IN ADULTS AGED 18+

YOU HAVE THE POWER TO HELP PROTECT BEYOND THE FLU FLUBLOK IS PROVEN TO HELP PREVENT INFLUENZA AND DEMONSTRATED TO REDUCE ITS COMPLICATIONS^{1,4*}

Flublok is a vaccine indicated for active immunization for the prevention of disease caused by influenza A virus subtypes and influenza type B virus represented by antigens contained in the vaccine. Flublok is approved for use in persons 18 years of age and older.

*Flublok (quadrivalent) was proven to prevent more flu in older adults than Fluarix (quadrivalent standard-dose vaccine). The efficacy of Flublok (quadrivalent) is relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.¹

IMPORTANT SAFETY INFORMATION

Do not administer Flublok to anyone with a history of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine.







FLUBLOK COMBINES THE ADVANTAGES OF RECOMBINANT TECHNOLOGY WITH A HIGHER DOSE^{4,6}



AN EXACT STRAIN MATCH^{6,7}

The only recombinant flu vaccine that has known and exact antigen content, Flublok ensures identical antigenic match with WHOand FDA-selected flu strains.



AVOIDS MUTATIONS⁶

Cell- and egg-based flu vaccines have the potential to develop mutations during production, which may reduce their effectiveness.



MAY PROVIDE CROSS-PROTECTION⁶

Recombinant technology leads to a broader immune response that may provide cross-protection, even in a mismatch season *

Flublok (quadrivalent) was evaluated in the pivotal trial against Fluarix (quadrivalent standard-dose vaccine). The efficacy of Flublok (quadrivalent) is relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.¹

*Flublok is produced using a novel production platform in which recombinant HA is expressed in insect cells using a baculovirus expression vector system (BEVS). Recombinant HA antigens produced using BEVS have been shown to induce significantly higher levels of broadly cross-reactive antibodies against highly conserved regions of HA compared with egg-derived vaccines, which may potentially protect against drift-variant influenza viruses.⁶

⁺Flublok contains 45 micrograms (mcg) of HA per strain vs 15 mcg of HA per strain in a standard-dose influenza vaccine.^{14,5}

CDC=Centers for Disease Control and Prevention; FDA=US Food and Drug Administration; WHO=World Health Organization.

IMPORTANT SAFETY INFORMATION

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Flublok.

Please see additional Important Safety Information throughout. Before administration, please see full Prescribing Information.



3x THE ANTIGEN^{1,4,5}

Flublok also contains 3x the hemagalutinin (HA) antigen content of standard-dose flu vaccines, which has been linked to greater immunogenicity vs standard-dose flu vaccines.⁺



MAY INDUCE A MORE ROBUST ANTIBODY RESPONSE⁸

According to a study published by the CDC in January 2024, vaccination with a higher-dose recombinant flu vaccine may induce a more robust antibody response than egg-based standard-dose vaccines.



IN A RANDOMIZED CONTROLLED TRIAL VS FLUARIX 30% RELATIVE REDUCTION IN PCR-CONFIRMED FLU IN ADULTS AGED 50+^{1,4}

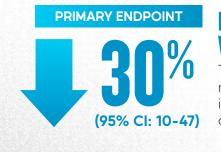
STUDY DESIGN^{1,4}

- Phase 3-4 randomized controlled trial in adults aged 50+ (N≈9000) during the 2014-2015 influenza season in which A (H3N2) was predominant and antigenically mismatched
- Patients were randomized 1:1 to receive Flublok or Fluarix*

*Flublok (quadrivalent) was proven to prevent more flu in older adults than Fluarix (quadrivalent standard-dose vaccine). The efficacy of Flublok (quadrivalent) is relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.¹

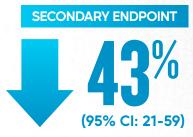
PROVEN TO HELP PREVENT MORE CASES OF THE FLU THAN FLUARIX IN PATIENTS AGED 50+14

Flublok prevented more cases of influenza than Fluarix, satisfying the primary criterion for noninferiority and the prespecified exploratory superiority criterion.⁴



FEWER INFLUENZA CASES WITH FLUBLOK

The primary endpoint was defined as relative vaccine efficacy (rVE) against influenza due to ANY PCR-confirmed circulating strains^{1,4}



FEWER INFLUENZA CASES WITH FLUBLOK

The secondary endpoint was defined as rVE against influenza due to ANY cultureconfirmed circulating strains^{1,4}

CI=confidence interval; PCR=polymerase chain reaction.

SAFETY IN ADULTS

- Comparable safety profile to a standard-dose quadrivalent inactivated influenza vaccine in adults aged 50+4
- Most common adverse events (≥10%) in the Flublok group in adults aged 50-64⁴:
- Injection-site reactions: tenderness (37%), pain (32%)
- Systemic adverse reactions: headache (17%), fatigue (13%), muscle pain (11%)

IMPORTANT SAFETY INFORMATION

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of the potential benefits and risks.



IN PATIENTS AGED 18-49 YEARS FLUBLOK: EFFECTIVE FLU PROTECTION, EVEN IN A SEASON WITH SIGNIFICANT ANTIGENIC MISMATCH^{1,9}

STUDY DESIGN

- Randomized, observer-blind, placebo-controlled trial to evaluate the protective efficacy and safety of Flublok (trivalent) against influenza in 4648 adults aged 18-49 years^{1,9}
- The study was undertaken during the 2007-2008 influenza season when there was significant mismatch between vaccine antigens and circulating viruses⁹
- Primary endpoint: CDC-defined influenza-like illness (ILI), defined by presence of documented fever ≥100 °F plus either sore throat or cough with positive culture for an influenza virus strain antigenically resembling a strain represented in Flublok. Vaccine efficacy against antigenically matched culture-confirmed CDC-ILI could not be determined reliably because 96% of the influenza isolates obtained were not antigenically matched to the strains represented in the vaccine¹

ADDITIONAL EFFICACY ENDPOINTS



FEWER FLU CASES WITH FLUBLOK

due to ANY culture-confirmed CDCdefined ILI strain, regardless of match to the vaccine¹ **44.8**% (95% CI: 24.4, 60.0)

FEWER FLU CASES WITH FLUBLOK

due to any culture-confirmed ILI strain, regardless of match to the vaccine¹

FLUBLOK WAS ASSOCIATED WITH PREVENTING CULTURE-CONFIRMED INFLUENZA DESPITE SIGNIFICANT ANTIGENIC MISMATCH BETWEEN THE VACCINE ANTIGENS AND CIRCULATING VIRUSES¹

IMPORTANT SAFETY INFORMATION

If Flublok is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.



THE LARGEST RANDOMIZED REAL-WORLD FLU EFFECTIVENESS STUDY TO DATE

STUDY DESIGN

- Modified cluster randomized observational study to evaluate Flublok vs standard-dose influenza vaccines^{10*}
- Study population: 1,630,328 members of the Kaiser Permanente Northern California (KPNC) healthcare system aged 18-64 years¹⁰
- Evaluated over 2 flu seasons: 2018-2019 influenza season, when A (H1N1) was predominant until March 2019, when A (H3N2) viruses became predominant, and 2019-2020 influenza season, when A (H1N1) was predominant with B cocirculation¹²⁻¹⁴
- Patients aged 50-64 with comorbid conditions: asthma: 14% (96,307); diabetes: 18% (119,430); chronic obstructive pulmonary disease: 2% (13,357); coronary heart disease: 4% (25,496)¹⁰

*Flublok (quadrivalent) was proven to prevent more flu in older adults than quadrivalent standard-dose vaccines. The efficacy of Flublok (quadrivalent) is relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.^{1,10}

FLUBLOK WAS ASSOCIATED WITH GREATER PROTECTION¹⁰

PRIMARY ENDPOINT:



559 patients (2.00 cases per 1000) had PCR-confirmed influenza in the Flublok cohort (N=279,400) vs 925 patients (2.34 cases per 1000) with standard-dose vaccines (N=395,852).

STUDY LIMITATIONS¹⁰

- Data were limited to 2 influenza seasons; rVE may vary across seasons depending on the vaccine match with circulating strains
- Primary outcome did not include infections in persons who did not undergo PCR testing, which limits generalizability
- Although KPNC has a diverse population, it may not be representative of other populations in the US
- Compliance with the weekly assigned vaccine schedule varied from time to time due to logistical constraints
- The study had limited power to detect a clinically meaningful benefit of Flublok vs standard-dose vaccines with respect to several less frequent outcomes, such as hospitalized, PCR-confirmed influenza

CONSIDERING FLU VACCINES TYPICALLY PREVENT 40% TO 60% OF FLU CASES IN A MATCHED FLU SEASON, COULD FLUBLOK MAKE A DIFFERENCE TO YOUR PATIENTS?¹⁰

IMPORTANT SAFETY INFORMATION

Vaccination with Flublok may not protect all recipients.

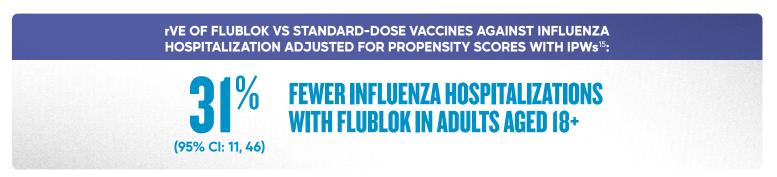


FLUBLOK WAS ASSOCIATED WITH FEWER INFLUENZA HOSPITALIZATIONS COMPARED TO STANDARD-DOSE VACCINES¹⁵

STUDY DESIGN

- Retrospective test-negative case-control study in approximately 15,000 patients aged 18+ to investigate the rVE of Flublok vs standard-dose vaccines against influenza hospitalization^{15*}
- In the primary analysis, Flublok was evaluated against standard-dose flu vaccines, including^{15,16}:
- Egg-based: Fluarix, Afluria, Flulaval, and Fluzone
- Cell-based: Flucelvax

*Flublok (quadrivalent) was evaluated against quadrivalent standard-dose vaccines.¹³ The efficacy of Flublok (quadrivalent formulation) is relevant to Flublok (trivalent formulation) because both vaccines are manufactured using the same process and have overlapping compositions.^{1,15}



Secondary endpoints: When adjusted for propensity scores with inverse probability weights (IPWs)¹⁵:

- Flublok was associated with providing greater protection against influenza hospitalization vs standard-dose vaccines for the following populations¹⁵:
- Female sex: 37% rVE (95% CI: 13, 54)
- Age 18-64 years: 28% rVE (95% CI: 3, 46)
- No high-risk condition: 60% rVE (95% CI: 29, 78)

IMPORTANT SAFETY INFORMATION

Syncope (fainting) has been reported following vaccination with Flublok. Procedures should be in place to avoid injury from fainting.



FLUBLOK WAS ASSOCIATED WITH FEWER INFLUENZA HOSPITALIZATIONS Compared to standard-dose vaccines (CONT'D)¹⁵

- Flublok was associated with providing greater (non-statistically significant) protection against influenza hospitalization vs standard-dose vaccines for the following populations¹⁵:
- Male sex: 23% rVE (95% CI: -14, 48)
- Age ≥65 years: 17% rVE (95% CI: -36, 48)
- High-risk condition: 20% rVE (95% CI: -7, 40)

STUDY STRENGTHS AND LIMITATIONS¹⁵

- The demographics of the study population were representative of the adult population of Allegheny County (which was 79% white and 51% female), which contributes to generalizability
- The University of Pittsburgh Medical Center hospitals in central and southwestern Pennsylvania are part of an integrated health system, with regular uploads of vaccination data from the state immunization registry; vaccination status was verified through the state registry with a specific data request
- Although the electronic medical record (EMR) system of University of Pittsburgh Medical Center hospitals in central and southwestern Pennsylvania is robust, if vaccinations were not captured in the EMRs or state registry, they were classified as unvaccinated
- Because data focused on hospitalizations, there may have been milder cases of influenza that were not captured in the EMRs because they didn't require medical care
- There is a possibility of selection bias among those who received influenza testing; for instance, clinicians might have preferentially tested unvaccinated subjects, which would increase the proportion of unvaccinated cases
- While a relatively large cohort of adults is included in this study, the sample size of standard-dose flu vaccine recipients may have been inadequate to detect meaningful rVE estimates for specific subgroups

IMPORTANT SAFETY INFORMATION

In adults 18 through 64 years of age, the most common injection site adverse reaction was pain; the most common solicited systemic adverse reactions were headache, fatigue, and myalgia. In adults 65 years of age and older, the most common injection-site adverse reaction was pain; the most common solicited systemic adverse reactions were fatigue and headache. Other adverse reactions may occur.



SAFETY PROFILE SUPPORTED IN ONE OF THE LARGEST SAFETY STUDIES OF A FLU VACCINE IN PREGNANT WOMEN, INCLUDING OVER 14,000 PATIENTS

STUDY DESIGN AND OUTCOMES

- This was a postlicensure, observational, retrospective safety surveillance study of over 14,000 pregnant individuals, including those with chronic conditions. 14,981 pregnant patients were exposed to Flublok Quadrivalent during the 28 days prior to conception (date of conception defined as the date of the last menstrual period [Day 0] plus 14 days) or during pregnancy¹
- The study was conducted during Northern Hemisphere influenza seasons 2018-2019 and 2019-2020. Prespecified outcomes included spontaneous abortion and congenital/fetal anomalies. Data were not collected on ectopic pregnancy or elective terminations¹
- Among 14,981 recipients of Flublok Quadrivalent with known pregnancy outcomes, 750 pregnant individuals received the vaccine during the 28 days prior to conception, 5092 during the first trimester, 4851 during the second trimester, and 4288 during the third trimester¹
- Among 5842 individuals exposed to Flublok Quadrivalent during the 28 days prior to conception or during the first trimester, miscarriage was reported in 464 (3.1%). Among individuals exposed to Flublok Quadrivalent at any time during pregnancy, 1113 pregnancies (7.7%) had infants with major birth defects (56, 360, 381, and 316 among individuals exposed during the 28 days prior to conception, the first trimester, the second trimester, and the third trimester, respectively)¹

*The data for Flublok (quadrivalent) are relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.¹

FLUBLOK DEMONSTRATED **NO INCREASED RISK** OF MAJOR BIRTH DEFECTS AND MISCARRIAGES¹





The CDC states that pregnant people are at higher risk of hospitalization due to flu and should receive an annual flu vaccine.¹⁷

IMPORTANT SAFETY INFORMATION

Do not administer Flublok to anyone with a history of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine.

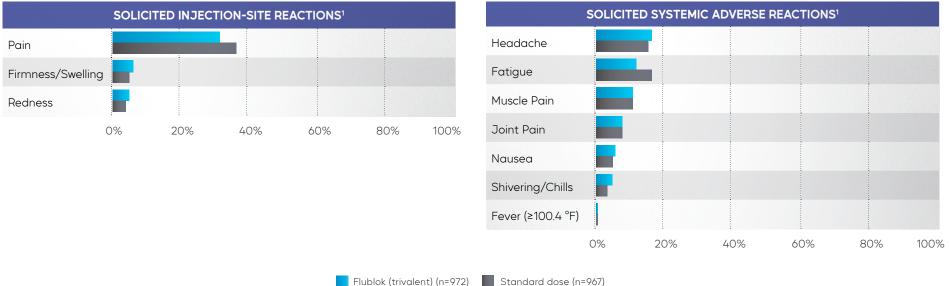
Please see additional Important Safety Information throughout. Before administration, please see full <u>Prescribing Information</u>.

Flublok[®] Influenza Vaccine

SIMILAR SAFETY PROFILE COMPARED TO STANDARD-DOSE FLU VACCINES

SAFETY IN ADULTS AGED 50-64¹

- Rates of local and systemic adverse reactions were similar within 7 days of Flublok (trivalent) or standard-dose influenza vaccine administration
- Pooled data from 2 studies; comparators were Fluzone (trivalent standard-dose formulation) and Afluria (trivalent standard-dose formulation)

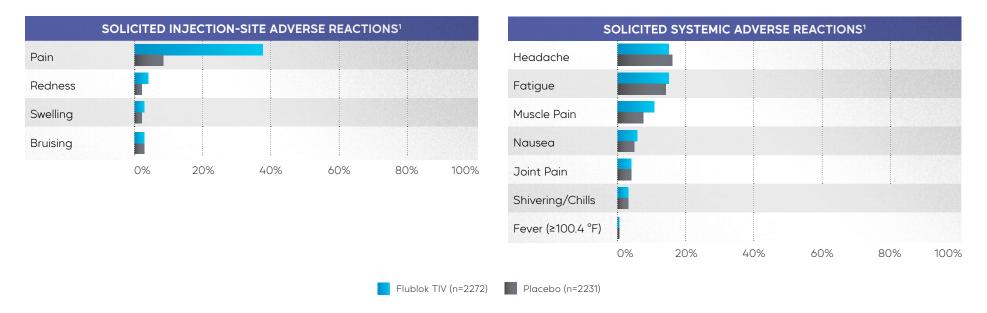




SAFETY PROFILE IN ADULTS AGED 18-49 COMPARED TO PLACEBO⁹

SAFETY IN ADULTS AGED 18-49⁹

- Safety data from a study of 4648 adults randomized to receive Flublok (trivalent; n=2344) or placebo (n=2304)
- Systemic symptoms following vaccination were similar between people receiving Flublok and placebo
- The most frequently reported systemic symptoms following vaccination were headache (15% with Flublok vs 16% with placebo) and fatigue (15% with Flublok vs 14% with placebo)
- 76% of headache complaints were mild
- Flublok was associated with local injection-site pain (37% with Flublok vs 8% with placebo) that was significantly more frequent than after saline placebo¹⁹
- 94% of all pain complaints after Flublok were rated as mild $^{\rm 9}$



TIV=trivalent.

INDICATION

Flublok is a vaccine indicated for active immunization for the prevention of disease caused by influenza A virus subtypes and influenza type B virus represented by antigens contained in the vaccine. Flublok is approved for use in persons 18 years of age and older.

IMPORTANT SAFETY INFORMATION

Do not administer Flublok to anyone with a history of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine.

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Flublok.

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of the potential benefits and risks.

If Flublok is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.

Vaccination with Flublok may not protect all recipients.

Syncope (fainting) has been reported following vaccination with Flublok. Procedures should be in place to avoid injury from fainting.

In adults 18 through 64 years of age, the most common injection site adverse reaction was pain; the most common solicited systemic adverse reactions were headache, fatigue, and myalgia. In adults 65 years of age and older, the most common injection-site adverse reaction was pain; the most common solicited systemic adverse reactions were fatigue and headache. Other adverse reactions may occur.

REFERENCES

1. Flublok, Prescribing Information, Protein Sciences Corporation, 2. Fluarix, Prescribing Information, GlaxoSmithKine, 3. Flucelvax, Prescribing Information, Segirus Inc. 4. Dunkle LM, Izikson R, Patriarca P, et al; PSC12 Study Team. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. N Engl J Med. 2017;376(25):2427-2436. doi:10.1056/NEJMoa1608862 5. Grohskopf LA, Blanton LH, Ferdinands JM, Chung JR, Broder KR, Talbot HK. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices–United States, 2023–24 influenza season. MMWR Recomm Rep. 2023;72(No. RR-2):1–25. doi:10.15585/mmwr.rr7101a1 6. Arunachalam AB, Post P, Rudin D. Unique features of a recombinant haemagalutinin influenza vaccine that influence vaccine performance. NPJ Vaccines. 2021;6:144. doi:10.1038/s41541-021-00403-77. Centers for Disease Control and Prevention. Influenza vaccines—United States, 2023–24 influenza season. August 24, 2023. Accessed June 5, 2024. https://www.cdc.gov/flu/professionals/acip/2022-2023/acip-table.htm 8. Liu F, Gross FL, Joshi S, et al. Redirecting antibody responses from egg-adapted epitopes following repeat vaccination with recombinant or cell culture-based versus egg-based influenza vaccines. Nat Commun. 2024;15(1):254. doi:10.1038/s41467-023-44551-x 9. Treanor JJ, El Sahly H, King J, et al. Protective efficacy of a trivalent recombinant hemagalutinin protein vaccine (Flublok®) against influenza in healthy adults: a randomized, placebo-controlled trial. Vaccine. 2011;29(44):7733-7739. doi:10.1016/ ivaccine.2011.07.128 10. Hsiao A, Yee A, Fireman B, Hansen J, Lewis N, Klein NP. Recombinant or standard dose influenza vaccine in adults under 65 years of age. N Engl J Med. 2023;389:2245-2255. doi:10.1056/NEJMoa2302099 11. Sanofi Pasteur Inc. Data on file. 12. Centers for Disease Control and Prevention. Estimated flu-related illness 2018-2019. September 29, 2021. Accessed June 5, 2024. https://archive.cdc.gov/#/details?url=https://www.cdc.gov/flu/about/burden/2018-2019.html 13. California Department of Public Health. Influenza surveillance report 2018-2019 season. December 2019. Accessed June 5, 2024. https://www.cdph.ca.gov/ Programs/CID/DCDC/CDPH%20Document%20Library/Immunization/Annual2018-19.pdf 14. California Department of Public Health. Influenza surveillance report 2019-2020 season. June 2021. Accessed June 5, 2024. https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Immunization/ Annual2019-20 FluReport.pdf 15. Zimmerman RK, Nowalk MP, Dauer K, et al. Vaccine effectiveness of recombinant and standard dose influenza vaccines against influenza-related hospitalization using a retrospective test-negative design. Vaccine. 2023;41:5134-5140. doi:10.1016/j.vaccine.2023.06.056 16. Rhodes RT. Choosing influenza vaccines. BioSupply Trends Quarterly. July 2013. Accessed June 5, 2024. https://www.bstquarterly.com/Assets/downloads/BSTQ/Articles/ BSTQ 2013-07 AR Choosing-Influenza-Vaccines.pdf 17. Centers for Disease Control and Prevention. Flu vaccine safety and pregnancy. September 2024. Accessed October 14, 2024, https://www.cdc.aov/flu/vaccine-safety/vaccine-preanant.html

Flublok[®] Influenza Vaccine

NEW DATA: ONE OF THE LARGEST FLU VACCINE STUDIES SUPPORTING THE SAFETY PROFILE IN PREGNANT WOMEN¹³

IN ADULTS AGED 18+

PROTECT BEYOND THE FLU WITH FLUBLOK: PROVEN TO HELP PREVENT INFLUENZA AND SHOWN TO REDUCE ITS COMPLICATIONS^{1,4*}

😴 COMBINES RECOMBINANT TECHNOLOGY WITH HIGHER ANTIGEN CONTENT4.6

- ONLY Flublok's recombinant technology ensures identical antigenic match with WHO- and FDAselected flu strains and also contains 3x the antigen content of standard-dose flu vaccines^{1,4-7†}
- PROVEN TO PREVENT MORE FLU CASES THAN A STANDARD-DOSE VACCINE IN A RANDOMIZED CONTROLLED TRIAL OF ADULTS AGED 50+1
- 😴 EVALUATED IN THE LARGEST REAL-WORLD FLU EFFECTIVENESS STUDY TO DATE 10,11
- S REAL-WORLD EVIDENCE IN INFLUENZA HOSPITALIZATIONS¹⁵

😒 ESTABLISHED SAFETY PROFILE4

- Similar safety profile compared to a standard-dose flu vaccine in adults aged 50-64⁴
- Outcomes from one of the largest safety studies of a flu vaccine in pregnant women support the safety profile of Flublok¹⁻³

*Flublok (quadrivalent) was proven to prevent more flu in older adults than Fluarix (quadrivalent standard-dose vaccine). The efficacy of Flublok (quadrivalent) is relevant to Flublok (trivalent) because both vaccines are manufactured using the same process and have overlapping compositions.¹

⁺ Flublok contains 45 mcg of hemagglutinin (HA) per strain compared with 15 mcg of HA in a standard-dose flu vaccine.¹⁴⁵

IMPORTANT SAFETY INFORMATION

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Flublok.

Please see additional Important Safety Information throughout and full Prescribing Information.

SolutionMAT-US-2400717-v3.0-10/2024© 2024 Sanofi Pasteur Inc.Sanofi1 Discovery Drive, Swiftwater, Pennsylvania 18370www.sanofi.us





