NEW INFORMATION REGARDING FLUMIST® QUADRIVALENT
(Influenza Vaccine Live, Intranasal)

June 23, 2016

Dear Healthcare Provider,

As you plan for the upcoming 2016-2017 influenza season, we are writing to inform you of the recent interim recommendations of the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) regarding the use of FluMist® Quadrivalent for the 2016-2017 season.

At the June 22 meeting of the ACIP, preliminary data were shared regarding the effectiveness of FluMist® Quadrivalent during the 2015-2016 influenza season. Based on a review of these data, the ACIP issued an interim recommendation that FluMist Quadrivalent should not be used in any setting for the 2016-2017 influenza season. This decision was based on CDC vaccine effectiveness study results from the last three influenza seasons, in which FluMist Quadrivalent did not demonstrate statistically significant effectiveness in children 2-17 years of age in the US.

Results are currently available from five observational vaccine effectiveness studies involving live attenuated (LAIV) and inactivated (IIV) influenza vaccines in children 2 to 17 years of age during 2015-2016.[1,2,3] These include studies in US children 2-17 years of age conducted by CDC, Department of Defense and AstraZeneca, a study in children 2-17 years of age in the United Kingdom conducted by Public Health England, and a study in children 24-35 months of age in Finland conducted by the National Institute of Health and Welfare.

- The CDC study did not demonstrate statistically significant effectiveness of FluMist Quadrivalent
- The other four studies demonstrated statistically significant moderate overall effectiveness of FluMist Quadrivalent, ranging from 46% to 58%
- FluMist Quadrivalent did not demonstrate statistically significant effectiveness against A/H1N1pdm09 viruses in 4 of the 5 studies
- In all studies, the overall effectiveness of FluMist Quadrivalent was lower than that observed with inactivated influenza vaccines (IIV)

Influenza vaccine effectiveness varies from season to season based on differences in circulating influenza strains and strains contained in the vaccines. The observed effectiveness of FluMist Quadrivalent in 2015-16 was driven by low to moderate effectiveness against circulating A/H1N1pdm09 influenza viruses, which was also observed in 2010-11 and 2013-14. Against other influenza viruses, FluMist® effectiveness in US children has ranged from 46% to 82% against vaccine-similar A/H3N2 and B viruses in 2010-11, 2011-12, 2012-13, 2013-14, and 2014-15 influenza seasons.

AstraZeneca places the highest priority on patient health and the impact our products have on public health. Our goal in sharing this information with you is to ensure you are fully informed as you plan for the upcoming 2016-2017 influenza season. We continue to evaluate the decision of making FluMist Quadrivalent available within the United States in the 2016-17 influenza season and will be providing additional information throughout the coming week. At this time you may reach out to your FluMist Quadrivalent distributor to make any order modifications you feel are necessary. The distribution of our vaccine in other countries is progressing as planned for the forthcoming influenza season, pending the annual release process from relevant regulatory authorities.

**Important Safety Information**

FluMist® Quadrivalent (Influenza Vaccine Live, Intranasal) is a vaccine indicated for active immunization of persons 2-49 years of age for the prevention of influenza disease caused by influenza A

subtype viruses and type B viruses contained in the vaccine. FluMist Quadrivalent is for intranasal administration only.

FluMist Quadrivalent is contraindicated in persons who have had a severe allergic reaction (e.g., anaphylaxis) to any vaccine component, including egg protein, or after a previous dose of any influenza vaccine, and in children and adolescents receiving concomitant aspirin or aspirin-containing therapy.

In clinical trials, the risks of hospitalization and wheezing were increased in children <24 months of age who received trivalent FluMist® (Influenza Vaccine Live, Intranasal). Children <5 years of age with recurrent wheezing and persons of any age with asthma may be at increased risk of wheezing following FluMist Quadrivalent administration. FluMist Quadrivalent has not been studied in persons with severe asthma or active wheezing. 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. FluMist Quadrivalent has not been studied in immunocompromised persons. The safety of FluMist Quadrivalent in individuals with underlying medical conditions predisposing them to wild-type influenza infection complications has not been established. FluMist Quadrivalent may not protect all individuals receiving the vaccine.

The most common solicited adverse reactions (occurring ≥10% in vaccine recipients and at least 5% greater than in placebo) reported after FluMist were runny nose or nasal congestion in all persons 2-49 years, fever >100°F in children 2-6 years, and sore throat in adults 18-49 years. Among children 2-17 years who received FluMist Quadrivalent, 32% reported runny nose or nasal congestion and 7% reported fever >100°F. Among adults 18-49 years who received FluMist Quadrivalent, 44% reported runny nose or nasal congestion and 19% reported sore throat.

**Please see accompanying full Prescribing Information for FluMist Quadrivalent, including Patient Information.**

If you have any questions regarding FluMist Quadrivalent, please feel free to contact AstraZeneca Medical Information at 1-877-633-4411.

Sincerely,

Marlyn Cascarina
Head of Infectious Disease Franchise

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[1] Advisory Committee on Immunization Practices (ACIP) Presentation on June 22, 2016.
[2] Public Health England. "Influenza vaccine effectiveness in adults and children in primary care in the UK: provisional end-of-season results 2015-16." Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/530756/Influenza_vaccine_effectiveness_in_primary_care_in_children.pdf. Accessed June 22, 2016.
[3] Data on File. MA1116 2015-16 VE Study Results. AstraZeneca. Presented at the Advisory Committee on Immunization Practices on June 22, 2016.