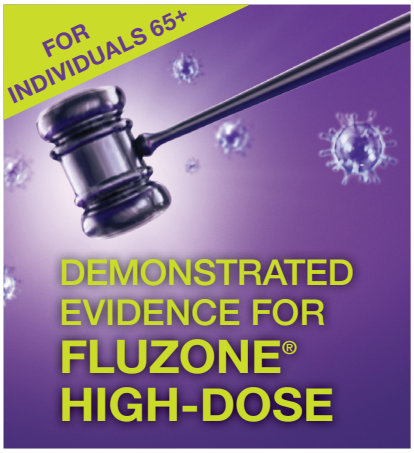
QUESTIONS·ANSWERS

ABOUT **FLUZONE® High-Dose**



What is FLUZONE® High-Dose?

FLUZONE® High-Dose is a trivalent, inactivated influenza vaccine.

FLUZONE® High-Dose contains 60 µg of hemagglutinin (HA), which is four times as much HA as in FLUZONE®, a standard-dose influenza vaccine with 15 µg HA.[1,2*]

What is FLUZONE® High-Dose indicated for?

FLUZONE® High-Dose is indicated for active immunization against influenza caused by the specific strains of influenza virus contained in the vaccine in adults 65 years of age and older. Annual flu vaccination using the most current vaccine is recommended as immunity declines in the year following vaccination.[1]

What are the risks of influenza for adults 65+?

Adults 65 years of age and older are particularly vulnerable to influenza[1,3], and suffer disproportionately from influenza-related morbidity and mortality.[4,5]

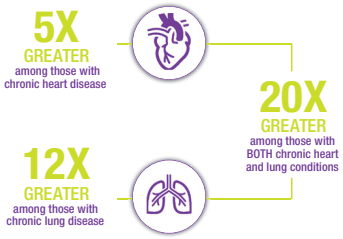
Hospitalizations and deaths

While Canadian adults age 65+ represented approximately 15% of the Canadian population, they accounted for up to:[6-12▲]

- **70%** of influenza-related hospitalizations
- **91%** of influenza-related deaths

Chronic conditions and mortality

Higher influenza-attributed mortality is associated with chronic conditions. For persons aged 65 years and over the risk for influenza-attributed death was:[3]



Functional status

One retrospective nursing home study in the United States found that influenza negatively affected the functional status of seniors and was associated with the decline of activities of daily living (ADL).[13]

FLUZONE® High-Dose is not indicated to reduce morbidity and mortality, complications associated with influenza such as pneumonia, hospitalizations, deaths, decline in independence or functional status, or to reduce influenza attributed mortality associated with chronic conditions such as chronic heart and lung disease.

What are the potential complications of influenza for adults 65+?

Direct Effects: Respiratory

Asthma & COPD Exacerbations[14,15] | Ear/Sinus Infections[15] | Bronchitis & Pneumonia[15,16]

Indirect Effects: Multi-Organ Systems

Trigger for:
Acute myocardial infarction, ischemic heart disease and cerebrovascular disease[17,18,19]

Exacerbation of:

Renal Disorder & Diabetes[5,20]

FLUZONE® High-Dose is not indicated for reduction of potential complications of influenza such as asthma, COPD, ear/sinus infections, bronchitis, pneumonia, acute myocardial infarction, ischemic heart disease, cerebrovascular disease, renal disorders or diabetes.

Why are adults 65+ more vulnerable to influenza?

Immunosenescence

Influenza infection in adults 65 years of age and older is associated with significant morbidity and mortality. The heightened susceptibility to influenza-related complications in older adults is due in large part to the natural and progressive weakening of the immune system over time—a phenomenon known as immunosenescence. Immunosenescence also renders seniors less responsive to standard-dose influenza vaccine.[1]

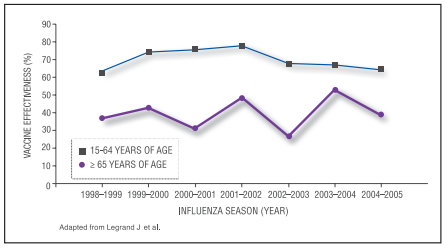
Reduced vaccine effectiveness

In the elderly, vaccine effectiveness is **~50% less** than in healthy adults, and varies depending on the outcome measures and the study population.[5]

A study showed that for the influenza seasons 1998–1999 through to 2004–2005, the range of standard-dose vaccine effectiveness was:[1†]

- 62% to 76% in persons 15-64 years of age
- 26% to 52% in persons ≥ 65 years of age

Effectiveness of standard-dose influenza vaccine[1, 21†]



How effective was FLUZONE® High-Dose in a multicentre clinical trial?

FLUZONE® High-Dose vaccine was demonstrated to provide **superior efficacy** for the 65+ population against laboratory-confirmed influenza illness compared to FLUZONE®, a standard-dose influenza vaccine.[1,2‡¥¶]

- **24.2% more efficacious** against laboratory-confirmed influenza illness caused by any virus type or subtype in adults 65 years of age and older (95% CI: 9.7; 36.5).[1,2]
- **35.4% more efficacious** against laboratory-confirmed influenza caused by strains similar to the vaccine components (secondary endpoint; 95% CI:12.5 to 52.5).[2]

* Comparative clinical significance has not been established.
▲ Public Health Agency of Canada, 2013-2018.
† Standard-dose trivalent influenza vaccine with 15 µg HA per strain/0.5 mL dose.

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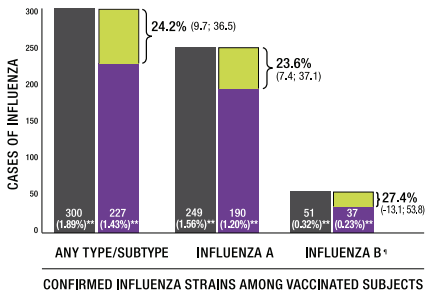
FLUZONE® High-Dose vaccine is the only vaccine demonstrated, through a large randomized study, to be more efficacious than FLUZONE® standard-dose vaccine in preventing influenza in adults over 65.[2,2]

Relative efficacy against lab-confirmed influenza-like illness caused by any strain compared to FLUZONE®, a standard-dose vaccine (phase 3B-4 trial) in adults 65 years of age and older.[1,2#]



FLUZONE® HIGH-DOSE VACCINE (N = 15,892)
FLUZONE® STANDARD-DOSE VACCINE (N = 15,911)
RELATIVE EFFICACY VACCINE % (95% CI)

** Percentages in parentheses refer to the percentage of FLUZONE® High-Dose or FLUZONE® vaccine recipients with laboratory-confirmed influenza in association with a protocol-define influenza-like illness.

Relative efficacy vs FLUZONE®, a standard-dose vaccine, was demonstrated across:

- **Two influenza seasons:** 2011–2012 and 2012–2013[1,2]
- **Influenza virus types:** Influenza A (H1N1), A (H3N2) and B strains[1,2]

What is the demonstrated safety profile of FLUZONE® High-Dose?

The safety profile of FLUZONE® was demonstrated in 2 large clinical trials comparing FLUZONE® High-Dose and FLUZONE®, a standard-dose vaccine.

Study 1 compared safety and immunogenicity in 3,833 individuals 65+:[1§]

- Within 6 months after vaccination, 6.1% of FLUZONE® High-Dose vaccine recipients and 7.4% of FLUZONE® vaccine recipients experienced a serious adverse event.

Study 2 compared efficacy and safety in 31,803 individuals 65+ over two influenza seasons:[1£]

- Within 6 to 8 months after vaccination, 8.3% of FLUZONE® High-Dose vaccine recipients and 9.0% of FLUZONE® vaccine recipients experienced a serious adverse event.

Frequency of solicited systemic adverse events and injection-site reactions within 7 days post-vaccination (phase 3 trial)[1]

		FLUZONE® HIGH-DOSE VACCINE (n = 2,569–2,572) %	FLUZONE® VACCINE (n = 1,258–1,260) %
SYSTEMIC	MYALGIA	21.4	18.3
	MALAISE	18.0	14.0
	HEADACHE	16.8	14.4
	FEVER	3.6	2.3
INJECTION-SITE REACTIONS	PAIN	35.6	24.3
	ERYTHEMA	14.9	10.8
	SWELLING	8.9	5.8

- Most of the reactions resolved within 3 days.[1]

How is FLUZONE® High-Dose administered?

FLUZONE® High-Dose should be administered as a single 0.5 mL injection by the intramuscular route.

- FLUZONE® does not contain gelatin, antibiotics, thimerosal or latex (natural rubber) and is considered safe for use in persons with latex allergies.
- FLUZONE® High-Dose is available in packages of 5 x 0.5 mL (single dose prefilled syringes.

Approximately 112 million doses have been distributed in the United States between 2009 and 2018.[2,3]

Contraindications:

- Known severe allergic reaction to egg protein or any component of the vaccine or after previous administration of FLUZONE® High-Dose or a vaccine containing the same components or constituents.

Relevant warnings and precautions:

- FLUZONE® High-Dose is not indicated for persons less than 65 years of age.
- As with any vaccine, immunization with FLUZONE® High-Dose may not protect 100% of individuals. Protection is limited to those strains of virus from which the vaccine is prepared or against closely related strains.
- Do not administer FLUZONE® High-Dose by intravascular injection. Do not administer into the buttocks.
- Postpone vaccination in case of moderate severe febrile illness or acute disease.
- Administer FLUZONE® High-Dose with caution in persons suffering fromcoagulation disorders or on anticoagulation therapy.
- Immunocompromised persons (whether from disease or treatment) may not elicit the expected immune response.
- Avoid vaccinating persons who are known to have experienced Guillain-Barré syndrome (GBS) within 6 weeks after a previous influenza vaccination.

For more information:

Consult the product monograph at http://products.sanofi.ca/en/fluzone-hd.pdf for important information relating to adverse reactions, drug interactions and dosing information which have not been discussed in this piece. The product monograph is also available through our medical department. Call us at 1-888-621-1146.

‡ The pre-specified statistical superiority criterion for the primary endpoint (lower limit of the 2-sided 95% CI of the vaccine efficacy of FLUZONE® High-Dose relative to FLUZONE® > 9.1%; p-value against H0:VE ≤ 9.1% = 0.022 one-sided) was met.

¥ In a multicentre study (FIM12) conducted in the United States and Canada, adults 65 years of age and older were randomized (1:1) to receive either FLUZONE® High-Dose or FLUZONE® Trivalent. The study was conducted over two influenza seasons (2011–2012 and 2012–2013). FLUZONE® High-Dose contained 60 µg of HA per strain while FLUZONE® Trivalent contained 15 µg of HA per strain. The per-protocol analysis set for efficacy assessments included 15,892 FLUZONE® High-Dose recipients and 15,911 FLUZONE® Trivalent recipients. The primary endpoint of the study was the occurrence of laboratory-confirmed influenza, defined as a new onset (or exacerbation) of at least one of the following respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing; concurrent with at least one of the following systemic signs or symptoms: temperature > 37.2°C, chills, tiredness, headaches or myalgia.

¶ In the first year of the study, the influenza B component of the vaccine and the majority of influenza B cases were of the Victoria lineage; in the second year, the influenza B component of the vaccine and the majority of influenza B cases were of the Yamagata lineage.

§ Laboratory confirmation by culture or polymerase chain reaction.

£ Randomized, double-blind, multicentre comparative trial with FLUZONE® High-Dose or FLUZONE® vaccine (2006-2007 formulation). Randomized, double-blind multicentre, efficacy trial with FLUZONE® High-Dose or FLUZONE® vaccine (2011–2012 and 2012–2013 formulations).

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Fluzone® High-Dose INFLUENZA VACCINE
Senior Influenza Protection

FLUZONE® is a trademark of Sanofi Pasteur. Sanofi Pasteur 1755 Steeles Avenue West, Toronto, Ontario M2R 3T4.

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