Approval Date: October 27, 2020

Product: VAXELIS

Proper Name: Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine

Manufacturer: MSP Vaccine Company

Indication: Active immunization against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive disease due to Haemophilus influenzae type b (Hib) in children 6 weeks through 4 years of age (prior to fifth birthday).

Description: VAXELIS (Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus b Conjugate and Hepatitis B Vaccine) is a sterile suspension for intramuscular injection.

BLA: 125563

Regulatory Milestone:

On September 21, 2010, Sanofi submitted an Investigational New Drug Application (IND). On August 13, 2014, MCM submitted a Biologics License Application (BLA) for PR5I to CBER, FDA which was assigned the STN 125563. The proprietary name of the vaccine at the time of the BLA submission was proposed as On February 14, 2018 Sanofi submitted a request to IND 14496 for withdrawing that proprietary name of the vaccine and on February 16, 2018, submitted a Proprietary Name Review (PNR) request to the same IND for changing the name of the product from to VAXELIS. CBER provisionally accepted VAXELIS as the proprietary name of the

vaccine on June 19, 2018. MCM submitted a PNR request to the BLA on August 27, 2018. The original PDUFA due date was August 12, 2015; however, this was extended to November 11, 2015 for a major amendment, submitted by MCM to the BLA on June 25, 2015. On May 25, 2017, Sanofi submitted an amendment to their IND 14496

PDUFA Goal Date: December 29, 2018

Package Insert: Package Insert - VAXELIS

Summary Basis for Regulatory Approval: December 18, 2018 Summary Basis for Regulatory Action - VAXELIS

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

Advisory Committee:

An Advisory Committee Meeting for VAXELIS vaccine was not held, because there were no issues pertaining to this BLA that required input from the Vaccines and Related Biological Products Advisory Committee.

Safety:

The safety evaluation for VAXELIS was based upon the two Phase 3 studies conducted in the U.S. under Protocols V419-005 and V419-006, as described above in Table 7, with supplementary safety data from two additional Phase 2 studies, V419-003 and V419-004, conducted in Canada, for the evaluation of Serious Adverse Events (SAEs). V419-005 and V419-006 studies enrolled a total of 4265 subjects (3380 received VAXELIS and 885 received control vaccines). Studies V419-003 and V419-004 enrolled a total of 495 subjects who received the

vaccine and 339 subjects who received control vaccines. In the phase 3 studies, V419-005 and V419-006, no clinically important imbalances for local solicited adverse events (AEs) (i.e., pain/tenderness, erythema, and swelling) or systemic AEs (i.e., crying, decreased appetite, irritability, pyrexia, somnolence and vomiting) were identified between groups for days 1-5 after each vaccination. However, in the combined Phase 3 studies, rates of fever (defined as ≥38◦C) were increased for VAXELIS (47.2%) as compared to the Control vaccines (33.6%); [difference 13.6% (95%CI: 9.7, 17.3)].

The most frequent SAE reported in both studies in the 30 days following any vaccination was respiratory syncytial virus-mediated bronchiolitis. The majority of SAEs that occurred during this time period in both studies were due to conditions commonly found in this age group, including gastroenteritis/dehydration, GERD, respiratory tract and other infections. AEs leading to study vaccine discontinuation were reported by 8 subjects (0.2%) in the VAXELIS group and 1 subject (0.1%) in the control group. Death was reported for 6 subjects (0.2%) in the VAXELIS group and 1 subject (0.1%) in the control group, all of which were considered unrelated to study vaccination.

NCT Numbers:

- NCT02759354
- NCT04535037
- NCT01480258
- NCT01553279
- NCT04490499
- NCT04016714
- NCT01839188

EudraCT Numbers:

- 2020-000126-26
- 2018-003788-70
- 2019-002988-10
- 2016-000274-37
- 2018-003451-38

Publications:

- Syed Y. Y. (2017). DTaP5-HB-IPV-Hib Vaccine (Vaxelis®): A Review of its Use in Primary and Booster Vaccination. *Paediatric drugs*, *19*(1), 69–80. https://doi.org/10.1007/s40272-016-0208-y
- Xu, J., Stek, J. E., Ziani, E., Liu, G. F., & Lee, A. W. (2019). Integrated Safety Profile of a New Approved, Fully Liquid DTaP5-HB-IPV-Hib Vaccine. *The Pediatric infectious disease journal*, *38*(4), 439–443. https://doi.org/10.1097/INF.0000000000002257
- Oliver, S. E., & Moore, K. L. (2020). Licensure of a Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, Haemophilus influenzae Type b Conjugate, and Hepatitis B Vaccine, and Guidance for Use in Infants. *MMWR. Morbidity and mortality weekly report*, *69*(5), 136–139. https://doi.org/10.15585/mmwr.mm6905a5
- Wilck, M. B., Xu, Z. J., Stek, J. E., & Lee, A. W. (2020). Safety and immunogenicity of a fully-liquid DTaP-IPV-Hib-HepB vaccine (Vaxelis™) in premature infants. *Human vaccines & immunotherapeutics*, 1–6. Advance online publication. https://doi.org/10.1080/21645515.2020.1756668
- Orsi, A., Azzari, C., Bozzola, E., Chiamenti, G., Chirico, G., Esposito, S., Francia, F., Lopalco, P., Prato, R., Russo, R., Villani, A., & Franco, E. (2018). Hexavalent vaccines: characteristics of available products and practical considerations from a panel of Italian experts. *Journal of preventive medicine and hygiene*, *59*(2), E107–E119.
- Vesikari, T., Becker, T., Vertruyen, A. F., Poschet, K., Flores, S. A., Pagnoni, M. F., Xu, J., Liu, G. F., Stek, J. E., Boisnard, F., Thomas, S., Ziani, E., & Lee, A. W. (2017). A Phase III Randomized, Double-blind, Clinical Trial of an Investigational Hexavalent Vaccine Given at Two, Three, Four and Twelve Months. *The Pediatric infectious disease journal*, *36*(2), 209–215. https://doi.org/10.1097/INF.0000000000001406
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- Puliyel, J., & Sathyamala, C. (2018). Infanrix hexa and sudden death: a review of the periodic safety update reports submitted to the European Medicines Agency. *Indian journal of medical ethics*, *3*(1), 43–47. https://doi.org/10.20529/IJME.2017.079
- Chiappini, E., Petrolini, C., Caffarelli, C., Calvani, M., Cardinale, F., Duse, M., Licari, A., Manti, S., Martelli, A., Minasi, D., Miraglia Del Giudice, M., Pajno, G. B., Pietrasanta, C., Pugni, L., Tosca, M. A., Mosca, F., & Marseglia, G. L. (2019). Hexavalent vaccines in preterm infants: an update by Italian Society of Pediatric Allergy and Immunology jointly with the Italian Society of Neonatology. *Italian journal of pediatrics*, *45*(1), 145. https://doi.org/10.1186/s13052-019-0742-7