

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE: EMERGENCY USE AUTHORIZATION 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

HIGHLIGHTS OF EMERGENCY USE AUTHORIZATION (EUA)

These highlights of the EUA do not include all the information needed to use JYNNEOS under the EUA. See the FULL FACT SHEET FOR HEALTHCARE PROVIDERS for JYNNEOS.

JYNNEOS (Smallpox and Mpox Vaccine, Live, Non-replicating) suspension for subcutaneous injection, suspension for intradermal injection

Original EUA Authorized Date: 08/2022

Most Recent EUA Authorized Date: 12/2024

RECENT MAJOR CHANGES

Warnings and Precautions (5.2)

10/2023

EMERGENCY USE AUTHORIZATION

The US Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of JYNNEOS for:

- active immunization by subcutaneous injection for prevention of mpox disease in individuals less than 18 years of age determined to be at high risk for mpox infection, and
- active immunization by intradermal injection for prevention of mpox disease in individuals 18 years of age and older determined to be at high risk for mpox infection. (1)

JYNNEOS is not approved for these uses.

See Full Fact Sheet for Healthcare Providers for the justification for emergency use of JYNNEOS, information on available alternatives, and additional information on mpox disease.

DOSAGE AND ADMINISTRATION

Individuals less than 18 years of age:

- For subcutaneous injection only.
- Administer two doses (0.5 mL each) 4 weeks apart. (2.1, 2.2)

Individuals 18 years of age and older:

- For intradermal injection only.
- Administer two doses (0.1 mL each) 4 weeks apart. (2.1, 2.2)

DOSAGE FORMS AND STRENGTHS

Suspension for injection. 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. (3)

CONTRAINDICATIONS

No contraindications have been identified based on the limited available data on the emergency uses of JYNNEOS authorized under this EUA. (4)

ADVERSE REACTIONS

- In smallpox vaccine-naïve healthy adults who received JYNNEOS subcutaneously, the most common (>10%) solicited injection site reactions were pain (84.9%), redness (60.8%), swelling (51.6%), induration (45.4%), and itching (43.1%); the most common solicited systemic adverse reactions were muscle pain (42.8%), headache (34.8%), fatigue (30.4%), nausea (17.3%) and chills (10.4%). (6.1)
- In healthy adults previously vaccinated with a smallpox vaccine who received JYNNEOS subcutaneously, the most common (>10%) solicited injection site reactions were redness (80.9%), pain (79.5%), induration (70.4%), swelling (67.2%), and itching (32.0%); the most common solicited systemic adverse reactions were fatigue (33.5%), headache (27.6%), and muscle pain (21.5%). (6.1)
- The frequencies of solicited local and systemic adverse reactions following subcutaneous administration among adults with HIV-infection and adults with atopic dermatitis were generally similar to those observed in healthy adults. (6.1)
- In smallpox vaccine-naïve healthy adults who received JYNNEOS intradermally, the most common (>10%) solicited reactions were erythema at injection site (99.5%), induration at injection site (99.5%), itchiness (89.0%), pain at injection site (65.4%), feeling tired (51.3%), headache (41.4%), muscle aches (30.4%), nausea (23.0%), underarm pain (20.9%), change in appetite (20.4%), joint pain (17.8%), chills (14.7%), and underarm swelling (10.5%). (6.1)

The vaccination provider must report all SERIOUS ADVERSE EVENTS and VACCINE ADMINISTRATION ERRORS to the Vaccine Adverse Event Reporting System (VAERS) by submitting [online at https://vaers.hhs.gov/reportevent.html](https://vaers.hhs.gov/reportevent.html). For further assistance with reporting to VAERS call 1-800-822-7967. Please also provide a copy of this form to Bavarian Nordic at 1-800-675-9596 (6.3).

See FACT SHEET FOR RECIPIENTS AND CAREGIVERS

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FULL FACT SHEET FOR HEALTHCARE PROVIDERS

1 EMERGENCY USE AUTHORIZATION

The US Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of JYNNEOS for:

- active immunization by subcutaneous injection for prevention of mpox disease in individuals less than 18 years of age determined to be at high risk for mpox infection, and
- active immunization by intradermal injection for prevention of mpox disease in individuals 18 years of age and older determined to be at high risk for mpox infection.

JYNNEOS is not approved for these uses.

Justification for Emergency Use of JYNNEOS During the Mpox Public Health Emergency

Following a 3-17 day incubation period, individuals infected with mpox virus develop painful lesions that progress sequentially through macular, papular, vesicular, and pustular stages, followed by scabbing over and desquamation. Lesions may occur anywhere on the body and may be limited to a single site or may be disseminated across many sites. Individuals may or may not experience prodromal symptoms (e.g., chills, lymphadenopathy, malaise, myalgias, or headache). Respiratory symptoms (e.g., sore throat, nasal congestion, or cough) can also occur. The clinical presentation of mpox disease is typically milder than smallpox disease but can be fatal, particularly in severely immunocompromised individuals who do not receive antiviral therapy. During the recent mpox outbreak, mpox cases and exposures have occurred in individuals across a wide range of ages, including infants and children.

On August 9, 2022, the Secretary of HHS has declared that:

- There is a public health emergency related to monkeypox, or significant potential for a public health emergency, that affects, or has the significant potential to affect, national security or the health and security of United States citizens living abroad that involves monkeypox virus; and
- On the basis of this determination, circumstances exist justifying the authorization of emergency use of vaccines.

An EUA is an FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency, or the significant potential for a public health emergency, that affects, or has significant potential to affect, the national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition;
- Based on the totality of the available scientific evidence (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that:
 - The product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition;

- The known and potential benefits of the product - when used to diagnose, prevent, or treat such disease or condition - outweigh the known and potential risks of the product, taking into consideration the material threat posed by the biological agent(s); and
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the serious or life-threatening disease or condition.

Information Regarding Available Alternatives for the EUA Authorized Use

JYNNEOS is approved for prevention of smallpox and mpox disease in adults 18 years of age and older determined to be at high risk for smallpox or mpox infection. The approved dosing regimen for JYNNEOS for use in adults 18 years of age and older is 2 doses (0.5 mL each), administered subcutaneously, 4 weeks apart.

ACAM2000 [Smallpox and Mpox (Vaccinia) Vaccine, Live] is FDA-approved for prevention of mpox disease in individuals determined to be at high risk for mpox infection. However, serious complications may follow vaccination with ACAM2000 and risks of these complications are increased in individuals with certain conditions.

For information on clinical studies of JYNNEOS for the prevention of mpox disease, see www.clinicaltrials.gov.

2 DOSAGE AND ADMINISTRATION

Individuals less than 18 years of age: for subcutaneous injection.

Individuals 18 years of age and older: for intradermal injection.

2.1 Dose and Schedule

Individuals less than 18 years of age: administer two doses (0.5 mL each) 4 weeks apart.

Individuals 18 years of age and older: administer two doses (0.1 mL each) 4 weeks apart.

2.2 Preparation and Administration

Allow the vaccine to thaw and reach room temperature before use. Once thawed, the vaccine may be kept at +2°C to +8°C (+36°F to +46°F) for 4 weeks. Certain lots may be kept at +2°C to +8°C (+36°F to +46°F) for up to 4 weeks. Certain lots may be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks¹. Do not refreeze.

When thawed, JYNNEOS is a milky, light yellow to pale white colored suspension.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered.

Swirl the vial gently for at least 30 seconds and cleanse the vial stopper with a single-use antiseptic swab before each use.

¹ Only certain lots may be held at +2°C to +8°C for up to 8 weeks. To confirm that a given lot may be held at +2°C to +8°C for up to 8 weeks, please verify that the lot is listed on this web page: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#mpoxvaccine>. If the lot number is not identified as being eligible for the 8-week hold time on this page, then the vaccine may only be kept at +2°C to +8°C (+36°F to +46°F) for up to 4 weeks.

Subcutaneous injection for individuals less than 18 years of age

Withdraw a dose of 0.5 mL into a sterile syringe for injection. Administer JYNNEOS by subcutaneous injection, preferably into the anterolateral thigh for infants less than 1 year of age, or into the upper arm (deltoid) for individuals 1 through 17 years of age.

Intradermal injection for individuals 18 years of age and older

Withdraw a dose of 0.1 mL into a sterile syringe for injection. Low dead volume syringes and/or needles can be used to extract 5 doses (0.1 mL each) for intradermal injection from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 5 doses from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.1 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.1 mL, discard the vial and its contents.
- Do not pool excess vaccine from multiple vials.
- Once the vial is punctured and a dose is withdrawn, if it is not used in its entirety it should be stored at +2°C to +8°C (+36°F to +46°F) and discarded within 8 hours of the first puncture.

Administer JYNNEOS by intradermal injection, preferably into the volar aspect (inner side) of the forearm.

3 DOSAGE FORMS AND STRENGTHS

JYNNEOS is a suspension for injection. Each subcutaneous dose is 0.5 mL. Each intradermal dose is 0.1 mL.

4 CONTRAINDICATIONS

No contraindications have been identified based on the limited available data on the emergency uses of JYNNEOS authorized under this EUA.

5 WARNINGS AND PRECAUTIONS

5.1 Severe Allergic Reactions

Appropriate medical treatment must be available to manage possible anaphylactic reactions following administration of JYNNEOS. Persons who experienced a severe allergic reaction following a previous dose of JYNNEOS or following exposure to any component of JYNNEOS may be at increased risk for severe allergic reactions after JYNNEOS. The risk for a severe allergic reaction should be weighed against the risk for disease due to mpox.

5.2 Syncope

Syncope (fainting) has been reported following vaccination with JYNNEOS. Procedures should be in place to avoid injury from fainting.

5.3 Altered Immunocompetence

Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response to JYNNEOS.

5.4 Limitations of Vaccine Effectiveness

Vaccination with JYNNEOS may not protect all recipients.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical studies of another vaccine and may not reflect the rates observed in clinical practice.

The following adverse reactions have been observed in the clinical studies of JYNNEOS that support the EUA. The overall clinical trial program included 22 studies and a total of 7,859 individuals 18 through 80 years of age who received at least 1 dose of JYNNEOS (7,093 smallpox vaccine-naïve and 766 smallpox vaccine-experienced individuals).

Solicited Adverse Reactions

Solicited Adverse Reactions Following Subcutaneous Administration to Smallpox Vaccine-Naïve Individuals

The safety of JYNNEOS administered subcutaneously in smallpox vaccine-naïve individuals was evaluated in Study 1 [1], a randomized, double-blind, placebo-controlled study conducted in the US in which vaccinia-naïve adults ages 18 to 40 years received either two doses of JYNNEOS (N=3003), or two injections of Tris-Buffered Saline (placebo, N=1002) four weeks apart. Both JYNNEOS and placebo were administered subcutaneously as a dose of 0.5 mL.

In the total study population, the mean age was 28 years; 47.9% of the subjects were men; 77.4% were white/Caucasian, 17.8% black/African American, 1.9% Asian, 0.5% American Indian/Alaska Native, 0.4% Native Hawaiian/Other Pacific, 1.9% other racial groups; and 11.4% of subjects were of Hispanic/Latino ethnicity. The demographic compositions of JYNNEOS and placebo groups were similar.

In Study 1, subjects were monitored for local and systemic adverse reactions using diary cards for an 8-day period starting on the day of each vaccination. The frequencies of solicited local and systemic adverse reactions following any dose of JYNNEOS are presented in Table 1.

Table 1: Percentages of Subjects with Solicited Local Injection Site Reactions and Systemic Adverse Reactions within 8 Days Following Any Dose of JYNNEOS in Adults 18 to 40 Years of Age, Study 1^x

Reaction	JYNNEOS ^d N=2943 %	Placebo N=980 %
Local (Injection site)	--	--
Pain	84.9	19.1
Pain, Grade 3 ^a	7.4	1.0
Redness	60.8	17.7
Redness ≥ 100 mm	1.5	0.0
Swelling	51.6	5.6
Swelling ≥ 100 mm	0.8	0.0
Induration	45.4	4.6
Induration ≥ 100 mm	0.3	0.0

Reaction	JYNNEOS ^d N=2943 %	Placebo N=980 %
Itching	43.1	11.7
Itching, Grade 3 ^b	1.6	0.2
Systemic	--	--
Muscle Pain	42.8	17.6
Muscle Pain, Grade 3 ^b	2.6	0.7
Headache	34.8	25.6
Headache, Grade 3 ^b	2.4	2.1
Fatigue	30.4	20.5
Fatigue, Grade 3 ^b	3.0	1.3
Nausea	17.3	13.1
Nausea, Grade 3 ^b	1.5	1.2
Chills	10.4	5.8
Chills, Grade 3 ^b	1.0	0.3
Fever ^c	1.7	0.9
Fever, Grade ≥ 3 ^c	0.2	0.0

^x NCT01144637

^a Grade 3 pain defined as spontaneously painful

^b Grade 3 itching, muscle pain, headache, fatigue, nausea and chills defined as preventing routine daily activities

^c Fever defined as oral temperature ≥ 100.4°F (≥ 38°C), Grade ≥ 3 fever defined as ≥ 102.2°F (≥ 39.0°C)

^d JYNNEOS was administered subcutaneously as a series of two doses (0.5 mL each dose), 4 weeks apart.

N=number of subjects

In Study 1, the majority of solicited local and systemic adverse reactions reported with JYNNEOS had a median duration of 1 to 6 days. In general, there were similar proportions of subjects reporting solicited local or systemic reactions of any severity after Dose 2 of JYNNEOS compared with Dose 1, with the exception of injection site pain, which was more commonly reported following Dose 1 (79.3%) than Dose 2 (69.9%).

Solicited Adverse Reactions Following Subcutaneous Administration to Persons Previously Vaccinated with a Smallpox Vaccine

Three studies (Study 2, Study 3, and Study 4, [2-4]) conducted in the US and Germany evaluated the safety of JYNNEOS in 409 persons previously vaccinated with a smallpox vaccine who received one or two doses of JYNNEOS, 0.5 mL administered subcutaneously (mean age 39 years, range 20-80 years; 59% women; 98.8% white/Caucasian; 0.7% Asian; 0.5% black/African American). Subjects were monitored for local and systemic adverse reactions using diary cards for an 8-day period starting on the day of each vaccination. Across all three studies, solicited local adverse reactions reported following any dose of JYNNEOS were redness (80.9%), pain (79.5%), induration (70.4%), swelling (67.2%), and itching (32.0%) at the injection site; solicited systemic adverse reactions reported following any dose of JYNNEOS were fatigue (33.5%), headache (27.6%), muscle pain (21.5%), nausea (9.8%), chills (0.7%), and fever (0.5%).

Solicited Adverse Reactions Following Subcutaneous Administration to HIV-infected Individuals

The safety of JYNNEOS in HIV-infected individuals was evaluated in Study 5 [5], an open label trial conducted in the US that included 351 HIV-infected smallpox vaccine-naïve subjects, 131 HIV-infected subjects who previously received smallpox vaccine, 88 non-HIV-infected smallpox vaccine-naïve subjects and 9 non-HIV-infected subjects who had previously received a smallpox vaccine.

Subjects in this study received 0.5 mL doses of JYNNEOS administered subcutaneously. The racial/ethnic and gender compositions of HIV-infected smallpox vaccine-naïve subjects and those who had previously received smallpox vaccine were similar and overall were 17.0% women; 45.8% white/Caucasian; 0.4% Asian; 33.2% black/African American; 19.0% Hispanic/Latino ethnicity; the HIV-infected smallpox vaccine-naïve group tended to be younger (mean age 37 years) compared to those who had previously received a smallpox vaccine (mean age 45 years). Subjects had CD4 counts ≥ 200 and ≤ 750 cells/ μL at study entry.

Solicited local and systemic adverse reactions were reported at similar or lower frequencies in HIV-infected smallpox vaccine-naïve subjects as compared to those seen in non-HIV-infected smallpox vaccine-naïve individuals in this study.

In HIV-infected subjects with previous smallpox vaccine exposure, fever and chills were reported in 1.5% and 8.4% of subjects respectively. Frequencies of other solicited local and general adverse reactions in this population were similar to those reported in Studies 2-4 in non-HIV-infected subjects who had previously received smallpox vaccination.

Solicited Adverse Reactions Following Subcutaneous Administration to Individuals with Atopic Dermatitis

The safety of JYNNEOS in smallpox vaccine-naïve subjects with currently active or a history of atopic dermatitis (AD) was evaluated in a multicenter, open-label clinical study (Study 6 [6]) conducted in the US and Mexico that included 350 subjects with AD and 282 subjects without AD. Subjects in this study received 0.5 mL doses of JYNNEOS administered subcutaneously. In the overall study the mean age of subjects was 27 years (range 18-42 years), and subjects were 59.0% women, 39.4% white/Caucasian, 10.9% Asian, 9.0% black/African American, 2.2% Other, and 38.4% Hispanic/Latino ethnicity. Demographic compositions were similar between subjects with and without AD. In subjects with AD, solicited local and systemic adverse reactions were reported at similar frequencies as those in subjects without AD in this study, with the exception of redness (61.2% with AD vs. 49.3% without AD), swelling (52.2% with AD vs. 40.8% without AD), chills (15.9% with AD vs. 7.8% without AD) and headache (47.2% with AD vs. 34.8% without AD).

Adverse Reactions Following Intradermal Administration to Smallpox Vaccine-Naïve Individuals

The safety of JYNNEOS administered intradermally was evaluated in a clinical study (Study 7 [7]) in the US with smallpox vaccine-naïve subjects, sponsored by the National Institutes of Health (NIH), which enrolled 191 subjects randomized to receive two intradermal (ID) doses of JYNNEOS (0.1 mL each) and 167 subjects randomized to receive two subcutaneous (SC) doses of JYNNEOS (0.5 mL each). Study vaccinations were administered 4 weeks apart to all subjects. An approximately equal number of males and females were enrolled into each of the groups. Most subjects were non-Hispanic and white, approximately 10% of the participants characterized their race as black and 4% as Asian.

The frequencies of systemic and local adverse reactions reported in greater than 10% of subjects within 15 days of vaccination are presented in Table 2.

Erythema at the injection site was reported by 81.4% and 99.5% of subjects in the SC and ID groups, respectively. In the SC group this was reported as resolved within 14 days following the second vaccine dose in all subjects, whereas in the ID arm 44% still had erythema at the end of this period. At Day 180, greater than a third of subjects in the ID group continued to have minimal induration or

erythema present on exam. Additionally, a few subjects receiving JYNNEOS on the ID arm developed small nodules or discoloration at the injection site.

Table 2. Adverse reactions reported in >10% of subjects within 15 days following any dose

Reactogenicity event	SC (%) N=166	ID (%) N=190
Feeling Tired	49.7	51.3
Muscle Aches	41.3	30.4
Headache	43.1	41.4
Nausea	21.6	23.0
Change in Appetite	15.0	20.4
Chills	12.6	14.7
Joint Pain	9.0	17.8
Pain at injection site	91.0	65.4
Erythema at injection site	81.4	99.5
Induration at injection site	69.5	99.5
Itchiness	48.5	89.0
Underarm pain	18.0	20.9
Underarm swelling	6.0	10.5

Data were not available for one individual in each of the two groups

Serious Adverse Events

The integrated analyses of serious adverse events (SAEs) pooled safety data across 22 studies, which included a total of 7,093 smallpox vaccine-naïve subjects and 766 smallpox vaccine-experienced subjects who received at least 1 dose of JYNNEOS and 1,206 smallpox vaccine-naïve subjects who received placebo only. Most subjects received JYNNEOS or placebo subcutaneously. SAEs were monitored from the day of the first study vaccination through at least 6 months after the last study vaccination.

Among the smallpox vaccine-naïve subjects, SAEs were reported for 1.5% of JYNNEOS recipients and 1.1% of placebo recipients. Among the smallpox vaccine-experienced subjects enrolled in studies without a placebo comparator, SAEs were reported for 2.3% of JYNNEOS recipients. Across all studies, a causal relationship to JYNNEOS could not be excluded for 4 SAEs, all non-fatal, which included Crohn's disease, sarcoidosis, extraocular muscle paresis and throat tightness.

Cardiac Adverse Events of Special Interest

Evaluation of cardiac adverse events of special interest (AESIs) included any cardiac signs or symptoms, ECG changes determined to be clinically significant, or troponin-I elevated above 2 times the upper limit of normal. In the 22 studies, subjects were monitored for cardiac-related signs or symptoms through at least 6 months after the last vaccination.

The numbers of JYNNEOS and placebo recipients, respectively, with troponin-I data were: baseline level (6,376 and 1,203); level two weeks after first dose (6,279 and 1,166); level two weeks after second dose (1,683 and 193); unscheduled visit, including for clinical evaluation of suspected cardiac adverse events (500 and 60).

Cardiac AESIs were reported to occur in 1.3% (95/7,093) of JYNNEOS recipients and 0.2% (3/1,206) of placebo recipients who were smallpox vaccine-naïve. Cardiac AESIs were reported to occur in 2.1% (16/766) of JYNNEOS recipients who were smallpox vaccine-experienced. The higher proportion of JYNNEOS recipients who experienced cardiac AESIs was driven by 28 cases of asymptomatic post-vaccination elevation of troponin-I in two studies: Study 5, which enrolled 482 HIV-infected subjects and 97 healthy subjects, and Study 6, which enrolled 350 subjects with atopic dermatitis and 282 healthy subjects. An additional 127 cases of asymptomatic post-vaccination elevation of troponin-I above the upper limit of normal but not above 2 times the upper limit of normal were documented in JYNNEOS recipients throughout the clinical development program, 124 of which occurred in Study 5 and Study 6. Proportions of subjects with troponin-I elevations were similar between healthy and HIV-infected subjects in Study 5 and between healthy and atopic dermatitis subjects in Study 6. A different troponin assay was used in these two studies compared to the other studies, and these two studies had no placebo controls. The clinical significance of these asymptomatic post-vaccination elevations of troponin-I is unknown.

Among the cardiac AESIs reported, 6 cases (0.08%) were considered to be causally related to JYNNEOS vaccination and included tachycardia, electrocardiogram T wave inversion, electrocardiogram abnormal, electrocardiogram ST segment elevation, electrocardiogram T wave abnormal, and palpitations.

None of the cardiac AESIs considered causally related to study vaccination were considered serious.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of JYNNEOS. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis

Immune System Disorders: hypersensitivity reactions, including angioedema, rash, and urticaria

Nervous System Disorders: dizziness, syncope, facial paralysis (Bell's palsy)

General disorders and administration site conditions: injection site warmth, injection site vesicles

6.3 Required Reporting for Adverse Events and Vaccine Administration Errors

The vaccination provider is responsible for MANDATORY reporting of the following listed events following JYNNEOS to the Vaccine Adverse Event Reporting System (VAERS):

- 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

*Serious adverse events are defined as:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions

- A congenital anomaly/birth defect
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above

Instructions for Reporting to VAERS

The vaccination provider should complete and submit a VAERS form to FDA using one of the following methods:

- Complete and submit the report online: <https://vaers.hhs.gov/reportevent.html>, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of JYNNEOS
- Pertinent laboratory information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on JYNNEOS and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within one month prior.
2. In Box 18, description of the event:
 - a. Write "JYNNEOS EUA" as the first line.
 - b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.
3. Contact information:
 - a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
 - b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.
 - c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Bavarian Nordic toll-free at 1-844-4BAVARIAN

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available human data on JYNNEOS administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

The effect of JYNNEOS on embryo-fetal and post-natal development was evaluated in four developmental toxicity studies conducted in female rats and rabbits. In two studies, rats were administered a single human dose of JYNNEOS (0.5 mL) once prior to mating and on one or two occasions during gestation. In the third study, rats were administered a single human dose of JYNNEOS (0.5 mL) on two occasions during gestation. In the fourth study, rabbits were administered a single human dose of JYNNEOS (0.5 mL) once prior to mating and on two occasions during gestation. These animal studies revealed no evidence of harm to the fetus [\[see Data\]](#).

Data

Animal Data

Developmental toxicity studies were conducted in female rats and rabbits. In one study, female rabbits were administered a single human dose of JYNNEOS (0.5 mL) by the subcutaneous route on three occasions: prior to mating, and on gestation days 0 and 14. Three studies were conducted in female rats administered a single human dose of JYNNEOS (0.5 mL) by the subcutaneous route on two or three occasions: prior to mating, and on gestation days 0 and 14; or prior to mating, and on gestation day 0; or on gestation days 0 and 6. No vaccine-related fetal malformations or variations and adverse effects on female fertility or pre-weaning development were reported in these studies.

8.2 Lactation

Risk Summary

It is not known whether JYNNEOS is excreted in human milk. Data are not available to assess the effects of JYNNEOS in the breastfed infant or on milk production/excretion.

The development and health benefits of breastfeeding should be considered along with the mother's clinical need for JYNNEOS and any potential adverse effects on the breastfed child from JYNNEOS or from the underlying maternal condition. For preventive vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

The safety and effectiveness of JYNNEOS have not been assessed in individuals less than 18 years of age. The FDA has granted an EUA for the emergency use of JYNNEOS for active immunization by subcutaneous injection for prevention of mpox disease in individuals less than 18 years of age

determined to be at high risk for mpox infection. This authorization is based on safety and effectiveness data from clinical trials in adults and efficacy data from animal challenge studies and historical data with use of live vaccinia virus smallpox vaccine in pediatric populations.

8.5 Geriatric Use

Forty-two smallpox vaccine-experienced adults 65 to 80 years of age received at least one dose of JYNNEOS (Study 4).

Clinical studies of JYNNEOS did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

When thawed, JYNNEOS (Smallpox and Mpox Vaccine, Live, Non-replicating) is a milky, light yellow to pale white colored suspension for subcutaneous injection.

JYNNEOS is a live vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus. MVA-BN is grown in primary Chicken Embryo Fibroblast (CEF) cells suspended in a serum-free medium containing no material of direct animal origin, harvested from the CEF cells, purified and concentrated by several Tangential Flow Filtration (TFF) steps including benzonase digestion. Each 0.5 mL dose for subcutaneous administration is formulated to contain 0.5×10^8 to 3.95×10^8 infectious units of MVA-BN live virus in 10 mM Tris (tromethamine), 140 mM sodium chloride at pH 7.7. Each 0.5 mL dose may contain residual amounts of host-cell DNA (≤ 20 mcg), protein (≤ 500 mcg), benzonase (≤ 0.0025 mcg), gentamicin (≤ 0.400 mcg) and ciprofloxacin (≤ 0.005 mcg). Each 0.1 mL dose for intradermal administration contains one-fifth of the ingredient content of a 0.5 mL dose.

JYNNEOS is a sterile vaccine formulated without preservatives. The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

JYNNEOS is an attenuated, live, non-replicating smallpox and mpox vaccine that elicits humoral and cellular immune responses to orthopoxviruses. Vaccinia neutralizing antibody responses in humans were evaluated to establish the effectiveness of JYNNEOS for prevention of smallpox and mpox.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

JYNNEOS has not been evaluated for carcinogenic or mutagenic potential, or for impairment of male fertility in animals. Developmental toxicity studies conducted in rats and rabbits vaccinated with JYNNEOS revealed no evidence of impaired female fertility [[see Use in Specific Populations \(8.1\)](#)].

13.2 Animal Toxicology and/or Pharmacology

The efficacy of JYNNEOS to protect cynomolgus macaques (*Macaca fascicularis*) against a mpox virus challenge was evaluated in several studies. Animals were administered Tris-Buffered Saline (placebo) or JYNNEOS (1×10^8 TCID₅₀) sub-cutaneously on day 0 and day 28. On day 63, animals were challenged with mpox virus delivered by aerosol (3×10^5 pfu), intravenous (5×10^7 pfu) or intratracheal (5×10^6 pfu) route. Across all studies, 80-100% of JYNNEOS-vaccinated animals survived compared to 0-40% of control animals.

14 CLINICAL STUDIES

14.1 Vaccine Effectiveness

Vaccine effectiveness against mpox was inferred from the immunogenicity of JYNNEOS in clinical studies and from efficacy data from animal challenge studies. [see [Nonclinical Toxicology \(13.2\)](#)]

14.2 Immunogenicity

Immunogenicity Following Subcutaneous Administration to Smallpox Vaccine-Naïve Individuals

Study 8 [8] was a randomized, open-label study conducted at US military facilities in South Korea to compare the immunogenicity of JYNNEOS to ACAM2000 in healthy smallpox vaccine-naïve adults 18 through 42 years of age. Subjects were randomized to receive either two doses of JYNNEOS (N=220) administered subcutaneously 4 weeks apart or one dose of ACAM2000 (N=213) administered percutaneously. In the total study population, the mean age was 24 years and 23 years in subjects receiving JYNNEOS and ACAM2000, respectively; 82.3% and 86.4% of the subjects were men; 57.3% and 63.8% were white/Caucasian, 21.8% and 18.8% black/African American, 6.4% and 5.6% Asian, 3.6% and 2.8% American Indian/Alaska Native, 2.3% and 1.4% Native Hawaiian/Other Pacific, 8.6% and 7.5% other racial groups, and 24.5% and 18.8% of Hispanic/Latino ethnicity (JYNNEOS and ACAM2000, respectively).

The primary immunogenicity endpoint was geometric mean titer (GMT) of vaccinia neutralizing antibodies assessed by PRNT at “peak visits” defined as two weeks after the second dose of JYNNEOS and four weeks after the single dose of ACAM2000. Analyses of antibody responses were performed in the per-protocol immunogenicity (PPI) population, consisting of individuals who received all vaccinations and completed all visits up until the peak visit without major protocol violations pertaining to immunogenicity assessments. Table 3 presents the pre-vaccination and “peak visit” PRNT GMTs from Study 8.

Table 3: Comparison of Vaccinia-Neutralizing Antibody Responses Following Vaccination with JYNNEOS or ACAM2000 in Healthy Smallpox Vaccine-Naïve Adults 18 through 42 Years of Age, Study 8^x, Per Protocol Set for Immunogenicity^y

Time Point	JYNNEOS ^a (N=185) GMT ^b [95% CI]	ACAM2000 ^a (N=186) GMT ^b [95% CI]
Pre-Vaccination	10.1 [9.9, 10.2]	10.0 [10.0, 10.0]
Post-Vaccination “Peak Visit” ^y	152.8 ^c [133.3, 175.0]	84.4 ^c [73.4, 97.0]

^x NCT01913353

^y Per Protocol Set for Immunogenicity included subjects who received all vaccinations, completed all visits up until the specified “peak visits” (two weeks after the second dose of JYNNEOS or 4 weeks after the single dose of ACAM2000) without major protocol violations pertaining to immunogenicity assessments.

^a JYNNEOS was administered subcutaneously as a series of two doses (0.5 mL each dose), 4 weeks apart, and ACAM2000 was administered percutaneously as a single dose.

^b GMT of vaccinia-neutralizing antibody titers assessed by plaque reduction neutralization test (PRNT) using the Western Reserve vaccinia strain. Values below the assay lower limit of quantitation (LLOQ) of 20 were imputed to a titer of 10; the proportions of subjects with pre-vaccination titers less than the assay lower limit of detection were 98.9% among subjects randomized to JYNNEOS and 97.8% among subjects randomized to ACAM2000, respectively.

^c Non-inferiority of the “peak visit” PRNT GMT for JYNNEOS compared to ACAM2000 was demonstrated as the lower bound of the 1-sided 97.5% CI for the GMT ratio (JYNNEOS/ACAM2000) was > 0.5.

N: Number of subjects in the specified treatment group; GMT: Geometric Mean Titer; 95% CI: 95% confidence interval, lower limit and upper limit.

PRNT GMTs were also evaluated at pre-specified time points post-vaccination and prior to the “peak visits”. The PRNT GMTs at two and four weeks after the first dose of JYNNEOS (prior to the second dose), were 23.4 (95% CI: 20.5, 26.7) and 23.5 (95% CI: 20.6, 26.9), respectively. The PRNT GMT at two weeks after the single dose of ACAM2000 was 23.7 (95% CI: 20.9, 26.8).

Immunogenicity Following Intradermal Administration to Smallpox Vaccine-Naïve Individuals

In a clinical trial (Study 7 [7]) conducted in the US with smallpox vaccine-naïve subjects and sponsored by the National Institutes of Health (NIH), 191 subjects were randomized to receive two intradermal doses of JYNNEOS (0.1 mL each), and 167 subjects were randomized to receive two subcutaneous doses of JYNNEOS (0.5 mL each). Study vaccinations were administered 4 weeks apart to all subjects. An approximately equal number of males and females were enrolled into each of the arms. Most subjects were non-Hispanic and white, approximately 10% of participants characterized their race as black and 4% as Asian.

Following vaccination with JYNNEOS administered subcutaneously and intradermally 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 enzyme 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 subcutaneous and intradermal administration was nearly identical, and the log₂ transformed peak titers obtained following intradermal administration were non-inferior to those obtained following subcutaneous administration (Table 4).

Table 4. Comparison of log₂ transformed peak titers following SC and ID vaccine administration

Assay	SC peak titer	ID peak titer	Difference	97.5% CI
SLU PRNT	8.37	8.36	0.005	0.43, 0.44
BN PRNT	5.63	5.90	-0.27	-0.77, 0.23
SLU ELISA	9.66	9.52	0.14	-0.21, 0.49
BN ELISA	9.59	9.57	0.02	-0.31, 0.35

CI, confidence interval

15 REFERENCES

1. Study 1: NCT01144637
2. Study 2: NCT00316524
3. Study 3: NCT00686582
4. Study 4: NCT00857493
5. Study 5: NCT00316589
6. Study 6: NCT00316602
7. Study 7: NCT00914732
8. Study 8: NCT01913353

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Package of 10 single-dose vials

(Package NDC number: 50632-001-03; Vial NDC number: 50632-001-01)

(Package NDC number: 50632-023-02; Vial NDC number: 50632-023-04)

Package of 20 single-dose vials

(Package NDC number: 50632-001-02; Vial NDC number: 50632-001-01)

(Package NDC number: 50632-022-02; Vial NDC number: 50632-022-04)

16.2 Storage Conditions

Keep frozen at -25°C to -15°C (-13°F to +5°F).

Store in the original package to protect from light.

Do not re-freeze a vial once it has been thawed.

Once thawed, the vaccine may be kept at +2°C to +8°C (+36°F to +46°F) for up to 4 weeks. Certain lots may be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks².

After first puncture vial can be stored at +2°C to +8°C (+36°F to +46°F) for up to 8 hours.

Do not use the vaccine after the expiration date shown on the vial label.

² Only certain lots may be held at +2°C to +8°C for up to 8 weeks. To confirm that a given lot may be held at +2°C to +8°C for up to 8 weeks, please verify that the lot is listed on this web page: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#mpoxvaccine>. If the lot number is not identified as being eligible for the 8 week hold time on this page, then the vaccine may only be kept at +2°C to +8°C (+36°F to +46°F) for up to 4 weeks.

17 PATIENT COUNSELING INFORMATION

As a healthcare practitioner, you must communicate to the patient and/or caregiver information consistent with the “FACT SHEET FOR RECIPIENTS AND CAREGIVERS” and provide them with a copy of this Fact Sheet prior to administration of JYNNEOS.

Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System at 1-800-822-7967 and www.vaers.hhs.gov.

This product’s labeling may have been updated

This Full EUA Fact Sheet may have been updated. For the most recent Full EUA Fact Sheet, please see <https://www.fda.gov/media/160774/download>.

Manufactured by:
Bavarian Nordic A/S
Hejreskovvej 10a
DK-3490 Kvistgaard
Denmark

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