U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30329-4027

June 23, 2022

Dear Colleague:

The Centers for Disease Control and Prevention (CDC) is tracking the outbreak of monkeypox that has occurred in several countries that do not normally report human cases of monkeypox, including the United States. As of June 22, 2022, more than 3,300 cases have been reported in 42 countries around the world, including 156 cases in the United States. There have been no deaths reported in the current outbreak. We do not yet know how all these cases are connected or how they were initially exposed to the virus that causes monkeypox. Many of these cases have occurred among gay, bisexual, or other men who have sex with men. CDC is urging healthcare providers in the United States to be alert for patients who have illnesses consistent with monkeypox (including rash, fever, and lymphadenopathy), regardless of gender and sexual orientation.

Enclosed is additional information regarding what we know about monkeypox, monkeypox infection prevention and control, what CDC is doing, and what you can do to help protect your patients.

Sincerely,

Rochelle P. Walensky, MD, MPH
Director, CDC

Enclosure

Enclosure

Centers for Disease Control and Prevention Information Regarding Monkeypox

What we know:
Monkeypox is a disease caused by monkeypox virus. It is a viral zoonotic disease, meaning that it can spread from animals to people. It can also spread when a person has contact with a person or materials (e.g., bedding, towels) that are contaminated with the virus. Monkeypox can spread through:

- Direct contact with monkeypox lesions on a person's skin
- Contact with contaminated objects, fabrics (clothing, bedding, or towels), and surfaces that have been in contact with someone with monkeypox
- Contact with respiratory secretions during prolonged, face-to-face contact, fluid from lesions, and sometimes tears from a person with monkeypox

Monkeypox can also be spread during intimate contact including:

- Oral, anal, and vaginal sex, or touching the genitals or anus of a person with monkeypox
- Hugging, massage, kissing, or talking closely
- Touching fabrics, shared surfaces, and objects (such as bedding, towels, and sex toys) that were used by a person with monkeypox

People with monkeypox may first develop symptoms including a flu-like illness with fever, headache, muscle aches, exhaustion, and enlarged lymph nodes. A few days later, a characteristic rash occurs. In recent cases, patients have developed localized rashes in the genital and perianal region without prior flu-like symptoms. The incubation period, the time from infection to onset of symptoms, is roughly 1-2 weeks. The illness typically lasts 2-4 weeks and usually resolves without specific treatment. Monkeypox symptoms can sometimes be confused with those associated with syphilis, herpes simplex virus, and chicken pox (varicella zoster virus).

For more information on the clinical recognition of monkeypox, please visit Clinical Recognition | Monkeypox | Poxvirus | CDC.[1]

At this time, researchers are investigating how long the virus has been circulating outside of endemic areas; how the virus was introduced into some of the current clusters of cases; whether asymptomatic spread is possible; and whether the virus is being spread through contact with semen, vaginal fluids, or other body fluids not already listed. We are working with our partners to answer these and other questions.

Infection Prevention and Control
Patients with suspected or confirmed monkeypox infection should be placed in a single-person room. A negative pressure room is not necessary for monkeypox patients. Healthcare personnel entering the room should use a gown, gloves, eye protection, and an N95 or higher-level respirator. Intubation and extubation, and any procedures on patients likely to spread oral

[1] https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

secretions, should be performed in an airborne infection isolation room. Information on infection prevention and control in healthcare settings for patients with suspected or confirmed monkeypox infection[2] is available.

Patients who do not require hospitalization for medical indications (including people who test positive for monkeypox or those waiting for monkeypox test results) may be isolated at home using protective measures,[3] such as wearing a well-fitting mask when in close contact with others. Individuals with extensive lesions that cannot be covered, have draining or weeping lesions or present with active respiratory symptoms (e.g., cough, runny nose) should avoid contact with other family members, including pets. Patients who are contacts of people confirmed to have monkeypox should be monitored for symptoms for 21 days after their last exposure. Contacts who remain asymptomatic can be permitted to continue routine daily activities (e.g., go to work and school).

What CDC is doing

CDC is closely tracking all reported cases of orthopoxvirus (a group of viruses that include smallpox, cowpox, vaccinia, and monkeypox) and monkeypox, specifically. CDC is also working to raise awareness among frontline healthcare providers and public health officials and provide information about what infection with monkeypox looks like and how to manage the illness.

We are also raising awareness of the current situation with the public. CDC has resources that are available to help support these efforts, including a website[4] with key information about monkeypox and a fact sheet for people who are sexually active.[5]

What You Can Do

Helping people make the best-informed decisions to protect their health and the health of their community from monkeypox requires a combination of providing key prevention information to the public and working with community partners and trusted messengers to ensure that information reaches the affected groups.

Partners can help with messaging to specific communities and channels to increase awareness of monkeypox while reducing the chances of stigmatizing those who may have contact with the virus. It is important to emphasize that anyone, regardless of gender or sexual orientation, can develop and spread monkeypox. Many of those affected in the current global outbreaks identify as gay or bisexual men; however, the current risk of exposure to monkeypox is not exclusive to the gay and bisexual community.

It will take a partnership between healthcare providers, affected patients, and public health

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[2] https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html
[3] https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html
[4] https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html
[5] https://www.cdc.gov/poxvirus/monkeypox/pdf/MonkeyPox-sexually-active-InfoSheet-508.pdf

officials to educate and intervene with stigma-free care. We thank the LGBTQIA+ community and its medical and community service providers for helping us in our efforts to raise the visibility of the current situation and the steps people can take to protect their health and the health of others.

More information on the current situation of monkeypox in the United States can be found at U.S. Monkeypox 2022: Situation Summary | Monkeypox | Poxvirus | CDC.[4]

Information about the monkeypox virus, specimen collection, treatment, and infection prevention and control can be found at Information For Clinicians | Monkeypox | Poxvirus | CDC.[6]

Resources:
U.S. Monkeypox 2022: Situation Summary | Monkeypox | Poxvirus | CDC[4]
Case Definition† | Monkeypox | Poxvirus | CDC[7]
Clinical Recognition | Monkeypox | Poxvirus | CDC[1]
Infection Control: Healthcare Settings | Monkeypox | Poxvirus | CDC[2]

Patient information
Monkeypox: Get the Facts (cdc.gov)[5]

[6] https://www.cdc.gov/poxvirus/monkeypox/clinicians/index.html
[7] https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html

Update on the Use of Medical Countermeasures for Monkeypox Infection

Medical Countermeasures Unit

Clinical Team

2022 Multi-National Monkeypox Response

23 June 2022

Agenda

- Available medical countermeasures and indications for use
  - Vaccines
  - Tecovirimat
  - Other
- Use of countermeasures in 2022 outbreak
- Regulatory framework
- Procurement processes
- Q&A

Medical countermeasures

- Important caveats
  - Developed for treatment of other viruses
  - Most are not FDA approved for monkeypox treatment or prevention; use is authorized under Expanded Access Investigational New Drug (EA IND) protocols
  - Limited data
  - Limited experience

Image: Getty images

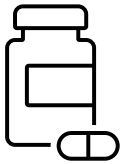
Image: Getty images

What tools are available for prevention and treatment of monkeypox infection?

Medical countermeasures

JYNNEOS

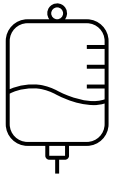
ACAM2000



Tecovirimat (TPOXX)

Cidofovir

Brincidofovir

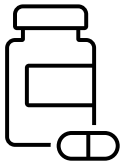


Vaccinia immune globulin

Medical countermeasures

JYNNEOS

ACAM2000



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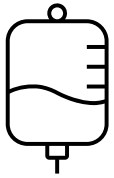


Vaccinia immune globulin

Medical countermeasures

- Pre-exposure prophylaxis (PrEP)
- Post-exposure prophylaxis (PEP)
- Treatment

Medical countermeasures: JYNNEOS vaccine

- Live, *non-replicating* vaccine
- Licensed by FDA in 2019 for prevention of smallpox and monkeypox disease in adults at least 18 years old
  - PrEP or PEP
- Administered as subcutaneous injection in 2 doses at least 4 weeks apart

Medical countermeasures: JYNNEOS vaccine

- Efficacy
  - Animal data, immunogenicity studies support efficacy as PrEP
  - Very limited evidence for efficacy as PEP
- Safety and side effects
  - Safe for use in immunocompromised, atopic dermatitis
  - Safety not established in pregnancy, breastfeeding, pediatrics; use might still be considered

Medical countermeasures: ACAM2000 vaccine

- Live, *replicating* vaccine
- Licensed by FDA in 2007 for active immunization against smallpox in adults at least 18 years old
- CDC holds expanded access investigational new drug (EA IND) protocol allowing use to prevent non-smallpox orthopoxviruses during an outbreak, including use as PEP
- Administered percutaneously using a multiple puncture “scarification” technique

Medical countermeasures: ACAM2000 vaccine

cdc.gov

Medical countermeasures: ACAM2000 vaccine

- Efficacy to prevent monkeypox infection
  - PrEP: likely similar to other live smallpox vaccines (>85%) in endemic countries (Fine et al 1988)
  - Efficacy as PEP uncertain
- Safety and side effects
  - Significant side effect profile: myo/pericarditis (1 in 175), progressive vaccinia, eczema vaccinatum, postvaccinial encephalitis, fetal vaccinia, inadvertent inoculation or autoinoculation
  - Risk of severe side effects: pregnancy, young children, immunocompromised, exfoliative skin condition

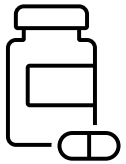
Medical countermeasures: ACAM2000 vaccine

MMWR 2007

Medical countermeasures

JYNNEOS

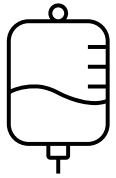
ACAM2000



Tecovirimat (TPOXX)

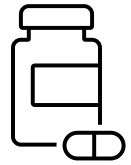
Cidofovir

Brincidofovir



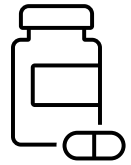
Vaccinia immune globulin

Medical countermeasures: Tecovirimat (TPOXX)



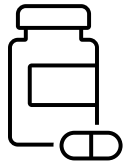
- Antiviral medication developed to treat smallpox
- Approved for treatment of smallpox in adults and children weighing at least 3kg
  - Oral capsule approved by FDA in 2018
  - IV formulation approved by FDA in May 2022
- CDC holds EA-IND allowing its use for other orthopoxviruses in adults and children

Medical countermeasures: Tecovirimat (TPOXX)



- Efficacy to treat monkeypox infection
  - Animal studies suggest mortality benefit
  - Case reports in humans suggest possible benefit on duration of illness, viral shedding
- Efficacy as PEP uncertain
- Safety and side effects
  - IV formulation contraindicated for creatinine clearance <30mL/min
  - Minor side effects in healthy subjects (headache, nausea, abdominal pain)
  - Not studied in pregnancy, breastfeeding, pediatrics

Medical countermeasures: Other medications

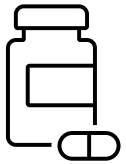


- Cidofovir
  - FDA-approved for cytomegalovirus retinitis
  - In vitro data suggest efficacy against orthopoxviruses
  - Available from the Strategic National Stockpile (SNS)
- Brincidofovir
  - FDA-approved for treatment of smallpox in children of all ages and adults
  - In vitro data suggest efficacy against orthopoxviruses
- Limitations of cidofovir and brincidofovir
  - Uncertain efficacy for treatment of monkeypox
  - Use limited by renal and hepatic toxicity
  - Brincidofovir not available through SNS

Medical countermeasures

JYNNEOS

ACAM2000



Tecovirimat (TPOXX)

Cidofovir

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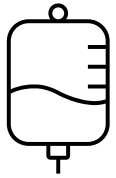
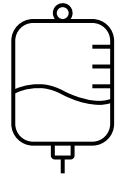


Vaccinia immune globulin

Medical countermeasures: VIGIV



- Vaccinia immune globulin (VIGIV)
  - FDA-approved for treatment of complications due to vaccinia vaccination (e.g. ACAM2000), including eczema vaccinatum, progressive vaccinia, and severe generalized vaccinia)
  - CDC holds EA IND allowing for use for prevention and treatment of complications from infection with orthopoxviruses
  - Unknown efficacy as PrEP, PEP, or treatment for monkeypox

Trifluridine (Viroptic)

- Antiviral medication licensed for treatment of herpes keratoconjunctivitis/keratitis
- In vitro evidence of activity against orthopoxviruses
- Case reports of use for orthopoxvirus infections

Am J Trop Med Hyg 2005

Medical countermeasures: summary

Based on current evidence…

- PrEP and PEP
  - JYNNEOS
  - ACAM2000 (for those without contraindications)
- Treatment
  - Tecovirimat
  - Other options might be considered in rare circumstances

When should PrEP, PEP, and antiviral treatments be given for monkeypox infection?

Pre-exposure prophylaxis (PrEP) indications

TABLE 1. Recommendations for ACAM2000 and JYNNEOS vaccines for persons at occupational risk for exposure to orthopoxviruses — Advisory Committee of Immunization Practices, United States, 2022

Recommendations	Vaccine product	
	ACAM2000	JYNNEOS
Who should receive the vaccine?	Persons at risk for occupational exposure to orthopoxviruses*	
Who should be offered the vaccine?	Persons who administer ACAM2000 or care for patients with infection with replication-competent viruses	

*1. Clinical laboratory personnel who perform testing to diagnose orthopoxviruses, including those who use polymerase chain reaction (PCR) assays for diagnosis of orthopoxviruses, including *Monkeypox virus*

2. Research laboratory workers who directly handle cultures or animals contaminated or infected with orthopoxviruses that infect humans, including *Monkeypox virus, replication-competent Vaccinia virus, or recombinant Vaccinia viruses derived from replication-competent Vaccinia virus strains*

3. Certain healthcare and public health response team members designated by public health authorities to be vaccinated for preparedness purposes

Pre-exposure prophylaxis (PrEP) indications

- At this time, most clinicians in the United States and laboratorians not performing orthopoxvirus testing are **not advised** to receive orthopoxvirus PrEP

Post-exposure prophylaxis (PEP) considerations

- Classify exposure using risk assessment tools
- Consider individual factors, e.g. risk for severe disease
- Provide reassurance when appropriate:
  - Primary mode of transmission is through prolonged, close contact with someone with lesions
- Facilitate prompt access to PEP when indicated:
  - Greatest efficacy when given within 4 days of exposure

Treatment considerations

- Persons with severe disease
- Persons at high risk of severe disease, including
  - People with immunocompromising conditions
  - Children, particularly those under 8 years of age
  - People who are pregnant or breastfeeding
  - People with a history of atopic dermatitis or exfoliative skin conditions
  - People with one or more complications
  - People with aberrant infections, including accidental implantation in eyes, mouth, or other anatomical areas where monkeypox lesions might constitute a special hazard, including genital and perianal areas
- Empiric treatment may be appropriate in some cases
- Benefit is likely greatest when antiviral treatment is started early in illness

How are medical countermeasures being used in the current monkeypox outbreak?

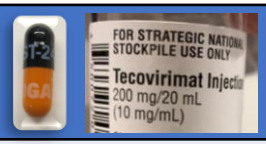
Use of medical countermeasures in 2022 outbreak

- PEP:
  - 4238 courses (8476 doses) of JYNNEOS requested by 28 jurisdictions
  - 200 courses of ACAM2000 distributed to 1 jurisdiction
- Treatment:
  - 197 courses of oral tecovirimat have been distributed
  - 18 patients in 8 jurisdictions have received oral tecovirimat
  - 3 courses of IV tecovirimat have been distributed
  - No patients have yet received IV tecovirimat

What regulatory framework is needed for use of medical countermeasures?

Regulatory mechanisms for stockpiled medical countermeasures (MCM)

- MCM regulatory status
  - FDA-approved MCM for approved use
  - Unapproved use of FDA-approved MCM
  - Unapproved MCM (e.g., investigational)
- Investigational New Drug Application (IND)
  - Product development through clinical trials
- Expanded Access IND (EA-IND)
  - “Compassionate use”; serious or immediately life-threatening disease or condition, favorable risk-benefit, evidence of safety and effectiveness
  - CDC-sponsored
    - CDC IRB serves as central IRB for review
    - FDA-reviewed and in effect
- Ensure any available HHS Public Readiness and Emergency Preparedness (PREP) Act protections apply

	Tecovirimat 	Jynneos*	ACAM2000
FDA-approved indication:	Treatment of smallpox in adults and pediatric patients	prevention of smallpox and monkeypox in adults ≥ 18 years	active immunization against smallpox in adults & children
EA-IND use:	Non-variola orthopoxvirus infection (e.g., monkeypox)	Children < 18 years of age	PEP of non-variola orthopoxvirus in adults & children
EA-IND includes:	Informed consent form		
	Statement of investigator (FDA Form 1572)		
	• Case report forms: ➢ Patient intake form ➢ Adverse events (AE) ➢ Progress and clinical outcomes ➢ Product accountability form • Photos and samples of lesions • PK sampling, serology	• Vaccination record form including AE reporting (AEs of special interest) • Product accountability form	

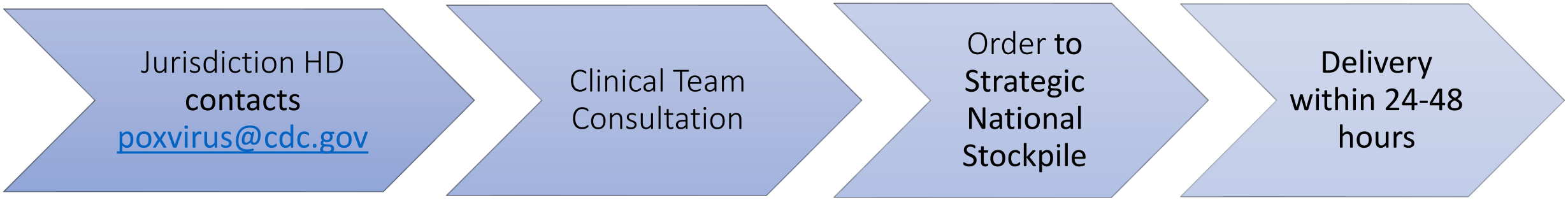
*Jynneos under single-patient EA-IND requiring FDA authorization prior to pediatric administration

regaffairs@cdc.gov

PEP: post-exposure prophylaxis

What is the process for procurement of medical countermeasures?

Procurement Processes



Deliveries from Strategic National Stockpile

- Free of charge
- Rapidly available
- Can be delivered directly to health departments, hospitals, or clinics
- Cannot be returned
- Come with required accountability forms

Take-aways

- Vaccines and antiviral treatment for monkeypox infection are available through the Strategic National Stockpile
- Health departments play a critical role:
  - Promote informed decision-making about use of vaccines and antiviral medications
  - Timely distribution during the current outbreak
  - Clinical, epidemiology, and treatment data
- The monkeypox clinical team is staffed 24/7

First point of contact

- CDC’s Emergency Operations Center: (770) 488-7100
- poxvirus@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov