Considerations for Monkeypox Vaccination

Updated July 28, 2022

What You Need to Know

- Two vaccines may be used for the prevention of *Monkeypox virus* infection:
  - JYNNEOS (also known as Imvamune or Imvanex), licensed (or approved) by the U.S. Food and Drug Administration (FDA) for the prevention of *Monkeypox virus* infection, and
  - ACAM2000, licensed (or approved) by FDA for use against smallpox and made available for use against monkeypox under an Expanded Access Investigational New Drug application.
- In the United States, there is currently a limited supply of JYNNEOS, although more is expected in the coming weeks and months.
- There is a larger supply of ACAM2000, but this vaccine should not be used in people who have certain health conditions, such as a weakened immune system, skin conditions like eczema or other exfoliative skin conditions, or pregnancy.
- No data are available yet on the effectiveness of these vaccines in the current outbreak.
- The immune response takes 14 days after the second dose of JYNNEOS and 4 weeks after the ACAM2000 dose for maximal development. People who get 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 monkeypox.
- To better understand the protective benefits of these vaccines in the current outbreak, CDC will collect data about adverse events and vaccine effectiveness, including whether the vaccine protects a person differently depending on how they were infected with *Monkeypox virus*.

Summary of Recent Changes

Updates as of July 28, 2022

- Additional special considerations for JYNNEOS vaccine, including
  - Exceptions to the two-dose vaccine series
  - Vaccine dosing interval clarifications
  - Guidance for coadministration with other vaccines
  - Guidance for contraindications and precautions
- Reporting of vaccine adverse events

Vaccine Strategies to Prevent Monkeypox

When properly administered before or after a recent exposure, vaccines can be effective tools at protecting people against monkeypox illness. The following vaccination strategies are being used in the United States:

Monkeypox Vaccine Post-Exposure Prophylaxis (PEP)

- For the current outbreak, this approach can be considered as “standard PEP” for monkeypox. People can be vaccinated following exposure to monkeypox to help prevent monkeypox illness. It is important that states and other jurisdictions identify contacts of confirmed or probable monkeypox cases to offer vaccine for PEP and to monitor for any early signs of illness.
- CDC recommends that the vaccine be given within 4 days from the date of exposure for the best chance to prevent onset of the disease.
- If given between 4 and 14 days after the date of exposure, vaccination may reduce the symptoms of disease, but may not prevent the disease. Benefits may still outweigh risks when giving vaccine more than 14 days after exposure in some clinical situations (e.g., high risk exposure in a person at high risk for severe disease, such as severe immune compromise). Vaccination given after the onset of signs or symptoms of monkeypox is not expected to provide benefit.
- When coupled with self-isolation and other prevention measures when symptoms first occur, PEP is important for controlling outbreaks and preventing further transmission of monkeypox.

Outbreak Response Monkeypox Vaccine Post-Exposure Prophylaxis (PEP)++

- For the current outbreak, this expanded approach can be considered as “individual-directed PEP” for monkeypox; public health officials refer to it as “expanded PEP” or “PEP plus-plus” or “PEP++”.
- People with certain risk factors are more likely to have been recently exposed to monkeypox. The PEP++ approach aims to reach these people for post-exposure prophylaxis, even if they have not had documented exposure to someone with confirmed monkeypox.
- When coupled with self-isolation and other prevention measures when symptoms first occur, PEP++ may help slow the spread of the disease in areas with large numbers of monkeypox cases—which would suggest a higher level of *Monkeypox virus* transmission.

Monkeypox Vaccine Pre-Exposure Prophylaxis (PrEP)

- This approach refers to administering vaccine to someone at high risk for monkeypox (for example, laboratory workers who perform diagnostic testing to diagnose monkeypox).
- ACIP recommendations regarding preexposure vaccination of persons at risk for occupational exposure to orthopoxviruses (such as laboratory workers who perform diagnostic testing to diagnose monkeypox), are available at: https://www.cdc.gov/mmwr/volumes/71/wr/mm7122e1.htm.
- At this time, most clinicians in the United States and laboratorians not performing the orthopoxvirus generic test to diagnose orthopoxviruses, including *Monkeypox virus*, are not advised to receive monkeypox vaccine PrEP.
- When more JYNNEOS vaccine is available, broader vaccination of people who may be at risk for future monkeypox exposure may be considered.

Vaccine Information (JYNNEOS and ACAM2000)

JYNNEOS vaccine is being allocated to jurisdictions for use for the following individuals:

- Known contacts who are identified by public health via case investigation, contact tracing, and risk exposure assessments
- Presumed contacts who may meet the following criteria:
  - Know that a sexual partner in the past 14 days was diagnosed with monkeypox
  - Had multiple sexual partners in the past 14 days in a jurisdiction with known monkeypox

> JYNNEOS doses should be prioritized for those people who are at risk for serious adverse events with ACAM2000 or severe disease from monkeypox (such as people with HIV or other immunocompromising conditions).

JYNNEOS

- JYNNEOS contains a live, [illegible] that does not replicate efficiently in human cells

- JYNNEOS contains a live *vaccinia virus* that does not replicate efficiently in human cells.
- It is administered as two (0.5 mL) subcutaneous (under the skin) injections 28 days apart.
- The immune response takes 14 days after the second dose for maximal development.
- JYNNEOS is licensed by the FDA for use in the prevention of smallpox or monkeypox in people ages 18 years and older. Use in younger populations currently requires requesting and obtaining a single patient emergency use authorization from FDA for each person under 18 years. CDC is developing an Expanded Access Investigational New Drug (IND) protocol to allow broader use of JYNNEOS in the pediatric population.
- The effectiveness of JYNNEOS against monkeypox is supported by clinical studies demonstrating a comparable immune response to ACAM2000 and animal studies.
- There are no data yet on the effectiveness of JYNNEOS for PEP, PEP++, or PrEP from the current outbreak. Although this is also true for ACAM2000, there is evidence that the precursor for ACAM2000 was effective in eradicating smallpox. Public health officials have concern about the lack of real-world effectiveness data for JYNNEOS, especially because a second dose of JYNNEOS was required in a clinical study to reach the same maximal antibody response seen with ACAM2000 at the 4-week timepoint, and a correlate of protection has not been defined (i.e., it is not known what level of antibodies is needed to prevent *Monkeypox virus* infection).
- Adverse reactions after JYNNEOS include injection site reactions such as pain, swelling, and redness. Fatigue, headache, and muscle pain were the most common systemic reactions observed after JYNNEOS in a clinical trial.
- JYNNEOS is safe to administer to people with HIV and eczema or other exfoliative skin conditions.
- While there are no data in people who are pregnant or breastfeeding, animal data do not show evidence of reproductive harm; pregnancy and breastfeeding are not contraindications to receiving JYNNEOS.
- Please see the JYNNEOS Special Considerations section for guidance on contraindications and precautions and additional clinical considerations for use of JYNNEOS.

ACAM2000

- ACAM2000 contains a live *Vaccinia virus* that is replication competent.
- It is administered as one percutaneous dose via multiple puncture technique with a bifurcated needle.
- The immune response takes 4 weeks for maximal development.
- Following a successful inoculation, a lesion (known as a “take”) will develop at the site of the vaccination; the lesion may take up to 6 weeks or more to heal.
- ACAM2000 is licensed by the FDA for use against smallpox; it is allowed for use against monkeypox under an Expanded Access IND (EA-IND) protocol, which requires informed consent along with completing additional forms.
- The effectiveness of ACAM2000 is supported by human clinical trials and animal studies.
- There are no data yet on the effectiveness of ACAM2000 for PEP, PEP++, or PrEP from the current monkeypox outbreak.
- Adverse reactions after ACAM2000 include injection site pain, swelling, and redness; fever; rash; lymph node swelling; and complications from inadvertent inoculation.
- ACAM2000 may cause myocarditis and pericarditis. In clinical trials about 1 in every 175 people who got the vaccine for the first time had myocarditis and/or pericarditis within 3 weeks after vaccination.
- People with severe allergy to any component of the vaccine should not receive it.
- In addition, people with severely weakened immune systems should not receive this vaccine.
- ACAM2000 should not be given to infants less than 12 months of age or to people with the following conditions:
  - Congenital or acquired immune deficiency disorders, including those taking immunosuppressive medications and people living with HIV (regardless of immune status)
  - Eczema or other exfoliative skin conditions, and people with a history of eczema or other exfoliative skin conditions
  - Pregnancy
  - Cardiac disease
  - Eye disease treated with topical steroids

Planning Considerations for Health Departments and Providers

Access to Vaccines

- Both vaccines are available from the Strategic National Stockpile (SNS).
- Potential adult or pediatric use of ACAM2000 and potential pediatric use of JYNNEOS should be requested in consultation with CDC.
- Either JYNNEOS or ACAM2000 can be used for PEP, PEP++, or PrEP, following risk-benefit discussions and a review of any conditions that could increase risk for serious adverse events.

Equity

When developing vaccine plans, consider the following approaches to ensure equitable distribution:

- Engage people from affected communities in planning for vaccine programs and as trusted sources of information about monkeypox and vaccination
- Use non-stigmatizing, plain language
- Reiterate privacy of information and how data will be used
- Engage diverse partners already working with special populations
- Bring vaccines to where people are through pop-up events and mobile outreach
- Leverage clinical venues that serve people who have historically had less access to primary care, including sexual health clinics, transgender health clinics, and pharmacies
- Use multiple channels (e.g., social media, website, flyers) to advertise and book appointments
- Minimize the use of systems that are first-come, first-served
- Equity interventions that prioritize populations less able to access vaccine should be implemented even if a first-come, first-served model is used

JYNNEOS Special Considerations

- Two doses of JYNNEOS are required, as this is the only FDA-approved dosing regimen.
- Exceptions to the two-dose vaccine series
    - In the context of the current monkeypox outbreak, and while the supply of JYNNEOS vaccine is limited:
        - A person who is diagnosed with *Monkeypox virus* infection after their first dose of JYNNEOS is not recommended to receive the second dose at this time, because *Monkeypox virus* infection likely confers additional immune protection.
        - A person who would be eligible for vaccination but has been diagnosed with *Monkeypox virus* infection during this outbreak, which started in the United States on May 17, 2022, is not recommended to be vaccinated at this time, because *Monkeypox virus* infection likely confers immune protection.
        - An immunocompromised person who is diagnosed with *Monkeypox virus* infection after their first dose of JYNNEOS may be eligible to receive the second dose of JYNNEOS on a case-by-case shared decision-making basis based on the clinical judgment of the healthcare provider.
    - These recommendations may be revised as data become available and/or as the supply of JYNNEOS increases to meet or exceed outbreak response needs.
- JYNNEOS has been evaluated in clinical studies involving people with HIV infection or eczema and shown to be safe and effective in eliciting an immune response in these populations. The recommended JYNNEOS dosing schedule is the same for people who are immunocompromised; however, people with immunocompromising conditions might be less likely to mount an effective response after any vaccination, and as a result people who are immunocompromised might be at increased risk for severe disease if an infection occurs, despite vaccination.
- People who receive JYNNEOS are considered to reach maximal immunity 14 days after their second dose.
- CDC will gather data about how well JYNNEOS will protect against monkeypox disease in this outbreak. Individuals wanting to minimize their risk of infection should continue to take steps to protect themselves from infection and self-

isolate as soon as they develop monkeypox symptoms, such as a rash. Infections despite vaccination may occur, and there are currently no data on effectiveness of JYNNEOS from the current outbreak.

- Vaccine dosing interval clarifications
  - The FDA-approved JYNNEOS vaccine dosing interval is 28 days.
  - The vaccine manufacturer has advised that it is not recommended to give the second dose before the minimum interval of 28 days; however, doses may be given up to 4 days before the minimum interval of 28 days (i.e., 24 days after the first dose) based on ACIP's general best practices.
  - Based on available clinical study data, the second dose may be given up to 7 days after the minimum interval of 28 days (i.e., 35 days after the first dose).
  - If there is a delay in administering the second dose and the interval becomes longer than 35 days, the second dose should be administered as soon as possible based on ACIP's general best practices. There is no need to restart the series.
- Guidance for coadministration with other vaccines
  - JYNNEOS typically may be administered without regard to timing of other vaccines. This includes simultaneous administration of JYNNEOS and other vaccines on the same day, but at different anatomic sites if possible. See ACIP's general best practices and *Epidemiology and Prevention of Vaccine-Preventable Diseases* (Pink Book) for further information.
  - However, because of the observed risk for myocarditis after receipt of ACAM2000 orthopoxvirus vaccine and mRNA (i.e., Moderna and Pfizer-BioNTech) and Novavax COVID-19 vaccines and the unknown risk for myocarditis after JYNNEOS, people, particularly adolescent or young adult males, might consider waiting 4 weeks after orthopoxvirus vaccination (either JYNNEOS or ACAM2000) before receiving a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine. However, if an orthopoxvirus vaccine is recommended for prophylaxis in the setting of an outbreak, orthopoxvirus vaccination should not be delayed because of recent receipt of a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine; no minimum interval between COVID-19 vaccination with these vaccines and orthopoxvirus vaccination is necessary. (See Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC)
- Guidance for contraindications and precautions
  - A severe allergic reaction (e.g., anaphylaxis) after a previous dose of JYNNEOS vaccine is a contraindication to receipt of a subsequent dose. Referral to an allergist-immunologist should be considered to assess the risks versus benefits of administering another dose.
  - JYNNEOS vaccine contains small amounts of gentamicin and ciprofloxacin and is produced using chicken embryo fibroblast cells.
  - People who have had a previous severe allergic reaction (e.g., anaphylaxis) following gentamicin or ciprofloxacin have a precaution for receiving JYNNEOS vaccine and should be informed about the potential for increased risk of allergic reaction if the vaccine is administered.
    - After discussing risks and benefits with the individual, these people may be vaccinated with a 30-minute observation period. Alternatively, taking into account the risk of acquiring monkeypox if the vaccination is delayed, an allergist-immunologist may be consulted before the vaccine is administered.
    - For individuals who have had Stevens-Johnson syndrome (SJS) or Toxic Epidermal Necrolysis (TEN) following either ciprofloxacin or gentamicin, the risk of this type of severe allergic reaction from JYNNEOS vaccine is considered to be low because of the small amounts of the antibiotics in the vaccine. The risks and benefits of the vaccination should be discussed with the individual. Alternatively, taking into account the risk of acquiring monkeypox if the vaccination is delayed, an allergist-immunologist may be consulted before the vaccine is administered.
  - People who have had a severe allergic reaction (e.g., anaphylaxis) to chicken or egg protein AND are currently avoiding exposure to all chicken or egg products have a precaution for receiving JYNNEOS vaccine and should be informed about the potential for increased risk of allergic reaction if the vaccine is administered.
    - After discussing risks and benefits with the individual, these people may be vaccinated with a 30-minute observation period. Alternatively, after taking into account the risk of acquiring monkeypox if the vaccination is delayed, an allergist-immunologist may be consulted before the vaccine is administered.
  - Vaccine providers should be familiar with identifying immediate-type allergic reactions, including anaphylaxis, and be competent in treating these events at the time of vaccine administration. Providers should also have a plan in place to contact emergency medical services immediately in the event of a severe acute vaccine reaction. (See ACIP Adverse Reactions Guidelines for Immunization | CDC)

ACAM2000 Special Considerations

- Adverse events following ACAM2000, including myocarditis and/or pericarditis or *Vaccinia virus* transmission to household contacts, can be serious. ACAM2000 will be made available for individuals who decide, in consultation with their healthcare provider, that the potential benefits of vaccination outweigh any potential risks from ACAM2000 adverse events.
- Recipients should be informed of the risks and benefits of ACAM2000 prior to vaccination. Because ACAM2000 is contraindicated in people with weakened immune systems, people who are eligible for and offered ACAM2000 should be tested for HIV to ensure they are HIV negative, counseled on potential side effects, and sign an informed consent. To avoid spread of *Vaccinia virus* infection to others or other parts of the body, recipients should be advised to keep the vaccination site covered and to avoid swimming, sharing of blankets and towels, and contact with people who might be at risk for serious adverse events, such as people with weakened immune systems, people with eczema or other exfoliative skin conditions, children younger than 12 months, or people who are pregnant.
- Providers should be properly trained on administration of ACAM2000 using a bifurcated needle and should follow up with the patient to assess the vaccination site for a vaccination "take." (See Smallpox Vaccination and Adverse Reactions).
- Any licensed provider can administer ACAM2000; training may be obtained online through a CDC training video.
- Providers should advise the vaccine recipient on how to keep the vaccination site clean and covered until the lesion completely heals (which may take up to 6 weeks or more). Vaccine recipients need to take specific precautions to prevent spread of the vaccine virus to others, including through direct contact (e.g., close, skin-to-skin contact, including intimate contact), during this time.
- People who receive ACAM2000 are considered to reach maximal immunity 4 weeks after their dose.
- Since there are currently no data on the effectiveness of ACAM2000 from the current outbreak, people who get this vaccine should continue to take steps to protect themselves from infection even after vaccination takes full effect.
- Vaccine providers should be familiar with identifying immediate-type allergic reactions, including anaphylaxis, and be competent in treating these events at the time of vaccine administration. Providers should also have a plan in place to contact emergency medical services immediately in the event of a severe acute vaccine reaction. (See ACIP Adverse Reactions Guidelines for Immunization | CDC)

How previous smallpox vaccination may affect current recommendations for JYNNEOS and ACAM2000 during the monkeypox outbreak

- Previous smallpox vaccination does provide protection, but it may not necessarily be lifelong. During the 2003 monkeypox outbreak and during the current monkeypox outbreak, several people who were infected with monkeypox had previously been vaccinated against smallpox decades prior.
- During this monkeypox outbreak response, vaccines and other medical measures should be given to eligible people who were previously vaccinated against smallpox, following the same schedules as for those who were not previously vaccinated.
    - See current ACIP recommendations for revaccination guidance for those at occupational risk of exposure.

Reporting of Vaccine Adverse Events

- Adverse events that occur in a recipient following monkeypox or smallpox vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reporting is encouraged for any clinically significant adverse event, even if it is uncertain whether the vaccine caused the event. Vaccine administration errors can be reported whether or not associated with an adverse event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov or by calling 1-800-822-7967.
- JYNNEOS (use in children) or ACAM2000 (use in adults or children for monkeypox prevention) administered under IND protocols are subject to adverse event reporting requirements per the IND regulations. The site investigator/treating physician/designee or vaccine administrator must follow safety reporting requirements as outlined in the IND protocols.
- CDC's Clinical Immunization Safety Assessment (CISA) Project is available to provide consultation to U.S. healthcare providers and health departments about complex monkeypox and smallpox vaccine safety questions for their patients. In case of an emergent clinical vaccine safety inquiry, healthcare providers and health department staff can call the CDC Emergency Operations Center (EOC) Watch Desk at (770) 488-7100.

Related Resources

JYNNEOS

- Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022 | MMWR (cdc.gov)

ACAM2000

- Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015 | MMWR (cdc.gov)
- Surveillance Guidelines for Smallpox Vaccine (vaccinia) Adverse Reactions (cdc.gov)
- Recommendations for Using Smallpox Vaccine in a Pre-Event Vaccination Program: Supplemental Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Healthcare Infection Control Practices Advisory Committee (HICPAC) (cdc.gov)
- Smallpox Vaccination and Adverse Reactions (cdc.gov)

More Information

Smallpox Vaccination Information

JYNNEOS Package Insert. Available from: https://www.fda.gov/media/131078/download

Vaccine Information Statement: Smallpox/Monkeypox Vaccine (JYNNEOS™): What You Need to Know (cdc.gov) [150 KB, 2 pages]

ACAM2000 Product Insert. Available from: https://www.fda.gov/media/75792/download

Medication Guide Smallpox Vaccine, Live ACAM2000 (fda.gov)

Administering ACAM2000 Smallpox Vaccine Videos | Smallpox | CDC

Smallpox (ACAM2000) | Health.mil

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