FluMist Quadrivalent is approved for use in persons 2 through 49 years of age. (1)

---

**INDICATIONS AND USAGE**

FluMist Quadrivalent is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. (1, 11)

FluMist Quadrivalent is approved for use in persons 2 through 49 years of age. (1)

---

**DOSAGE AND ADMINISTRATION**

For intranasal administration by a healthcare provider. (2)

**Age** | **Dose** | **Schedule**
---|---|---
2 years through 8 years | 1 or 2 doses, 0.2 mL each | If 2 doses, administer at least 1 month apart
9 years through 49 years | 1 dose, 0.2 mL | -

* 1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.
* Administer as 0.1 mL per nostril.

---

**Invoice to Patients**

- Severe allergic reaction (e.g., anaphylaxis) to any component of FluMist Quadrivalent, including egg protein, or after a previous dose of any influenza vaccine. (4.1, 11)
- Concomitant aspirin therapy in children and adolescents. (4.2)

---

**WARNINGs AND PRECAUTIONS**

- In clinical trials, risks of hospitalization and wheezing were increased in children younger than 2 years of age who received FluMist (trivalent Influenza Vaccine Live, Intranasal). (5.1)
- Children younger than 5 years of age with recurrent wheezing and persons of any age with asthma may be at increased risk of wheezing following the administration of FluMist Quadrivalent. (5.2)
- If Guillain-Barré syndrome has occurred within 6 weeks of any prior influenza vaccination, the decision to give FluMist Quadrivalent should be based on careful consideration of the potential benefits and risks. (5.3)
- FluMist Quadrivalent has not been studied in immunocompromised persons. (5.4)

---

**ADVERSE REACTIONS**

The most common solicited adverse reactions (≥10% in vaccine recipients and at least 5% greater than in placebo recipients) reported for FluMist were runny nose or nasal congestion (ages 2 years through 49 years), fever over 100°F (children ages 2 years through 6 years), and sore throat (adults ages 18 years through 49 years). Among children and adolescents 2 through 17 years of age who received FluMist Quadrivalent, 32% reported runny nose or nasal congestion and 7% reported fever over 100°F. Among adults 18 through 49 years of age who received FluMist Quadrivalent, 44% reported runny nose or nasal congestion and 19% reported sore throat. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact MedImmune at 1-877-633-4411 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

---

**USE IN SPECIFIC POPULATIONS**

- Safety and effectiveness of FluMist Quadrivalent have not been established in pregnant women, nursing mothers, geriatric adults, or children less than 2 years of age. (8.1, 8.2, 8.4, 8.5)
- In clinical trials, in children 6 through 23 months of age, FluMist was associated with an increased risk of hospitalization and wheezing. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

**DRUG INTERACTIONS**

- Antiviral drugs that are active against influenza A and/or B may reduce the effectiveness of FluMist Quadrivalent if administered within 48 hours before, or within 2 weeks after, receipt of the vaccine. (7.2)

---

**FULL PRESCRIBING INFORMATION: CONTENTS**

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

6 ADVERSE REACTIONS

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

9 DESCRIPTION

10 CLINICAL PHARMACOLOGY

11 NONCLINICAL TOXICOLOGY

12 REFERENCES

13 HOW SUPPLIED/STORAGE AND HANDLING

14 PATIENT COUNSELING INFORMATION

15 ADVERSE REACTIONS

16 WARNINGS AND PRECAUTIONS

17 USE IN SPECIFIC POPULATIONS

18 DESCRIPTION

19 CLINICAL PHARMACOLOGY

20 NONCLINICAL TOXICOLOGY

21 REFERENCES

22 PATIENT COUNSELING INFORMATION

---

**FULL PRESCRIBING INFORMATION**

1 INDICATIONS AND USAGE

FluMist Quadrivalent is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. (see Description [11]).

FluMist Quadrivalent is approved for use in persons 2 through 49 years of age.

2 DOSAGE AND ADMINISTRATION

FOR INTRANASAL ADMINISTRATION BY A HEALTHCARE PROVIDER.

2.1 Dosing Information

Administer FluMist Quadrivalent according to the following schedule:

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 years through 8 years</td>
<td>1 or 2 doses, 0.2 mL each</td>
<td>If 2 doses, administer at least 1 month apart</td>
</tr>
<tr>
<td>9 years through 49 years</td>
<td>1 dose, 0.2 mL</td>
<td>-</td>
</tr>
</tbody>
</table>

* 1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.
* Administer as 0.1 mL per nostril.

---

**Administration Instructions**

Each sprayer contains a single dose (0.2 mL) of FluMist Quadrivalent; administer approximately one half of the contents of the single-dose intranasal sprayer into each nostril (each sprayer contains 0.2 mL of vaccine). Refer to Figure 1 for step-by-step administration instructions. Following administration, dispose of the sprayer according to the standard procedures for medical waste (e.g., sharps container or biohazard container).

---

**Note**: Active inhalation (i.e., sniffing) is not required by the patient during vaccine administration.
3. DOSAGE FORMS AND STRENGTHS
Each 0.2 mL dose is a suspension supplied in a single-dose pre-filled intranasal sprayer.

4. CONTRAINDICATIONS
4.1 Severe Allergic Reactions
Do not administer FluMist Quadrivalent to persons who have had a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine [see Description (11)] including egg protein, or after a previous dose of any influenza vaccine.

4.2 Concomitant Aspirin Therapy and Reye's Syndrome in Children and Adolescents
Do not administer FluMist Quadrivalent to children and adolescents through 17 years of age who are receiving aspirin therapy or aspirin-containing therapy because of the association of Reye's syndrome with aspirin and wild-type influenza infection [see Drug Interactions (7.1)].

5. WARNINGS AND PRECAUTIONS
5.1 Risks of Hospitalization and Wheezing in Children Younger than 24 Months of Age
In clinical trials, risks of hospitalization and wheezing were increased in children younger than 2 years of age who received FluMist (trivalent Influenza Vaccine Live, Intranasal) [see Adverse Reactions (6.1)]. This observation with FluMist is relevant to FluMist Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions [see Description (11)].

5.2 Asthma, Recurrent Wheezing, and Active Wheezing
Children younger than 5 years of age with recurrent wheezing and persons of any age with asthma may be at increased risk of wheezing following administration of FluMist Quadrivalent. FluMist Quadrivalent has not been studied in persons with severe asthma or active wheezing.

5.3 Guillain-Barré Syndrome
The 1976 swine influenza vaccine (inactivated) was associated with an elevated risk of Guillain-Barré syndrome (GBS). Evidence for causal relation of GBS with other influenza vaccines is inconclusive; if an excess risk exists, based on data for inactivated influenza vaccines, it is probably slightly more than 1 additional case per 1 million persons vaccinated.

5.4 Altered Immunocompetence
FluMist Quadrivalent has not been studied in immunocompromised persons. The effectiveness of FluMist has not been studied in immunocompromised persons. Data on safety and shedding of vaccine virus after administration of FluMist in immunocompromised persons are limited to 173 persons with HIV infection and 10 mild to moderately immunocompromised children and adolescents with cancer [see Clinical Pharmacology (12.2)].

5.5 Medical Conditions Predisposing to Influenza Complications
The safety of FluMist Quadrivalent in individuals with underlying medical conditions that may predispose them to complications following wild-type influenza infection has not been established.

5.6 Management of Acute Allergic Reactions
Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine [see Contraindications (4.1)].

5.7 Limitations of Vaccine Effectiveness
FluMist Quadrivalent may not protect all individuals receiving the vaccine.

6. ADVERSE REACTIONS
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

This safety experience with FluMist is relevant to FluMist Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions [see Description (11)].

A total of 1382 children and adolescents 1 through 17 years of age who received FluMist Quadrivalent in randomized, placebo-controlled studies D153-P501, AV06, D153-P526, A019, and AV009 [3 used Inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc., and 2 used saline placebo] were observed at a lower frequency [see Table 4: Summary of Solicited Adverse Reactions occurring in at least 1% of FluMist recipients and at a 1% rate difference after rounding] compared to active control was sneezing (2% FluMist recipients and at a higher rate (≥1% rate difference after rounding) compared to placebo). In post-hoc analysis, rates of hospitalization in children 6 through 11 months of age were 6.1% (42/684) in FluMist recipients and 2.6% (18/683) in inactivated Influenza Virus Vaccine recipients.

Table 2 shows pooled solicited adverse reactions occurring in at least 1% of FluMist recipients and at a higher rate (≥1% rate difference after rounding) compared to placebo post Dose 1 for Studies D153-P501 and AV006, and solicited adverse reactions post Dose 1 for Study MI-CPI111. Solicited adverse reactions were those that about which parents/guardians were specifically queried after receipt of FluMist, placebo, or control vaccine. In these studies, solicited reactions were documented for 10 days post vaccination. Solicited reactions following the second dose of FluMist were similar to those following the first dose and were generally observed at a lower frequency.

Table 2: Summary of Solicited Adverse Reactions Observed Within 10 Days after Dose 1 for FluMist and Either Placebo or Active Control Recipients in Children 2 through 6 Years of Age

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist N</th>
<th>Placebo N</th>
<th>FluMist Active Control N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>16%</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>&gt;100°F Oral</td>
<td>9%</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>&gt;101°F Oral</td>
<td>4%</td>
<td>3%</td>
<td>4%</td>
</tr>
</tbody>
</table>

In clinical studies D153-P501 and AV006, unsolicited adverse reactions in children occurring in at least 1% of FluMist recipients and at a higher rate (>1% rate difference after rounding) compared to placebo were abdominal pain (2% FluMist vs. 0% placebo) and otitis media (3% FluMist vs. 1% placebo). An additional adverse reaction identified in the active-controlled trial MI-CPI111 occurring in at least 1% of FluMist recipients and at a higher rate (>1% rate difference after rounding) compared to active control was sneezing (2% FluMist vs. 1% active control).

In a separate saline placebo-controlled trial (D153-P526) in a subset of older children and adolescents 9 through 17 years of age who received one dose of FluMist, the solicited adverse reactions as well as unsolicited adverse reactions reported were generally consistent with observations from the trials in Table 2. Abdominal pain was reported in 12% of FluMist recipients compared to 4% of placebo recipients and decreased activity was reported in 6% of FluMist recipients compared to 0% of placebo recipients.

In Study AV018, in which FluMist was concomitantly administered with Measles, Mumps, and Rubella Virus Vaccine Live (MMR, manufactured by Merck & Co., Inc.) and Varicella Virus Vaccine Live (manufactured by Merck & Co., Inc.) to children 12 through 15 months of age, adverse reactions were similar to those seen in other clinical trials of FluMist.

FluMist Quadrivalent in Children and Adolescents
In the randomized, active-controlled Study MI-CPI208 that compared FluMist Quadrivalent and FluMist in children and adolescents 2 through 17 years of age, the rates of solicited adverse reactions reported were similar between subjects who received FluMist Quadrivalent and FluMist. Table 3 includes solicited adverse reactions post Dose 1 from Study MI-CPI208 that either occurred at a higher rate (>1% rate difference after rounding) in FluMist Quadrivalent recipients compared to FluMist recipients or were identified in previous FluMist clinical studies (see Table 2). In this study, solicited adverse reactions were documented for 14 days post vaccination. Solicited adverse reactions post Dose 2 were observed at a lower frequency compared to Dose 1 for FluMist Quadrivalent and were similar between subjects who received FluMist Quadrivalent and FluMist.

FluMist® Quadrivalent

Table 1: Percentages of Children with Hospitalizations and Wheezing from Study MI-CPI111

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist (n/N)</th>
<th>Active Control (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations</td>
<td>6-23 months: 4.2% (84/2029)</td>
<td>3.2% (63/1975)</td>
</tr>
<tr>
<td>24-59 months: 2.1% (46/2187)</td>
<td>2.5% (56/2188)</td>
<td></td>
</tr>
<tr>
<td>Wheezing</td>
<td>6-23 months: 5.9% (117/1992)</td>
<td>3.8% (75/1975)</td>
</tr>
<tr>
<td>24-59 months: 2.1% (47/2187)</td>
<td>2.5% (56/2188)</td>
<td></td>
</tr>
</tbody>
</table>

NCT00128167; see www.clinicaltrials.gov

Inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc., administered intramuscularly.

Hospitalization due to any cause from randomized through 180 days post last vaccination.

Painting requiring bronchodilator therapy or accompanied by respiratory distress or hypoxia evaluated from randomized through 42 days post last vaccination.

NCT010192244; see www.clinicaltrials.gov

NCT0123167; see www.clinicaltrials.gov

Study D153-P501 used saline placebo; Study AV006 used SPG placebo.

Inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc., administered intramuscularly.

Number of evaluable subjects (subjects who returned diary cards) for each reaction. Range reflects differences in data collection between the 2 pooled studies.

In clinical studies D153-P501 and AV006, unsolicited adverse reactions in children occurring in at least 1% of FluMist recipients and at a higher rate (>1% rate difference after rounding) compared to placebo were abdominal pain (2% FluMist vs. 0% placebo) and otitis media (3% FluMist vs. 1% placebo). An additional adverse reaction identified in the active-controlled trial MI-CPI111 occurring in at least 1% of FluMist recipients and at a higher rate (>1% rate difference after rounding) compared to active control was sneezing (2% FluMist vs. 1% active control).

In a separate saline placebo-controlled trial (D153-P526) in a subset of older children and adolescents 9 through 17 years of age who received one dose of FluMist, the solicited adverse reactions as well as unsolicited adverse reactions reported were generally consistent with observations from the trials in Table 2. Abdominal pain was reported in 12% of FluMist recipients compared to 4% of placebo recipients and decreased activity was reported in 6% of FluMist recipients compared to 0% of placebo recipients.

In Study AV018, in which FluMist was concomitantly administered with Measles, Mumps, and Rubella Virus Vaccine Live (MMR, manufactured by Merck & Co., Inc.) and Varicella Virus Vaccine Live (manufactured by Merck & Co., Inc.) to children 12 through 15 months of age, adverse reactions were similar to those seen in other clinical trials of FluMist.
Table 3: Summary of Solicited Adverse Reactionsb Observed Within 14 Days after Dose 1 for FluMist Quadrivalent and FluMist Recipients in Study MI-CP208b in Children and Adolescents 2 through 17 Years of Age

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist Quadrivalenta</th>
<th>FluMista</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 1341-1377b</td>
<td>N = 901-920b</td>
</tr>
<tr>
<td>Runny Nose/Nasal Congestion</td>
<td>32%</td>
<td>%</td>
</tr>
<tr>
<td>Headache</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>Decreased Activity (Lethargy)</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Sore Throat</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Muscle Aches</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Fever</td>
<td>&gt;100°F by any route</td>
<td>7%</td>
</tr>
<tr>
<td>&gt;100°F to &lt;101°F by any route</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>&gt;101°F to &lt;102°F by any route</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

a Solicited adverse reactions that occurred at a higher rate (>1% rate difference after rounding) in FluMist Quadrivalent recipients compared to FluMist recipients or were identified in previous FluMist trials (see Table 2).  
b NCT01091246; see www.clinicaltrials.gov  
c Represents pooled data from the FluMist study arms [see Clinical Studies (14.2)].  
d Number of evaluable subjects for each event.

In Study MI-CP208, no unsolicited adverse reactions occurred at a higher rate (1% or greater) in FluMist Quadrivalent recipients compared to FluMist recipients.

Table 4: Summary of Solicited Adverse Reactionsb Observed Within 14 Days after Dose 1 for FluMist Quadrivalent and FluMist Recipients in Study MI-CP185b in Adults 18 through 49 Years of Age

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist Quadrivalenta</th>
<th>FluMista</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 1197b</td>
<td>N = 597b</td>
</tr>
<tr>
<td>Runny Nose/Nasal Congestion</td>
<td>44%</td>
<td>40%</td>
</tr>
<tr>
<td>Headache</td>
<td>29%</td>
<td>27%</td>
</tr>
<tr>
<td>Sore Throat</td>
<td>19%</td>
<td>20%</td>
</tr>
<tr>
<td>Decreased Activity (Lethargy)</td>
<td>18%</td>
<td>17%</td>
</tr>
<tr>
<td>Cough</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Muscle Aches</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>6%</td>
<td>5%</td>
</tr>
</tbody>
</table>

a Solicited adverse reactions that occurred at a higher rate (>1% rate difference after rounding) in FluMist Quadrivalent recipients compared to FluMist recipients or were identified in Study AV009.  
b NCT01091246; see www.clinicaltrials.gov  
c Represents pooled data from the two FluMist study arms [see Clinical Studies (14.4)].  
d Number of evaluable subjects for each event.

In Study MI-CP185, no unsolicited adverse reactions occurred at a higher rate (1% or greater) in FluMist Quadrivalent recipients compared to FluMist recipients.
A prospective, randomized, double-blind, placebo-controlled trial was performed in a daycare setting in children younger than 3 years of age to assess the transmission of vaccine viruses from a vaccinated individual to a non-vaccinated individual. A total of 197 children 8 through 36 months of age were randomized to receive one dose of FluMist (N = 98) or AS-PS placebo (N = 99). Virus shedding was evaluated for 21 days by culture of nasal swab specimens. Wild-type A (A/Hong Kong/4806/2001) influenza virus documented to have circulated in the community and in the study population during the trial, whereas Type B (A/H1N1) and B strains did not.

At least one vaccine strain was isolated from 80% of FluMist recipients; strains were recovered from 1-21 days post vaccination (mean duration of 7.6 days ± 3.4 days). The cold-adapted (ca) and temperature-sensitive (ts) phenotypes were preserved in 135 tested of 250 strains isolated at the local laboratory. Ten influenza isolates (9 influenza A, 1 influenza B) were cultured from a total of seven placebo subjects. One sample of each of the cultured Type B influenza virus confirmed as a transmitted vaccine virus by a FluMist recipient in the same playgroup. This Type B isolate retained the ca, ts, and att phenotypes of the vaccine strain and had the same genetic sequence when compared to a Type B virus cultured from a vaccine recipient within the same playgroup. Four of the influenza Type A isolates were confirmed as wild-type A/Panama (H2N2). The remaining isolates are characterized as attenuated.

Assuming a single transmission event (isolation of the Type B vaccine strain), the probability of a young child acquiring vaccine virus following close contact with a single FluMist vaccinee in this daycare setting was 0.95% (95% CI: 0.1, 1.7) based on the Reed-Frost model. With documented transmission of one Type B in one placebo subject and possible transmission of Type A viruses in four placebo subjects, the probability of acquiring a transmitted vaccine virus was estimated to be 2.4% (95% CI: 0.13, 4.6) using the Reed-Frost model.

### 13 NONCLINICAL TOXICOLOGY

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

FluMist Quadrivalent has not been evaluated for its carcinogenic or mutagenic potential or its inability to impair fertility.

### 14 CLINICAL STUDIES

The effectiveness of FluMist Quadrivalent is based on data demonstrating the clinical efficacy of FluMist in children and the effectiveness of FluMist in adults, and a comparison of vaccine virus shedding to that seen in healthy children and adolescents. The effectiveness of FluMist and FluMist Quadrivalent in preventing influenza illness due to antigenically matched wild-type influenza is assessed using a multifaceted approach.

**Peak Titer**

The highest proportion of subjects in each group shed one or more vaccine strains on Days 2-3 post vaccination. After Day 11 among individuals 2 through 49 years of age (n = 443), virus titers did not exceed 1.5 log_{10} TCID_{50}/mL.

**Studies in Immunocompromised Individuals**

Safety and shedding of vaccine virus following FluMist administration were evaluated in 28 HIV-infected adults with median CD4 cell count of 417 cells/mm^3 and 27 HIV-negative adults 18 through 58 years of age. No serious adverse events were reported during the one-month follow-up period. Vaccine strain (type B) virus was detected in 1 of 28 HIV-infected subjects on Day 5 only, and in none of the HIV-negative FluMist recipients.

Safety and shedding of vaccine virus following FluMist administration were also evaluated in children in a randomized (1:1:1) cross-over, double-blind, AF-SPG placebo-controlled trial in 24 HIV-infected children with median CD4 cell count of 1013 cells/mm^3 and 25 HIV-negative children 1 through 7 years of age, and in a randomized (1:1), open-label, inactivated influenza vaccine-controlled trial in 24 HIV-infected children who were also enrolled in an earlier study with a daily dose of 20 days of vaccination (days 17 and 13, respectively). The effectiveness of FluMist and FluMist Quadrivalent in preventing influenza illness in HIV-infected individuals has not been evaluated.

Transmission Study

Twenty mild to moderately immunocompromised children and adolescents 5 through 17 years of age (receiving chemotherapy and/or radiation therapy or who had received chemotherapy in the 12 weeks prior to the study) were randomly assigned to receive 1:1:1 to receive FluMist or AS-PS placebo. Frequency and duration of vaccine virus shedding in these immunocompromised children and adolescents were comparable to that seen in healthy children and adolescents. The effectiveness of FluMist and FluMist Quadrivalent in preventing influenza illness in immunocompromised individuals has not been evaluated.

### Table 1: Comparative Efficacy Against Culture-Confirmed Modified CDC-ILI Caused by Wild-Type Strains (Study MI-CP111)^e

<table>
<thead>
<tr>
<th>Matched Strains</th>
<th>All Strains</th>
<th>Mismatched Strains</th>
<th>Regardless of Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3916</td>
<td>3936</td>
<td>3916</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>5.4%</td>
<td>22.4%</td>
<td>38.9%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>4.7%</td>
<td>21.9%</td>
<td>45.4%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>N</td>
<td>3916</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>6.9%</td>
<td>17.2%</td>
<td>36.0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>7.5%</td>
<td>20.3%</td>
<td>40.9%</td>
</tr>
</tbody>
</table>

### Table 2: Comparative Efficacy Against Culture-Confirmed Modified CDC-ILI Caused by Wild-Type Strains (Study MI-CP111)^e

<table>
<thead>
<tr>
<th>Matched Strains</th>
<th>All Strains</th>
<th>Mismatched Strains</th>
<th>Regardless of Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3916</td>
<td>3936</td>
<td>3916</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>5.4%</td>
<td>22.4%</td>
<td>38.9%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>4.7%</td>
<td>21.9%</td>
<td>45.4%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>6.9%</td>
<td>17.2%</td>
<td>36.0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>7.5%</td>
<td>20.3%</td>
<td>40.9%</td>
</tr>
</tbody>
</table>

### Table 3: Comparative Efficacy Against Culture-Confirmed Modified CDC-ILI Caused by Wild-Type Strains (Study MI-CP111)^e

<table>
<thead>
<tr>
<th>Matched Strains</th>
<th>All Strains</th>
<th>Mismatched Strains</th>
<th>Regardless of Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3916</td>
<td>3936</td>
<td>3916</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>5.4%</td>
<td>22.4%</td>
<td>38.9%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>4.7%</td>
<td>21.9%</td>
<td>45.4%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>6.9%</td>
<td>17.2%</td>
<td>36.0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>7.5%</td>
<td>20.3%</td>
<td>40.9%</td>
</tr>
</tbody>
</table>

### Table 4: Comparative Efficacy Against Culture-Confirmed Modified CDC-ILI Caused by Wild-Type Strains (Study MI-CP111)^e

<table>
<thead>
<tr>
<th>Matched Strains</th>
<th>All Strains</th>
<th>Mismatched Strains</th>
<th>Regardless of Match</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3916</td>
<td>3936</td>
<td>3916</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>5.4%</td>
<td>22.4%</td>
<td>38.9%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>4.7%</td>
<td>21.9%</td>
<td>45.4%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>6.9%</td>
<td>17.2%</td>
<td>36.0%</td>
</tr>
<tr>
<td>N</td>
<td>3936</td>
<td>3936</td>
<td>3936</td>
</tr>
<tr>
<td>Rate (cases/N)</td>
<td>7.5%</td>
<td>20.3%</td>
<td>40.9%</td>
</tr>
</tbody>
</table>
Study AV006 was a second multi-center, randomized, double-blind, AF-SPG placebo-controlled trial performed in U.S. children without high-risk medical conditions to evaluate the efficacy of FluMist against culture-confirmed influenza over two successive seasons (1996-1997 and 1997-1998). The primary endpoint of the trial was the prevention of culture-confirmed influenza illness due to antigenically matched wild-type influenza in children who received two doses of vaccine in the first year and a single revaccination dose in the second year. Respiratory illness that prompted an influenza culture was defined as at least one of the following: fever (≥ 101.5°F rectal or oral; or ≥ 100.4°F axillary), wheezing, shortness of breath, pulmonary congestion, pneumonia, or otitis media; or two of the following: runny nose/nasal congestion, sore throat, cough, muscle aches, chills, headache, irritability, decreased activity, or vomiting. During the first year of the study, 1602 children 15 through 71 months of age were randomized 2:1 (vaccine/placebo). See Table 7 for a description of the results.

Table 7: Efficacy of FluMist vs. Placebo Against Culture-Confirmed Influenza Illness Due to Antigenically Matched Wild-Type Strains (Studies D153-P501 and AV006, Year 1)

<table>
<thead>
<tr>
<th>Strain</th>
<th>FluMist Placebo</th>
<th>FluMist Placebo</th>
<th>FluMist Placebo</th>
<th>FluMist Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>23 (1.4%)</td>
<td>81 (7.1%)</td>
<td>7 (0.5%)</td>
<td>24 (2.1%)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>4 (0.2%)</td>
<td>27 (2.4%)</td>
<td>26 (2.2%)</td>
<td>49 (4.4%)</td>
</tr>
<tr>
<td>B</td>
<td>29 (1.8%)</td>
<td>35 (3.2%)</td>
<td>35 (3.2%)</td>
<td>35 (3.2%)</td>
</tr>
</tbody>
</table>

The predominantly circulating virus during the trial period was A/Sydney/05/97 (H3N2), an antigenic variant not included in the vaccine.

1.5 Effectiveness was shown in a post-hoc analysis using an endpoint of CDC-ILI in the age group 18 through 49 years of age.

14.4 Immune Response Study of FluMist Quadrivalent in Adults

A multicenter, randomized, double-blind, active-controlled, and non-inferiority study (MI-CP185) was performed to assess the safety and immunogenicity of FluMist Quadrivalent compared to those of FluMist (active control) in adults 18 through 49 years of age. A total of 1800 subjects were randomized by site at a 1:1 ratio to receive either one dose of FluMist Quadrivalent or one dose of one of two formulations of comparator vaccine, FluMist, each containing a B strain that corresponded to one of the two B strains in FluMist Quadrivalent (a B strain of the Yamagata lineage and a B strain of the Victoria lineage).

Immunogenicity in study MI-CP185 was evaluated by comparing the 4 strain-specific serum hemagglutination inhibition (HAI) antibody geometric mean titers (GMTs) post dosing and provided evidence that the addition of the second B strain did not result in immune interference to other strains included in the vaccine.

15.3 Concomitantly Administered Live Virus Vaccines

In Study AV018, concomitant administration of FluMist, MMR (manufactured by Merck & Co., Inc.) and Varicella Virus Live (manufactured by Merck & Co., Inc.) was studied in 1245 subjects 12 through 15 months of age. Subjects were randomized in a 1:1:1 ratio to MMR, Varicella vaccine and FluMist placebo (group 1); MMR, Varicella vaccine and FluMist (group 2); or FluMist alone (group 3). Immune responses to MMR and Varicella vaccines were evaluated 6 weeks post-vaccination while the immune responses to FluMist were evaluated 4 weeks after the second dose. No evidence of interference with immune response to measles, mumps, rubella, varicella and FluMist vaccines was observed.

15. REFERENCES


16. HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

FluMist Quadrivalent is supplied in a package of 10 pre-filled, single-dose (0.2 mL) intranasal sprays. The single-use intranasal sprayer is not made with natural rubber latex. Carton containing 10 intranasal sprays: NDC 66019-305-10 Single intranasal sprayer: NDC 66019-305-01

16.2 Storage and Handling

The cold chain [2-8°C (35-46°F)] must be maintained when transporting FluMist Quadrivalent.

FLUIMIST QUADRIVALENT SHOULD BE STORED IN A REFRIGERATOR BETWEEN 2-8°C (35-46°F) UPON RECEIPT. THE PRODUCT MUST BE USED BEFORE THE EXPIRATION DATE ON THE SPREYER LABEL. DO NOT FREEZE.

Keep FluMist Quadrivalent sprayer in outer carton in order to protect from light.

A single temperature excursion up to 25°C (77°F) for 12 hours has been shown to have no adverse impact on the vaccine. After a temperature excursion, the vaccine should be returned immediately to the recommended storage condition (2°C – 8°C) and used as soon as feasible. Subsequent excursions are not permitted.

Once FluMist Quadrivalent has been administered or has expired, the sprayer should be disposed of according to the standard procedures for medical waste (e.g., sharps container or biohazard container).

17. PATIENT COUNSELING INFORMATION

Advise the vaccine recipient or caregiver to read the FDA-approved patient labeling (Information for Patients and Their Caregivers).

Inform vaccine recipients or their parents/guardians of the need for two doses at least 1 month apart in children 2 through 8 years of age, depending on vaccination history. Provide the Vaccine Information Statements (VIS) which are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization.

17.1 Asthma and Recurrent Wheezing

Ask the vaccinee or their parent/guardian if the vaccinee has asthma. For children younger than 5 years of age, also ask if the vaccinee has recurrent wheezing since this may be an asthma equivalent in this age group. Inform the vaccinee or their parent/guardian that there may be an increased risk of wheezing associated with FluMist Quadrivalent in persons younger than 5 years of age with recurrent wheezing and persons of any age with asthma [see Warnings and Precautions (5.2)].

17.2 Vaccination with a Live Virus Vaccine

Inform vaccine recipients or their parents/guardians that FluMist Quadrivalent is an attenuated live virus vaccine and has the potential for transmission to immunocompromised household contacts.

17.3 Adverse Event Reporting

Instruct the vaccine recipient or their parent/guardian to report adverse reactions to their healthcare provider.

FluMist® is a registered trademark of MedImmune, LLC.
Information for Patients and Their Caregivers

FluMist® Quadrivalent (pronounced FLEW-mist Kwá-dre-VĀ-lent)
(Influenza Vaccine Live, Intranasal)

Please read this Patient Information carefully before you or your child is vaccinated with FluMist Quadrivalent.

This is a summary of information about FluMist Quadrivalent. It does not take the place of talking with your healthcare provider about influenza vaccination. If you have questions or would like more information, please talk with your healthcare provider.

What is FluMist Quadrivalent?

FluMist Quadrivalent is a vaccine that is sprayed into the nose to help protect against influenza. It can be used in children, adolescents, and adults ages 2 through 49. FluMist Quadrivalent is similar to MedImmune’s trivalent Influenza Vaccine Live, Intranasal (Flumist), except FluMist Quadrivalent provides protection against an additional influenza strain. FluMist Quadrivalent may not prevent influenza in everyone who gets vaccinated.

Who should not get FluMist Quadrivalent?

You should not get FluMist Quadrivalent if you:

- have a severe allergy to eggs or to any inactive ingredient in the vaccine (see “What are the ingredients in FluMist Quadrivalent?”)
- have ever had a life-threatening reaction to influenza vaccinations
- are 2 through 17 years old and take aspirin or medicines containing aspirin. Children or adolescents should not be given aspirin for 4 weeks after getting FluMist or FluMist Quadrivalent unless your healthcare provider tells you otherwise.

Please talk to your healthcare provider if you are not sure if the items listed above apply to you or your child.

Children under 2 years old have an increased risk of wheezing (difficulty with breathing) after getting FluMist Quadrivalent.

Who may not be able to get FluMist Quadrivalent?

Tell your healthcare provider if you or your child:

- are currently wheezing
- have a history of wheezing if under 5 years old
- have had Guillain-Barré syndrome
- have a weakened immune system or live with someone who has a severely weakened immune system
- have problems with your heart, kidneys, or lungs
- have diabetes
- are pregnant or nursing
- are taking Tamiflu®, Relenza®, amantadine, or rimantadine

If you or your child cannot take FluMist Quadrivalent, you may still be able to get an influenza shot. Talk to your healthcare provider about this.

How is FluMist Quadrivalent given?

- FluMist Quadrivalent is a liquid that is sprayed into the nose.
- You can breathe normally while getting FluMist Quadrivalent. There is no need to inhale or “sniff” it.
- People 9 years of age and older need one dose of FluMist Quadrivalent each year.
- Children 2 through 8 years old may need 2 doses of FluMist Quadrivalent, depending on their history of previous influenza vaccination. Your healthcare provider will decide if your child needs to come back for a second dose.

What are the possible side effects of FluMist Quadrivalent?

The most common side effects are:

- runny or stuffy nose
- sore throat
- fever over 100°F

Other possible side effects include:

- decreased appetite
- headache
- irritability
- muscle ache
- tiredness
- chills
- cough

Call your healthcare provider or go to the emergency department right away if you or your child experience:

- hives or a bad rash
- trouble breathing
- swelling of the face, tongue, or throat

These are not all the possible side effects of FluMist Quadrivalent. You can ask your healthcare provider for a complete list of side effects that is available to healthcare professionals.

Call your healthcare provider for medical advice about side effects. You may report side effects to VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

What are the ingredients in FluMist Quadrivalent?

Active Ingredients: FluMist Quadrivalent contains 4 influenza virus strains that are weakened (A(H1N1), A(H3N2), B Yamagata lineage, and B Victoria lineage).

Inactive Ingredients: monosodium glutamate, gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, and gentamicin.

FluMist Quadrivalent does not contain preservatives.

How is FluMist Quadrivalent Stored?

FluMist Quadrivalent is stored in a refrigerator (not the freezer) between 35-46°F (2-8°C) upon receipt. FluMist Quadrivalent sprayer must be kept in the carton until use in order to protect from light. FluMist Quadrivalent must be used before the expiration date on the sprayer label.

If you would like more information, talk to your healthcare provider or visit www.flumistquadrivalent.com or call 1-877-833-4411.

FluMist® is a registered trademark of MedImmune, LLC.

Other brands listed are registered trademarks of their respective owners and are not trademarks of MedImmune, LLC.

MedImmune

Manufactured by:
MedImmune, LLC
Gaithersburg, MD 20878

Issue date: August 2018   US-20839   8/18   RAL-FLUQV7