

Clinical guidance for the use of JYNNEOS

Brett Petersen, MD, MPH

United States Public Health Service
Poxvirus and Rabies Branch
Centers for Disease Control and Prevention

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Outline

- **Contraindications and precautions / warnings**
- **Guidance for minimizing the risk of occupational exposure**
- **Titer testing and starting work in laboratories**

ACAM2000 and JYNNEOS®

	ACAM2000	JYNNEOS®
Vaccine virus	Replication-competent vaccinia virus	Replication-deficient Modified vaccinia Ankara
“Take”	“Take” occurs	No “take” after vaccination
Inadvertent inoculation and autoinoculation	Risk exists	No risk
Serious adverse event	Risk exists	Fewer expected
Cardiac adverse events	Myopericarditis in 5.7 per 1,000 primary vaccinees	Risk believed to be lower than that for ACAM2000
Effectiveness	FDA assessed by comparing immunologic response and “take” rates to Dryvax*	FDA assessed by comparing immunologic response to ACAM2000 & animal studies
Administration	Percutaneously by multiple puncture technique in single dose	Subcutaneously in 2 doses, 28 days apart

*Both ACAM2000 and Dryvax are derived from the NYC Board of Health strain of vaccinia; ACAM2000 is a “second generation” smallpox vaccine derived from a clone of Dryvax, purified, and produced using modern cell culture technology.

Proposed recommendations for JYNNEOS[®] compared to ACAM2000

	ACAM2000	JYNNEOS [®]
Population recommended	Persons at occupational risk for orthopoxviruses (i.e., research laboratory personnel, diagnostic laboratorians, response team members)	
Populations offered	Persons who administer ACAM2000 or care for patients with infection or after vaccination with replication competent virus	
Populations for whom booster is recommended at specific intervals	Persons who are at continued or sustained risk for orthopoxviruses [Note: Response teams are not at continued risk and will receive boosters only at the time of a smallpox/monkeypox event]	
Frequency of boosters: Those working with smallpox and monkeypox	Every 3 years (had previously been every year)	Every 2 years
Frequency of boosters: Those working with less virulent orthopoxviruses	At least every 10 years	

Severe Vaccinia Virus Complications

Uncontrolled Viral Replication

- Progressive vaccinia
- Eczema vaccinatum



Progressive vaccinia

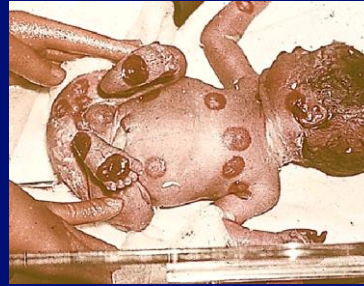


Eczema vaccinatum

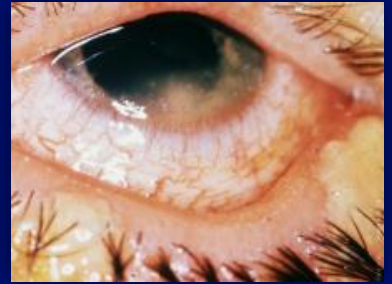
Severe Vaccinia Virus Complications

Inadvertent Transmission

- Fetal vaccinia
- Autoinoculation / inadvertent inoculation
 - Ocular infections



Fetal vaccinia



Ocular vaccinia

Severe Vaccinia Virus Complications

Uncertain Etiology

- Postvaccinial encephalitis
- Myopericarditis

Proposed ACIP Contraindications for ACAM2000 and JYNNEOS

Contraindication	ACAM2000 Primary Vaccinees	ACAM2000 Revaccinees	ACAM2000 Household Contacts ¹	JYNNEOS
History or presence of atopic dermatitis	X	X	X	
Other active exfoliative skin conditions ²	X	X	X	
Conditions associated with immunosuppression ³	X	X	X	
Pregnancy ⁴	X	X	X	
Aged <1 year ⁵	X	X	X	
Breastfeeding ⁶	X	X		
Serious vaccine component allergy	X	X		X
Known underlying heart disease (e.g., coronary artery disease or cardiomyopathy)	X	X		
Three or more known major cardiac risk factors ⁷	X			

1. Household contacts

- Household contacts include persons with prolonged intimate contact with the potential vaccinee (e.g., sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (e.g., dressings or clothing)
- **JYNNEOS is a replication-deficient vaccine and therefore should not present a risk of transmission to household contacts**

2. Atopic dermatitis / eczema and other active exfoliative skin conditions

- Conditions include eczema, burns, impetigo, varicella-zoster, herpes, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease (keratosis follicularis)
- Studies evaluating JYNNEOS in persons with atopic dermatitis have demonstrated immunogenicity in eliciting a neutralizing antibody response and did not reveal any significant safety concerns

3. Conditions associated with immunosuppression

- Conditions include human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component
- **Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response to JYNNEOS because of their immunocompromised status**

4. Pregnancy

- Available human data on JYNNEOS administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy
- However, animal models, including rats and rabbits, have shown no evidence of harm to a developing fetus

5. Aged <1 year

- Vaccination of infants aged <1 year is contraindicated for **ACAM2000**
- **JYNNEOS is not licensed for persons <18 years and has not been rigorously evaluated in this population**
- **Caution should be used when considering the administration of ACAM2000 or JYNNEOS to children and adolescents aged <18 years**

6. Breastfeeding

- **The safety and efficacy of JYNNEOS has not been evaluated in breastfeeding women**
- **It is not known whether JYNNEOS is excreted in human milk and data are not available to assess the impact of JYNNEOS on milk production or the safety of JYNNEOS in breastfed infants**
- **However, JYNNEOS vaccine is replication deficient and therefore should not present a risk of transmission to breastfeeding infants**
- **Caution should be used when considering the administration of JYNNEOS to breastfeeding women**

7. Three or more known major cardiac risk factors

- Major cardiac risk factors include hypertension, diabetes, hypercholesterolemia, heart disease at age 50 years in a first-degree relative, and smoking
- Clinical studies have not detected an increased risk of myopericarditis in recipients of JYNNEOS
- Persons with underlying heart disease or ≥ 3 major cardiac risk factors should be counseled on the theoretical risk of myopericarditis given the uncertain etiology of myopericarditis associated with replication-competent smallpox vaccines

Guidance for Minimizing the Risk of Occupational Exposure

- **Many persons with contraindications to vaccination with ACAM2000 (e.g., atopic dermatitis, immunocompromising conditions, breastfeeding, or pregnancy) may receive vaccination with JYNNEOS**
- **However, such persons may be at increased risk for severe disease if an occupational infection occurs despite vaccination**
- **Persons with immunocompromising conditions may be less likely to mount an effective response after any vaccination, including after JYNNEOS even though JYNNEOS can be safely administered to such persons**

Guidance for Minimizing the Risk of Occupational Exposure

- **Persons who are pregnant, immunocompromised, with atopic dermatitis, or breastfeeding may receive JYNNEOS when it is considered imperative to provide protection against orthopoxvirus infections and after careful consideration of the risk/benefit ratio**
- **To find more information about the risk for severe outcomes if orthopoxvirus infections are acquired, please see [Smallpox Vaccination and Adverse Reactions: Guidance for Clinicians, 2003. MMWR 2003, 52(RR04);1-28]**

Titer Testing

- As a replication-deficient vaccine, JYNNEOS does not produce a vaccine site lesion (also known as a “take”) that can be used as a marker of successful vaccination
- Routine titer testing is not recommended following vaccination with JYNNEOS to confirm successful administration of vaccine given that high rates of seroconversion were demonstrated in clinical trials
- However, titer testing could be considered on a case-by-case basis after consultation with public health authorities for select persons with immunocompromising conditions or those working with more virulent orthopoxviruses (e.g., variola virus and monkeypox virus) to confirm an immune response has been achieved

Titer Testing

- A correlate of protection has not been established and there is no known antibody titer level that will ensure protection
- Titer results should be interpreted with caution in such cases to avoid providing a false sense of security

Starting Work in Laboratories

- **A person can be considered fully immunized 2 weeks following administration of the second dose of JYNNEOS when clinical studies have demonstrated maximal antibody titers**

Questions?

Brett W. Petersen, MD, MPH
1600 Clifton Road NE, Mail Stop H24-12
Atlanta, GA 30333
Phone: 404-639-5464
E-Mail: bpetersen@cdc.gov

**For more information please contact Centers for Disease
Control and Prevention**

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov

Web: <http://www.cdc.gov>

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



ACAM2000 Package Insert

Contraindications, Warnings, and Precautions

- **Contraindication**

- Individuals with severe immunodeficiency who are not expected to benefit from the vaccine. These individuals may include persons who are undergoing bone marrow transplantation or persons with primary or acquired immunodeficiency states who require isolation

- **Black Box Warning**

- Myocarditis and pericarditis (suspect cases observed at a rate of 5.7 per 1000 primary vaccinees (95% CI: 1.9-13.3)), encephalitis, encephalomyelitis, encephalopathy, progressive vaccinia, generalized vaccinia, severe vaccinia skin infections, erythema multiforme major (including STEVENS-JOHNSON SYNDROME), eczema vaccinatum resulting in permanent sequelae or death, ocular complications, blindness and fetal death, have occurred following either primary vaccination or revaccination with live vaccinia virus smallpox vaccines. These risks are increased in certain individuals and may result in severe disability, permanent neurological sequelae and/or death [see Warnings and Precautions]

ACAM2000 Package Insert

Contraindications, Warnings, and Precautions

■ Warnings and Precautions

- Myocarditis and/or pericarditis, ischemic heart disease and non-ischemic dilated cardiomyopathy
- Encephalitis, encephalomyelitis, encephalopathy, progressive vaccinia (vaccinia necrosum), generalized vaccinia, severe vaccinia skin infections, erythema multiforme major (including Stevens-Johnson syndrome), eczema vaccinatum, fetal vaccinia and fetal death
- Ocular vaccinia and blindness
- These risks, including risks of severe disability and/or death, are increased in vaccinees with:
 - Cardiac disease
 - Eye disease treated with topical steroids
 - Congenital or acquired immune deficiency disorders
 - History or presence of eczema and other skin conditions
 - Infants < 12 months of age
 - Pregnancy
- ACAM2000 is a live vaccinia virus that can be transmitted to persons who have close contact with the vaccinee and the risks in contacts are the same as those stated for vaccinees

JYNNEOS Package Insert

Warnings and Precautions

▪ 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 smallpox or monkeypox

▪ Altered Immunocompetence

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

▪ Limitations of Vaccine Effectiveness

- Vaccination with JYNNEOS may not protect all recipients