Approval Date: October 28, 2020

Product: FLUAD

Proper Name: Influenza Vaccine, Adjuvanted

Manufacturer: Seqirus, Inc.

Indication: For active immunization of persons 65 years of age and older against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

Description: FLUAD (Influenza Vaccine, Adjuvanted), a sterile injectable emulsion for intramuscular use, is a trivalent, inactivated influenza vaccine prepared from virus propagated in the allantoic cavity of embryonated hens' eggs inoculated with a specific type of influenza virus.

BLA: 125510

Regulatory Milestone:

CBER held a pre-BLA meeting with Novartis on December 16, 2011, and a type C meeting on September 20, 2013, to discuss the manufacturing, pre-clinical and clinical information to be included in a BLA submission for Fluad. On November 25, 2014, Novartis submitted a BLA for Fluad to CBER, FDA. This BLA was denoted STN 125510. The PDUFA Action Due date is November 25, 2015. Fluad was first registered in Italy in 1997 and is currently authorized in 38 countries including Canada, and 15 European countries through individualized regulatory authorities, but not through the centralized European Medicines Agency (EMA).

PDUFA Goal Date: November 25, 2015

Package Insert: Package Insert - FLUAD

Summary Basis for Regulatory Approval: November 23, 2015 Summary Basis for Regulatory Action - FLUAD

European Public Assessment Report: Human medicine European public assessment report (EPAR): Fluad Tetra

Advisory Committee:

On September 15, 2015, CBER convened a Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting to review and discuss presentations of safety and immunogenicity data derived from studies conducted with Fluad and submitted in the BLA. The committee voted affirmatively that the available data support the safety (10 yes, 2 no, 1 abstain) and effectiveness (11 yes, 1 no, 1 abstain) of Fluad and approval under the accelerated approval regulations for the proposed indication in adults aged 65 years of age and older.

NCT Numbers:

- NCT03694808
- NCT03183908
- NCT02215863
- NCT01258023
- NCT02523287
- NCT03603509
- NCT00434733
- NCT01771367
- NCT01222403
- NCT02225327
- NCT02882100
- NCT02686398
- NCT00956761
- NCT00734734
- NCT01651104
- NCT01344057
- NCT01346592
- NCT01152814
- NCT01682369
- NCT03669627
- NCT02871206
- NCT02560909
- NCT04077424
- NCT02368327
- NCT02529904
- NCT00478816
- NCT00522236
- NCT01879540
- NCT00841763
- NCT01819155
- NCT01162122
- NCT01032395
- NCT00522067
- NCT04101838
- NCT00644059
- NCT03314662
- NCT03312699
- NCT01368796
- NCT02872311
- NCT00971906
- NCT00971542
- NCT00971100
- NCT00970177
- NCT04515368

- NCT02362919
- NCT02933723
- NCT03838497
- NCT03698279
- NCT03699839
- NCT03330132

EudraCT Numbers:

- 2007-003339-22
- 2005-005871-14
- 2004-002225-45
- 2006-004063-66
- 2010-023791-63
- 2014-005053-40
- 2005-000621-38
- 2007-003786-41
- 2006-005558-63
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- 2010-021841-38
- 2006-005203-33
- 2012-000085-38
- 2006-005428-18
- 2008-003871-32
- 2006-000610-20
- 2007-000964-26
- 2010-018603-29
- 2007-000966-19
- 2013-000607-16
- 2007-005233-11
- 2012-002443-26
- 2014-003543-35
- 2007-000165-38
- 2009-010586-23
- 2009-013639-39
- 2015-001648-12
- 2009-013671-21
- 2008-000895-25
- 2010-022871-78
- 2011-003603-37
- 2019-001974-27
- 2009-013640-37
- 2011-003573-28
- 2008-001047-19
- 2009-013672-45
- 2014-004248-36
- 2007-002480-27
- 2018-005026-39
- 2009-013904-30
- 2008-002602-20

Publications:

- Durando, P., Fenoglio, D., Boschini, A., Ansaldi, F., Icardi, G., Sticchi, L., Renzoni, A., Fabbri, P., Ferrera, A., Parodi, A., Bruzzone, B., Gabutti, G., Podda, A., Del Giudice, G., Fragapane, E., Indiveri, F., Crovari, P., & Gasparini, R. (2008). Safety and immunogenicity of two influenza virus subunit vaccines, with or without MF59 adjuvant, administered to human immunodeficiency virus type 1-seropositive and -seronegative adults. *Clinical and vaccine immunology: CVI*, *15*(2), 253–259. https://doi.org/10.1128/CVI.00316-07
- Seo, Y. B., Choi, W. S., Lee, J., Song, J. Y., Cheong, H. J., & Kim, W. J. (2014). Comparison of the immunogenicity and safety of the conventional subunit, MF59-

adjuvanted, and intradermal influenza vaccines in the elderly. *Clinical and vaccine immunology : CVI*, *21*(7), 989–996. https://doi.org/10.1128/CVI.00615-13

- Levin, Y., Kochba, E., Shukarev, G., Rusch, S., Herrera-Taracena, G., & van Damme, P. (2016). A phase 1, open-label, randomized study to compare the immunogenicity and safety of different administration routes and doses of virosomal influenza vaccine in elderly. *Vaccine*, *34*(44), 5262–5272. https://doi.org/10.1016/j.vaccine.2016.09.008
- Akmatov, M. K., Riese, P., May, M., Jentsch, L., Ahmed, M. W., Werner, D., Rösel, A., Tyler, M., Pessler, K., Prokein, J., Bernemann, I., Klopp, N., Prochnow, B., Trittel, S., Tallam, A., Illig, T., Schindler, C., Guzmán, C. A., & Pessler, F. (2017). Establishment of a cohort for deep phenotyping of the immune response to influenza vaccination among elderly individuals recruited from the general population. *Human vaccines & immunotherapeutics*, *13*(7), 1630–1639. https://doi.org/10.1080/21645515.2017.1299300
- de Wolf, A., van Aalst, S., Ludwig, I. S., Bodinham, C. L., Lewis, D. J., van der Zee, R., van Eden, W., & Broere, F. (2017). Regulatory T cell frequencies and phenotypes following anti-viral vaccination. *PloS one*, *12*(6), e0179942. https://doi.org/10.1371/journal.pone.0179942
- Cruz-Valdez, A., Valdez-Zapata, G., Patel, S. S., Castelli, F. V., Garcia, M. G., Jansen, W. T., Arora, A. K., & Heijnen, E. (2018). MF59-adjuvanted influenza vaccine (FLUAD®) elicits higher immune responses than a non-adjuvanted influenza vaccine (Fluzone®): A randomized, multicenter, Phase III pediatric trial in Mexico. *Human vaccines & immunotherapeutics*, *14*(2), 386–395. https://doi.org/10.1080/21645515.2017.1373227