Approval Date: July 9, 2020

Product: FluMist Quadrivalent

Proper Name: Influenza Vaccine

Manufacturer: MedImmune LLC

Indication: For active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine.

Description: FluMist Quadrivalent (Influenza Vaccine Live, Intranasal) is a live quadrivalent 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.

BLA: 125020

Regulatory Milestone: No data

PDUFA Goal Date: None

Date of Submission: April 5, 2011

Refusal to File Letter Issued: April 29, 2011

Application Filed Over Protest: May 26, 2011

Package Insert: Package Insert - FluMist Quadrivalent

Summary Basis for Regulatory Approval: February 29, 2012 Summary Basis for Regulatory Action - FluMist Quadrivalent

European Public Assessment Report: No data

Advisory Committee:

It was determined that review of the sBLA for FluMist® Quadrivalent by the Vaccines and Related Biological Products Advisory Committee (VRBPAC) was not required because of CBER's experience with the currently licensed FluMist® and because FluMist® Quadrivalent manufacturing is similar to the procedures used for the currently licensed FluMist® formulation. Furthermore, because our review of information submitted in the supplement, including the clinical study design and trial results, did not raise concerns or controversial issues which would have benefited from an advisory committee discussion, it was agreed that discussion of the review of this sBLA by the VRBPAC was not necessary.

Safety:

In two pivotal studies FluMist® Quadrivalent was administered to children 2-17 years of age and adults 18-49 years of age. Solicited adverse events were monitored during Days 0-14 post-vaccination; serious and non-serious unsolicited adverse events were monitored during Days 0-28 post-vaccination; and specific adverse events of interest (SAEs, new onset chronic disease) were followed for 6 months following the last immunization in these studies. The pivotal studies raised no new safety concerns. In general, the safety and reactogenicity profile of FluMist® Quadrivalent appeared similar to that of FluMist® in both adults and children. Runny/stuffy nose was the most frequently reported solicited reaction, and the median duration of any reactogenicity symptoms was < 4 days.

NCT Numbers:

- NCT03088904
- NCT02950688
- NCT03564444
- NCT02474901

- NCT03158038
- NCT02473510
- NCT01859143
- NCT02743117
- NCT03143101
- NCT03453801
- NCT03028974
- NCT01997450
- NCT02222870
- NCT02539108
- NCT01946425
- NCT02908269
- NCT03438487
- NCT04109222
- NCT03965195
- NCT01959945
- NCT04551677
- NCT04460781
- NCT02148211
- NCT03686514
- NCT02563184
- NCT03888989
- NCT03328325
- NCT03694392
- NCT03617523
- NCT03701061
- NCT03308825
- NCT04439695
- NCT03553940
- NCT01991587
- NCT02258334
- NCT02563093
- NCT01946438
- NCT02233816
- NCT03598439
- NCT03028987
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- NCT02015494
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- NCT01827462
- NCT04487041
- NCT02307851
- NCT04304768
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- NCT02212106
- NCT03301051
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- NCT01091246
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- NCT03501576
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- NCT03945825
- NCT02623075
- NCT02783170
- NCT00952705
- NCT02787044
- NCT03314662
- NCT03845231
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- NCT01198756
- NCT03275389
- NCT01992107
- NCT03658629
- NCT01992094
- NCT03312699
- NCT03615482
- NCT03318315
- NCT03068949
- NCT01954251
- NCT02860039
- NCT03734237

EudraCT Numbers:

- 2018-003701-26
- 2014-004634-26

Publications:

- Chandler, J. C., Schaeffer, J. W., Davidson, M., Magzamen, S. L., Pérez-Méndez, A., Reynolds, S. J., Goodridge, L. D., Volckens, J., Franklin, A. B., Shriner, S. A., & Bisha, B. (2017). A method for the improved detection of aerosolized influenza viruses and the male-

specific (F+) RNA coliphage MS2. *Journal of virological methods*, *246*, 38–41. https://doi.org/10.1016/j.jviromet.2017.04.004

- Grohskopf, L. A., Sokolow, L. Z., Fry, A. M., Walter, E. B., & Jernigan, D. B. (2018). Update: ACIP Recommendations for the Use of Quadrivalent Live Attenuated Influenza Vaccine (LAIV4) - United States, 2018-19 Influenza Season. *MMWR. Morbidity and mortality weekly report*, *67*(22), 643–645. https://doi.org/10.15585/mmwr.mm6722a5
- Kirtland, K. A., Lin, X., Kroger, A. T., Myerburg, S., & Rodgers, L. (2019). Frequency and cost of live vaccines administered too soon after prior live vaccine in children aged 12 months through 6 years, 2014-2017. *Vaccine*, *37*(46), 6868–6873. https://doi.org/10.1016/j.vaccine.2019.09.058
- Hawksworth, A., Jayachander, M., Hester, S., Mohammed, S., & Hutchinson, E. (2020). Proteomics as a tool for live attenuated influenza vaccine characterisation. *Vaccine*, *38*(4), 868–877. https://doi.org/10.1016/j.vaccine.2019.10.082
- Hawksworth, A., Lockhart, R., Crowe, J., Maeso, R., Ritter, L., Dibben, O., & Bright, H. (2020). Replication of live attenuated influenza vaccine viruses in human nasal epithelial cells is associated with H1N1 vaccine effectiveness. *Vaccine*, *38*(26), 4209–4218. https://doi.org/10.1016/j.vaccine.2020.04.004