December 23, 2024

John Beigel, M.D.
Associate Director for Clinical Research
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases (NIAID)

Dear Dr. Beigel:

On August 9, 2022, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States (U.S.) citizens living abroad, and that involves monkeypox virus. On the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of vaccines for use against the monkeypox virus, pursuant to Section 564 of the Act, subject to terms of any authorization issued under that section.[1]

On August 9, 2022, pursuant to Section 564 of the Act. the FDA issued an EUA for the emergency use of Jynneos to prevent monkeypox infection in 1) individuals less than 18 years of age determined to be at high risk of monkeypox infection when two 0.5 mL doses are administered subcutaneously 4 weeks apart, and individuals 18 years of age and older determined to be at high risk of monkeypox infection when two 0.1 mL doses are administered intradermally 4 weeks apart. Subsequently on August 16, 2022, data was reviewed to support extending the hold time of Jynneos lots to allow the vaccine to be stored at 2-8C for 8 weeks once thawed.

On December 23, 2024, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the August 9, 2022 letter of authorization in its entirety with revisions to: 1) remove the requirement that use of Jynneos under the EUA is limited to doses supplied by the Administration for Strategic Preparedness & Response (ASPR) 2) clarify storage time for certain lots of Jynneos vaccine held at +2°C to +8°C (+36°F to +46°F) after thawing; and 3) revise condition J to provide flexibility to determine a different reporting interval for periodic safety reports, if appropriate.

[1] U.S. Department of Health and Human Services, Determination of Public Health Emergency or Significant Potential for a Public Health Emergency and Declaration that Circumstances Exist Justifying an Authorization Pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b).

Additionally, FDA is authorizing the EUA Fact Sheets for Jynneos to replace "monkeypox" with the WHO new preferred term[2] "mpox," and to reflect this and other relevant changes. FDA is also updating the postmarketing experience section of the EUA Fact Sheet for Healthcare Providers Administering Vaccine.

Jynneos is a live vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus. Each 0.5 mL single dose is formulated to contain 0.5×10^8 to 3.95×10^8 infectious units of MVA-BN live virus. Jynneos is licensed for active immunization to prevent smallpox and mpox disease in adults 18 years of age and older determined to be at high risk for smallpox or mpox infection. It is FDA-approved as a two-dose series, with each 0.5 mL dose given subcutaneously (SC) 4 weeks apart.

For the authorization of intradermal administration of two doses (0.1 mL each) of Jynneos to individuals 18 years of age and older, FDA reviewed immunogenicity and safety data from a completed phase 2 trial in which 191 subjects received two intradermal (ID) doses of Jynneos (0.1 mL each), and 167 subjects received two SC doses of Jynneos (0.5 mL each). Study vaccinations were administered 4 weeks apart to all subjects. FDA's review of the available safety data did not identify specific safety concerns that would preclude issuance of an EUA. Following vaccination with Jynneos SC and ID immunogenicity was evaluated using 4 different assays. Plaque reduction neutralizing antibody titers (PRNT) were obtained using assays performed at St. Louis University (SLU) and Bavarian-Nordic (BN) and enyzme linked immunosorbent assay (ELISA) values were obtained from assays conducted at SLU and BN. The development of the immune response to Jynneos over time following SC and ID administration was nearly identical, and the $\log_2$ transformed peak titers obtained following ID administration were non-inferior those obtained following SC administration. For the authorization of SC administration of two doses (0.5 mL each) of Jynneos to individuals younger than 18 years of age FDA has considered the available Jynneos safety and immunogenicity data in adults as well as the historical data with use of live vaccinia virus smallpox vaccines in pediatric populations. Based on these data, FDA concluded that it is reasonable to believe, based on the totality of scientific evidence available, that Jynneos may be effective and that the known and potential benefits of Jynneos outweigh the known and potential risks of the vaccine, for the prevention of mpox disease in individuals less than 18 years of age determined to be at high risk of mpox infection when two 0.5 mL doses are administered subcutaneously 4 weeks apart, and in individuals 18 years of age and older determined to be at high risk of mpox infection when two 0.1 mL doses are administered intradermally 4 weeks apart.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of Jynneos for the prevention of mpox disease as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

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[2] On November 28, 2022, following a series of consultations with global experts, the World Health Organization (WHO) began using a new preferred term "mpox" as a synonym for monkeypox, the disease caused by the monkeypox virus. Refer to: https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Jynneos for the prevention of mpox disease when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1) The monkeypox virus can cause a serious or life-threatening disease or condition to humans infected by this virus;

2) Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the use of Jynneos under this authorization may be effective in preventing mpox disease, and that, when used under the conditions described in this authorization, the known and potential benefits of this use when used to prevent mpox disease outweigh its known and potential risks; and

3) There is no adequate, approved, and available alternative[3] for the unapproved uses of Jynneos to prevent mpox disease.[4]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Use of Jynneos in accordance with this authorization will be administered by vaccination providers[5] and used only to prevent mpox disease in:
  1. individuals less than 18 years of age determined to be at high risk of mpox infection when two 0.5 mL doses are administered subcutaneously 4 weeks apart, and
  2. individuals 18 years of age and older determined to be at high risk of mpox infection when two 0.1 mL doses are administered intradermally 4 weeks apart.
- Jynneos may be administered by a vaccination provider without an individual prescription for each vaccine recipient.

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[3] Although the ACAM2000 vaccine and Jynneos (0.5 mL per dose) are approved to prevent mpox disease in certain individuals determined to be at high risk of mpox infection, available information indicates that availability of mpox vaccine is needed. Additionally, Jynneos is not approved to provide vaccination in the pediatric population.

[4] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

[5] For purposes of this letter, "vaccination provider" refers to anyone who is licensed or otherwise authorized to administer or provide vaccination services (e.g., non-physician healthcare professionals, such as nurses and pharmacists pursuant to state law under a standing order issued by the state health officer) in accordance with State law. For purposes of this letter, "vaccination provider" also includes a person authorized by the U.S. Department of Health and Human Services (e.g., under the PREP Act Declaration pertaining to monkeypox virus) to administer mpox vaccines in accordance with an FDA authorization. See, e.g., HHS, *Notice of Amendment to the January 1, 2016 Republished Declaration Under the Public Readiness and Emergency Preparedness Act* (87 FR 59799, October 3, 2022). In addition, for purposes of this letter, the term "State" includes any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. See Section 201(a)(1) of the Act.

Product Description

Jynneos is supplied as a suspension and does not contain a preservative. Jynneos is approved for use in individuals 18 years of age and older. The FDA-approved dosing regimen is two doses (0.5 mL each) given subcutaneously 4 weeks apart. Under the license, Jynneos is supplied in a single dose vial. Once thawed, Jynneos is licensed to be kept at +2°C to +8°C (+36°F to +46°F) for 4 weeks.

Under this authorization, each vial contains a single dose (0.5 mL) for subcutaneous injection in individuals less than 18 years of age or up to 5 doses (0.1 mL each) for intradermal injection in individuals 18 years of age and older.

Jynneos lots listed in Appendix A are authorized to be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks after thawing Future lots may be authorized to be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks if FDA determines that the data support such expiry. All lots that are authorized to be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks can be found on the following website, and FDA will update this website if the agency authorizes future lots for this extended expiry: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#mpoxvaccine.

Jynneos is authorized for the emergency uses described in Scope of Authorization (Section II) with the following product-specific information that is available to vaccination providers and recipients, respectively (referred to as "authorized labeling"):

- Fact Sheet for Healthcare Providers Administering Vaccine: Emergency Use Authorization (EUA) of Jynneos (Smallpox and Mpox Vaccine, Live, Non-Replicating) for Prevention of Mpox Disease in Individuals Determined to be at High Risk for Mpox Infection

- Fact Sheet for Recipients and Caregivers About Jynneos (Smallpox and Mpox Vaccine, Live, Non-Replicating) to Prevent Mpox Disease in Individuals Determined to be at High Risk for Mpox Infection

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of use of Jynneos under this authorization, when used to prevent mpox disease and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that use of Jynneos under this authorization may be effective in preventing mpox disease when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that use of Jynneos (as

described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The authorized emergency use of Jynneos under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), use of Jynneos is authorized to prevent mpox disease as described in the Scope of Authorization (Section II) under this EUA, despite the fact that such use does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:[6]

The Administration for Strategic Preparedness & Response (ASPR)

A. ASPR will ensure that the authorized labeling (i.e., Fact Sheets) and the terms of this EUA are made available to relevant stakeholders (i.e., State public health agencies and other authorized distributors of which ASPR is aware) involved in distributing or receiving Jynneos under this authorization. ASPR will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized labeling (i.e., Fact Sheets).

ASPR and Bavarian Nordic A/S Distribution Under the EUA:

B. ASPR and Bavarian Nordic A/S, as applicable,[7] will ensure that appropriate storage and cold chain is maintained until delivered to healthcare facilities or other vaccine receipt sites.

C. ASPR and Bavarian Nordic A/S may develop and disseminate instructional and educational materials (e.g., video regarding vaccine handling, storage/cold-chain management, preparation, disposal) that are consistent with the authorized emergency use of the vaccine as described in the letter of authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs during an emergency. Any instructional and educational materials that are inconsistent with the authorized labeling are prohibited.

[6] The conditions in this EUA do not restrict distribution or administration of the vaccine when distributed or administered for the licensed use.

[7] In Conditions B through E of this Letter of Authorization, a condition is applicable to ASPR if ASPR is responsible for distribution of the vaccine under the EUA and a condition is applicable to Bavarian Nordic A/S if Bavarian Nordic A/S is responsible for distribution of the vaccine under the EUA. A condition is not applicable if the vaccine is being distributed for the licensed use only and a condition is not applicable to ASPR or Bavarian Nordic A/S when neither entity distributes the vaccine for the emergency uses authorized under the EUA.

D. ASPR and Bavarian Nordic A/S, as applicable, will maintain records regarding release of Jynneos for distribution (i.e., lot numbers, quantity, release date).

E. ASPR and Bavarian Nordic A/S, as applicable, will make available to FDA upon request any records maintained in connection with this EUA.

National Institute of Allergy and Infectious Diseases (NIAID)

F. NIAID may request changes to this authorization, including to the authorized Fact Sheets for Jynneos. Any request for changes to this EUA must be submitted to the Office of Vaccines Research and Review (OVRR)/Center for Biologics Evaluation and Research (CBER). Such changes require appropriate authorization prior to implementation.[8]

Bavarian Nordic A/S

G. Bavarian Nordic A/S will submit to the STN 125678 file quarterly manufacturing reports that include a listing of all drug substance and drug product lots produced after issuance of this authorization. This report must include lot number, manufacturing site, date of manufacture, and lot disposition, including those lots that were quarantined for investigation or those lots that were rejected. Information on the reasons for lot quarantine or rejection must be included in the report. The first report is due November 9, 2022. This EUA does not supersede requirements under the biologics license applicable to facilities, equipment, manufacturing, and lot release.

H. Bavarian Nordic A/S must submit reports to Vaccine Adverse Event Reporting System (VAERS) for the following:
   - Serious adverse events (irrespective of attribution to vaccination)
   - Cases of cardiac events including myocarditis and pericarditis (regardless of seriousness or expectedness)
   - Cases of thromboembolic events and neurovascular events

   These reports should be submitted to VAERS as soon as possible but no later than 15 calendar days from initial receipt of the information by Bavarian Nordic A/S. All other adverse events must be submitted to VAERS as periodic (non-expedited) reports in compliance with 21 CFR 600.80.

I. Bavarian Nordic A/S must submit to STN 125678 periodic safety reports for Jynneos at monthly intervals, or at another appropriate reporting interval determined by the Office of Biostatistics and Pharmacovigilance (OBPV)/CBER, in accordance with a due date agreed

[8] The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study. All changes to the authorization require review and concurrence from OVRR. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), or (7), review and concurrence is also required from the Preparedness and Response Team (PREP)/Office of the Center Director (OD)/CBER and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS).

upon with the Office of Biostatistics and Pharmacovigilance (OBPV)/CBER, beginning after the first full calendar month after authorization. Each periodic safety report must contain consolidated aggregate analysis for all postmarketing and post-authorization spontaneous adverse event reports, and descriptive information which includes:

- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant individuals), and adverse events of special interest;
- A narrative summary and analysis of vaccine administration errors, whether or not associated with an adverse event, that were identified since the last reporting interval;
- Newly identified safety concerns in the interval; and
- Actions taken since the last report because of adverse experiences (for example, changes made to Healthcare Providers Administering Vaccine (Vaccination Providers) Fact Sheet, changes made to studies or studies initiated).

Vaccination Providers Administering Jynneos Under the EUA:

J. Vaccination providers will administer the vaccine in accordance with the authorization.

K. Vaccination providers will provide the Fact Sheet for Recipients and Caregivers to each individual receiving vaccination and provide the necessary information for receiving their second dose.

L. Vaccination providers administering Jynneos must report the following information associated with the administration of Jynneos of which they become aware to VAERS in accordance with the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events (irrespective of attribution to vaccination)
- Cases of cardiac events including myocarditis and pericarditis
- Cases of thromboembolic events and neurovascular events

Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. The VAERS reports should include the words "Jynneos" in the description section of the report. More information is available at vaers.hhs.gov or by calling 1-800-822-7967. Please also provide a copy of the VAERS form to Bavarian Nordic at 1-800-675-9596.

M. Vaccination providers will conduct any follow-up requested by the U.S. government, including ASPR, CDC, FDA, or other designee, regarding adverse events to the extent feasible given the emergency circumstances.

N. Vaccination providers will monitor and comply with CDC vaccine management requirements (e.g., requirements concerning obtaining, tracking, and handling vaccine) and with requirements concerning reporting of vaccine administration data to CDC.

O. Vaccination providers will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to CDC, and FDA for inspection upon request.

P. Vaccination providers receiving Jynneos will ensure that appropriate storage and cold chain is maintained.

Conditions Related to Printed Matter, Advertising, and Promotion Under the EUA

Q. All descriptive printed matter, advertising, and promotional material, relating to the use of Jynneos under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in section 502(a) and (n) of the FD&C Act and FDA implementing regulations.

R. All descriptive printed matter, advertising, and promotional material relating to the use of Jynneos under this authorization clearly and conspicuously shall state that:
   - This product has not been approved or licensed by FDA for use in individuals less than 18 years of age, or as two 0.1 mL doses administered intradermally 4 weeks apart in individuals 18 years of age and older determined to be at high risk of mpox infection but has been authorized for emergency use by FDA, under an EUA to prevent mpox disease; and
   - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of the medical product under Section 564(b)(1) of the FD&C Act unless the declaration is terminated or authorization revoked sooner.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of vaccines for use to prevent mpox disease is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

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Peter W. Marks, M.D., Ph.D.
Director
Center of Biologics Evaluation and Research
Food and Drug Administration

Enclosures

Appendix A: Lots of Jynneos authorized to have an 8-week expiry when held at +2°C to +8°C (+36°F to +46°F) after thawing

JYNNEOS Lot number	Expiry date (at −20°C)	JYNNEOS Lot number	Expiry date (at −20°C)
FDP00002	AUG-2023	87580	FEB-2026
FDP00003	AUG-2023	87578	FEB-2026
FDP00004	AUG-2023	87579	FEB-2026
FDP00005	AUG-2023	96845	FEB-2026
FDP00009	MAY-2024	96847	FEB-2026
FDP00012	AUG-2024	96848	FEB-2026
FDP00013	SEP-2024	96849	MAR-2026
FDP00014	SEP-2024	96854	MAR-2026
FDP00015	SEP-2024	96850	MAR-2026
FDP00016	OCT-2024	96851	MAR-2026
FDP00017	OCT-2024	96852	MAR-2026
FDP00018	OCT-2024	96844	FEB-2026
FDP00019	OCT-2024	87570	NOV-2025
FDP00020	OCT-2024	87572	DEC-2025
FDP00074	JUL-2025	96853	MAR-2026
FDP00115	JUL-2025	96855	MAR-2026
FDP00117	JUL-2025	96856	MAR-2026
FDP00118	JUL-2025	96858	MAR-2026
FDP00119	AUG-2025	96859	MAR-2026
FDP00120	AUG-2025	96860	MAR-2026
FDP00125	AUG-2025	96861	APR-2026
FDP00144	SEP-2025	96862	APR-2026
FDP00147	SEP-2025	96863	APR-2026
FDP00148	SEP-2025	96865	APR-2026
FDP00160	OCT-2025	96867	APR-2026
FDP00161	OCT-2025	96868	APR-2026
FDP00162	OCT-2025	FDP00287	MAR-2026
FDP00193	OCT-2025	FDP00289	APR-2026
FDP00195	NOV-2025	96866	APR-2026
FDP00196	NOV-2025	106902	APR-2026
FDP00197	NOV-2025	FDP00288	MAR-2026
80897	OCT-2025	FDP00278	FEB-2026
80898	OCT-2025	96857	MAR-2026
80899	OCT-2025	96864	APR-2026
FDP00202	FEB-2026	FDP00326	MAY-2026
87574	JAN-2026	142054	JUN-2027
87575	JAN-2026	FDP00639	SEP-2027
87576	JAN-2026	FDP00640	SEP-2027
87577	FEB-2026	FDP00641	SEP-2027