Centers for Disease Control and Prevention

Smallpox Vaccines

Safety Information

This information is about the safety of smallpox vaccines. For the latest information about the safety of mpox vaccines, including side effects, please visit CDC's mpox vaccine safety site. For information about the current mpox outbreak, including information on symptoms and prevention, please visit CDC's mpox site.

About the Disease

Smallpox is a serious infectious disease caused by the variola virus. The disease spreads easily from person to person, causing high fever, and a distinctive, progressive skin rash.

Since 1980, smallpox has been considered eradicated. Learn more about smallpox.

Available Vaccines

Vaccine Information Statements

Vaccine Information Statements (VISs) are information sheets produced by CDC that explain both the benefits and risks of a vaccine.

ACAM2000 [PDF - 7 Pages]

Medication guide for the Smallpox (Vaccinia) vaccine. This guide replaced the VIS in December 2015.

JYNNEOS

Smallpox/Mpox vaccine for people ages 18 years and older at risk for smallpox or mpox infection.

The virus that causes smallpox is part of the genus (group) Orthopoxvirus. The vaccines available that provide protection against smallpox can also provide cross-protection against other orthopoxviruses.

There are two types of vaccines licensed in the United States that can prevent smallpox disease. Both vaccines are made from a virus called **vaccinia**, which is a poxvirus similar to variola virus, but less harmful.

ACAM2000 is approved for the prevention of smallpox only. This vaccine contains a poxvirus strain that can cause a clinical infection in humans that can be transmitted to others. However, this vaccine cannot cause smallpox. ACAM2000 is the preferred vaccine to protect against smallpox except in persons who are severely immunodeficient or with relative contraindications.

JYNNEOS (also known as Imvamune or Imvanex in other countries) is approved for the prevention of smallpox and mpox. This vaccine contains a poxvirus strain that does not cause clinical infections. JYNNEOS is the preferred vaccine to protect against mpox.

Who Should Be Vaccinated Against Smallpox

After smallpox eradication, routine vaccination against smallpox among the general public was stopped because it was no longer needed. However, because of concern that variola virus might be used as an agent of bioterrorism, the U.S. government stockpiled enough smallpox vaccine to vaccinate everyone in the United States if a smallpox outbreak occurs.

When there is **NO** smallpox outbreak, CDC recommends routine smallpox vaccination for people at risk for occupational exposure to orthopoxviruses, including:

- Research laboratory personnel working with orthopoxviruses (such as mpox, cowpox and variola)
- Clinical laboratory personnel performing diagnostic testing for orthopoxviruses
- Orthopoxvirus and healthcare worker response teams designated by appropriate public health and antiterror authorities

Routine vaccination is not recommended, but should be offered to:

- Healthcare personnel who currently treat or anticipate treating patients with orthopoxvirus infections
- Anyone administering ACAM2000

Booster doses are recommended every two years (JYNNEOS) or every 3 years (ACAM2000) if a person remains at continued risk for exposure to more virulent (harmful) orthopoxviruses (e.g., variola virus and mpox virus).

Learn more about who should get smallpox vaccination.

Administering Smallpox Vaccination

The route of administration is different for ACAM2000 and JYNNEOS. ACAM2000 is administered as a single dose by the percutaneous route using the multiple puncture technique using a bifurcated (two-pronged) needle.

JYNNEOS is administered as a series of two injections, four weeks apart. People who received a smallpox vaccine in the past might only need one dose.

Manufacturer Package Inserts

ACAM2000

> ACAM2000 [PDF – 11 Pages] : The U.S. Food and Drug Administration (FDA) approved this vaccine in 2007. It is approved for use in people who have a high chance of getting smallpox. During the 2022 mpox outbreak, ACAM2000 is allowed to be used under the Expanded Access Investigation New Drug Application (EA-IND) .

JYNNEOS

JYNNEOS [PDF – 11 Pages] : FDA approved this vaccine in 2019 for use in people ages 18 years and older and determined to be at high risk for smallpox or mpox infection. The FDA also issued an EUA for JYNNEOS use in people under ages 18 years and for alternative routes of administration for those ages 18 years and older during the 2022 mpox outbreak. The EUA is listed on the FDA's page on Mpox EUA Information .

Common Side Effects

Vaccines, like any medicine, can have side effects. The most common side effects are usually mild and go away on their own.

Severe allergic reactions following vaccination are rare, but can be life threatening.
Symptoms of a severe allergic reaction can include hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, and weakness.

If such reactions occur, call 9-1-1 and get the person to the nearest hospital.

Smallpox (Vaccinia) Vaccine, Live – ACAM2000

Healthcare providers should consult CDC's Interim Clinical Considerations for the most current information on who should or should not get a vaccine to prevent mpox. Learn more about Interim Clinical Considerations for Use of JYNNEOS and ACAM2000 Vaccines during the 2022 U.S. Mpox Outbreak.

Common Side Effects

- Itching
- Swollen lymph nodes
- Sore arm
- Fever
- Headache
- Body ache
- Mild rash
- Fatigue (tiredness)

Serious Side Effects

- Heart problems (including myocarditis and pericarditis)
- Swelling of the brain or spinal cord
- Problems with the vaccination site blister, including infection
- Spreading the virus to other parts of the body or to another person
- Severe allergic reaction after vaccination
- Accidental infection of the eye (may cause swelling of the cornea, causing watery, painful eyes and blurred vision, scarring of the cornea, and blindness)

Who Should Not Get ACAM2000

People who have immune system related illnesses, such as HIV, should not get ACAM2000. Infants younger than age 12 months should not receive ACAM2000.

The risk for serious ACAM2000 vaccine side effects are greater in people with certain conditions, and they should not get the vaccine. People with the following conditions should talk to their doctor about ACAM2000:

- Have three or more of the following risk factors for heart disease: high blood pressure, high cholesterol, diabetes, high blood sugar, a family history of heart problems, or smoking
- Have heart or blood vessel problems, including angina, previous heart attack, artery disease, congestive heart failure, stroke, or other cardiac issues
- Have skin problems, such as eczema, atopic dermatitis, burns, impetigo, contact dermatitis, chickenpox, shingles, psoriasis, or uncontrolled acne
- Are pregnant, could be pregnant, plan to become pregnant or breastfeeding
- Are taking steroid eye drops or ointment
- Have had problems after previous doses of smallpox vaccine or are allergic to any part of smallpox vaccine, such as antibiotics neomycin or polymyxin B

People with minor illnesses, such as a cold, may be vaccinated.

In some cases, the healthcare provider may decide to postpone vaccination with ACAM2000 or vaccinate with JYNNEOS. For children and adolescents ages 1 to 16 years, the safety and effectiveness has not been evaluated; assess risks versus benefits before administering ACAM2000.

Smallpox and Mpox Vaccine, Live, Non-replicating – JYNNEOS

Common Side Effects

- Injection site reactions, including pain, redness, swelling, hardening of the skin, and itching. Injection site reactions, except for pain, may occur more frequently after intradermal administration than after subcutaneous administration)
- Headache
- Muscle pain
- Fatigue (tiredness)
- Nausea
- Change in appetite
- Chills
- Fever

Before Getting JYNNEOS

People who have certain health conditions may not be able to get JYNNEOS. People should talk to their healthcare provider before getting JYNNEOS if they:

- Have had a severe allergic reaction (e.g., anaphylaxis) after a previous dose of JYNNEOS or another smallpox vaccine
- Have a history of severe allergic reaction (e.g., anaphylaxis) following gentamicin or ciprofloxacin
- Have a history of severe allergic reaction to chicken or egg protein AND are currently avoiding exposure to all chicken or egg proteins

People with minor illnesses, such as a cold, may be vaccinated.

People who have been recommended to receive JYNNEOS due to exposure to smallpox virus should be vaccinated regardless of concurrent illness, pregnancy, breastfeeding, or weakened immune system.

More information about contraindications and precautions.

Report Possible Adverse Events To VAERS

The Vaccine Adverse Event Reporting System (VAERS) is an early warning system, co-managed by CDC and FDA, that monitors for potential vaccine safety problems.

Healthcare providers and vaccine manufacturers are required by law to report certain adverse events following vaccination to VAERS; patients and caregivers can also submit reports.

For more information, see Report an Adverse Event to VAERS .

More Information

Smallpox Vaccination: What everyone Should Know
What everyone should know about smallpox vaccines.

Who Should Not Get Vaccinated?
Some people should not get certain vaccines or should wait before getting them. Read the CDC guidelines for each vaccine.

Orthopoxviruses (Smallpox and Mpox) Vaccines – ACIP Recommendations and Guidance
Official guidance on smallpox and mpox vaccines from the Advisory Committee on Immunization Practices (ACIP).

Smallpox Vaccination: Information for Healthcare Providers
Information for healthcare professionals on smallpox vaccines.

Mpox and Smallpox Vaccine Guidance
Information for healthcare professionals on mpox and smallpox vaccine guidance.

A Closer Look at the Safety Data

ACAM2000

There are several serious adverse events that have been reported following the first vaccination or revaccination at a later date with live vaccinia virus smallpox vaccine (ACAM2000). Serious adverse events that have occurred include:

- **Myocarditis and pericarditis:**

  The heart muscle and lining become inflamed. The package insert states the suspected cases were observed at a rate of 5.7 per 1,000 primary vaccinees.
- **General, progressive, and severe vaccinia:**

  This condition can occur in immunocompromised people and is caused by the uncontrolled replication of the vaccinia virus. The virus causes open wounds, and depending on the severity, can lead to death.
- **Eczema vaccinatum resulting in permanent sequelae or death:**

  This occurs when the vaccinia virus spreads and causes an overall rash and systemic reactions.
- **Fetal death:**

  Pregnant people who have received a live vaccinia virus vaccine are more susceptible to spontaneous abortion (miscarriage).
- **Encephalitis, Encephalomyelitis and Encephalopathy:**

  These are conditions of inflammation of brain, spinal cord, or both.
- **Erythema multiforme major (EMM), including Stevens-Johnson Syndrome (SJS):**

  EMM is a skin reaction from an infection or medication. SJS is a rare and serious disorder that affects skin, moist surfaces of the body (such as inside of mouth and throat), genitals, and eyes.
- **Ocular complications and blindness:**

  When the vaccinia virus enters the eye region, it can cause eyelid infections, swelling, sensitivity to light, irritation and damage to the cornea, and possible blindness.

Which adverse events are considered "serious?"

By the Code of Federal Regulations (CFR) Title 21, an adverse event is defined as serious if it involves any of the following outcomes:

- Death
- A life-threatening adverse event
- A persistent or significant disability or incapacity
- A congenital anomaly or birth defect
- Hospitalization, or prolongation of existing hospitalization

Learn more about adverse events.

These are serious risks and certain individuals who receive live vaccinia virus vaccine are more prone to these adverse events.

Source: ACAM2000 Product Insert (fda.gov) [PDF – 11 Pages]

In March 2008, ACAM2000 replaced the previous stockpiled smallpox vaccine, Dryvax®, as the only licensed smallpox vaccine at the time. While not routinely administered, ACAM2000 was administered to people entering military service and those working in labs handling variola (smallpox) virus. As part of the post-licensure marketing commitments for ACAM2000, FDA, CDC, Department of Defense, and the vaccine manufacturer, gathered additional safety data on adverse events following vaccination. In March 2011, a routine safety data review within Vaccine Adverse Event Reporting System (VAERS), co-managed by CDC and FDA, identified a safety concern of acute ischemic cardiac events (ICE) following ACAM2000 vaccination.

Researchers reviewed all reports to VAERS submitted from March 1, 2008 through June 30, 2013, following ACAM2000 vaccination. Possible ICE cases were identified by searching for specific medical terms, including myocardial ischemia (lack of blood flow back to the heart), acute myocardial infarction (heart attack), and ischemia (restriction of blood supply to any part of the body). A clinical review of the cardiovascular reports identified 16 cases of myocarditis/pericarditis (inflammation of the heart muscle or lining of the heart) and 15 ICE cases. This review did not confirm the concerns of ICE following ACAM2000. The study also suggested that with pre-vaccination screening of ACAM2000, cardiac events in a generally healthy population remain uncommon.

Source:

Ischemic Cardiac Events and Other Adverse Events following ACAM2000® Smallpox Vaccine in the Vaccine Adverse Event Reporting System [Vaccine. 2018]

JYNNEOS

The modified vaccinia Ankara vaccine (JYNNEOS) was developed to offer a safer smallpox vaccine option for people who would not be able to safely receive ACAM2000 (live vaccinia virus vaccine). When JYNNEOS received FDA approval, it was approved to prevent smallpox and mpox. JYNNEOS is the preferred vaccine to protect against mpox.

The overall JYNNEOS clinical trial program included 22 studies and a total of 7,859 people ages 18 through 80 years of age who received at least 1 dose of JYNNEOS.

In one clinical trial study, researchers found people with skin conditions (either active or history of skin conditions such as eczema or atopic dermatitis) who received JYNNEOS experienced mild to moderate skin reactions from the vaccine. No safety concerns were found during this study in people with skin conditions.

Several studies assessed the cardiac safety of people who received JYNNEOS. During a study of the vaccine and placebo groups, there were three cases of heart palpitations, two cases of tachycardia, and no cases of myocarditis or pericarditis detected. Overall, data did not suggest an increased risk of myocarditis or pericarditis after vaccination with JYNNEOS compared with placebo controls.

Across all 22 clinical trials, the safety profile of JYNNEOS was favorable in all populations, including people with HIV or other immunocompromising conditions. There were no clinically relevant differences in the safety or the reactogenicity of JYNNEOS in populations who were or were not previously exposed to a vaccinia virus vaccine.

The reported complications from live vaccinia virus vaccines, such as rashes caused by the virus (including generalized and progressive vaccinia), erythema multiforme (skin reaction from an infection or medication), or encephalitis, were not observed during the clinical trials for JYNNEOS.

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Phase 3 Efficacy Trial of Modified Vaccinia Ankara as a Vaccine against Smallpox. [N Engl J Med. 2019]

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A Multicenter, Open-Label, Controlled Phase II Study to Evaluate Safety and Immunogenicity of MVA Smallpox Vaccine (IMVAMUNE) in 18-40 Year Old Subjects with Diagnoses Atopic Dermatitis. [PLoS One. 2015]

Safety and Immunogenicity of Modified Vaccinia Anakara-Bavarian Nordic Smallpox Vaccine in Vaccinia-Naïve and Experienced Human Immunodeficiency Virus-Infected Individuals: An Open-Label, Controlled Clinical Phase II Trial. [Open Forum Infect Dis. 2015]

Cardiac Safety of Modified Vaccinia Ankara for vaccination against smallpox in a young, healthy study population. [PLoS One. 2015]

How CDC Monitors Vaccine Safety

CDC and FDA monitor the safety of vaccines after they are approved or authorized. If a problem is found with a vaccine, CDC and FDA will inform health officials, health care providers, and the public.

CDC uses 3 systems to monitor vaccine safety:

- The Vaccine Adverse Event Reporting System (VAERS): an early warning system, co-managed by CDC and FDA, to monitor for potential vaccine safety problems. Anyone can report possible vaccine side effects to VAERS.
- The Vaccine Safety Datalink (VSD): a collaboration between CDC and 13 healthcare organizations that conducts vaccine safety monitoring and research.
- The Clinical Immunization Safety Assessment (CISA) Project: a partnership between CDC and several medical research centers that provides expert consultation and conducts clinical research on vaccine-associated health risks.

Related Scientific Articles

2015 to Present

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