Smallpox and Mpox Vaccine Live (AHFS DI)
Generic Name: Smallpox and Mpox Vaccine, Live, Non-replicating
Brand Information: Jynneos®

Introduction
Smallpox and mpox vaccine live is a live, attenuated, non-replicating virus vaccine produced using modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus.[1]

Uses
Smallpox
Smallpox and mpox vaccine live (JYNNEOS®) is indicated for prevention of smallpox disease in adults 18 years of age and older determined to be at high risk for smallpox.[1]

Effectiveness of JYNNEOS against smallpox has been inferred by comparing the immunogenicity of the vaccine to smallpox vaccine live (ACAM2000®) based on a plaque reduction neutralization test (PRNT) using the Western Reserve strain of vaccinia virus and was supported by efficacy data from animal challenge studies.[1]

The US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) has issued recommendations and clinical considerations for the use of vaccines in preventing smallpox.[2] Although routine vaccination against smallpox in the US ended in the 1970s, ACIP recommends that certain populations at high risk of occupational exposure to orthopoxviruses be vaccinated.[2] For additional information, consult the CDC website at https://www.cdc.gov/smallpox/clinicians/vaccines.html.

Mpox
Smallpox and mpox vaccine live (JYNNEOS®) is indicated for prevention of mpox disease in adults 18 years of age and older determined to be at high risk for mpox.[1]

Effectiveness of JYNNEOS against mpox has been inferred from immunogenicity studies and efficacy data from animal challenge studies.[1] Additional data accumulated since the 2022 mpox outbreak in the US support the efficacy and safety of the 2-dose vaccine series in preventing mpox infection.[5,6,9] Infections that have occurred after vaccination with 2 doses are typically milder than infections among unvaccinated individuals.[7]

The CDC ACIP has issued recommendations and clinical considerations for the use of vaccines for mpox prevention in the US.[6] There are 2 vaccines (JYNNEOS [also known internationally as Imvamune® or Imvanex®] and ACAM2000®) currently available.[6,7] During the current clade II mpox outbreak that started in the US on May 17, 2022, JYNNEOS has been the main vaccine used in the US.[6] The ACAM2000 vaccine is approved for immunization against smallpox and can also be made available for use against mpox under an Expanded Access Investigational New Drug (EA-IND) protocol; however, this

vaccine has not been used during the current mpox outbreak and is associated with more adverse effects and contraindications.[6]

ACIP currently recommends vaccination with a 2-dose JYNNEOS vaccine series (2 subcutaneous doses administered 28 days apart) for people 18 years of age and older at risk for mpox, in line with the FDA-approved labeling.[6] In addition, FDA issued an Emergency Use Authorization (EUA) in August 2022 to permit use of the vaccine by *intradermal* injection for prevention of mpox disease in individuals 18 years of age and older at high risk for mpox, and by subcutaneous injection for prevention of mpox disease in individuals younger than 18 years of age determined to be at high risk of mpox.[6,7,8] Because there is currently an adequate supply of the JYNNEOS vaccine, clinicians can preferentially administer the vaccine by the subcutaneous route per FDA licensure.[7] Doses that were previously administered intradermally are equally effective as doses administered subcutaneously and do not need to be repeated.[7] ACIP also recommends vaccination with JYNNEOS in selected individuals at occupational risk of exposure to orthopoxviruses (as an alternative to ACAM2000) and for post-exposure prophylaxis in certain individuals.[6,7] People who are vaccinated should continue to take steps to protect themselves from infection by avoiding close, skin-to-skin contact, including intimate contact, with someone who has mpox.[6] For additional information on ACIP recommendations, consult the CDC website at https://www.cdc.gov/poxvirus/mpox.

Dosage and Administration

General

Smallpox and mpox vaccine live (JYNNEOS) is available in the following dosage form(s) and strength(s):

- Suspension, for subcutaneous use: Single-dose vial containing one 0.5-mL dose.[1]

Administration and Preparation

For subcutaneous injection, preferably into the upper arm.[1] The vaccine also has been administered intradermally (off-label) in select situations for active immunization against mpox disease.[8]

Administer as a 2-dose vaccine series.[1,7,8]

Allow the vaccine to thaw and reach room temperature before use.[1] Once thawed, the vaccine may be kept at 2–8ºC for 4 weeks; do not refreeze.[1]

Swirl the vial gently before use for at least 30 seconds; withdraw a dose of 0.5 mL into a sterile syringe for injection.[1]

Dosage

It is essential that the manufacturer's labeling be consulted for more detailed information on dosage and administration of this drug.

Dosage summary:
Pediatric Patients
Mpox

1. In individuals younger than 18 years of age (off-label), administer 2 doses (0.5 mL each) 4 weeks apart by subcutaneous injection, preferably into the anterolateral thigh for infants less than 1 year of age, or into the upper arm for individuals 1 through 17 years of age.[8]
2. Peak immunity is expected to be reached 14 days after the second dose is administered.[7] Administration of more than 2 doses is currently not recommended for most people.[7]

Adults
Smallpox

1. Administer 2 doses (0.5 mL each) 4 weeks apart by subcutaneous injection.[1]

Mpox

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Cautions
Contraindications
None.[1]

Warnings and Precautions
Severe Allergic Reactions
Appropriate medical treatment must be available to manage possible anaphylactic reactions following administration of smallpox and mpox vaccine live.[1]

Individuals who experienced a severe allergic reaction following a previous dose of smallpox and mpox vaccine live or following exposure to any component of the vaccine may be at increased risk for severe allergic reactions to smallpox and mpox vaccine live.[1] The risk for a severe allergic reaction should be weighed against the risk for disease due to smallpox or mpox.[1]

Syncope
Syncope (fainting) has been reported following vaccination with smallpox and mpox vaccine live.[1] Procedures should be in place to avoid injury from fainting.[1]

Altered Immunocompetence

Immunocompromised individuals, including those receiving immunosuppressive therapy, may have a diminished immune response to smallpox and mpox vaccine live.[1]

Because smallpox and mpox vaccine live contains non-replicating virus, the vaccine can be used in adults with certain immunodeficiencies or conditions, such as human immunodeficiency virus (HIV) infection or atopic dermatitis.[2]

Limitations of Vaccine Effectiveness
Vaccination with smallpox and mpox vaccine live may not protect all recipients.[1]

For primary immunization, smallpox and mpox vaccine live is administered in a series of 2 doses given 4 weeks apart;[1] full immunity may not develop until 2 weeks after the second dose.[2]

Specific Populations
Pregnancy
Available human data on smallpox and mpox vaccine live administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.[1] All pregnancies have a risk of birth defect, loss, or other adverse outcomes.[1] In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.[1]

The effect of smallpox and mpox vaccine live on embryofetal and postnatal development was evaluated in 4 developmental toxicity studies conducted in female rats and rabbits.[1] These animal studies revealed no evidence of harm to the fetus.[1]

Lactation
It is not known whether smallpox and mpox vaccine live is distributed in human milk.[1] Data are not available to assess the effects of the vaccine on the breast-fed infant or on milk production/distribution.[1]

The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for smallpox and mpox vaccine live and any potential adverse effects on the breast-fed infant from the vaccine or from the underlying maternal condition.[1] For preventive vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.[1]

Pediatric Use
Safety and effectiveness of smallpox and mpox vaccine live have not been established in individuals younger than 18 years of age.[1] However, the vaccine (JYNNEOS) is available under an FDA Emergency Use Authorization (EUA) for use in the prevention of mpox disease in individuals younger than 18 years of age who are determined to be at high risk of mpox.[6,7,8]

Geriatric Use
Clinical studies of smallpox and mpox vaccine live did not include sufficient numbers of adults 65 years of age and older to determine whether they respond differently than younger individuals.[1]

In one clinical study, 42 adults 65–80 years of age previously vaccinated with a smallpox vaccine received at least one dose of smallpox and mpox vaccine live.[1]

Common Adverse Effects
Healthy adults not previously vaccinated with a smallpox vaccine: Most common (>10%) solicited injection site reactions were pain (85%), redness (61%), swelling (52%), induration (45%), and itching (43%); most common solicited systemic adverse reactions were muscle pain (43%), headache (35%), fatigue (30%), nausea (17%), and chills (10%).[1]

Healthy adults previously vaccinated with a smallpox vaccine: Most common (>10%) solicited injection site reactions were redness (81%), pain (80%), induration (70%), swelling (67%), and itching (32%); most common solicited systemic adverse reactions were fatigue (34%), headache (28%), and muscle pain (22%).[1]

Adults with HIV infection or atopic dermatitis: Frequencies of solicited local and systemic adverse reactions were generally similar to those observed in healthy adults.[1]

Drug Interactions
Vaccines
Currently, there are no data on administering smallpox and mpox vaccine live (JYNNEOS) vaccine at the same time as other vaccines.[7] Because JYNNEOS is based on a live, attenuated, non-replicating orthopoxvirus, ACIP states that JYNNEOS typically may be administered without regard to timing of most other vaccines.[7] This includes simultaneous administration of JYNNEOS and other vaccines, including influenza vaccine, on the same day, but at different anatomic sites if possible.[7]

There is no required minimum interval between receiving any COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech) and the JYNNEOS vaccine, regardless of which vaccine is administered first.[7] People, particularly adolescent or young adult males, who are recommended to receive both vaccines might consider waiting 4 weeks between vaccines because of the observed risk for myocarditis and pericarditis after receipt of ACAM2000 orthopoxvirus vaccine and COVID-19 vaccines, and the hypothetical risk for myocarditis and pericarditis after the JYNNEOS vaccine.[7] However, if a patient is at increased risk for mpox or severe disease due to COVID-19, administration of JYNNEOS and COVID-19 vaccines should not be delayed.[7]

Actions
Mechanism of Action

Smallpox and mpox vaccine live is a live, attenuated, non-replicating virus vaccine that contains a modified vaccinia virus (MVA-BN) and elicits humoral and cellular immune responses to orthopoxviruses.[1] Vaccinia virus, variola virus (causative agent of smallpox), and mpox virus are all orthopoxviruses.[2]

Smallpox and mpox vaccine live does not contain smallpox (variola) virus and cannot cause smallpox.[4]

Vaccinia neutralizing antibody responses in humans following vaccination with smallpox and mpox vaccine live were evaluated to establish the effectiveness of the vaccine for prevention of smallpox and mpox.[1]

Advice to Patients

1. Inform vaccine recipient of the potential benefits and risks of vaccination with smallpox and mpox vaccine live.[1]

2. Inform vaccine recipient of the importance of completing the 2-dose vaccination series.[1]

3. Advise vaccine recipient to report any adverse events to their healthcare provider or to the Vaccine Adverse Event Reporting System (VAERS) at 800-822-7967 or https://www.vaers.hhs.gov.[1]

AHFSfirstRelease™. For additional information until a more detailed monograph is developed and published, the manufacturer's labeling should be consulted. It is essential that the manufacturer's labeling be consulted for more detailed information on usual uses, dosage and administration, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.

Preparations

Restricted Distribution

Smallpox and mpox vaccine live (JYNNEOS) is stored in the US Strategic National Stockpile (SNS).[2] The SNS ensures that certain drugs and medical supplies are readily available to prevent or treat specific diseases, including during public health emergencies, and is managed by the US Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR).[3]

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Smallpox and Mpox Vaccine, Live, Non-replicating
Suspension, for subcutaneous use
0.5 x 10^8 to 3.95 x 10^8 infectious units of MVA-BN live virus per 0.5 mL
Jynneos®, Bavarian Nordic A/S

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