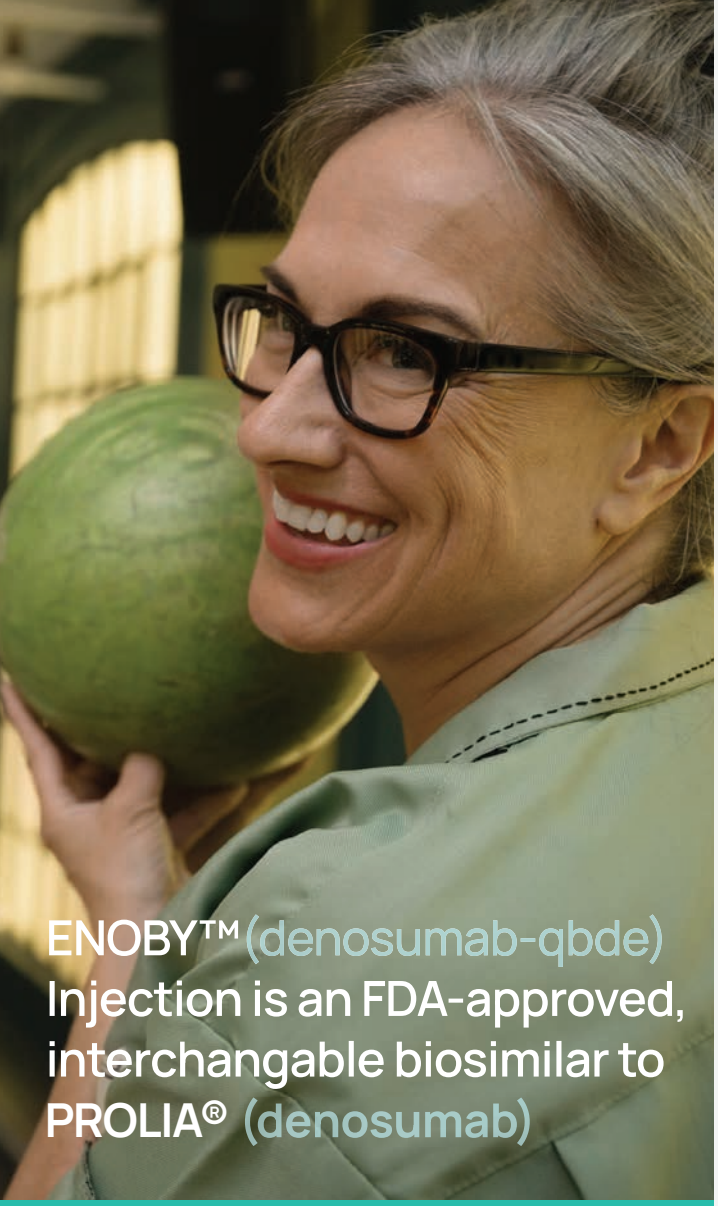
**The integration of biosimilars into clinical practice increasingly requires physicians to consider both clinical and economic factors when making treatment decisions.**

Continuity of care is another important factor. For patients with chronic conditions, even small disruptions in treatment can affect disease control. While biosimilars have been shown to perform comparably to their reference products, changes in therapy, especially those driven by external factors such as formulary adjustments, may come with uncertainty. In these situations, maintaining a stable treatment plan and minimizing unnecessary changes can be just as important as the choice of therapy itself.

A patient with inflammatory bowel disease who has been stable for several years on a biologic therapy may be asked to transition to a biosimilar due to a formulary change. While clinical evidence supports comparable outcomes, the change itself can create uncertainty for the patient, particularly when symptoms have been well-controlled. Questions about effectiveness, potential side effects or loss of disease control may affect confidence in the treatment plan. In these situations, clear communication and careful monitoring can help make sure the transition is successful and that continuity of care is maintained.

Patient experience also extends to how and when treatment is initiated. Earlier access to biologic therapies may allow physicians and care teams to intervene before disease progression leads to irreversible damage. In conditions such as rheumatoid arthritis or inflammatory bowel disease, timely and sustained treatment can significantly influence long-term outcomes. Biosimilars, when integrated effectively into care plans, can support this earlier intervention without compromising clinical effectiveness.

Over time, the consistency of treatment can have a measurable impact on long-term outcomes. In chronic diseases, gaps in therapy or delayed initiation can contribute to disease progression, increased symptom burden and the need for more intensive interventions. By supporting more consistent access to biologic therapies, biosimilars may help reduce these risks and contribute to more stable disease management. In this way, their impact extends beyond immediate



# ENOBY™ (denosumab-qbde) Injection is an FDA-approved, interchangable biosimilar to PROLIA® (denosumab)

- ✓ FDA-approved interchangeable* biosimilar available as an alternative to PROLIA®[2]
- ✓ Approved for the same five (5) indications as PROLIA®[1, 3]
- ✓ Same dosing and administration as PROLIA®[1, 3]
- ✓ Highly similar safety, efficacy and quality as PROLIA®[1, 3]

*An interchangeable biological product is a biosimilar that meets additional requirements and may be substituted for the reference product at the pharmacy, depending on state pharmacy laws.[4]

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hikma.



## Important Safety Information for ENOBY™ (denosumab-qbde) Injection

**WARNING: SEVERE HYPOCALCEMIA IN PATIENTS WITH ADVANCED KIDNEY DISEASE**

- **Patients with advanced chronic kidney disease (eGFR <30 mL/min/1.73 m²), including dialysis-dependent patients, are at greater risk of severe hypocalcemia following denosumab products administration. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported [see Warnings and Precautions (5.1)].**
- **The presence of chronic kidney disease–mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia in these patients [see Warnings and Precautions (5.1)].**
- **Prior to initiating ENOBY™ in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with ENOBY™ in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD [see Dosage and Administration (2.2) and Warnings and Precautions (5.1)].**

### CONTRAINDICATIONS

ENOBY™ is contraindicated in:

- Patients with hypocalcemia: Pre-existing hypocalcemia must be corrected prior to initiating therapy with ENOBY™.
- Pregnant women: Denosumab products may cause fetal harm when administered to a pregnant woman. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with ENOBY™.
- Patients with hypersensitivity to denosumab products: ENOBY™ is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling, and urticaria.

### WARNINGS & PRECAUTIONS

- **Severe Hypocalcemia and Mineral Metabolism Changes –** Denosumab products can cause severe hypocalcemia and fatal cases have been reported. Patients with advanced chronic kidney disease including dialysis-dependent patients are at greater risk for severe hypocalcemia following denosumab products administration.
- **Drug Products with Same Active Ingredient –** Patients receiving ENOBY™ should not receive other denosumab products concomitantly.
- **Hypersensitivity –** Clinically significant hypersensitivity including anaphylaxis has been reported with denosumab products. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus, and urticaria.
- **Osteonecrosis of the Jaw –** Osteonecrosis of the jaw (ONJ), which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing. ONJ has been reported in patients receiving denosumab products.
- **Atypical Subtrochanteric and Diaphyseal Femoral Fractures –** Atypical low energy or low trauma fractures of the shaft have been reported in patients receiving denosumab products.
- **Multiple Vertebral Fractures (MVF) Following Treatment Discontinuation –** Following discontinuation of denosumab treatment, fracture risk increases, including the risk of multiple vertebral fractures.
- **Serious Infections –** In a clinical trial of over 7,800 women with postmenopausal osteoporosis, serious infections leading to hospitalization were reported more frequently in the denosumab group than in the placebo group.
- **Dermatologic Adverse Reactions –** In a large clinical trial of over 7,800 women with postmenopausal osteoporosis, epidermal and dermal adverse events such as dermatitis, eczema, and rashes occurred at a significantly higher rate in the denosumab group compared to the placebo group.
- **Musculoskeletal Pain –** In postmarketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking denosumab products.
- **Suppression of Bone Turnover –** In clinical trials in women with postmenopausal osteoporosis, treatment with denosumab resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry.
- **Hypercalcemia in Pediatric Patients with Osteogenesis Imperfecta –** ENOBY™ is not approved for use in pediatric patients. Hypercalcemia has been reported in pediatric patients with osteogenesis imperfecta treated with denosumab products. Some cases required hospitalization.

### ADVERSE REACTIONS

The most common adverse reactions reported with denosumab products in patients with postmenopausal osteoporosis are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis.

The most common adverse reactions reported with denosumab products in men with osteoporosis are back pain, arthralgia, and nasopharyngitis.

The most common adverse reactions reported with denosumab products in patients with glucocorticoid-induced osteoporosis are back pain, hypertension, bronchitis, and headache.

The most common (per patient incidence ≥ 10%) adverse reactions reported with denosumab products in patients with bone loss receiving androgen deprivation therapy for prostate cancer or adjuvant aromatase inhibitor therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.

### USE IN SPECIFIC POPULATIONS

**Pregnancy:** ENOBY™ is contraindicated for use in pregnant women because it may cause harm to a fetus. There are insufficient data with denosumab products use in pregnant women to inform any drug-associated risks for adverse developmental outcomes.

**Females of Reproductive Potential:** Advise females of reproductive potential to use effective contraception during therapy, and for at least 5 months after the last dose of ENOBY™.

### INDICATIONS AND USAGE

**Treatment of Postmenopausal Women with Osteoporosis at High Risk for Fracture**

ENOBY™ is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, denosumab reduces the incidence of vertebral, nonvertebral, and hip fractures.

**Treatment to Increase Bone Mass in Men with Osteoporosis**

ENOBY™ is indicated for treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

**Treatment of Glucocorticoid-Induced Osteoporosis**

ENOBY™ is indicated for the treatment of glucocorticoid-induced osteoporosis in men and women at high risk of fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 6 months. High risk of fracture is defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

**Treatment of Bone Loss in Men Receiving Androgen Deprivation Therapy for Prostate Cancer**

ENOBY™ is indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy (ADT) for nonmetastatic prostate cancer. In these patients denosumab also reduced the incidence of vertebral fractures.

**Treatment of Bone Loss in Women Receiving Adjuvant Aromatase Inhibitor Therapy for Breast Cancer**

ENOBY™ is indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

### ENDING INFORMATION

**Patient Counseling Information should be shared with the patient prior to administration.**

**For additional information, please refer to the Package Insert for full prescribing information, available on www.hikma.com.**

**To report SUSPECTED ADVERSE REACTIONS, contact Hikma Pharmaceuticals USA Inc. at 1-877-845-0689 or FDA at 1-800 FDA-1088 or www.fda.gov/medwatch.**

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treatment decisions to influence the overall trajectory of care.

## Physician Considerations

The integration of biosimilars into clinical practice increasingly requires physicians to consider both clinical and economic factors when making treatment decisions. While therapeutic equivalence is well-established, prescribing is often influenced by formulary design, coverage limitations and institutional cost-containment strategies. Incorporating biosimilars into cost-conscious prescribing does not require compromising clinical judgment but, rather, understanding when their use aligns with both patient needs and system constraints.

In addition to clinical and economic considerations, physicians must also determine when switching is appropriate on an individual patient basis. While evidence supports the safety of transitioning to biosimilars, factors such as disease stability, patient preference and prior treatment response should inform these decisions. For patients who are well controlled on a current biologic, the potential benefits of switching must be weighed against the risk of disrupting a stable treatment regimen. In these cases, shared decision-making becomes particularly important, allowing patients to participate in treatment choices and helping to maintain confidence in the care plan.

Effective patient communication is essential, particularly when initiating or transitioning therapy. Patients may have questions about the differences between biosimilars and the original brand-name biologic drug that the biosimilar is based on, especially when a change occurs after a disease has been stabilized for a period. For physicians to help maintain trust and support adherence, they need to address these concerns with clear, evidence-based explanations. In many cases, the way they communicate a treatment is as important as the decision itself.

Policies from organizations such as the Centers for Medicare and Medicaid Services and private insurers shape formulary preferences and coverage decisions, so physicians must also navigate ever-evolving payer rules. Familiarity with these frameworks can help clinicians anticipate treatment pathways and reduce administrative barriers to make sure patients receive timely and appropriate care within the constraints of the healthcare system.

Administrative considerations also play a role in biosimilar adoption. Prior authorization requirements, step therapy protocols and formulary changes can create additional workload for clinical teams and may delay treatment initiation or continuation. Understanding these processes and anticipating potential barriers can help streamline care delivery and reduce disruptions for patients. In many practices, coordination between physicians, pharmacists and support staff is essential to successfully integrating biosimilars into routine care.

Many practices are also turning to technology to manage these demands more efficiently, particularly for prior authorizations and payer communication. Artificial intelligence-driven tools can help automate parts of the documentation process, flag missing information before submission and streamline interactions with payers, reducing delays and administrative back-and-forth. In some settings, these tools are being integrated into electronic health record platforms to support more timely access to therapy while reducing the burden on clinical staff.

## Takeaway

Biosimilars have demonstrated comparable clinical outcomes to their reference biologics while offering a clear opportunity to reduce the cost of care. Across multiple therapeutic areas, evidence from clinical trials and real-world studies has consistently shown no meaningful differences in efficacy, safety or immunogenicity. These findings have supported their growing role in routine clinical practice.

However, the impact of biosimilars is not determined by evidence alone. In practice, their success depends on how they are incorporated into treatment decisions, particularly in the context of patient stability, communication and system-level constraints. Decisions around initiation or switching must be made thoughtfully, considering both clinical factors and the broader realities of payer requirements and patient preferences.

As their use continues to expand, physicians play a central role in how biosimilars deliver on their promise. Through careful clinical judgment and clear communication, along with an understanding of the systems that shape access to care, clinicians can help translate cost savings into consistent, high-quality patient outcomes. In this way, the value of biosimilars is realized not simply through reduced spending, but through their effective integration into patient-centered care. Ultimately, their impact will be defined not by cost alone, but by how they are used in practice. ❖

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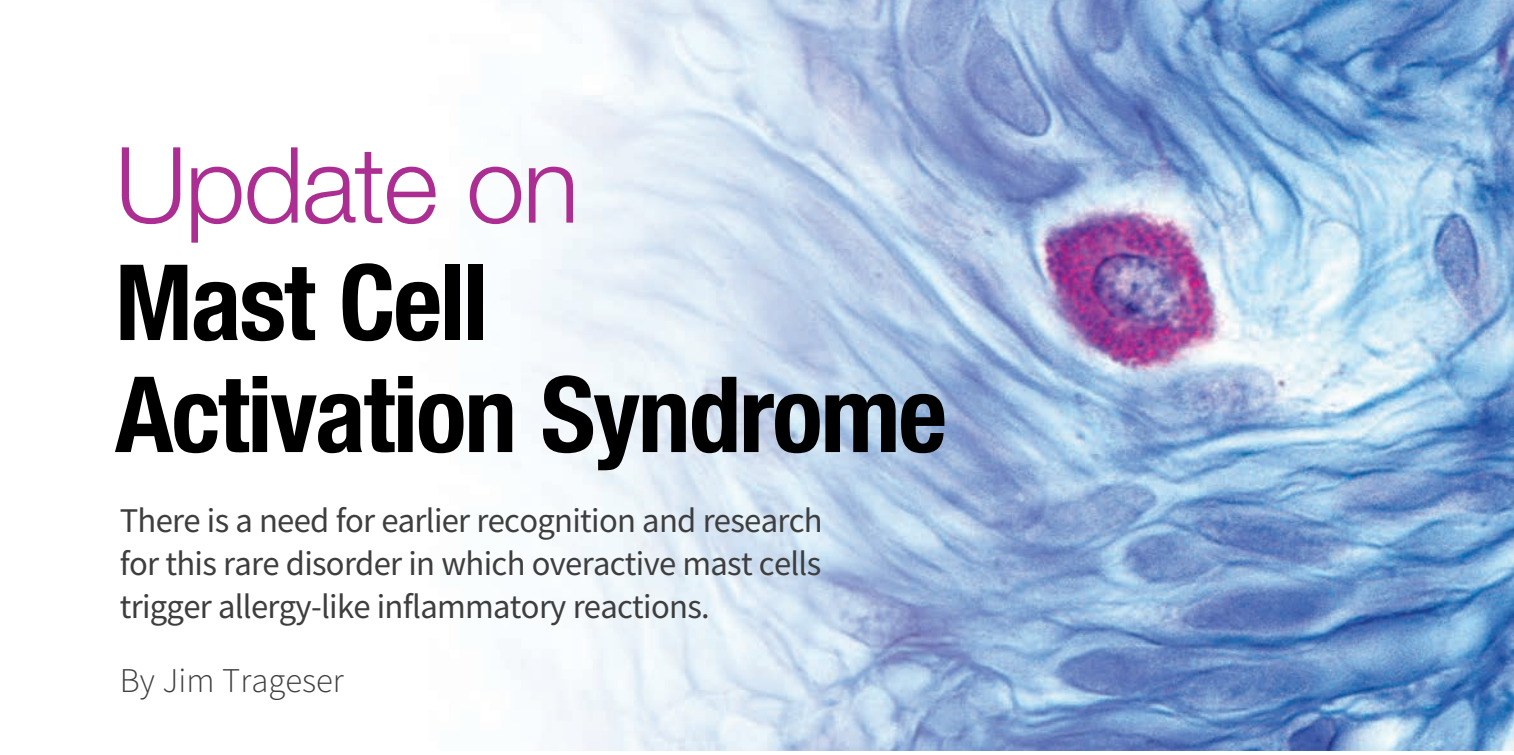

# Update on Mast Cell Activation Syndrome

There is a need for earlier recognition and research for this rare disorder in which overactive mast cells trigger allergy-like inflammatory reactions.

By Jim Trageser

**MAST CELLS** — specialized white blood cells that reside in tissue rather than the bloodstream or lymphatic system — are a key component of a body's immune system. They serve as sentinels, and warn the body when they detect invading bacteria, viruses or fungi — even venom and toxins.[1]

But as with just about every system in individuals' bodies, mast cells are prone to various disorders. While mast cell disorders are fortunately rare (the most common, mastrocytosis, which is an overaccumulation of mast cells in tissue, affects only about one in 10,000 people[2]), when they do occur, the effects can be life-threatening.

While even less common than mastrocytosis, mast cell activation syndrome, or MCAS, involves malfunctioning mast cells sending out chemical signals for an infection or poisoning that isn't actually occurring. Similar to an allergy, the immune system ramps up to fight the nonexistent threat, leading to an inflammatory response that is similar to an allergic reaction: racing heart, lowered blood pressure, itchy or flushed skin, possibly hives and difficulty breathing.[3] In extreme cases, MCAS can lead to anaphylaxis — a systemic failure of the body that can quickly lead to death if not immediately treated.

While there is neither a cure nor a vaccine, MCAS usually can be successfully managed by addressing symptom relief and trigger avoidance.

## What Is MCAS?

Mast cells were first described in 1863, but their role in the immune system was suspected since 1949. It was only in 2010 that our understanding of mast cell disorders was classified in its current form.[4]

Mast cells are produced in the bone marrow and circulate as stem cells before migrating into tissue: lungs, digestive tract and connective tissue, as well as the skin and mucus membrane. They are particularly common in any part of the body that may come in contact with the external world — and, thus, infectious agents or toxins.

These cells have a unique structure: They are covered with a series of pattern recognition receptors that will react to specific molecular components associated with bacteria, viruses, fungi or parasites. On the interior, but near the surface, are dozens to as many as 1,000 granules, each containing a specific chemical that will stimulate or regulate the immune system if released.[5]

In some people (and researchers do not yet understand the underyling causes of MCAS), the mast cells are chronically overactive. Those chemical mediators, primarily histamine, are released frequently — sometimes in overreaction to a known allergen, and other times for no discernible reason.[6]

Because the immune system isn't attacking the person's body, MCAS is not considered an autoimmune disease.[7]

Researchers classify MCAS into a variety of subtypes based on either the suspected underyling cause,[8] other co-existing conditions,[4] the severity of symptoms or organs involved[9] and others. There is no single, accepted classifcation system at this time.

The three most common classifications fall into these groups:

• Genetic: Certain mutations in a person's DNA are linked to an increased likelihood of developing MCAS. Hereditary alpha tryptasemia (HαT), for instance, is linked to a duplicate

TPSAB1 gene, leading the mast cells to increase production of the α-tryptase enzyme.[10] Other genetic abnormalities thought to play a role in MCAS include the KIT gene and the RCCX complex.[11] Importantly, some of these mutations are not inherited, but may be acquired after conception through random mutations triggered by radiation, toxins or aging, or just chance.

• Hypersensitivity: MCAS flare-ups can be caused by a variety of triggers, from temperature changes to stress, food and odors, or even medications.[4]

• Idiopathic: In some cases, no particular cause can be determined. (A recent study determined that relatively few cases of MCAS are actually idiopathic.[12])

Women are significantly more likely to be diagnosed with MCAS than men, and those with a Caucasian family background are also more heavily represented among MCAS diagnoses.[13] It is also known that MCAS runs in families — although it is thought that it is not an inherited gene that regulates mast cells, but rather an inherited epigenetic mutation.[14] (Epigenetics is the ability of the body to turn certain genes off through enzyme regulation. One well-known example is that while humans still carry the gene for fur, as our distant ancestors had, somehow the gene is not activated in modern humans. Researchers do not yet understand this mechanism very well.)

It is also notable that symptoms generally begin in childhood — although there is a well-documented pattern of diagnosis often not being made until middle age[15] (frequently due to individuals not bringing symptoms to the attention of their physician).

In addition, individuals who have certain other conditions or disorders are also more likely to develop MCAS. These include Ehlers-Danlos syndrome,[16] postural orthostatic tachycardia syndrome,[17] primary immunodeficiency, CD4 lymphocytopenia,[19] IgE-dependent allergy[9] and mastocytosis — although MCAS can develop first, and then mastocytosis. Researchers are unclear about the link between the two disorders involving mast cells.[19]

## MCAS Symptoms and Progression

MCAS usually manifests with symptoms similar to those of common allergies:

- Itchy skin
- Flushing
- Low blood pressure
- Hives
- Feeling light-headed
- Abdominal pain
- Constipation or diarrhea
- Congestion
- Shortness of breath

But an MCAS flare-up is differentiated from an allergic reaction in that it will involve at least two bodily systems:[20]

- Skin
- Respiratory system
- Cardiovscular system
- Digestive tract

With MCAS, flare-ups will grow not only more severe over time, but are also likely to increase in frequency. However, within that larger time frame measured in years and decades, there are also often periods of relative calm. In addition, many individuals with MCAS will find that flare-ups are triggered by a widening pool of catalysts.

And, any specific flare-up can progress rapidly. If not treated, a severe flare-up can lead to anaphylaxis as quickly as an allergic reaction, even within minutes, requiring immediate hospitalization.[20]

## MCAS Diagnosis

There is no single test to confirm a diagnosis of MCAS, and the initial symptoms are similar to, and even indistinguishable from, numerous other conditions.

However, the 2010 Working Conference on Mast Cells (held in Vienna) came up with a three-part diagnostic standard:[21]

1) Individual presents with the above symptoms, including at least two systems being affected

2) Mast cell-derived mediators are found at elevated levels in the individual's blood or urine during a symptomatic episode

3) The individual's symptoms respond to treatment for MCAS

If an individual presents with symptoms consistent with MCAS, a blood test may be ordered during the next flare-up to compare with a test from the same individual during a symptom-free period. The two samples will be compared for tryptase levels. An elevated measurement (above 11.4 ng/mL) may be an indicator of MCAS.[4] Elevated levels of other mediators, including histamine (blood), histamine metabolites (urine) and prostaglandin D2 metabolites (urine) may help confirm a suspected diagnosis of MCAS, particularly if the tryptase results are not clear cut.[9]

Final confirmation will generally come from prescribing drugs to stabilize the mast cells, or to counter the mediators. Cromolyn sodium (Gastrocom) can be given orally to prevent mast cells from releasing mediators from their granules.[20] If an individual meeting the above criteria responds positively, this is generally enough to make a positive diagnosis.

## MCAS Treatment

Since there is presently no cure for MCAS, treatment consists of addressing symptoms and, if triggers for previous flare-ups are known, avoiding them as much as possible.

As mentioned previously, cromolyn

sodium can help stop flare-ups by preventing degranulation in mast cells. Additional drugs that may be tried are antihistamines to counter the mediators released by the mast cells, and aspirin (which blocks production of prostaglandin $D_2$) to reduce inflammation. Individuals should also be instructed to carry at least two epinephrine self-injectors in case of a severe flare-up.[9]

In serious flare-ups in which anaphylaxis is developing, hospitalization is needed.

Future flare-ups can be reduced by prescribing a histamine receptor blocker, including famotidine when the gastrointestinal tract is a frequent source of symptoms and cetirizine or fexofenadine when the skin is a primary source of symptoms.[22] Leukotriene inhibitors, including montelukast and zafirlukast, help relieve wheezing, while zileuton blocks production of $LTC_4$, achieving the same result.

In individuals in which none of the above treatments are providing an adequate level of relief, there is some evidence that combining naltrexone and immune globulin can be effective, particularly in patients with both MCAS and postural orthostatic tachycardia syndrome.[23]

Individuals who are dealing with multiple conditions will be treated to address all of them, in addition to MCAS.

## Ongoing Research

Since it is believed that epigenetics may be the underyling cause of MCAS, one promising area of research is in treating epigenetic disease.[24]

However, because MCAS is such a rare condition, there is relatively little primary research listed on the U.S. Food and Drug Administration's ClinicalTrials.gov website.

Other studies are looking into mast cell disease as a whole, with just under 200 recent or ongoing trials, some of which may create spillover progress in understanding MCAS. Among those trials are one ongoing study to build a baseline of KIT D816V mutation rates in patients with suspected clonal mast cell disease.[25] Another is an effort to create a tissue bank built around samples from individuals who suffer from, or are suspected to have, an allergic or mast cell disease. This biobank would be used to benefit future research into these conditions.[26]

Lastly, recent studies were conducting primary research into mast cell precursors (the stem cells created in the marrow that then travel through the blood until embedding in tissue), primary research into how mast cell proliferation is regulated, and determining the normal range of tryptase levels in premature newborns.

## Looking Ahead

Until researchers are able to determine the specific reasons some patients develop MCAS, treatment improvements will largely involve faster diagnosis.[15] If there is an average gap of three decades between the onset of symptoms and diagnosis, that is one area that is clearly ripe for improvement. Better communication with individuals affected by MCAS, and encouraging them to share symptoms they may not feel are serious enough to warrant sharing, are the most likely path to earlier treatment. ❖

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# MCAS: *A Patient's Perspective*

By Trudie Mitschang

**CAROLINE CRAY QUINN** measures her life in breaths, movements and bites of food. Every action carries a weight most people never notice. Diagnosed with mast cell activation syndrome (MCAS), a rare and unpredictable immune disorder, Caroline lives with the constant threat of anaphylaxis — an extreme allergic reaction that can strike without warning.

Her struggles began in early childhood. At age 2, a snack containing trace amounts of nuts triggered her first severe reaction. Through her early years, she navigated allergies cautiously, but everything changed during her freshman year at university in Massachusetts. "I was with friends and grabbed some mint chocolate-chip ice cream," she recalls. "Before I knew it, I went into anaphylaxis, and my friends rushed me to the hospital."

After that episode, Caroline's immune system seemed to treat nearly every food as a threat, turning routine activities into high-risk endeavors. Specialists at Brigham and Women's Hospital in Boston diagnosed her with MCAS, explaining why her body reacted as if under constant attack. At her most restricted, she could tolerate only oats and a hypoallergenic toddler formula. "At the time, the only alternative was a feeding tube," she says. "You can't escape your body. To feel like it's your enemy is devastating."

For years, Caroline lived cautiously, often in isolation. Social situations required constant strategizing; exposure to pets, feathers or wool could provoke life-threatening reactions. Her work as a healthcare recruiter necessitated adapting to remote work to minimize risk, and personal relationships required extraordinary precautions. "You name it, I can't be near it. Even kissing my boyfriend was risky," she admits. Friends and family often had to avoid allergens for hours or even change clothes before seeing her.

Even with these obstacles, Caroline sought ways to reclaim her life. Mast cell stabilizers and antihistamines allowed her to expand her diet slightly and tolerate brief exposures to animals. Travel became possible, though never without caution. A Caribbean trip ended in anaphylaxis after just two bites of salad, a stark reminder of her condition's fragility. Over time, she relied on her safe staples — oats and formula — finding both nourishment and security in routine.

Seven years into her journey, Caroline began experimenting with cooking to bring variety to her limited diet. She discovered oat-based recipes — cookies, pancakes, even savory dishes — and started documenting her process online. Her posts and videos struck a chord with thousands facing similar challenges, offering practical guidance and emotional support. "I started sharing my experiences online to raise awareness," she explains. "It's become a two-way conversation — strangers give me ideas to try new recipes, and I hope my story helps them feel less alone." Her social media presence is more than a cookbook; it's a platform for education and advocacy. Caroline frequently discusses the realities of MCAS, the precautions required to live safely and the emotional toll of invisible chronic conditions. By opening a window into what life with chronic illness looks like, she encourages empathy and understanding for others navigating hidden disabilities.

For Caroline, daily life still requires meticulous planning. She carries EpiPens, Benadryl and inhalers with her at all times. When it comes to travel, flying remains too risky, but road trips with family provide a safe and needed escape. She notes she finds a silver lining in the perspective her condition has given her. "I'd like to think that by being open about my condition, I can help change the way people interact with others and be more mindful of accommodating all kinds of allergies," she says.

Looking ahead, Caroline remains cautiously optimistic. Under the guidance of her medical team, she is slowly reintroducing foods, aware that each new ingredient carries potential risk. Working with her MCAS therapist, she has tried chicken, lamb, sweet potato and broccoli, but so far, each attempt has triggered an allergic reaction. "We introduce small amounts of a single food to see how I react — or if I react at all," she explains. "It's a long and grueling process. I hope one day I can expand my diet, but there's no guarantee. I just focus on getting through each day."

Caroline's life is a testament to resilience and adaptability in the face of relentless adversity. From severe allergic reactions at age 2 to becoming a content creator who documents her routines for a fascinated online audience, she has transformed her limitations into an avenue for awareness, education and connection. In a world where safety and risk must constantly be balanced, Caroline navigates life with courage, creativity and an unwavering commitment to both survival and community. ❖

Editor's note: Follow Caroline on Instagram and TikTok: @carolinecray2

# MCAS: *A Physician's Perspective*

**KELLY MCCANN**, MD, MPH, is an integrative and functional medicine physician based in Costa Mesa, Calif. She earned her degrees in tropical medicine from Tulane University, and completed residencies in internal medicine and pediatrics. She is among a select group of physicians to complete the University of Arizona's Residential Fellowship in Integrative Medicine under Andrew Weil, MD, and is certified by the Institute of Functional Medicine and board certified in integrative medicine.

**BSTQ:** What is mast cell activation syndrome (MCAS)?

**Dr. McCann:** MCAS is a condition in which mast cells, key immune "sentinel" cells, become dysregulated and overly reactive. Instead of responding appropriately to threats, they release chemical mediators like histamine, prostaglandins and cytokines too easily and too often, reactions that are often to things that do not really pose a threat such as smells or other common substances. This leads to widespread, multisystem symptoms that can appear inconsistent or unrelated. Unlike classic allergic reactions, MCAS is diffuse, unpredictable and frequently missed in conventional clinical settings.

**BSTQ:** How do patients with MCAS typically present?

**Dr. McCann:** Patients often arrive with a long list of symptoms affecting multiple organ systems. Common presentations include dermatologic symptoms like flushing, rashes and hives; gastrointestinal complaints such as abdominal pain, bloating and diarrhea; neurologic issues like headaches or dizziness; and cardiovascular symptoms, including palpitations or lightheadedness. Many also report anxiety or panic-like episodes. What's striking is the pattern: Symptoms are episodic, encompass multiple systems of the body, triggered by seemingly unrelated exposures, and often occur despite normal standard lab work. Patients frequently describe a growing sensitivity to foods, environmental factors or even stress.

**BSTQ:** What do we know about the prevalence of MCAS?

**Dr. McCann:** Emerging data suggest MCAS may be far more common than previously thought, with some estimates indicating it could affect a significant portion of the population, up to 17 percent of the population or more. There also appears to be a genetic component, as individuals with a first-degree relative affected by MCAS have a higher likelihood of developing it.

**BSTQ:** How do you approach diagnosing MCAS in clinical practice?

**Dr. McCann:** Diagnosis is both clinical and laboratory-based. A thorough history is critical, looking for multisystem involvement, trigger patterns and symptom variability. Laboratory testing can include markers such as serum tryptase, histamine, prostaglandins and their metabolites, though these are not always elevated. Timing is important; testing during or shortly after a flare increases diagnostic yield. Equally important is assessing the patient's environmental exposures, infectious history and nervous system regulation. MCAS rarely exists in isolation.

**BSTQ:** Once diagnosed, what does treatment typically involve?

**Dr. McCann:** Treatment is multifaceted and individualized. Broadly, we focus on three pillars: 1) trigger identification and removal, which may involve environmental testing for mold, addressing chronic infections and reducing toxic exposures; 2) mast cell stabilization, using both pharmacologic and non-pharmacologic approaches; and 3) nervous system regulation techniques that support autonomic balance, such as breathwork, vagal nerve stimulation and trauma-informed therapies. The goal is not just symptom suppression but restoring stability to the system.

**BSTQ:** There's growing discussion about reframing MCAS. Can you explain that perspective?

**Dr. McCann:** MCAS has been viewed as a condition of dysfunction requiring suppression management. An emerging perspective is that mast cell activation is an exaggerated but meaningful response to perceived threat. Symptoms, then, are signals rather than random malfunctions pointing to underlying environmental, infectious or physiologic stressors that need to be addressed. For clinicians, this framework encourages a more comprehensive, root-cause approach rather than focusing solely on symptom control. And beneath the physical symptoms and stressors are even deeper patterns of beliefs, trauma and lack of safety that drive the threat response. ❖

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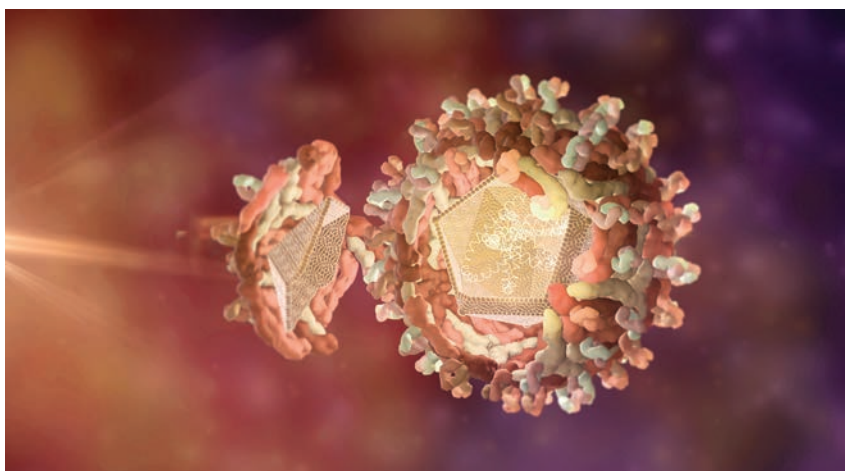
# Early Vaccine Development: The Challenging Case of the West Nile Virus

By Brian Gaul, PharmD



**NEW TECHNOLOGY** has spurred advances in medicine, including the development of vaccines against problematic pathogens. However, despite those breakthroughs, not every promising vaccine has made it to market. One example is the West Nile virus (WNV) vaccine. Efforts to create vaccines to control the virus have stalled at the Phase II level, an illustration of the challenges of early vaccine development.

## What is WNV?

WNV, a member of the flavivirus family, is a growing health challenge in the U.S. and Europe, driven by climate change. Spread by the Culex mosquito and migratory birds, WNV reached the U.S. in 1999; by 2003, it was a major arthropod-borne disease.[1]

While 80 percent of infections are asymptomatic, 20 percent result in a febrile illness characterized by fever, muscle aches and gastrointestinal complaints.[2] Less than one percent of infections cause serious neuroinvasive diseases like meningitis, encephalitis and acute flaccid paralysis.[1,3]

From 1999 to 2021, there have been 55,000 reported cases of WNV in the U.S., with 27,000 of them neuroinvasive and 2,600 leading to deaths.[4] Most neuroinvasive cases are in the north-central to south-central U.S.[5]

Unfortunately, new tools to combat WNV have not been developed since its emergence in the northern hemisphere. Prevention is limited to personal protective measures such as clothing and insect repellent, which can be effective but have low adherence. Chemical mosquito control efforts are available in less than 60 percent of U.S. counties, with variable capabilities and coverage.[2]

A vaccine solution is an unmet need.

## Early Vaccine Development

The COVID-19 pandemic accelerated a trend away from traditional vaccine approaches toward newer modalities. Classical approaches were difficult to scale and had long development times; newer technologies are more adaptive, scalable and agile.[6]

Advances in RNA stabilization, lipid nanoparticle delivery systems and mass production led to breakthroughs with messenger RNA (mRNA) technology.[6] However, challenges include the need for ultracold storage, variable expression profiles and rare immune-mediated adverse events.[7]

Traditional approaches included inactivated, live attenuated and toxoid-based vaccines. Inactivated vaccines are whole pathogens rendered non-replicative ("killed") by chemical agents such as formaldehyde, heat or radiation.[6] Examples are the inactivated poliovirus or hepatitis A vaccines. Live attenuated viruses are weak, replicative strains lacking complete virulence.[6] Examples are measles-mumps-rubella and oral poliovirus. Toxoid-based vaccines use killed bacterial exotoxins that preserve immunogenicity while eliminating toxicity.[6] Examples include the diphtheria and tetanus components in the diphtheria-tetanus-pertussis (D-T-P) vaccine.

Bridging the gap between traditional and new technology are the recombinant DNA vaccines. Recombinant vaccines feature peptides or proteins from the pathogen that are produced in a cell factory, such as yeast, insects or mammalian cells. They may also be created as pathogen subunits, such as surface or viral envelope proteins, presented as antigens.[6] An example is the

hepatitis B surface protein vaccine.

The newest technology includes viral vectors, mRNA vaccines and DNA vaccines. Viral vectors are modified viruses used as carriers coding protein antigens such as the Johnson & Johnson COVID-19 vaccine.[6] mRNA vaccines present synthetic mRNA encoding a target antigen to host cells, where it is expressed and recognized by the immune system.[6] Examples include the Moderna and Pfizer-BioNTech COVID-19 vaccines. DNA vaccines, meanwhile, introduce circular plasmid DNA that codes a target antigen through mRNA.[6] They have been studied in the context of the Zika virus, HIV and COVID-19.

Recent advances in the development pathway, such as the ability to manufacture mRNA and DNA vaccines, have sparked innovation in the field. But not every vaccine has been a beneficiary.

## WNV Vaccine Pipeline

Sometimes, the development pathway is not the bottleneck for a new vaccine. It may be logistics.

While seven vaccines have been developed and tested for WNV, none have advanced past Phase II in the U.S. Food and Drug Administration (FDA) pipeline.[1]

Among those studied to date are the following:

- Chimerivax-WN02: a chimeric live attenuated virus with seroconversion above 90 percent after a single dose in clinical trials, including one in Phase II.[4,8] This vaccine program is no longer active.[2]
- WN/DENV4-3'Δ30: a live attenuated chimeric vaccine that showed seroconversion between 65 and 95 percent based on dosing schedule.[4,8] The National Institutes for Health developed it and is awaiting a commercial partnership to enter Phase II.[2]
- Two DNA-based candidates (WRC-WNVDNA-017-00 and VRC-WNVDNA020-00-VP) showed strong neutralizing antibody responses and seroconversion rates exceeding 96 percent after a three-dose regimen.[4,8]
- A recombinant subunit WN-80E/SLA-LSQ, which has shown neutralizing antibody response and safety in a preclinical setting and is awaiting a Phase I trial.[2]
- Inactivated whole virus formulations have been studied; one has a moderate seroconversion rate (31 to 50 percent) after two doses, and another, a formalin-inactivated vaccine, peaked after a booster dose.[8]

Ironically, WNV vaccine development for veterinary use has been available since 2001.[1,2] These vaccines are effective at reducing infection, morbidity and mortality in animals like horses.[2]

## Barriers to Traditional Trials in Humans

Scientific, safety and economic obstacles have prevented WNV vaccine candidates from advancing to Phase III trials in the U.S.[4]

The unpredictable course of infection outbreaks makes it difficult to assess vaccine efficacy.[4] Finding a region with endemic levels of the disease would be preferred; however, even in regions of high incidence, such as Maricopa County, Ariz., the number of cases may vary by year. In 2021, for example, Maricopa reported 1,400 WNV cases and 100 resulting deaths, compared to three cases the previous year. Low case counts and the need for ethics approval for Phase III trials may result in enrollment that takes years to complete. As a result, the traditional pathway may be time-consuming and expensive for potential vaccine manufacturers.[4]

Factors that influence reporting rates also include changes in bird or mosquito populations, weather patterns, the time people spend outdoors and healthcare-seeking behavior.[2] The most consistent predictor of future WNV cases is past incidence, even though it is inconsistent.[9] The fact that most diseases are asymptomatic or mild in nature also limits the number of case reports.

Finally, cost-effectiveness is a concern. One study found that vaccinating the general public against WNV was not cost-effective, although targeting older adults may be worthwhile.[10]

## Nontraditional Approval Options

If Phase III trials prove to be too costly or difficult to implement, options exist. The possibilities were discussed at a one-day Centers for Disease Control and Prevention meeting in April 2024, specifically addressing WNV and vaccine issues.[2]

While seven vaccines have been developed and tested for WNV, none have advanced past Phase II in the FDA pipeline.

Among the options are the following:[4]

- Using surrogate endpoints like immune protection in animal models to argue for the value of the WNV (as has

been done with chikungunya vaccines)

- Comparing immunological markers with other flaviviruses, like the Japanese encephalitis vaccine
- Approving an FDA investigational new drug application with an expanded access system
- Creating an emergency use authorization, like those used for early approval of COVID-19 vaccines

WNV vaccines may be candidates for the expedited programs due to their ability to address unmet needs in morbidity and mortality prevention.[2]

## Safety with WNV Vaccines

Even if approved, WNV vaccines may cause safety concerns. The use of live vaccines in older adults and the immunocompromised may lead to reactivation if not handled carefully. For inactivated options, the need for multiple doses and boosters may be an obstacle. Veterinary WNV vaccines, for example, require a two-dose primary series and annual boosters.[4]

## Future Outlook

Current prevention strategies continue to be insufficient to control the morbidity and mortality associated with WNV. Overcoming the obstacles that have stalled the early development of a WNV vaccine is crucial to controlling the impact of the disease. ❖

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# Optimizing the Operating Room

By Rachel Maier, MS

**AN EFFICIENT** operating room (OR) aims to ensure patients receive the highest level of care in a safe, well-managed environment. The surgical team manages a wide variety of tasks, including performing pre-operative care, administering anesthesia, conducting a time-out safety procedure and performing the surgery itself, all while maintaining a sterile environment, preventing infection and managing surgical equipment. Patients, protocols, processes and products all demand attention at once, and this perioperative dance requires everyone in the room to know their role and do their part. The team's success ensures patient safety and success.

It's a tall order for any surgical team, but new data-driven, technologically savvy, customizable solutions are optimizing OR workflow to bolster surgical success and patient outcomes. From customizable tool trays to optimized OR scheduling, the following tools can help make any OR run more smoothly. Harnessing the power of artificial intelligence (AI) and cloud-based technology, these tools can increase your OR's workflow and throughput.

## DinamicOR Customizable Back Table Solutions

Combining technology with efficiency, DinamicOR offers multi-tiered back tables for surgical tools, custom-fitted drapes and a powerful workflow management app to revolutionize the OR experience.

The four-in-one adjustable back table allows your team to adjust shelf positions and table height. Available in double-wide (fitting up to eight trays) or triple-wide (fitting up to 12 trays), it gives you 92 percent visibility of surgical tools without moving trays, reduces setup and takedown time by 33 percent and decreases staff tray movements by 88 percent. Durable, custom-fitted drapes work with the table to reduce the risk of sterile field violations. The drape features numbered placement icons to help your surgical team create repeatable tray setups, streamlining the process and minimizing errors. The Workflow Management App guides your team through an optimized, streamlined, repeatable tray setup process. It also offers an instrument database and a procedure encyclopedia with a wealth of information on new instruments and unfamiliar procedures. For more information, visit *www.dinamicor.com*.

## QVENTUS Perioperative Solution

Surgery scheduling often complicates OR efficiency, and more than 30 percent of OR time goes unused. Quventus AI-powered Surgical Growth Solution puts the right cases in the right rooms at the right times, ensuring ORs are used to their full potential. Two perioperative solutions help increase surgical volume, maximize robotic asset utilization and attract best-fit surgeons, while reducing care teams' administrative workload. For more information, visit *www.qventus.com/solutions/surgical-services*.

## PROXIMIE Operating System

The Proximie operating system for intelligent operating rooms links people, data, devices and workflow to improve surgical throughput and quality using real-time, AI-powered insight and orchestration. This secure, scalable, cloud-based platform optimizes the schedule, reduces underutilization, drives efficiency and increases case volume. AI and computer vision detect surgical events and capture real-time OR data, replacing the need for manual data entry. It also improves collaboration and training, discovers patterns and reduces variations and adverse events. This tool integrates with electronic health records and combines predictive analytics and automated notifications. The intelligence suite streamlines workflows and increases throughput, helping ORs operate at their highest level. For more information or to request a demo, visit *www.proximie.com*.

**RACHEL MAIER**, MS, is a Kansas City-based freelance writer and editor.

## Clinical Research Design Simplified: A Step-by-Step Guide for Nurses, Physicians, and Allied Health Researchers (Healthcare Research Simplified Book 1)

*Author: Rafiq Muhammad, MD, PhD*

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*Author: Healthcare AI Institute*

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## Healthcare Cybersecurity, Privacy, and Data Protection (HIMSS Book Series)

*Author: Lee Kim, JD, CISSP, CIPP/US*

Healthcare cybersecurity, privacy and data protection are foundational to healthcare organizations that operate in complex environments that rely on trusted virtual and physical access by both human and nonhuman entities, as well as an extensive network of vendors, service providers and third parties that support clinical, administrative and technical functions. This book offers practical guidance for individuals involved in healthcare cybersecurity, privacy and data protection, as well as international stakeholders, to safeguard patient information, systems, networks, devices, applications, data and other resources.

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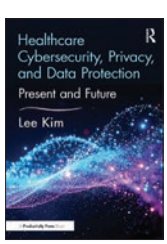


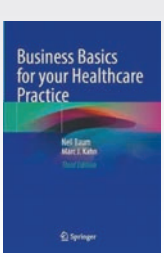


## Business Basics for your Healthcare Practice, Third Edition

*Authors: Neil Baum, MD, and Marc J. Kahn, MD*

Building on the foundation of the previous editions, this book takes readers to the next level of management of medical practices for the 21st century. Opening chapters revisit the basic business concepts, from accounting and contracts to managing people and personal finances. The next set of chapters offers a roadmap for doctors who are beginning a medical practice and includes new methods and procedures that have become available since the original edition, defining the various options for doctors' employment such as solo practice, group practice and organized medicine. The final chapters emphasize strategies on how to build and grow a successful practice, including the use of technology and telemedicine, cybersecurity, marketing and much more.

www.amazon.com/Business-Basics-your-Healthcare-Practice/dp/3032252407

# Medicare Immune Globulin Reimbursement Rates

Rates are effective July 1, 2026, through Sept. 30, 2026

| | Product | Manufacturer | J Codes | ASP + 6% (before sequestration) | ASP + 4.3% (after sequestration) |
|---|---|---|---|---|---|
| IVIG | ALYGLO® | GC Biopharma | J1552 | $243.09 | $239.19 |
| | ASCENIV™ | ADMA Biologics | J1554 | $1018.28 | $1001.95 |
| | BIVIGAM® | ADMA Biologics | J1556 | $162.48 | $159.88 |
| | GAMMAGARD® SD | Takeda | J1566 | $161.92 | $159.33 |
| | GAMMAPLEX® | BPL/Kedrion | J1557 | $132.54 | $130.42 |
| | OCTAGAM® | Octapharma | J1568 | $94.11 | $92.60 |
| | PANZYGA® | Octapharma/Pfizer | J1576 | $142.70 | $140.40 |
| | PRIVIGEN® | CSL Behring | J1459 | $102.44 | $100.79 |
| | YIMMUGO® | Kedrion | J1553 | $48.29 | $47.52 |
| IVIG/SCIG | GAMMAGARD LIQUID® | Takeda | J1569 | $98.61 | $97.02 |
| | GAMMAKED™ | Kedrion | J1561 | $98.03 | $96.46 |
| | GAMUNEX®-C | Grifols | J1561 | $98.03 | $96.46 |
| SCIG | CUTAQUIG® | Octapharma | J1551 | $140.30 | $138.05 |
| | CUVITRU® | Takeda | J1555 | $181.47 | $178.56 |
| | HIZENTRA® | CSL Behring | J1559 | $148.83 | $146.44 |
| | HYQVIA® | Takeda | J1575 | $183.47 | $180.53 |
| | XEMBIFY® | Grifols | J1558 | $152.43 | $149.99 |

* ASP-based Medicare payment rate not yet available; payment rate assigned by your Medicare Administrative Contractor.

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# Immune Globulin Reference Table

| | Product | Manufacturer | Indication | Size |
|---|---|---|---|---|
| IVIG | ALYGLO® | GC Biopharma | PI | 5 g, 10 g, 20 g |
| | ASCENIV™ LIQUID, 10% | ADMA Biologics | PI | 5 g |
| | BIVIGAM® LIQUID, 10% | ADMA Biologics | PI | 5 g, 10 g |
| | GAMMAGARD® S/D Lyophilized, 5% (Low IgA) | Takeda | PI, ITP, B-cell CLL, KD | 5 g, 10 g |
| | GAMMAPLEX® Liquid, 5% | BPL/Kedrion | PI, ITP | 5 g, 10 g, 20 g |
| | GAMMAPLEX® Liquid, 10% | BPL/Kedrion | PI, ITP | 5 g, 10 g, 20 g |
| | OCTAGAM® Liquid, 5% | Octapharma | PI | 1 g, 2.5 g, 5 g, 10 g, 25 g |
| | OCTAGAM® Liquid, 10% | Octapharma | ITP, DM | 2 g, 5 g, 10 g, 20 g, 30 g |
| | PANZYGA® Liquid, 10% | Octapharma/Pfizer | PI, ITP, CIDP | 1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g |
| | PRIVIGEN® Liquid, 10% | CSL Behring | PI, ITP, CIDP | 5 g, 10 g, 20 g, 40 g |
| | YIMMUGO®, 10% | Kedrion | PI | 5 g, 10 g, 20 g |
| IVIG/SCIG | GAMMAGARD Liquid®, 10% | Takeda | IVIG: PI, MMN, CIDP | 1 g, 2.5 g, 5 g, 10 g, 20 g, 30 g |
| | | | SCIG: PI | |
| | GAMMAKED™ Liquid, 10% | Kedrion | IVIG: PI, ITP, CIDP | 1 g, 2.5 g, 5 g, 10 g, 20 g |
| | | | SCIG: PI | |
| | GAMUNEX®-C Liquid, 10% | Grifols | IVIG: PI, ITP, CIDP | 1 g, 2.5 g, 5 g, 10 g, 20 g, 40 g |
| | | | SCIG: PI | |
| SCIG | CUTAQUIG® Liquid, 16.5% | Octapharma | PI | 1 g, 1.65 g, 2 g, 3.3 g, 4 g, 8 g |
| | CUVITRU® Liquid, 20% | Takeda | PI | 1 g, 2 g, 4 g, 8 g, 10 g |
| | HIZENTRA® Liquid, 20% | CSL Behring | PI, CIDP | 1 g PFS, 2 g PFS, 4 g PFS, 10 g PFS |
| | HYQVIA® Liquid, 10% | Takeda | PI, CIDP | 2.5 g, 5 g, 10 g, 20 g, 30 g |
| | XEMBIFY® Liquid, 20% | Grifols | PI | 1 g, 2 g, 4 g, 10 g |

**CIDP** Chronic inflammatory demyelinating polyneuropathy
**CLL** Chronic lymphocytic leukemia
**DM** Dermatomyositis
**ITP** Immune thrombocytopenic purpura
**KD** Kawasaki disease
**MMN** Multifocal motor neuropathy
**PI** Primary immune deficiency disease
**PFS** Prefilled syringes

## 2026-2027 Influenza Vaccines

**Administration Codes:** G0008 (Medicare plans)
**Diagnosis Code:** V04.81

| Product | Manufacturer | Presentation | Age Group | Code |
|---|---|---|---|---|
| FLUAD® (IIV4) | CSL Seqirus | 0.5 mL PFS 10-bx | 65 years+ | 90674 |
| FLUARIX® (IIV4) | GSK | 0.5 mL PFS 10-bx | 6 months+ | 90686 |
| FLUBLOK® (ccIIV4) | Sanofi | 0.5 mL PFS 10-bx | 9 years+ | 90682 |
| FLUCELVAX® (ccIIV4) | CSL Seqirus | 0.5 mL PFS 10-bx | 6 months+ | 90674 |
| FLULAVAL® (IIV4) | GSK | 0.5 mL PFS 10-bx | 6 months+ | 90686 |
| FLUMIST® (LAIV4) | AstraZeneca | 0.2 mL PFS nasal spray 10-bx | 2–49 years | 90672 |
| FLUZONE® (IIV4) | Sanofi | 0.5 mL PFS 10-bx | 6 months+ | 90686 |
| FLUZONE® (IIV4) | Sanofi | 5 mL MDV | 6 months+ | 90685 |
| FLUZONE® HIGH-DOSE (IIV4) | Sanofi | 0.5 mL PFS 10-bx | 65 years+ | 90662 |

**ccIIV4** Cell culture-based trivalent inactivated injectable
**IIV4** Egg-based trivalent inactivated injectable
**LAIV4** Egg-based live attenuated trivalent nasal spray

## 2026-2027 COVID-19 Vaccines

| Product | Manufacturer | Presentation | Age Group | Code |
|---|---|---|---|---|
| COMIRNATY® (COVID-19 Vaccine, mRNA) | Pfizer-BioNTech | 0.3 mL PFS 10-bx | 65 years+; 5–64 years with underlying condition | TBD |
| mNEXSPIKE® (COVID-19 Vaccine, mRNA) | Moderna US, Inc. | 0.2 mL PFS 10-bx | 65 years+; 12–64 years with underlying condition | TBD |
| NUVAXOVID™ (COVID-19 Vaccine, Adjuvanted) | Sanofi | 0.5 mL PFS 10-bx | 65 years+; 12–64 years with underlying condition | TBD |
| SPIKEVAX® (COVID-19 Vaccine, mRNA) | Moderna US, Inc. | 0.5 mL PFS 10-bx | 12 year+ | TBD |
| SPIKEVAX® (COVID-19 Vaccine, mRNA) | Moderna US, Inc. | 0.25 mL PFS 10-bx | 6 months to 11 years | TBD |

## Respiratory Syncytical Virus (RSV) Products

| Product | Manufacturer | Presentation | Age Group | Code |
|---|---|---|---|---|
| ABRYSVO™ | Pfizer | 0.5 mL PFS 1-bx | 60 years+; 50–59 years at increased risk for LRTD caused by RSV; pregnant individuals 32–36 weeks gestation | 90678 |
| ABRYSVO™ | Pfizer | 0.5 mL PFS 10-bx | | |
| AREXVY | GSK | 0.5 mL SDV 10-bx | 60 years+; 50–59 years at increased risk for LRTD caused by RSV | 90679 |
| BEYFORTUS® | Sanofi | 0.5 mL PFS 5-bx | Neonates and infants born during or entering first RSV season; children up to 24 months who remain vulnerable to severe RSV through second RSV season | 90380 |
| BEYFORTUS® | Sanofi | 1 mL PFS 5-bx | | 90381 |
| ENFLONSIA™ | Merck | 0.7 mL PFS 10-bx | Neonates and infants born during or entering first RSV season | 90382 |
| mRESVIA® | Moderna US, Inc. | 0.5 mL PFS 2-bx | 60 years+; 18-59 years at increased risk for LRTD caused by RSV | 90683 |
| mRESVIA® | Moderna US, Inc. | 0.5 mL PFS 10-bx | | |

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