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

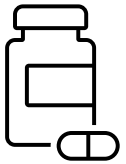
Image: Getty images

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

Medical countermeasures

JYNNEOS

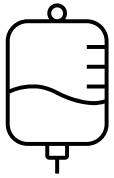
ACAM2000



Tecovirimat (TPOXX)

Cidofovir

Brincidofovir

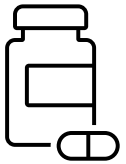


Vaccinia immune globulin

Medical countermeasures

JYNNEOS

ACAM2000



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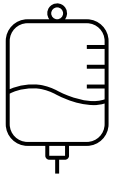


Vaccinia immune globulin

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

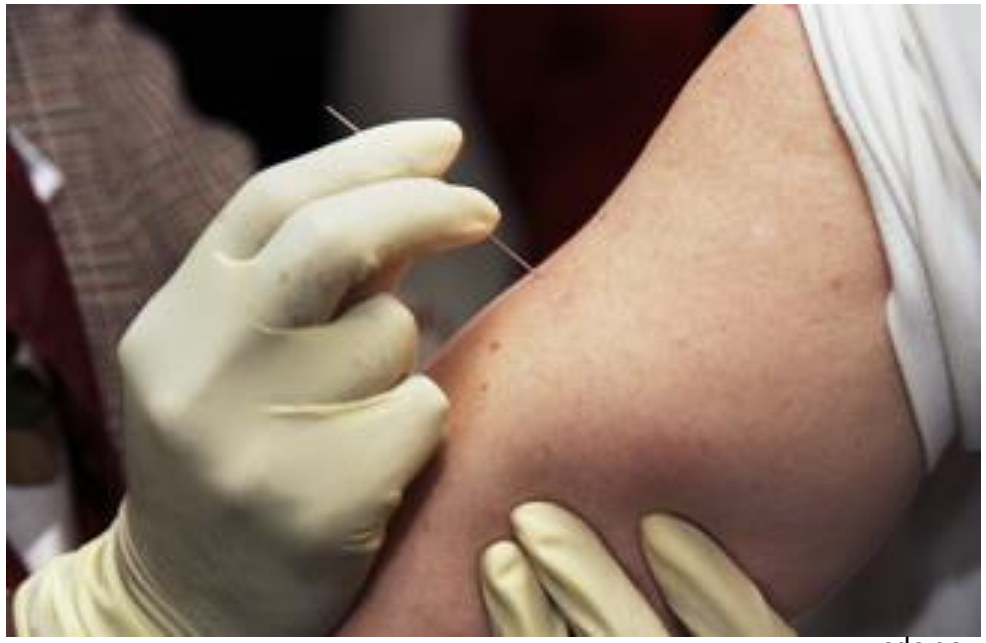
Medical countermeasures: JYNNEOS vaccine

- 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

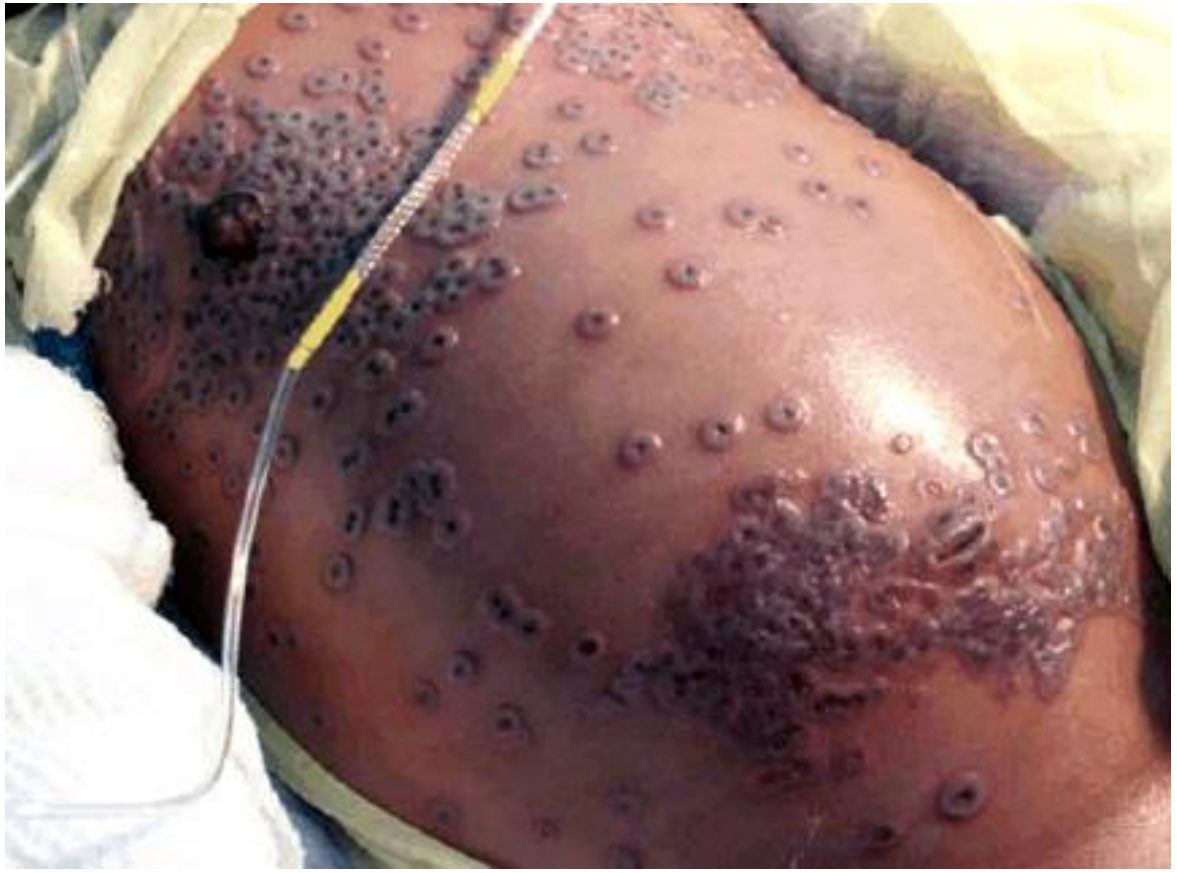


cdc.gov

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

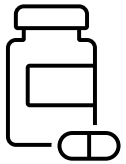


MMWR 2007

Medical countermeasures

JYNNEOS

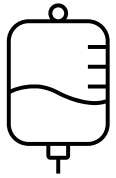
ACAM2000



Tecovirimat (TPOXX)

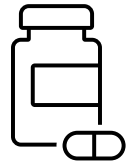
Cidofovir

Brincidofovir



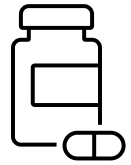
Vaccinia immune globulin

Medical countermeasures: Tecovirimat (TPOXX)



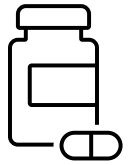
- Antiviral medication developed to treat smallpox
- Approved for treatment of smallpox in adults and children weighing at least 3kg
  - Oral capsule approved by FDA in 2018
  - IV formulation approved by FDA in May 2022
- CDC holds EA-IND allowing its use for other orthopoxviruses in adults and children

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

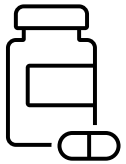


- Cidofovir
  - FDA-approved for cytomegalovirus retinitis
  - In vitro data suggest efficacy against orthopoxviruses
  - Available from the Strategic National Stockpile (SNS)
- Brincidofovir
  - FDA-approved for treatment of smallpox in children of all ages and adults
  - In vitro data suggest efficacy 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



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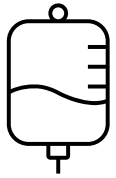
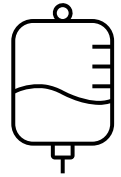


Vaccinia immune globulin

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?

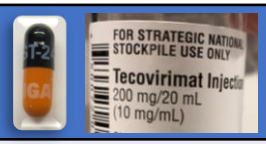
Use of medical countermeasures in 2022 outbreak

- 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	

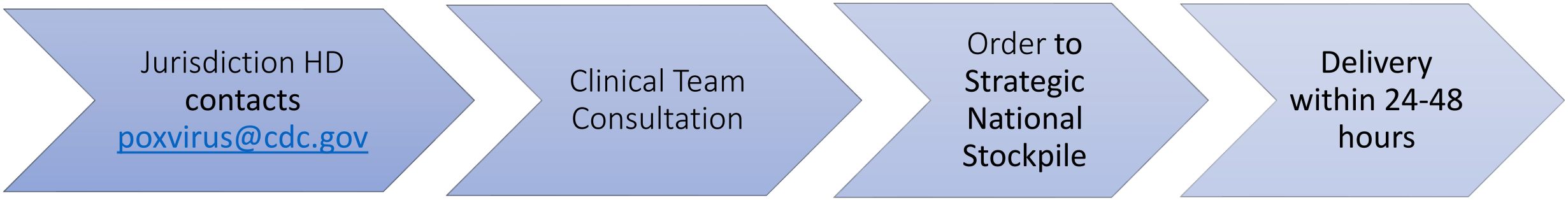
*Jynneos under single-patient EA-IND requiring FDA authorization prior to pediatric administration

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