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A Revolution in Flu Vaccine Technology

Flublok represents a new class of influenza vaccine and is the world's first protein-based flu vaccine. It is approved by the FDA for adults 18 years and older. Unlike other flu vaccines, Flublok does not use the influenza virus or eggs in its production. Hemagglutinin (HA) is a part of the virus that is essential for entry of the virus into cells in the body. HA is the primary component in all inactivated vaccines and the novel manufacturing technology of Flublok allows for the production of large quantities of this protein. The majority of antibodies that prevent influenza virus infection are directed against HA. Although the technology is new to flu vaccine production, it is used to make vaccines that have been approved by the FDA to prevent other infectious diseases.¹

Flublok is highly pure as it is manufactured without:

- the use of eggs
- live or inactivated flu virus
- (making it ideal for individuals with egg allergies)
- latex
- preservatives, such as thimerosal
- formaldehyde
- gelatin
- antibiotics

Flublok is manufactured using the genetic information derived from the wild-type influenza virus and is not subject to the mutations sometimes introduced into vaccines during the process of egg adaptation. This reduces the possibility of decreased effectiveness due to a mismatch between the wild-type virus and an egg-adapted vaccine, as was repeatedly reported in the literature most recently during the 2012-2013 season.² During that same flu season, vaccine effectiveness

Table 1. Efficacy of Flublok (Trivalent) vs Culture-Confirmed Influenza in Healthy Adults 18-49 Years of Age⁶

Case definition	Flublok Vaccine Efficacy (%)
Positive culture with a strain represented in the vaccine	
CDC-ILI: all matched strains	75.4
Any ILI: all matched strains	67.2
Positive culture with any strain, regardless of match to the vaccine	
CDC-ILI: all strains	44.6
Subtype A	54.4
Type B	23.1
Any ILI: all strains	44.8
Subtype A	49
Type B	37.2

ILI= influenza-like illness; CDC-ILI=ILI+fever \geq 100°F

Talking to Your Patients—Key Points

- Assess patients' immunization status
- Discuss the importance of receiving an influenza vaccination:
- Vaccine efficacy varies, but getting vaccinated remains the best protection against the flu and will reduce the severity and duration if patients do become infected with influenza
- Reassure patients of vaccine safety
- Offer to administer the influenza vaccine that best meets individual patients' needs. Flublok is a good choice for all people 18 years of age and older and is especially ideal for older adults or patients with egg allergies, are vegan, or are allergic to other ingredients typically found in conventional vaccines.

Table 2. Immunogenicity of Flublok (Trivalent) vs Another Standard Flu Vaccine in Adults 50 Years and Older⁶

Study of Patients 50-64 Years	Flublok (GMT)	Other Flu Vaccine (GMT)
A strain (H1N1)	181.3	139.7
A strain (H3N2)	105.4	60.9
B strain	110.9	116
Study of Patients \geq 65 Years	Flublok (GMT)	Other Flu Vaccine (GMT)
A strain (H1N1)	176.8	148.1
A strain (H3N2)	338.5	199.2
B strain*	149.6	194.8

GMT=geometric mean titers

*B immunogenicity comparison is confounded as the B-component differed in this study.

against the H3N2 strain for egg-based influenza vaccines was estimated at 9% for individuals 65 years and older.^{2,3}

Flublok's production technology has other advantages as well. The vaccine manufacturing process can be started quickly if an unexpected need arises, such as an influenza pandemic or during seasons when flu is particularly widespread.⁴ The process is also important if egg supplies are compromised or an influenza virus is particularly dangerous. Additionally, some flu strains do not grow well in eggs or cells, and Flublok's technology can speed up vaccine production and availability.

New Data Demonstrate Increased Efficacy

Flublok is currently available as a trivalent formulation, offering protection against two influenza A strains (H1N1 and H3N2) and one influenza B strain, and contains 3 times the amount of antigen than standard flu vaccines (3x45 mcg versus 3x15 mcg HA protein). In adults 18 to 49 years of age, studies showed Flublok to be 75.4% effective against matched strains of flu and 44.6% effective against all circulating strains of flu (Table 1).^{5,6} Studies in adults 50 years of age and older showed a higher rate of immunogenicity against A strains in people administered Flublok compared with conventional trivalent flu vaccine; immunogenicity rates were comparable for the B strain (Table 2).⁶⁻⁸

A post-marketing efficacy study of Flublok using a formulation that protected against two influenza A strains and two B strains was recently performed in more than 8,500 adults 50 years and older (Table 3).⁹ Among patients reporting flu symptoms, 2.2% of those given Flublok were

laboratory-confirmed to have flu compared with 3.2% of those given a traditional inactivated egg-based influenza vaccine protecting against the same four strains. These top-line data results showed Flublok to be 31% more effective in preventing flu compared with those who received the traditional vaccine. A pre-specified exploratory analysis confirmed the superior efficacy of Flublok over the traditional vaccine ($P < 0.001$). A quadrivalent formulation of Flublok is being studied in children 6 to 17 years of age.

Comparable Safety

Flublok has a safety profile similar to that of inactivated influenza vaccines, with pain at the injection site the most commonly reported adverse reaction. Headache, fatigue, and muscle aches were also reported in clinical trials.⁶

Individuals having any known severe allergic reactions to any of the components in Flublok should not receive the vaccine. Flublok does not contain any egg protein, preservatives, latex, antibiotics, or gelatin, and is safe and recommended by the CDC Advisory Committee on Immunization Practices (ACIP) for adults 18 years of age and older, including those with known or suspected egg allergies.

If patients have experienced Guillain Barré Syndrome within 6 weeks of a prior flu vaccine, the decision to administer Flublok should be made with careful consideration of the potential benefits and risks.⁶ Further, the immune response of Flublok may be diminished if given to an immunocompromised person.

Reimbursement

Flublok is fully covered for all adults 18 years and older by most insurance providers, including Medicare. Under the Affordable Care Act, individuals may receive ACIP-recommended influenza vaccines without any cost sharing requirements when administered by an in-network provider. Pharmacists should check with the patient's medical or pharmacy benefits administrator to determine coverage for the vaccine and its administration by your practice. Effective January 1, 2014, Flublok has a specific CPT code, which should be used when submitting reimbursement claims: 90673. (This is a code specific for Flublok and will ensure compensation occurs at an appropriate rate.)

The NDC numbers for Flublok are:
Box: 42874-015-10

Single-dose vial: 42874-015-01

How to Order

Flublok is available as single-dose vials in boxes of 10. The FDA-approved shelf life of Flublok is 6 months. To order Flublok, please contact one of the following distributors:

FFF Enterprises: 800-843-7477 or www.myfluvaccine.com
Cardinal Health: 866-677-4844 or www.cardinal.com/us/en/SPD/Ordering
McKesson: 877-MCK-4FLU or <https://mms.mckesson.com/index.mck>
Henry Schein Medical: 800-772-4346 or www.henryschein.com/flu

NEW Table 3. Efficacy of Flublok vs Another Standard Flu Vaccine⁹

	Flublok (n=4,303)	Other Flu Vaccine (n=4,302)
Patients with confirmed influenza*	96 (2.2%)	138 (3.2%)

Relative vaccine efficacy for Flublok was 31%, meeting pre-specified conditions for superiority.

*187/234 (or 80%) virus isolates were subtyped as influenza A. Efficacy against the B strains was comparable between vaccines.
Both vaccines used in this study were quadrivalent.

Please see complete Package Insert information at www.flublok.com or call 203-686-0800 for more information.

The flu (influenza) is a serious respiratory illness that causes fever and chills; cough; sore throat; runny nose; muscle or body aches; headache; and fatigue. Diarrhea and vomiting may also occur but are more common in children. Each year, the Centers for Disease Control and Prevention (CDC) estimate that 5% to 20% of people in the United States get the flu and more than 200,000 are hospitalized because of flu-related complications.¹⁰ These complications can include pneumonia and inflammation of the heart, and can be serious enough to result in death. This is why the best protection against the flu is to get a flu shot (vaccine) every year. It is recommended that everyone older than 6 months of age receive a flu shot.

However, research has shown less than half of people in the United States receive a flu shot. This may be due to several reasons, including having an egg allergy (conventional flu vaccines are grown in eggs and are not suitable for people with egg allergies) or they do not wish to get a shot that contains preservatives, such as the mercury-based preservative called thimerosal, or the flu virus. Some choose not to get a flu shot for reasons that are not true: they believe they can get the flu from the vaccine, or they believe that the vaccine is not very effective.

A New Class of Flu Vaccine

Flublok is a new class of flu vaccine that is approved by the FDA for adults 18 years and older. Flublok is different than conventional flu vaccines as it is the world's first protein-based flu vaccine. Conventional flu vaccines are grown in eggs or sometimes in cell culture.

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ELSEVIER

**Flublok®**
Influenza vaccine

Using revolutionary production technology, Flublok is highly pure as it is made without:

- the use of eggs
- preservatives, such as thimerosal
- live or inactivated flu virus
- latex
- formaldehyde
- gelatin
- antibiotics

Flublok is made with just the protective ingredients needed (called hemagglutinin [HA] protein) without growing the flu virus. This makes Flublok ideal for people who have allergies to or concerns with any of those ingredients listed above or who are vegan. This HA protein is what the body needs so it can make antibodies to protect against flu infection. It is important to note that flu vaccines grown in eggs can mutate, or change, resulting in a mismatch between the vaccines that grew in the eggs and the flu viruses that are actually circulating that season. This leads to a less effective flu vaccine. Flublok is different and does not contain egg-based mutations.

This new technology has other advantages as well. The manufacturing process that Flublok utilizes can be started quickly (unlike processes that use eggs) in case of an increased demand, such as a pandemic or during seasons when flu has become widespread.

How Does Flublok Work?

Commercially available Flublok is a trivalent formulation, which means it offers protection against two influenza A strains (H1N1 and H3N2) and one influenza B strain. Importantly, Flublok contains 3 times the amount of antigen (the HA protein) than standard flu vaccines. Studies have shown that in adults 18 to 49 years of age, Flublok was 75.4% effective in preventing flu against matched strains of flu (the strains included in the vaccine) and 44.6% effective against all circulating strains of flu (not just the flu strains included in the vaccine, but all strains present during that flu season).^{5,6} Studies in adults 50 years of age and older showed more antibodies were produced against

A strains of the flu in people who received Flublok compared with conventional trivalent flu vaccine; antibody levels were comparable for the B strain.^{7,8} A new study of Flublok was recently performed in adults (this formulation included two A strains and two B strains), and showed 31% improved performance in preventing the flu compared with a standard egg-based flu vaccine.⁹ Flublok is also being studied in children 6 to 17 years of age.

Safety of Flublok

Flublok is just as safe as conventional flu vaccines. The most commonly reported side effect is pain at the injection site. Other side effects include headache, fatigue, and muscle aches.⁶

Anyone with a known severe allergic reaction to any of the ingredients in Flublok should not receive the vaccine. Flublok does not contain any egg protein, preservatives, latex, antibiotics, or gelatin, and is safe and recommended for use in all adults 18 years and older, including those with known or suspected egg allergies.

If a person has experienced Guillain Barré Syndrome (severe muscle weakness) within 6 weeks of a prior flu shot, patients should talk with their doctor or pharmacist about the potential benefits and risks of receiving Flublok.⁶ The immune response of Flublok may be less if given to a person with a weakened immune system.

How Can I Find Flublok?

You can ask your doctor or pharmacist to order Flublok or visit our Flublok Finder at www.flublok.com to find a location that carries Flublok near you.

Cost/Reimbursement

Flublok is fully covered by most insurance providers, including Medicare.

Contact your insurance provider, employer, or school to find out more information on your specific flu vaccine coverage.

For more information on Flublok, visit www.flublok.com or call 203-686-0800.

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