



Review Memo: Priority Review Request

Date: August 12, 2019

BLA STN#: 125678/0

Product: Smallpox (Modified Vaccinia Ankara) vaccine, live, non-replicating

Proprietary Name: JYNNEOS

Sponsor: Bavarian Nordic A/S

Indication: JYNNEOS is a vaccine indicated for prevention of smallpox or monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection

Date of Submission: October 25, 2018

From: Bharat Khurana, DVM, PhD, MBA
Chair of the Review Committee

Through: Rakesh Pandey, PhD, Branch Chief

To: STN 125678/0

Background

Bavarian Nordic A/S submitted IND 11596, entitled, "Modified Vaccinia Ankara (MVA; chick embryo fibroblast cells) Smallpox Vaccine, Live" (MVA-BN Smallpox Vaccine) which was received at CBER on March 08, 2004. Subsequently, Bavarian Nordic submitted a request for Fast Track Designation in an amendment dated May 11, 2004, received on May 12, 2004 (IND 11596/04). On July 12, 2004, Fast Track designation was granted for development of MVA-BN Smallpox Vaccine for active immunization against smallpox infection in special populations for which Dryvax is contraindicated. At the time of submission of their Biologics License Application (BLA), Bavarian Nordic requested Priority Review of the BLA for MVA-BN Smallpox Vaccine (STN 125678) for the prevention of smallpox in adults aged 18 years and older, determined to be at high risk for smallpox infection. In the cover letter (dated October 25, 2018) of the original BLA application Bavarian Nordic requested priority review designation "based on smallpox being a serious condition for which MV A-BN provides a significant improvement in safety, particularly in multiple subpopulations of individuals for whom the currently licensed vaccine, ACAM2000, is either contraindicated or could have severe and potentially life-threatening clinical consequences."

Smallpox is a serious, highly contagious, and sometimes fatal infectious disease and is considered as a high-priority threat under the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan (2017-2018). Dryvax, a smallpox vaccine, originally licensed in 1944 to Wyeth Laboratories, Inc. of Madison, N.J., was manufactured until the mid-1980s when the World Health Organization declared that smallpox had been eradicated. Currently, there is only one US-licensed smallpox vaccine: ACAM2000, licensed on August 31, 2007, which is manufactured by Emergent Product Development Gaithersburg, Inc. and is based on the same strain of vaccinia virus as Dryvax. ACAM2000 is indicated for active immunization against smallpox disease for persons determined to be at high risk for smallpox infection. ACAM2000 is contraindicated for use in individuals with severe immunodeficiency who are not expected to benefit from the vaccine. The Warnings and Precautions section of the package insert for ACAM2000 describes a number of clinically significant adverse reactions including generalized vaccinia, progressive vaccinia (in immunocompromised individuals), eczema vaccinatum (in individuals with atopic dermatitis), fetal vaccinia (in pregnant women), and inadvertent inoculation of contacts of vaccinees. Thus, there is an unmet need for a smallpox vaccine with an improved safety profile.

Sponsor's rationale for Priority Review:

Bavarian Nordic stated that they are requesting Priority Review for JYNNEOS (STN 125678) for the following reasons:

- 1) JYNNEOS targets a serious condition (smallpox).

Rationale: Smallpox is a high-priority threat under the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan (2017-2018)

- 2) JYNNEOS offers a significant improvement in safety over currently licensed vaccine, ACAM2000.

Rationale: JYNNEOS “provides a significant improvement in safety particularly in multiple subpopulations of individuals for whom the currently licensed vaccine, ACAM2000, is either contraindicated or could have severe and potentially life-threatening clinical consequences.”

Recommendations for Priority Review Determination:

The Review Committee recommends Priority Review be granted for STN 125678/0. The serious risks associated with ACAM2000 outlined above are directly related to replication of the vaccine virus at and beyond the vaccination site. JYNNEOS is incapable of replication in human cells and tissues, and preliminary review of the safety data accumulated in the JYNNEOS clinical development program support the safety profile.

JYNNEOS is intended to prevent a serious condition and, if approved, would provide a significant improvement in safety. As the Chair of the Review Committee, I

recommended that Priority Review be granted for STN 125678/0. The decision to grant Priority Review was conveyed to Bavarian Nordic in the December 19, 2018, BLA filing notification letter.

Reference:

Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics

(<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf>).