Monkeypox Emergency Could Change Vaccine Strategy

The FDA has authorized a new administration method that splits a single Jynneos vial to vaccinate five people.

August 9, 2022 By Liz Highleyman

UPDATE: On August 9, the Food and Drug Administration issued an emergency use authorization that allows the Jynneos monkeypox vaccine to be administered by intradermal injection, splitting a single vial into five doses to stretch the limited supply.

This article was originally published on August 5, 2022.

On August 4, Department of Health and Human Services Secretary Xavier Becerra declared the growing monkeypox outbreak a public health emergency. This follows emergency declarations by the World Health Organization; states including California, Illinois and New York; and several cities with high case numbers.

"Ending the monkeypox outbreak is a critical priority for the Biden-Harris Administration. We are taking our response to the next level by declaring a public health emergency," Becerra said in a statement. "With today's declaration we can further strengthen and accelerate our response further."

> In light of evolving circumstances on the ground, I am declaring a public health emergency on #monkeypox. We are prepared to take our response to the next level in addressing this virus. We urge every American to take monkeypox seriously.
> — Secretary Xavier Becerra (@SecBecerra) August 4,

2022

Earlier this week, President Biden named FEMA's Robert Fenton as the White House national monkeypox response coordinator and Demetre Daskalakis, MD, MPH, director of the CDC's Division of HIV Prevention, as deputy coordinator.

As of August 5, the Centers for Disease Control and Prevention (CDC) has identified 7,510 monkeypox cases in the United States. Worldwide, there are now more than 28,000 cases, most of them in countries where monkeypox had not been reported prior to this outbreak.

While anyone can get monkeypox through close physical contact, cases remain overwhelmingly concentrated among gay, bisexual, transgender and other men who have sex with men, even as testing for other groups has increased. A new report from the CDC describing the first 1,195 U.S. cases shows that 99% were among men.

The emergency declaration enables the federal government to devote more resources to the crisis, allows exploration of a new a dose-sparing strategy to vaccinate more people and encourages states to share data with the CDC.

Increasing Vaccine Access

Monkeypox is related to smallpox, but is less severe, and smallpox vaccines can prevent monkeypox as well. A safe nonreplicating smallpox and monkeypox vaccine (brand names Jynneos, Imvanex and Imvamune) was approved in 2019. It is administered as two doses, four weeks apart. An older vaccine (ACAM2000) can cause severe side effects, especially for immunocompromised people, and produces a lesion that sheds live virus.

Because the monkeypox virus has a long incubation period, vaccines may be used either as post-exposure prophylaxis (PEP) within several days after exposure or as pre-exposure prophylaxis (PrEP) for those at risk. Vaccines are indicated for people with a known close-contact exposure. Based on supply, various cities have expanded eligibility to include men who have recently had sex with multiple partners, those who attended venues or events where exposure might have occurred, transgender people and sex workers of any gender or orientation.

But the vaccine supply has been severely limited, leading to long queues and growing frustration in hard-hit cities. The rollout has been beset by blunders, including allowing millions of Jynneos doses to expire and letting some 800,000 finished Jynneos doses sit unused at a factory in Denmark awaiting a delayed Food and Drug Administration (FDA) inspection.

And while gay men in the United States may be frustrated, people in many other countries—including countries in Africa that have been facing monkeypox for decades—don't have access at all. Adequate vaccine supply and equitable access were among the demands of a protest on Monday at the International AIDS Conference in Montreal.

HHS indicated that, as of August 4, it had shipped more than 602,000 Jynneos doses to states and jurisdictions and has allocated a total of 1.1 million doses. The government anticipates that an additional 150,000 doses will arrive in the U.S. next month. But Daskalakis told reporters that the supply and demand mismatch will probably continue through the summer and into the fall.

The FDA maintains that Jynneos is a two-dose vaccine, and says people need both shots. However, due to supply constraints, many cities have resorted to a one-dose strategy to give twice as many people partial protection as soon as possible, rather than holding second doses in reserve. But given the shortage, it is unclear whether people will be able to get their second dose on schedule.

The efficacy of a single Jynneos dose—or even two doses—in real-world use is unknown; what we do know is based on antibody responses. In a Phase III clinical trial, antibody levels increased for two weeks after the first dose, reached a plateau, then rose to a high level after the second shot.

Another study (MVA-011) found that 67% of HIV-positive people and 83% of HIV-negative people had an adequate immune response four weeks after the first Jynneos dose, rising to 96% and 98%, respectively, after the second shot. This suggest that people living with HIV should be prioritized for second doses, Chloe Orkin, MD, of Queen Mary University in London said at an AIDS 2022 media briefing.

In an effort to stretch the limited vaccine supply, the U.S. is exploring an alternative administration method in which a single-dose vial of Jynneos, which is now given as a subcutaneous injection, is split into five doses injected under the upper layer of the skin, known as intradermal administration. (ACAM2000, in contrast, is administered via a scarification process using a two-pronged needle.)

The skin contains plentiful immune cells, known as dendritic cells, that can recognize viral antigens in the vaccine and trigger a strong immune response. The intradermal method is already used for other vaccines, including the BCG tuberculosis vaccine, but it requires special training and can cause worse injection site reactions site as redness and itching.

So first, why Intradermally? Surprisingly enough, your skin is chockful of cells that can efficiently utilize the antigens from the smaller dose (even if it’s a fraction) and sense, process, and present these in a way that facilitates immune responses (yay for Langerhan cells!) pic.twitter.com/8mqUyUnc4t

— Dr. Neuro ???????? ???????????? (@Neurofourier)

August 5, 2022

A small study in 2015 showed that antibody response rates were similar with subcutaneous or intradermal administration. Researchers were preparing to launch a larger clinical trial to evaluate this approach, but federal officials have apparently decided not to wait. A decision about the alternative method, which would require emergency use authorization, will likely come within the next few days, FDA commissioner Robert Califf, MD, told reporters during an August 4 telebriefing.

“There are some advantages to intradermal administration, including an improved immune response to the vaccine,” Califf said. “It’s important to know that that overall safety and efficacy profile will not be sacrificed with this approach.”

Community Reaction

Experts and advocates generally applauded the decision to declare the monkeypox emergency.

“We urgently need an enhanced and better-coordinated plan to drive our response, including new federal funding and resources for states, cities, health care systems, and sexual health and community-based clinics to support the ramp up of testing, vaccinations and treatment access,” Infectious Diseases Society of America president Daniel McQuillen, MD, said in a statement. “While we have seen some progress in vaccine supply and treatment access, much more is needed to ensure we can equitably reach all of those in need and stop the spread of the virus.”

“Monkeypox has been a health emergency for many in the LGBTQ community for months,” said GLAAD president and CEO Sarah Kate Ellis. “This fast-moving public health emergency requires every possible effort to escalate equitable delivery and production of MPV vaccines and treatments, coupled with urgent, clear and transparent information for every healthcare provider and every American.”

But, some say, words without action are not enough.

“This declaration of a national emergency on monkeypox is a good first step from the federal government. This declaration will allow federal agencies to prioritize resources to provide vaccinations and outreach for those at risk of infection,” said NMAC executive director Paul Kawata.

“However, it is only a first step and there are many questions that must be answered,” he continued. “How will vaccinations be rolled out? How will the federal government ensure not just access to vaccinations but equity in that access? When will the CDC recommend that all gay, bisexual, and other men who have sex with men get vaccinated? How will they make that happen, given issues of stigma and vaccine hesitancy? And how can this be done in the current political

climate without further stigmatizing the LGBTQ community? “Immediate clarity must be provided beyond this federal declaration. Making a declaration of an emergency is an easy step. The hard part starts now. How do we make this all happen?”

Click here for more news about monkeypox.
