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)

For intranasal administration by a healthcare provider. (2)

<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 a, 0.2 mL b 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 b</td>
<td>-</td>
</tr>
</tbody>
</table>

a Or 2 doses depend on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.

b Administer as 0.1 mL per nostril.

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)
- 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 8 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.

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)

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.

Revised: 8/2018

**FULL PRESCRIBING INFORMATION: CONTENTS**

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:

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b Administer as 0.1 mL per nostril.

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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).

**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)
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**ADVERSE REACTIONS**

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**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.

Revised: 8/2018

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**ADVERSE REACTIONS**

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**USE IN SPECIFIC POPULATIONS**

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See 17 for Patient Counseling Information and FDA-Approved Patient Labeling.

Revised: 8/2018
randomization through 180 days post last vaccination.

Most hospitalizations observed were due to gastrointestinal and respiratory tract infections and occurred comparably to those post Dose 1 for FluMist, in post-hoc analysis, rates of hospitalization in children 2 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-CP111. Solicited adverse reactions were those 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</th>
<th>Placebo</th>
<th>FluMist Active Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>&gt;100°F Oral</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>&gt;100 - &lt;101°F Oral</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>&gt;101 - &lt;102°F Oral</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

The safety of FluMist Quadrivalent in children and adolescents 2 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. Adenoidal 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 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. Adenoidal 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-CP208 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-CP208 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

The safety of FluMist was evaluated in an AF-SPG placebo-controlled study (AV019) conducted in a Health Maintenance Organization (HMO) in children 1 through 17 years of age (FluMist = 6473, placebo = 5216). An increase in asthma events, captured by review of diagnostic codes, was observed in children younger than 2 years of age who received FluMist compared to those who received placebo (Relative Risk 1.53, 90% CI 1.1, 1.57). In Study MI-CP111, children 6 through 59 months of age were randomized to receive FluMist or inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc. Wheezing requiring bronchodilator therapy or accompanied by respiratory distress or hypoxia was prospectively monitored from randomization through 42 days post last vaccination. Hospitalization due to all causes was prospectively monitored from randomization through 180 days post last vaccination. Increases in wheezing and hospitalization (for any cause) were observed in children 6 months through 23 months of age who received FluMist compared to those who received inactivated Influenza Virus Vaccine, as shown in Table 1.
**Table 3: Summary of Solicited Adverse Reactions* Observed Within 14 Days after Dose 1 for FluMist Quadrivalent and FluMist Recipients in Study MI-CP208® in Children and Adolescents 2 through 17 Years of Age**

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist Quadrivalent</th>
<th>FluMist®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 1341-13774</td>
<td>N = 901-9204</td>
</tr>
<tr>
<td>Runny Nose/Nasal Congestion</td>
<td>32%</td>
<td>32%</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; 10°F by any route</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>&gt; 100 - &lt; 101°F by any route</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>&gt; 101 - ≤ 102°F by any route</td>
<td>2%</td>
</tr>
</tbody>
</table>

* 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).

**Table 4: Summary of Solicited Adverse Reactions* Observed Within 14 Days after Dose 1 for FluMist Quadrivalent and FluMist Recipients in Study MI-CP185® in Adults 18 through 49 Years of Age**

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist Quadrivalent</th>
<th>FluMist®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 1197</td>
<td>N = 597</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>18%</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>

* 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.

6.2 Postmarketing Experience

The following events have been spontaneously reported during post approval use of FluMist. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Cardiac disorders. Pericarditis. Congenital, familial, and genetic disorders: Exacerabation of symptoms of mitochondrial encephalomyopathy (Leigh syndrome). Gastrointestinal disorders: Nausea, vomiting, diarrhea Immune system disorders: Hypersensitivity reactions (including anaphylactic reaction, facial edema, and urticaria) Nervous system disorders: Guillain-Barré syndrome, Bell’s Palsy, meningitis, eosinophilic meningitis, vaccine-associated encephalitis Respiratory, thoracic, and mediastinal disorders: Epistaxis Skin and subcutaneous tissue disorders: Rash

7 DRUG INTERACTIONS

7.1 Aspirin Therapy

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 [see Contraindications (4.2)]. Avoid aspirin-containing therapy in these age groups during the first 4 weeks after vaccination with FluMist Quadrivalent unless clearly needed.

7.2 Antiviral Agents Against Influenza A and/or B

Antiviral drugs that are active against influenza A and/or B viruses may reduce the effectiveness of FluMist Quadrivalent if administered within 48 hours before, or within 2 weeks after vaccination. The concurrent use of FluMist Quadrivalent with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. If antiviral agents and FluMist Quadrivalent are administered concomitantly, revaccination should be considered when appropriate.

7.3 Concomitant Administration with Inactivated Vaccines

The safety and immunogenicity of FluMist Quadrivalent when administered concomitantly with inactivated vaccines have not been determined. Studies of FluMist and FluMist Quadrivalent excluded subjects who received any inactivated or subunit vaccine within two weeks of enrollment.

7.4 Concomitant Administration with Other Live Vaccines

Concomitant administration of FluMist Quadrivalent with Measles, Mumps, and Rubella Virus Vaccine Live (MMR, manufactured by Merck & Co., Inc.), or the Varicella Virus Vaccine Live (manufactured by Merck & Co., Inc.) has not been studied. Concomitant administration of FluMist with MMR and the varicella vaccine was studied in children 12 through 15 months of age [see Clinical Studies (14.5)]. Concomitant administration of FluMist with the MMR and the varicella vaccine in children older than 15 months of age has not been studied.

7.5 Intranasal Products

There are no data regarding co-administration of FluMist Quadrivalent with other intranasal preparations.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

FluMist Quadrivalent is not absorbed systemically following intranasal administration and maternal use is not expected to result in fetal exposure to the drug.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: Pregnant women infected with seasonal influenza are at increased risk of severe illness associated with influenza infection compared with nonpregnant women. Pregnant women with influenza may be at increased risk for adverse pregnancy outcomes, including preterm labor and delivery.

Data

Animal Data: In a developmental and reproductive toxicity study, female rats were administered FluMist Quadrivalent either three times (during the period of organogenesis) or six times (prior to gestation and during the period of organogenesis), 200 microliter/rat/occasion (approximately 150 human dose equivalents), by intranasal instillation revealing no evidence of impaired fertility or harm to the fetus due to FluMist Quadrivalent.

8.2 Lactation

Risk Summary

FluMist is not absorbed systemically by the mother following intranasal administration and breastfeeding is not expected to result in exposure of the child to FluMist.

8.4 Pediatric Use

Safety and effectiveness of FluMist Quadrivalent in children 24 months of age and older is based on data from FluMist clinical studies and a comparison of post-vaccination antibody titers between persons who received FluMist Quadrivalent and those who received FluMist [see Clinical Studies (14.1, 14.2)]. FluMist Quadrivalent is not approved for use in children younger than 24 months of age because use of FluMist in children 6 through 23 months has been associated with increased risks of hospitalization and wheezing in clinical trials [see Warnings and Precautions (5.1) and Adverse Reactions (6.1)].

8.5 Geriatric Use

FluMist Quadrivalent is not approved for use in persons 65 years of age and older because in a clinical study (AV009), effectiveness of FluMist Quadrivalent to prevent febrile illness was not demonstrated in adults 55 through 64 years of age [see Clinical Studies (14.3)]. In this study, solicited events among individuals 50 through 64 years of age were similar in type and frequency to those reported in younger adults. In a clinical study of FluMist in persons 65 years of age and older, subjects with underlying high-risk medical conditions (N = 203) were studied for safety. Compared to controls, FluMist recipients had a higher rate of sore throat.

11 DESCRIPTION

FluMist Quadrivalent (Influenza Vaccine Live, Intranasal) is a live vaccine quadrivalent for administration by intranasal spray. FluMist Quadrivalent contains four vaccine virus strains: an A/H1N1 strain, an A/H3N2 strain and two B strains. FluMist Quadrivalent contains B strains from both the B/Yamagata/16/88 and the B/Victoria/2/87 lineages. FluMist Quadrivalent is manufactured according to the same process as FluMist.

The influenza virus strains in FluMist Quadrivalent are (a) cold-adapted (ca) (i.e., they replicate efficiently at 22°C, a temperature that is restrictive for replication of many wild-type influenza viruses); (b) temperature-sensitive (ts) (i.e., they are restricted in replication at 37°C [Type B strains] or 39°C [Type A strains], temperatures at which many wild-type influenza viruses grow efficiently); and (c) attenuated (att) (i.e., they do not produce classic influenza-like illness in the ferret model of human influenza infection).

No evidence of reversion has been observed in the recovered vaccine strains that have been tested (135 passages) in cell culture and positive selection of vaccine virus strains [see Clinical Pharmacology (12.2)]. For each of the four reassortant strains in FluMist Quadrivalent, the six internal gene segments responsible for ca, ts, and att phenotypes are derived from a master donor virus (MDV), and the two segments that encode the two surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), are derived from the corresponding antigenically relevant wild-type influenza viruses. Thus, the four viruses contained in FluMist Quadrivalent maintain the replication characteristics and phenotypic properties of the MDV and express the HA and NA of wild-type viruses. For the Type A MDV, at least five genetic loci in three different internal gene segments contribute to the ts and att phenotypes. For the Type B MDV, at least three genetic loci in two different internal gene segments contribute to both the ts and att properties; five genetic loci in three gene segments control the ca phenotype.

Each of the reassortant strains in FluMist Quadrivalent express the HA and NA of wild-type viruses that are related to strains expected to circulate during the 2018-2019 influenza season. Three of the viruses (A/H1N1, A/H3N2 and one B strain) have been recommended by the United States Public Health Service (USPHS) for inclusion in the annual trivalent and quadrivalent influenza vaccine formulations. An additional B strain has been recommended by the USPHS for inclusion in the quadrivalent influenza vaccine formulation. Specific pathogen-free (SPF) eggs are inoculated with each of the reassortant strains and incubated to allow virus vaccine replication. The allantoic fluid of these eggs is harvested, pooled, and then clarified by filtration. The virus is concentrated by ultracentrifugation and dialized with stabilizing buffer to obtain the final sucrose and potassium phosphate concentrations. The viral harvests are then sterile filtered to produce the monovalent bulks. Each lot is tested for ca, ts, and att phenotypes and is also tested...
Studies in Immunocompromised Individuals

preventing influenza illness in immunocompromised individuals has not been evaluated. The effectiveness of FluMist and FluMist Quadrivalent in preventing influenza illness in HIV-infected individuals was comparable to that seen in healthy children and adolescents. The effectiveness of FluMist Quadrivalent has not been evaluated for its carcinogenic or mutagenic potential or its potential to impair fertility. A randomized, double-blind, saline placebo-controlled trial (D153-P501) was performed to assess the efficacy of FluMist compared to an intramuscularly administered, inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc. (active control) in children 6 to 42 months of age during the 2004-2005 influenza season. A total of 3916 children were included in the trial, of whom 2016 were randomized to receive FluMist and 1900 to receive the active control. The primary endpoint was culture-confirmed modified CDC-ILI (CDC-defined influenza illness) among children. Modified CDC-ILI was defined as fever (temperature ≥ 100°F oral or equivalent) plus cough, sore throat, or runny nose/nasal congestion on the same or consecutive days.

In the primary efficacy analysis, FluMist demonstrated a 44.9% (95% CI: 24.2, 60.6) reduction in influenza rate compared to active control as measured by culture-confirmed modified CDC-ILI caused by wild-type strains antigenically similar to those contained in the vaccine. See Table 6 for a description of the results by strain and antigenic similarity.
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 (1997-1998 and 1998-1999). 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°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-PS01 and AV006, Year 1)

<table>
<thead>
<tr>
<th>Strain</th>
<th>FluMist</th>
<th>Placebo</th>
<th>% Efficacy (95% CI)</th>
<th>FluMist n (%)</th>
<th>Placebo n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/HA1N1</td>
<td>23 (1.4%)</td>
<td>81 (7.0%)</td>
<td>72.9% (62.8, 80.5)</td>
<td>10 (17%)</td>
<td>73 (18%)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>4 (0.2%)</td>
<td>27 (2.4%)</td>
<td>30.0% (7.4, 56.9)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>29 (1.8%)</td>
<td>35 (2.3%)</td>
<td>44.3% (6.2, 66.2)</td>
<td>6 (0.7%)</td>
<td>31 (7.1%)</td>
</tr>
</tbody>
</table>

### Notes:
- D153-PS01 and AV006 data are for subjects who received two doses of study vaccine.
- In children 12 through 35 months of age.
- In children 15 through 71 months of age.
- NCT01992244; see www.clinicaltrials.gov.
- NCT01992197; see www.clinicaltrials.gov.
- Number and percent of subjects in per-protocol efficacy analysis population with culture-confirmed influenza illness.
- Number of subjects in per-protocol efficacy analysis population of each treatment group for each strain analysis.
- For D153-PS01, influenza circulated through 12 months following vaccination.

Evaluate the immunogenicity of FluMist Quadrivalent in children and adolescents. A multicenter, randomized, double-blind, active-controlled, non-inferiority study (MI-CP208) was performed to assess the immunogenicity of FluMist Quadrivalent compared to FluMist (active control) in children and adolescents 2 through 17 years of age. A total of 2312 subjects were randomized by site at a 3:1:1 ratio to receive either FluMist Quadrivalent or 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.

### Immune Response Study of FluMist Quadrivalent in Children and Adolescents

A multicenter, randomized, double-blind, active-controlled, non-inferiority study (MI-CP208) was performed to assess the immunogenicity of FluMist Quadrivalent compared to FluMist (active control) in children and adolescents 2 through 17 years of age. A total of 2312 subjects were randomized by site at a 3:1:1 ratio to receive either FluMist Quadrivalent or 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). Children 2 through 8 years of age received 2 doses of vaccine approximately 30 days apart; children 9 through 17 years of age received 1 dose. For children 2 through 8 years of age with a history of influenza vaccination, immunogenicity assessments were performed prior to vaccination and at 28 days after the first dose. For children 2 through 8 years of age without a history of influenza vaccination, immunogenicity assessments were performed prior to vaccination and 28 days after the second dose. For children 9 years of age and older, immunogenicity assessments were performed prior to vaccination and at 28 days after vaccination. Immunogenicity 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.

### Effectiveness of FluMist to Prevent Febrile Illness in Adults 18 through 49 Years of Age During the 7-Week Site-Specific Outbreak Period (Study AV009)

**Table 8:**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>FluMist N = 2411</th>
<th>Placebo N = 1226</th>
<th>Percent Reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants with one or more events of:*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any febrile illness</td>
<td>331 (13.7%)</td>
<td>189 (15.4%)</td>
<td>10.9% (-5.1, 24.4)</td>
</tr>
<tr>
<td>Severe febrile illness</td>
<td>250 (10.3%)</td>
<td>158 (12.8%)</td>
<td>19.5% (3.0, 33.2)</td>
</tr>
<tr>
<td>Febrile upper respiratory illness</td>
<td>213 (8.63)</td>
<td>142 (11.5%)</td>
<td>23.7% (6.7, 37.5)</td>
</tr>
</tbody>
</table>

* Number of evaluable subjects (92.3% and 92.0% of FluMist and placebo recipients, respectively).

**Participants with or more events of:**

- Any febrile illness
- Severe febrile illness
- Febrile upper respiratory illness

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

### Concomitantly Administered Live Virus Vaccines

In Study AV108, concomitant administration of FluMist, MMR (manufactured by Merck & Co., Inc.) and Varicella virus Vaccine 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 (group 1); 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.

### References


### How Supplied/Storage and Handling

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 sprayers: NDC 66019-305-10

Single intranasal sprayer: NDC 66019-305-01

### Storage and Handling

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

**Flumist 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 Sprayer 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).

### 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.

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 Information for Patients and Their Caregivers

FluMist® Quadrivalent (pronounced FLEW-mist Kwä-drä-VÄ-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 Ingredient: 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 1-877-633-4411.

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MedImmune

Manufactured by:
MedImmune, LLC
Gaithersburg, MD 20878

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