## 1. NAME OF THE MEDICINAL PRODUCT

Fluenz nasal spray, suspension
Influenza vaccine (live, nasal)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Reassortant influenza virus* (live attenuated) of the following three strains**:

A/Missouri/11/2025 (H1N1)pdm09-like strain
(A/Switzerland/6849/2025, MEDI 400592) $10^{7.0\pm0.5}$ FFU***

A/Darwin/1454/2025 (H3N2)-like strain
(A/Darwin/1369/2025, MEDI 406666) $10^{7.0\pm0.5}$ FFU***

B/Tokyo/EIS13-175/2025-like strain
(B/Perth/115/2025, MEDI 407730) $10^{7.0\pm0.5}$ FFU***

.....per 0.2 ml dose

* Propagated in fertilised hens' eggs from healthy chicken flocks.
** Produced in VERO cells by reverse genetic technology. This product contains genetically modified organisms (GMOs).
*** Fluorescent Focus Units.

This vaccine complies with the WHO recommendation (Northern Hemisphere) and EU decision for the 2026/2027 season.

The vaccine may contain traces of the following substances: egg proteins (e.g. ovalbumin) and gentamicin. The maximum amount of ovalbumin is less than 0.024 micrograms per 0.2 ml dose (0.12 micrograms per ml), see section 4.3.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Nasal spray, suspension (nasal spray)

Colourless to pale yellow, clear to opalescent suspension with a pH of approximately 7.2. Small white particles may be present.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Fluenz is indicated for active immunisation for the prevention of influenza disease in children and adolescents from 2 years to less than 18 years of age.

Fluenz should be used in accordance with official recommendations.

## 4.2 Posology and method of administration

Posology

*Children and adolescents from 2 years to < 18 years of age*

The recommended dose is 0.2 ml, administered as 0.1 ml in each nostril.

For children 2 to 8 years of age who have not previously been vaccinated against seasonal influenza, a second dose should be given after an interval of at least 4 weeks.

*Infants and toddlers < 2 years of age*

Fluenz should not be used in infants and toddlers below 2 years of age because of safety concerns regarding increased rates of hospitalisation and wheezing in this population (see section 4.8).

Method of administration

For nasal use only.

**Fluenz should under no circumstances be injected**.

Fluenz is administered as a divided dose in both nostrils. After administering half of the dose in one nostril, administer the other half of the dose in the other nostril immediately or shortly thereafter. The vaccine recipient can breathe normally while the vaccine is being administered – there is no need to actively inhale or sniff.

Fluenz should be administered by or under supervision of a healthcare professional.

For instructions on the handling of the vaccine before administration, see section 6.6.

Detailed instructions on the preparation and administration of the vaccine are provided in the Instructions for Use.

## 4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or to gentamicin (a possible trace residue).
- Severe allergic reaction (e.g. anaphylaxis) to eggs or to egg proteins (e.g. ovalbumin).
- Children and adolescents with clinical immunodeficiency due to conditions or immunosuppressive therapy such as acute and chronic leukaemias, lymphoma, symptomatic HIV infection, cellular immune deficiencies, and high-dose corticosteroids. Fluenz is not contraindicated for use in individuals with asymptomatic HIV infection, or individuals who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids, or those receiving corticosteroids as replacement therapy, e.g. for adrenal insufficiency.
- Children and adolescents younger than 18 years of age receiving salicylate therapy because of the association of Reye's syndrome with salicylates and wild-type influenza infection (see section 4.5).

## 4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

As with most vaccines, appropriate medical treatment and supervision should always be readily available to manage an anaphylactic event or serious hypersensitivity event following the administration of Fluenz.

Concurrent illness and chronic conditions

Fluenz should not be administered to children and adolescents with severe asthma or who are currently wheezing, because these individuals have not been adequately studied in clinical studies (see section 4.8).

Administration of Fluenz should be postponed in individuals suffering from severe acute febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not result in the deferral of vaccination.

Vaccination should also be postponed in individuals with nasal blockage, due to the potential for reduced vaccine uptake and the absence of efficacy data in this population. The presence of mild symptoms of a common cold without nasal blockage should not result in the deferral of vaccination.

Syncope

Syncope (fainting) has been observed following intranasal administration of Fluenz (see section 4.8). Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

Immunocompromised individuals

Vaccine recipients should be informed that Fluenz is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1-2 weeks following vaccination. Peak incidence of vaccine virus recovery occurred 2-3 days post-vaccination in clinical studies. In circumstances where contact with severely immunocompromised individuals is unavoidable, the potential risk of transmission of the influenza vaccine virus should be weighed against the risk of acquiring and transmitting wild-type influenza virus. The effectiveness of Fluenz preventing influenza disease in immunocompromised individuals has not been evaluated (see section 4.8).

General

**Fluenz should under no circumstances be injected.**

No data exist regarding the safety of intranasal administration of Fluenz in children with unrepaired craniofacial malformations.

## 4.5 Interaction with other medicinal products and other forms of interaction

Fluenz must not be administered to children and adolescents receiving salicylate therapy (see section 4.3). Salicylates should not be used in children and adolescents for 4 weeks after vaccination unless medically indicated, as Reye's syndrome has been reported following the use of salicylates during wild-type influenza infection.

Fluenz can be administered concomitantly with the live attenuated vaccines: measles, mumps, rubella, varicella, and orally-administered poliovirus.

The co-administration of Fluenz with inactivated vaccines has not been studied.

The concurrent use of Fluenz with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for influenza antiviral agents to reduce the effectiveness of Fluenz, it is recommended not to administer the vaccine until 48 hours after the cessation of influenza antiviral therapy. Administration of influenza antiviral agents within two weeks of vaccination may affect the response of the vaccine.

If influenza antiviral agents and Fluenz are administered concomitantly, revaccination should be considered based on clinical judgement.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There is a moderate amount of data from the use of Fluenz in pregnant women. There was no evidence of significant maternal adverse outcomes in 138 pregnant women who had a record of receiving Fluenz in a US-based health insurance claims database.

In more than 300 case reports in the AstraZeneca safety database of vaccine administration to pregnant women, no unusual patterns of pregnancy complications or foetal outcomes were observed.

While animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity, and post-marketing data offer some reassurance in the event of inadvertent administration of the vaccine, Fluenz is not recommended during pregnancy.

Breast-feeding

Limited available evidence suggests that Fluenz is not excreted in human milk. However, because there are limited data to assess the effects on the breast-fed infant and as some viruses are excreted in human milk, Fluenz should not be used during breast-feeding.

Fertility

No data exist regarding the possible effects of Fluenz on male and female fertility.

## 4.7 Effects on ability to drive and use machines

Fluenz has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

Summary of the safety profile

The most common adverse reaction is nasal congestion/rhinorrhoea (56.7%).

Tabulated list of adverse reactions

The following adverse reactions have been reported with influenza vaccines (live, nasal) trivalent and tetravalent during clinical studies and post-marketing experience. Adverse reactions are listed by MedDRA System Organ Class (SOC). Within each SOC, adverse reactions are presented by decreasing frequency. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from available data).

**Table 1 Adverse reactions**

| MedDRA SOC | Adverse reaction | Frequency |
|---|---|---|
| Immune system disorders | Hypersensitivity reactions (including facial oedema, urticaria) | Uncommon |
| | Anaphylactic reactions | Very rare |
| Metabolism and nutrition disorders | Decreased appetite | Very common |
| Nervous system disorders | Headache | Common |
| | Syncope | Not known[a] |
| | Guillain-Barré syndrome | Not known[a] |
| Respiratory, thoracic and mediastinal disorders | Nasal congestion/rhinorrhoea | Very common |
| | Epistaxis | Uncommon |
| Skin and subcutaneous tissue disorders | Rash | Uncommon |
| Musculoskeletal and connective tissue disorders | Myalgia | Common |
| Congenital, familial, and genetic disorders | Exacerbation of symptoms of Leigh syndrome (mitochondrial encephalomyopathy) | Not known[a] |
| General disorders and administration site conditions | Malaise | Very common |
| | Pyrexia | Common |

[a] Post-marketing experience

Paediatric population

In an active-controlled clinical study (MI-CP111), an increased rate of hospitalisations (for any cause) through 180 days after final vaccination dose was observed in infants and toddlers 6-11 months of age (6.1% Fluenz versus 2.6% injectable influenza vaccine). Most hospitalisations were due to gastrointestinal and respiratory tract infections and occurred more than 6 weeks post vaccination. The rate of hospitalisations was not increased in Fluenz recipients 12 months and older. In the same study, an increased rate of wheezing through 42 days was observed in infants and toddlers 6-23 months of age (5.9% Fluenz versus 3.8% injectable influenza vaccine). The rate of wheezing was not increased in Fluenz recipients 2 years and older. Fluenz is not indicated for use in infants and toddlers younger than 2 years (see section 4.2).

*Concurrent illness and chronic conditions*

In a study (D153-P515) of children 6 to 17 years of age with asthma (Fluenz: n=1 114, trivalent injectable influenza vaccine: n=1 115), there were no significant differences between treatment groups in the incidence of asthma exacerbations, mean peak expiratory flow rate, asthma symptom scores, or night-time awakening scores. The incidence of wheezing within 15 days after vaccination was lower in Fluenz recipients relative to inactivated vaccine recipients (19.5% vs. 23.8%, P=0.02).

In a study of children and adolescents 9 to 17 years of age with moderate to severe asthma (Fluenz: n=24, placebo: n=24), the primary safety criterion, change in percent predicted forced

expiratory volume in 1 second ($FEV_1$) measured before and after vaccination, did not differ between treatment arms.

Although safety in children and adolescents with mild to moderate asthma has been established, data in children with other pulmonary diseases or with chronic cardiovascular, metabolic or renal diseases, or other underlying chronic medical conditions are limited. In a study of adults 60 years of age and older (n=3 242), a high percentage of individuals had underlying chronic medical conditions (87%), including cardiac disorders (15%), respiratory, thoracic and mediastinal disorders (13%), and diabetes mellitus (9.6%). The safety profile of Fluenz in these individuals was comparable to the safety profile observed in individuals without these conditions.

*Immunocompromised individuals*

In HIV-infected children (n=24) and HIV-negative children (n=25) 1 through 7 years of age, and in HIV-infected children and adolescents 5 through 17 years of age receiving stable anti-retroviral therapy (Fluenz: n=122, trivalent injectable vaccine: n=121), the frequency and duration of vaccine virus shedding were comparable to that seen in healthy individuals. No adverse effects on HIV viral load or CD4 counts were identified following Fluenz administration.

Twenty mild to moderately immunocompromised children and adolescents 5 through 17 years of age (receiving chemotherapy and/or radiation therapy or who had recently received chemotherapy) were randomised 1:1 to Fluenz or placebo. Frequency and duration of vaccine virus shedding in these immunocompromised children and adolescents were comparable to that seen in healthy children and adolescents.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

**Ireland**
HPRA Pharmacovigilance
Website: www.hpra.ie

**Malta**
ADR Reporting Website: https://medicinesauthority.gov.mt/adrportal

### 4.9 Overdose

Overdose with Fluenz is unlikely due to its presentation as a single pre-filled nasal applicator. Administration of a higher than recommended dose of Fluenz was reported rarely and the adverse reaction profile was comparable to that observed with the recommended dose of Fluenz.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, influenza vaccines, ATC code: J07BB03

Mechanism of action

Fluenz is a trivalent vaccine that contains three *cold-adapted (ca)*; *temperature-sensitive (ts)*; and *attenuated (att)* influenza virus strains, an A/(H1N1) strain, an A/(H3N2) strain, and a B strain from the Victoria lineage. After intranasal administration, the live attenuated influenza virus strains in

Fluenz replicate in the nasopharynx and induce immune responses against the three influenza strains contained in the vaccine.

Clinical efficacy

Fluenz efficacy data in the paediatric population consist of 9 controlled studies comprising over 20 000 infants and toddlers, children and adolescents, conducted during 7 influenza seasons. Four placebo-controlled studies included second season revaccination. Fluenz has demonstrated superiority in 3 active-controlled studies with injectable influenza vaccine. See Table 2 and 3 for a summary of efficacy results in the paediatric population.

**Table 2 Fluenz efficacy after 2 doses against culture-confirmed influenza illness in placebo controlled paediatric studies**

| Study number[a] | Region | Age range[b] | Number of study participants | Influenza season | Efficacy (95% CI) matched strains | Efficacy (95% CI) all strains regardless of match |
|---|---|---|---|---|---|---|
| D153-P502 | Europe | 6 to 35 M | 1 616 | 2000-2001 | 85.4% (74.3, 92.2) | 85.9% (76.3, 92.0) |
| D153-P504 | Africa, Latin America | 6 to 35 M | 1 886 | 2001 | 73.5% (63.6, 81.0)[c] | 72.0% (61.9, 79.8)[c] |
| D153-P513 | Asia/ Oceania | 6 to 35 M | 1 041 | 2002 | 62.2% (43.6, 75.2) | 48.6% (28.8, 63.3) |
| D153-P522 | Europe, Asia/ Oceania, Latin America | 11 to 23 M | 1 150 | 2002-2003 | 78.4% (50.9, 91.3) | 63.8% (36.2, 79.8) |
| D153-P501 | Asia/ Oceania | 12 to 35 M | 2 764 | 2000-2001 | 72.9% (62.8, 80.5) | 70.1% (60.9, 77.3) |
| AV006 | USA | 15 to 71 M | 1 259[c] | 1996-1997 | 93.4% (87.5, 96.5) | N/A |

[a] Per protocol population, except where noted otherwise; none of the participants were previously vaccinated against influenza
[b] Age range as described in the study protocol. M=months.
[c] Data presented are for study participants who received two doses (ITT population).

In clinical studies AV006 and D153-P504, the efficacy of a single dose of Fluenz was evaluated in previously unvaccinated children aged 15-71 months (n=288) and aged 6-35 months (n=1 877). The efficacy against culture-confirmed influenza caused by any matched strain was 88.8% (95% CI: 64.5, 96.5) and 57.7% (95% CI: 44.7, 67.9), respectively.

Fluenz efficacy estimates against all matched strains in children who received 2 doses in year 1 and revaccination in year 2 was 100% (95% CI: 38.2, 100; n=1 110) in AV006, 84.3% (95% CI: 70.1, 92.4; n=1 265) in D153-P501, 88.7% (95% CI: 82.0, 93.2; n=1 090) in D153-P502 and 73.6% (95% CI: 33.3, 91.2; n=680) in D153-P504.

Fluenz efficacy estimates against all matched strains in children who received 2 doses in year 1 and placebo in year 2 were lower: 56.2% (95% CI: 30.5, 72.7; n=1 253) in D153-P501 and 57.0% (95% CI: 6.1, 81.7; n=718) in D153-P504.

**Table 3 Fluenz relative efficacy against culture-confirmed influenza illness in active-controlled paediatric studies with injectable influenza vaccine**

| Study number[a] | Region | Age range[b] | Number of study participants | Influenza season | Improved efficacy (95% CI) matched strains | Improved efficacy (95% CI) all strains regardless of match |
|---|---|---|---|---|---|---|
| MI-CP111 | USA, Europe, Asia/Oceania | 6 to 59 M | 7 852[c] | 2004-2005 | 44.5% (22.4, 60.6) | 54.9% (45.4, 62.9)[d] |
| D153-P514 | Europe | 6 to 71 M | 2 085[e] | 2002-2003 | 52.7% (21.6, 72.2) | 52.4% (24.6, 70.5)[f] |
| D153-P515 | Europe | 6 to 17 Y | 2 211[g] | 2002-2003 | 34.7% (3.9, 56.0) | 31.9% (1.1, 53.5) |

[a] Per protocol population
[b] Age range as described in the study protocol. M=months. Y=years.
[c] Data presented are for study participants who received two doses if unvaccinated or vaccination history was unknown, and one dose for those previously vaccinated.
[d] Fluenz demonstrated 55.7% (39.9, 67.6) fewer cases than injectable influenza vaccine in 3 686 infants and toddlers 6-23 months of age and 54.4% (41.8, 64.5) fewer cases in 4 166 children 24-59 months of age.
[e] Data presented are for study participants with a history of recurrent respiratory tract infections who received two doses of intranasal influenza vaccine compared to those who received two doses of injectable influenza vaccine.
[f] Fluenz demonstrated 64.4% (1.4, 88.8) fewer cases than injectable influenza vaccine in 476 infants and toddlers 6-23 months of age and 48.2% (12.7, 70.0) fewer cases in 1 609 children 24-71 months of age.
[g] Data presented are for study participants clinically diagnosed with asthma who received one dose of intranasal influenza vaccine compared to those who received one dose of injectable influenza vaccine.

### 5.2 Pharmacokinetic properties

Not applicable.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional non-clinical studies of repeated dose toxicity, reproduction and developmental toxicity, local tolerance and neurovirulence.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Sucrose
Dipotassium phosphate
Potassium dihydrogen phosphate
Gelatin
Arginine hydrochloride
Monosodium glutamate monohydrate
Water for injections

### 6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

## 6.3 Shelf life

15 weeks

## 6.4 Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).

Do not freeze.

Keep the nasal applicator in the outer carton in order to protect from light.

Before use, the vaccine may be taken out of the refrigerator once for a maximum period of 12 hours at a temperature not above 25 °C. Stability data indicate that the vaccine components are stable for 12 hours when stored at temperatures from 8 °C to 25 °C. At the end of this period, Fluenz should be used immediately or discarded.

## 6.5 Nature and contents of container

Fluenz is supplied as a nasal spray, suspension (0.2 ml) in a single-use nasal applicator (Type 1 glass), with nozzle (polypropylene with polyethylene transfer valve), nozzle tip-protector cap (synthetic rubber), plunger rod, plunger-stopper (butyl rubber) and a dose-divider clip.

Pack sizes of 1 or 10 nasal applicators.

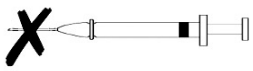
Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

Handling

Fluenz is for single nasal use only.

- Do not use with a needle. Do not inject.



- Do not use Fluenz if the expiry date has passed or the spray container appears damaged, for example, if the plunger is loose or displaced from the spray container or if there are any signs of leakage.
- Check the appearance of the vaccine before administration. The suspension should be colourless to pale yellow, clear to opalescent. Do not use the vaccine if the liquid contents of the spray container appear discoloured. Small white particles may be present.
- Do not prime or attempt to remove bubbles from the spray container.

Detailed instructions for the preparation and administration of Fluenz using the spray container are provided in the Instructions for Use.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements for medical waste.

## 7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1816/001
EU/1/24/1816/002

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 June 2024

## 10. DATE OF REVISION OF THE TEXT

15 July 2026

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

INF 26 0002