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
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
- Tecovirimat (TPOXX)
- Cidofovir
- Brincidofovir
- 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
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
- Brincidofovir
- 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

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Vaccine product</th>
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<tbody>
<tr>
<td>Who should receive the vaccine?</td>
<td>ACAM2000</td>
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<tr>
<td>Who should receive the vaccine?</td>
<td>JYNNEOS</td>
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<tr>
<td>Who should be offered the vaccine?</td>
<td>Persons at risk for occupational exposure to orthopoxviruses*</td>
</tr>
<tr>
<td>Who should be offered the vaccine?</td>
<td>Persons who administer ACAM2000 or care for patients with infection with replication-competent viruses</td>
</tr>
</tbody>
</table>

*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
<table>
<thead>
<tr>
<th><strong>Tecovirimat</strong></th>
<th><strong>Jynneos</strong>*</th>
<th><strong>ACAM2000</strong></th>
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<tbody>
<tr>
<td><strong>FDA-approved indication:</strong></td>
<td>Treatment of smallpox in adults and pediatric patients</td>
<td>prevention of smallpox and monkeypox in adults ≥ 18 years</td>
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<td><strong>EA-IND use:</strong></td>
<td>Non-variola orthopoxvirus infection (e.g., monkeypox)</td>
<td>Children &lt; 18 years of age</td>
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<tr>
<td><strong>EA-IND includes:</strong></td>
<td>Informed consent form</td>
<td>Statement of investigator (FDA Form 1572)</td>
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<td>• Case report forms:</td>
<td>• Vaccination record form including AE reporting (AEs of special interest)</td>
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<tr>
<td></td>
<td>➢ Patient intake form</td>
<td>➢ Product accountability form</td>
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<tr>
<td></td>
<td>➢ Adverse events (AE)</td>
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<td>➢ Progress and clinical outcomes</td>
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<tr>
<td></td>
<td>➢ Product accountability form</td>
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<tr>
<td></td>
<td>• Photos and samples of lesions</td>
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<tr>
<td></td>
<td>• PK sampling, serology</td>
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*Jynneos under single-patient EA-IND requiring FDA authorization prior to pediatric administration

PEP: post-exposure prophylaxis

regaffairs@cdc.gov
What is the process for procurement of medical countermeasures?
Procurement Processes

Jurisdiction HD contacts poxvirus@cdc.gov

Clinical Team Consultation

Order to Strategic National Stockpile

Delivery within 24-48 hours
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