**FULL PRESCRIBING INFORMATION**

**INDICATIONS AND USAGE**

FluMist® Quadrivalent (Influenza Vaccine Live, Intranasal)

**FOR INTRANASAL ADMINISTRATION BY A HEALTHCARE PROVIDER.**

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>

\(^a\) 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.

\(^b\) Administer as 0.1 mL per nostril.

\("-" indicates information is not applicable

**DOSE FORMS AND STRENGTHS**

Each 0.2 mL dose is a suspension supplied in a single-dose pre-filled intranasal sprayer. (3)

**CONTRAINDICATIONS**

- 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 with 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 after 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)

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

Revised: 7/2016

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**Figure 1**

1. **Check expiration date.** Product must be used before the date on the sprayer label.
2. **Remove rubber tip protector.** Do not remove if single-dose sprayer. Do not remove dose-divider clip at the other end of the sprayer.
3. **Remove tuberculin syringe.** Do not remove dose-divider clip at the other end of the sprayer. With the patient in an upright position, place the tip just inside the nostril to ensure the vaccine is delivered into the nose.
4. **Place the tip just inside the nostril.** Press and remove the dose-divider clip from the nozzle.
5. **Pinch and remove the dose-divider clip from the nozzle.**

Note: Active inhalation (i.e., snifffing) is not required by the patient during vaccine administration.
Clinical randomization through 180 those who received inactivated Influenza Virus Vaccine, as shown in Table 1. An increase in asthma events, captured by review of diagnostic codes, was observed in children younger than 5 years.

FluMist in Children and Adolescents

Among pediatric FluMist Quadrivalent recipients 2 through 17 years of age who received FluMist (trivalent Influenza Vaccine Live, Intranasal) [see Adverse Reactions (6.4)]. 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 viruses 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 [1]. If GBS 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 potential risks.

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)].

FluMist Quadrivalent may not protect all individuals receiving the vaccine. Do not give FluMist Quadrivalent should be based on careful consideration of the potential benefits and potential risks.

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.

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

Limitations of Vaccine Effectiveness

FluMist Quadrivalent may not protect all individuals receiving the vaccine.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

A total of 9537 children and adolescents 1 through 17 years of age and 3041 adults 18 through 64 years of age received FluMist in randomized, placebo-controlled Studies D153-P501, AV006, D153-P526, AV019, and AV009 [3 used Allantoic Fluid containing Sucrose-Phosphate-Glutamate (AF-SPG) placebo, and 2 used saline placebo]. In addition, 4179 children 6 through 17 years of age received FluMist Quadrivalent in Study MI-CP111, a randomized, active-controlled trial. Among pediatric 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.

FluMist® Quadrivalent 2

Table 1: Percentages of Children with Hospitalizations and Wheezing from Study MI-CP111

<table>
<thead>
<tr>
<th>Event</th>
<th>FluMist (%)</th>
<th>Active Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>2.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>&gt;100°F Oral</td>
<td>6.6%</td>
<td>6.6%</td>
</tr>
<tr>
<td>100-&lt;101°F Oral</td>
<td>9.4%</td>
<td>9.4%</td>
</tr>
<tr>
<td>&lt;101-&lt;102°F Oral</td>
<td>3.9%</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

6.2 Medical Conditions Predisposing to Influenza Complications

<table>
<thead>
<tr>
<th>Phone Number</th>
<th>FluMist (%)</th>
<th>Active Control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phone Number</td>
<td>FluMist (%)</td>
<td>Active Control (%)</td>
</tr>
<tr>
<td>Phone Number</td>
<td>FluMist (%)</td>
<td>Active Control (%)</td>
</tr>
</tbody>
</table>

FluMist Quadrivalent and were similar between subjects who received FluMist Quadrivalent and were different between subjects who received FluMist Quadrivalent and FluMist. 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-CP111 occurring in at least 1% of FluMist recipients and at a higher rate (≥1% rate difference after rounding) compared to active control was sneezing (in 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

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 = 4734, placebo = 4216). An increase in asthma events, captured by review of diagnostic codes, was observed in children younger than 5 years of age who received FluMist compared to those who received placebo (Relative Risk 3.53, 90% CI: 1.1, 15.7).

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. Wearing 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.
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 (14.4, 14.5)).

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 to prevent febrile illness was not demonstrated in adults 50 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 = 200) 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, cold-adapted vaccine 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 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 (i.e., they replicate efficiently at 25°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 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 possible inactivated or subunit vaccine within two weeks of enrollment.

The concurrent use of FluMist Quadrivalent with antiviral agents that are active against influenza A and/or B viruses may not be effective. If antiviral agents and FluMist Quadrivalent are administered concomitantly, revaccination should be considered when appropriate.

7.3 Concomitant Administration with Other Live Vaccines

Concomitant administration of FluMist Quadrivalent with measles, mumps, and rubella virus live vaccine MMR (manufactured by Merck & Co., Inc.) and other inactivated or subunit influenza vaccines has not been demonstrated. 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 live vaccine MMR (manufactured by Merck & Co., Inc.) and other inactivated or subunit influenza vaccines has not been demonstrated. Studies of FluMist and FluMist Quadrivalent excluded subjects who received any inactivated or subunit vaccine within two weeks of enrollment.

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

Pregnancy Category B

A developmental and reproductive toxicity study has been performed in female rats administered FluMist Quadrivalent either three times (during the period of organogenesis) or six times (prior to gestation and during the period of organogenesis). 210 micrograms/rat/occasion (approximately 159 human dose equivalents) was administered and has revealed no evidence of impaired fertility or harm to the fetus due to FluMist Quadrivalent. There are however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human response FluMist Quadrivalent should be administered during pregnancy only if clearly needed.

8.2 Nursing Mothers

It is not known whether FluMist Quadrivalent is excreted in human milk. Because some viruses are excreted in human milk, caution should be exercised when FluMist Quadrivalent is administered to a nursing woman.

8.3 Other Vaccines

FluMist Quadrivalent is not recommended for use with any other live vaccines or live or inactivated influenza vaccine within two weeks of enrollment.

8.4 Antiviral Agents

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.5 Immunocompromised Persons

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.6 Women of Childbearing Age

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.7 Infants and Children

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.8 Hepatitis B Vaccine

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.9 Tuberculosis Vaccines

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.10 Bacille Calmette-Guérin (BCG) Vaccine

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.11 Inactivated and Subunit Influenza Vaccines

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.12 Other Vaccines

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.13 Menopausal Hormone Therapy

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.14 Concomitant Administration

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.15 Other Medications

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.16 Alcohol, Tobacco, or Illicit Drug Use

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.17 Physical and Mental Health Conditions

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.

8.18 Other Factors

FluMist Quadrivalent is not recommended for use within 14 days of any immunosuppressive or antiviral agents that are used during the period of organogenesis.
A New Caledonia/7/2014 (H3N2), (an A/Hong Kong/4801/2014 (H1N1)-like virus), B/Phuket/03/2013 (B/Victoria/02/2009 lineage), and B/Brisbane/60/2008 (B/Victoria/2/2007 lineage). Each 0.2 mL dose also contains 0.188 mg/mg monosodium glutamate, 2.0 mg/mg dextrose, 2.42 mg/mg arginine, 13.68 mg/dose sucrose, 2.26 mg/dose dibasic potassium phosphate, and 0.96 mg/dose monobasic potassium phosphate. Each dose contains residual amounts of gentamicin sulfate (< 0.015 mg/mL) and ethylenediaminetetraacetic acid (EDTA) (< 0.37 mg/mL). FluMist Quadrivalent contains no preservatives.

The tip attached to the sprayer is equipped with a nozzle that produces a fine mist that is primarily deposited in the nose and nasopharynx. FluMist Quadrivalent is a colorless to pale yellow suspension and is clear to slightly cloudy.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Immune mechanisms conferring protection against influenza following receipt of FluMist Quadrivalent vaccine are not fully understood; serum antibodies, mucosal antibodies, and influenza-specific T cells may play a role.

FluMist and FluMist Quadrivalent contain live attenuated influenza viruses that must infect and replicate in cells lining the nasopharynx of the recipient to induce immunity. Vaccine viruses capable of infection and replication can be cultured from nasal secretions obtained from vaccine recipients (shedding) [see Pharmacodynamics (12.2)].

12.2 Pharmacodynamics

**Shedding Studies**

Shedding of vaccine viruses within 28 days of vaccination with FluMist was evaluated in (1) multi-center study MI-CP129 which enrolled healthy individuals 6 through 59 months of age (N = 200), and (2) multi-center study FM026 which enrolled healthy individuals 5 through 49 years of age (N = 778). In each study, nasal secretions were obtained daily for the first 7 days and every other day either through Day 28 and on Day 28 or through Day 28. In study MI-CP129, individuals with a positive shedding sample at Day 25 or Day 28 were to have additional shedding samples collected every 7 days until culture negative on 2 consecutive samples. Results of these studies are presented in Table 5.

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Number of Subjects</th>
<th>% Shedding</th>
<th>Peak Titer (TCID50/mL)</th>
<th>% Shedding After Day 11</th>
<th>Day of Last Positive Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-23 months</td>
<td>95</td>
<td>69</td>
<td>&lt; 5 log10</td>
<td>7.0</td>
<td>Day 23</td>
</tr>
<tr>
<td>24-59 months</td>
<td>100</td>
<td>69</td>
<td>&lt; 5 log10</td>
<td>1.0</td>
<td>Day 23</td>
</tr>
<tr>
<td>5-8 years</td>
<td>102</td>
<td>50</td>
<td>&lt; 5 log10</td>
<td>2.9</td>
<td>Day 23</td>
</tr>
<tr>
<td>9-18 years</td>
<td>126</td>
<td>29</td>
<td>&lt; 4 log10</td>
<td>1.6</td>
<td>Day 28</td>
</tr>
<tr>
<td>19-49 years</td>
<td>115</td>
<td>20</td>
<td>&lt; 3 log10</td>
<td>0.9</td>
<td>Day 17</td>
</tr>
</tbody>
</table>

**FluMist and FluMist Quadrivalent** are not approved for use in children younger than 24 months of age [see Adverse Reactions (11)].

A single subject who had previously received 1 dose of FluMist/MLD/mL was less than 1.5 log10, on Day 23.

A single subject who did not shed previously; TCIID/mL was less than 1.5 log10,

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 titters did not exceed 1.5 log10/mL.

**Studies in Immunocompromised Individuals**

Safety and shedding of vaccine virus following FluMist administration were evaluated in 28 HIV-infected adults [median CD4 cell count of 541 cells/mm3] and 27 HIV-negative adults 18 through 58 years of age. No serious adverse events were reported during the four-month follow-up period. Vaccine strain (type B) virus was detected in 1 of 28 HIV-infected individuals 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), cross-over, double-blind, AF-SPG placebo-controlled trial in 24 HIV-infected children [median CD4 cell count of 1013 cells/mm3] and 25 HIV-negative children 1 through 7 years of age, and in a randomized (1:1), open-label, uncontrolled influenza-vaccine-controlled trial in 24 HIV-infected children and adolescents 5 through 17 years of age (N = 606) receiving placebo or vaccine. Frequency and duration of vaccine virus shedding in HIV-infected individuals were comparable to that seen in healthy individuals. In general, adverse events in HIV-infected children following receipt of vaccine were mild and similar to those observed in vaccine recipients outside the HIV-infected group.

**ATP Population.**

An additional study involving intranasally administered placebo was conducted in healthy adults and children. The results of this study are not included in the shedding data provided in Table 5.

**Reactions (6.1)**

Inactivated Influenza Virus Vaccine manufactured by Sanofi Pasteur Inc. (active control) in children 6 to less than 5 years of age compared to any intranasally administered influenza vaccine. See Table 5 for a description of the results by strain and antigenic similarity.

### Table 6: Comparative Effectiveness Against Culture-Confirmed Modified CDC-IL-12a,b Strains (Study MI-CP111)

<table>
<thead>
<tr>
<th>Matched Strains</th>
<th>Active Control</th>
<th>Reduction in Rate of Disease Due to Wild-Type Strains Compared to Active Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N # of Cases</td>
<td>Active Control for Active Control</td>
<td>N # of Cases</td>
</tr>
<tr>
<td># of Cases/N</td>
<td>Rate (cases/N)</td>
<td>N # of Cases</td>
</tr>
<tr>
<td>4396 35</td>
<td>14.4%</td>
<td>3936 93</td>
</tr>
<tr>
<td>1501 0</td>
<td>&lt; 0.0%</td>
<td>&lt; 0.0%</td>
</tr>
<tr>
<td>4396 35</td>
<td>14.4%</td>
<td>3936 93</td>
</tr>
<tr>
<td>67</td>
<td>1.8%</td>
<td>4396 67 1.8%</td>
</tr>
<tr>
<td>4396 35</td>
<td>14.4%</td>
<td>3936 93</td>
</tr>
<tr>
<td>1501 0</td>
<td>&lt; 0.0%</td>
<td>&lt; 0.0%</td>
</tr>
<tr>
<td>4396 35</td>
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</tr>
<tr>
<td>4396 35</td>
<td>14.4%</td>
<td>3936 93</td>
</tr>
</tbody>
</table>

**ATP Population.**

A randomized, double-blind, saline placebo-controlled trial (DI53-F501) was performed to evaluate the efficacy of FluMist in children 12 through 35 months of age without high-risk medical conditions against culture-confirmed influenza. This study was performed for two consecutive seasons (2000-2001 and 2001-2002). The primary endpoint of the trial was the prevention of culture-confirmed influenza illness due to antigenically matched wild-type influenza. Respiratory illness that prompted an influenza vaccinee to seek medical care was defined as a Modified CDC-ILI (CDC-defined influenza-like illness) was defined as a positive culture for a wild-type influenza virus associated with at least 7 days of symptoms (temperature ≥ 100°F oral or equivalent) with cough, sore throat, or runny nose/nasal congestion on the same or consecutive days.

In the primary efficacy analysis, FluMist demonstrated a 44.5% (95% CI: 22.4, 66.0) reduction in influenza rate compared to active control as measured by culture-confirmed modified CDC-IL-12a,b due to 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.
Table 7: Efficacy of FluMist vs. Placebo Against Culture-Conferred Influenza Illness Due to Antigenically Matched Wild-Type Strains (Studies D153-PS01* & AV006*, Year 1)

<table>
<thead>
<tr>
<th>Strain</th>
<th>FluMist</th>
<th>Placebo</th>
<th>% Efficacy (95% CI)</th>
<th>FluMist</th>
<th>Placebo</th>
<th>% Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any strain</td>
<td>56 (3.4%)</td>
<td>139 (12.5%)</td>
<td>72.9% (62.8, 80.5)</td>
<td>10 (17%)</td>
<td>73 (18%)</td>
<td>93.5% (97.5, 99.5)</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>81 (7.3%)</td>
<td>22 (1.9%)</td>
<td>90.9% (69.4, 88.55)</td>
<td>4 (0.5%)</td>
<td>48 (12%)</td>
<td>90.0% (78.4, 91.9)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>35 (3.2%)</td>
<td>72 (9.0%)</td>
<td>44.3% (27.4, 62.7)</td>
<td>6 (0.7%)</td>
<td>31 (7%)</td>
<td>90.5% (78.0, 92.9)</td>
</tr>
</tbody>
</table>

* A D153-PS01 and AV006 data are for subjects who received two doses of study vaccine.
* In children 12 through 35 months of age.
* For children 2 through 8 years of age without 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 with a history of influenza vaccination, immunogenicity assessments were performed prior to vaccination and 28 days after the second dose.

In Study AV006, children 2 through 8 years of age without a history of influenza vaccination received 2 doses of FluMist Quadrivalent (strain H1N1 and H3N2 strains). Both strains were considered antigenically similar to the vaccine. 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.

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 spray is not made with natural rubber latex. Carton containing 10 intranasal sprays: NDC 66019-303-10 Single intranasal sprayer: NDC 66019-303-01

16.2 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.

17. PATIENT COUNSELING INFORMATION

Advising the vaccine recipient or their 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 Kwā-drĭ-Vā-lēnt) (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 of age 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.
• 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
• have a history of wheezing if under 5
• 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 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 degrees 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 degrees F (2-8 degrees 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

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Issue date: July 2016  3271103  7/16

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