CDC COCA Call: Mpox Update: Clinical Management and Outbreaks—June 27, 2024

Good afternoon. I'm Nikki Grimsley, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Office of Emergency Risk Communication at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call, Mpox Update: Clinician Management and Outbreaks. All participants joining us today are in listen only mode. Free continuing education is offered for this webinar, and instructions on how to earn continuing education will be provided at the end of the call.

In compliance with continuing education requirements, all planners, presenters, and moderators must disclose all financial relationships in any amount with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use. CDC, our planners, presenters, and moderators wish to disclose they have no financial relationships with any ineligible companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients. Content will not include any discussion of the unlabeled use of a product, or product under investigational use, with the exception of Dr. Meghan Pennini, who will discuss using Jynneos for populations who are currently covered under EAU, but not on the approved label.

And Dr. Yon Yu, who will provide an update on the eligibility criteria for using tecovirimat for treating mpox, which is an unapproved or investigational use of an approved drug only available in the United States through the USG stockpile. CDC did not accept any financial or in-kind support from ineligible companies for this continuing education. At the conclusion of today's sessions, participants will be able to accomplish the following: discuss the epidemiology of clade II mpox virus and U. S. clinical and vaccine guidance, describe the Jynneos vaccine commercialization, and explain TPOXX EA IND eligibility criteria for treating mpox. After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentation. To ask a question, click the Q&A button at the bottom of your screen. Then type your question in the Q&A box.

Please note that we receive many more questions than we can answer during our webinars. If you are a patient, please refer your question to your healthcare provider. If you are a member of the media, please contact CDC Media Relations at 404 639 3286, or send an email to media@cdc.gov. I would now like to welcome our presenters for today's COCA call.

We are pleased to have with us Dr. Agam Rao, Chief Medical Officer for the Poxvirus and Rabies Branch in the Division of High Consequence Pathogens and Pathology at the Centers for Disease Control and Prevention. Dr. Meghan Pennini, Chief Science Officer for the HHS Coordination Operations and Response Element and the Administration of Strategic Preparedness and Response at the U.S. Department of Health and Human Services. And Dr. Yon Yu, who is leads the Medical Countermeasures Regulatory Support Team in the Office of Readiness and Response at the Centers for Disease Control and Prevention. I will now turn it over to Dr. Rao.

Dr. Rao, please proceed.

Thank you, Nikki. Next slide. Mpox is caused by monkeypox virus, or MPXV, so the name of the illness has changed to mpox, but the name of the virus is still monkeypox virus, or MPXV. There are two clades, or subtypes of MPXV. Clade II is historically known to have been endemic in five countries in Africa, and for decades.

This is not a new phenomenon. And those countries are Nigeria, Sierra Leone, Liberia, Cameroon, and Cote D'Ivoire. Next slide. In 2017, a large MPXV clade II outbreaks started in Nigeria. Next.

In the years between 2017 and 2022, non-endemic countries, like the United States, had some sporadic travel associated mpox cases from Nigeria. There was very little human to human spread associated with those cases. Next. Then during 2022, a cluster of cases was detected in the United Kingdom, and this was a cluster among men who have sex with men, or MSM. The first cases in the U. S. that were associated with that were MSM who had traveled recently from Europe. And then subsequently there was human to human spread in the United States, which has been the main source of cases for the last many, many months or years. Next. Sorry.

Next, sex was found to be an effective means of spread, unlike what has previously been observed with mpox. Next. And men who have sex with men, or MSM, have been most affected. Next. So, what has happened since that May 2022 outbreak has first started? Next.

This is an epi curve depicting months beginning in 2022 by probable or confirmed mpox cases on the y axis. Next. As you can see in August is when the peak number of cases occurred. Actually, late July, early August. Next.

At that time, there were 3,274 cases occurring in that week. And then case counts actually ended up decreasing soon after that. Next. And they went down to very low numbers at the tail end, beginning at the tail end of 2022 and into early 2023, but they never went down to 0. So, mpox cases in the United States have never been zero per year.

Next. And then during, since October of 2023, cases increased a bit, but nothing like the case counts of the peak of this outbreak. They've been stable since that time period, so since October 2023 to present time, the case counts have been stable nationally at 58 cases per week. Next. And this is 2% of the case counts at the outbreak peak.

Next. Okay, now let's take a closer look. Actually, it looks like we may have lost a slide here, but let's take a closer look. I'll just speak to this. A closer look at the time period between October and present time, there have been asynchronous mpox clusters that have been occurring in some jurisdictions.

And you might know that this is attracted some media attention. But these have been asynchronous, meaning that one, a jurisdiction may have a cluster of cases this week, but then next week they have a very low number of cases. And so it's for that reason that the average number of cases per week nationally has stayed at 58 cases per week since October. New York City, though, is an exception. Case counts have not fluctuated as much.

They've remained at a slightly higher level since October of 2023. However, that is still just a fraction of the case counts at the peak of the outbreak in New York City. About 1/20 of the case counts in New York City during the outbreak, and less than 20 cases on a weekly basis. So, even with that slightly higher, the higher numbers that are occurring in New York City since October, the national case counts have remained stable. Next.

I'm sorry, you can stay on that slide. Oh, see those two reverse. Nationally, the demographics are unchanged. But, regionally, demographics and reasons for the cases may differ by jurisdiction. And there are many reasons that regionally the demographics may differ.

There might be low vaccine coverage, particularly in certain racial and ethnic groups. So, if a certain ethnic group has not been getting very many vaccinations, then perhaps they comprise more of the cases in that jurisdiction. Frequent behaviors associated with mpox transmission might also be part of the reason that certain populations have increased cases. So, on this slide, you can see a screenshot from a manuscript that we recently published about an investigation that the Chicago Department of Public Health led into a cluster of cases that occurred in March, sorry, in May of last year, in particular, is when the attention, when there was attention involving a lot of people who were previously vaccinated. And in that manuscript, the authors concluded that perhaps there were increased opportunities for people to have mpox, and that that was the reason for the cluster.

And there may be other reasons as well that we're not aware of that might explain why in individual regions the demographics for patients may differ. But nationally, those have been unchanged. Next. I already went over this, so if you could next, and then next again, and then next again, and then next again. So, at this time, vaccine effectiveness is not waning.

Serologic studies have shown vaccine titers decrease a few months after vaccination. We know that this has gathered a lot of media attention. But levels of circulating titers are not the only marker of protection. There's other markers of protection; cell mediated immunity, innate immunity. And those things haven't been measured.

So, the actual clinical significance of waning vaccine titers is really not known. It's typically real-world data that helps guide our decisions about policy. And there has been some analyses that we performed that were published. And that has shown that infections after 2 Jynneos doses in the United States, or breakthrough infections, as we call them, are very rare. They've occurred in less than 1% of people who were fully vaccinated have been associated with less severe infections when they occur.

And they've occurred at disparate time intervals after vaccination. So, even as recently as a few weeks after the second dose was administered, all the way to several months or even years after vaccination. Next. All of this has led to a CDC recommendation that booster doses are not recommended at this time for people who were vaccinated as part of this outbreak. And if you're interested in seeing more information about the data that went into that, then I would suggest reading the *MMWR* publication, the reference of which is at the bottom of this slide.

Next. So, just to reiterate, at this time, the vaccine recommendations for people impacted by the ongoing outbreak are unchanged. People who have recovered from mpox, or people who have received the recommended two dose Jynneos series, even if it's been two years since they were vaccinated, do not need any additional mpox vaccinations at this time. Mpox vaccinations are recommended, though, for people with certain mpox risk factors who have not been previously vaccinated with both doses, and also not previously recovered from mpox. And I'll go over that on the next slide.

Other people who should be vaccinated now are people who received only one vaccine dose and never had mpox. And those people should receive the second dose as soon as possible, regardless of the amount of time that has lapsed since that first dose was given. They should not have the series restarted. Next. And I just want to highlight that those are the recommendations that are the ACIP recommendations as well.

Next. So, as of October of 2024, when ACIP voted, they recommend vaccination with the two dose Jynneos vaccine series for persons aged 18 years and older at risk for mpox. And when we say a person's at risk, it is referring to the following; gay, bisexual, and other men who have sex with men, transgender people, or non-binary people, who in the past six months have had any of the following; a new diagnosis of greater than or equal to 1 sexually transmitted disease, more than 1 sex partner, sex at a commercial venue, sex and association with a large public event in geographic area where mpox transmission is occurring, the sexual partners of people with the risks described above, so that includes heterosexual woman, for example, who may have sex with bisexual men who have the above risk, risks. And it also includes people who anticipate experiencing any of the above. So, if someone currently does not have more than one sex partner, but they're anticipating having more than one sex partner, then they too would be included if they are gay, bisexual, and other men who have sex with men.

Next slide. After this ACIP vote, the mpox vaccine became, became one of the vaccines on the routine immunization schedule. And this slide shows the routine immunization schedule that is on the CDC website. And on the very last row, you can see that mpox vaccine is indicated for the populations that I just described in detail. Next.

Now, despite this vaccine being available for as long as it has, and the interest that was in the vaccine very early on, there hasn't been that much uptake in the vaccine or interest in getting both doses of the vaccine. The data on this slide is through January 9th of 2024. But we believe that it's not too much different at this time. And at that time, only 25% of the people who are recommended to receive two doses of the vaccine had received both doses of the vaccine. We understand from various focus groups that our experts in the Division of STD Prevention, have conducted that some of the reason might be related to not thinking that mpox is in the news.

What we're hoping that now that this is on the routine immunization schedule, and that clinicians know that it is still a problem in the United States, including causing very severe infections, such as, that result in death, that there may be more, more coverage, vaccine coverage for the individuals most at risk. Next. And then other than vaccine, there's other prevention strategies that are important. Clinicians can counsel patients so that the patients speak with their sex partners about any mpox signs and symptoms and are aware of any unexplained rashes or lesions

on a partner's body. Those patients might also benefit from knowing that close or intimate contact, if they or a sex partner becomes six with mpox, or experience mpox like rash, should be avoided.

Next. So, at this juncture, I'm going to bring up the self-knowledge check question and give you a few, a few seconds here to see if you know the answer. Which of the following is true regarding mpox in the United States? A, nationally case counts are exponentially increasing. B, a booster dose of Jynneos is recommended for anyone who received both doses of the two dose vaccine series during 2022, see people eligible to be vaccinated who have received only one Jynneos dose and then never had mpox, should receive a second Jynneos dose as soon as possible Jynneos dose as soon as possible; i.e., complete the two-dose series. And D, Jynneos vaccine is recommended for all men who have sex with men, including those in a monogamous relationship. Okay, next slide. And the answer here is C, people eligible to be vaccinated who have received only one Jynneos dose and have never had mpox should receive a second Jynneos dose as soon as possible; i.e. complete the two-dose series. And the rationale for this is that U. S. case counts have been stable since October of 2023, as I mentioned. Vaccine effectiveness is not waning.

And, therefore, booster doses are not recommended at this time. People who received one dose of the vaccine should receive the second dose as soon as possible; i.e., not restart the series. And people in monogamous relationships do not have the sexual risk factors for which ACIP recommends vaccination.

If we were to recommend vaccination for everyone who is a gay or bisexual man, then we would, we would just be alarming people unnecessarily when they do not have the risk. And we'd be increasing the number of people who are recommended to receive the vaccine from roughly 2 million to 6 million. And so we do want to make sure that the criteria is followed. Next slide. And now I'm just going to spend a few minutes talking a little bit about clade I MPXV.

Next. Most importantly, I want to start by saying at this time, there were no clade I cases identified outside of countries known to be endemic for this MPXV clade. Next. Similar to clade II, clade I MPXV has historically known for decades to be endemic in certain countries. And when I say for decades, I'm saying 1970 was the first human case recognized in the Democratic Republic of Congo.

Other than the Democratic Republic of Congo, or DRC, Central African Republic, Republic of Congo, Cameroon, and Gabon all have, all are endemic for MPXV clade I. Next, next slide. There's a large outbreak right now that has been recognized in DRC, or the Democratic Republic of Congo, since 2023. So, there are some notes of sort of what happened in Nigeria, where there was initially a large outbreak in Nigeria, and then travel associated cases to other countries. So far, there have been no other cases, no cases outside of endemic countries.

But what makes this outbreak in DRC particularly concerning is that cases have an identified in parts of the country from which cases were not previously reported, including those in conflict regions, and those on the border with other countries. Some cases are associated with sex. However, both genders are involved, and children are also impacted, so there is more going on.

Next slide. This table depicts the number of suspected and confirmed cases, and also suspected deaths that have occurred in DRC since 2021.

And, as you can see from the last two rows of the table, the number of suspected cases and suspected deaths during 2023, and so far in 2024, have been higher than in previous years. Only a fraction of these cases are laboratory confirmed. And there remains a lot of other unknowns. For example, the suspected cases, some of them, at least, might be due to other, other infections, other outbreaks, like measles. But the large number of cases still is concerning, including that there are confirmed cases that have occurred in other parts of the country.

Next slide. There are several ways that clade I and clade II MPXV are similar. First off, with the clinical presentation. Both of them have a similar clinical presentation of firm, deep seated, sometimes umbilicated lesions. And they both present along the clinical continuum.

So, some cases are mild, and some cases are severe in both MPXV clade I and clade II. The transmission of the viruses are similar, so contact with skin lesions is the most common way that fomites and respiratory secretions, like, for example, via kissing, are all ways that these can spread. Contact with infected animals in endemic settings has also, is also known to be a problem, but wouldn't be an issue here in the U. S. Diagnostic testing wise, FDA cleared non variola orthopoxvirus, or NVO, test, used by many laboratories, and could be used for both.

As far as hospital waste management goes, both of them are considered Category B. In terms of IPC for healthcare providers, it's the same protection; gowns, gloves, eye protection, N 95s. And in addition, there needs to be standard precautions. I'm sorry, in addition to standard precautions, suspected mpox infections have additional IPC precautions. Patient management is dependent on the severity of the illness, potential for severe illness, and the use of the Jynneos vaccine and therapeutics is expected to be effective regardless of the clade.

The two viruses are very similar. There's no difference expected for Jynneos, for Tecovirimat, for any of those, regardless of the clade. Next slide. There are ways, though, that these two are different. The populations impacted might not be exclusively or predominantly MSM, if clade I were to spread to the United States.

It's uncertain if other populations could be impacted. But we are most concerned about the fact that sexual contact seems to have been a very effective means of spread. Transmissibility wise, clade I MPXV is associated with more viral shedding, and so we could see more secondary cases as a result of that. Clinical presentation, more of the severe cases could occur with clade I MPXV, but as I mentioned, there's still that continuum of some cases being mild, and some cases being severe. Disseminated lesions, prodromal symptoms, and hospitalization all occur with both, but might be more obvious with clade I infection.

Diagnostic testing wise, clade II specific testing is available in some laboratories, but not others, to distinguish between the two. And from an IPC standpoint, patients may shed more virus. And so adherence to IPC practices are particularly important. They're important for both, bullet just saying that knowing that there is going to be, there is the likelihood of more viral shedding with clade I, IPC practices should be particularly adhered to. Next slide.

So, if clade I cases were to occur in the United States, we're recommending that similar clade II spread, there might be travel from other countries that is the source of the earliest infections. We would still expect close to stay in contact for transmission to occur. And we are concerned about sexual exposures, because of how efficient that means of, that has been as a means of spread, particularly among men who have sex with men. If clade I cases occurred in the U.S., then there would be further specific guidance that would be issued. At this time, we have a practice enhanced precautions clinical guidance for people who travel to the Democratic Republic of Congo, and do not have a recommendation for vaccination. Next slide. CDC is working really hard on a lot of clade I specific preparedness activities, clade I specific testing is occurring for positive specimens in the United States. Some commercial laboratory tests can rule out clade I and CDC is collaborating with many private and public health laboratories as well for patients with suspected mpox, and a history of recent travel to DRC.

We're recommending that clinicians contact public health authorities as soon as possible, because even though this clade specific testing is occurring, if you have that high suspicion, then clade specific testing can be expedited. We are asking that people be vaccinated who are at risk for mpox because of the ongoing clade II outbreak, because of the chance that those are the, those individuals may also be at increased risk for clade I, should there be cases in the United States. And for awareness purposes, CDC is assisting public health authorities in DRC. We have had a history of over 15 years of collaborating with DRC colleagues about mpox in particular and have staff who are in the DRC and who are trying to assist the country with their country led effort to respond to this outbreak. And then as I already mentioned, at this time, because the outbreak in the DRC is still, it's still considered a rare illness, there's still a lot that needs to be sorted out, there is no recommendation for vaccination before travel to the DRC.

Next slide. And then just to conclude with some take home messages, as far as clade II goes, it continues to circulate in the U. S. Nationally, clade II MPXV case counts have been stable since October of 2023. Regionally, clusters have occurred, and there are differing reasons that may explain these cases, but waning, waning protection is an unlikely reason.

Increasing the two-dose vaccination coverage and counseling patients about other prevention strategies are the best ways for clinicians to prevent cases. And if clade I, at this time, there are no clade I Mpox cases outside of endemic countries. Clinicians should contact public health authorities if they suspect clade I in a patient with recent travel to DRC, and CDC is engaged in the clade I response in DRC, and actively preparing in the event of spread to the United States. And I'll now pass it over to the next speaker. Next slide.

And then next.

All right, thank you so much, Agam. Hi, everyone. Glad to be here. And just have a few slides to update you on where we are with Jynneos mpox vaccine availability. So, I am Meghan Pennini.

I am working for ASPR. Next. So, we just heard a great breakdown of the epidemiology of mpox and where we are now. As you just heard, the case counts do remain low. However, we know, right, that vaccination remains an important way to ensure individuals, at risk individuals are protected, and that we keep those case counts low.

Next slide. As a reminder, Jynneos is an FDA approved vaccine for prevention of both smallpox and mpox disease, and has approval for adults 18 years and older, who are at high risk for infection. And as we just heard, currently this vaccine is on ACIP routine immunization schedule, again, for certain individuals, as we just heard. Jynneos also has an active EUA, an emergency use authorization. And that is for subcu injection for prevention of mpox disease in individuals younger than 18 years of age who are determined to be at high risk for mpox infection.

So, that EUA is still active. Jynneos should be administered as two injections. And that's a two-dose series. Those two doses should be given ideally around 28 days apart. Or as soon as possible, if more time has elapsed since the first dose, again, as we just heard.

Next slide. So, for those of you who have been paying attention to this outbreak, you may remember that beginning in May of 2022, HHS did make a Jynneos vaccine available from our strategic national stockpile under the national mpox vaccination strategy that was stood up at that time. And we're now working to transition away from distribution for the strategic national stockpile and get things over to the commercial market. So, here are some timelines that just sort of, or some of the important states that represent the timeline of this transition. So, as you may recall back in February of 2023, there was an ACIP recommendation for at risk adults during an outbreak.

But as we just heard, the October 2023 ACIP recommendation is the one that is updated, and that is for routine vaccination of adults at risk of mpox infection. So, that is the current ACIP recommendation. On April 1st of this year, Bavarian Nordic, who is the manufacturer of Jynneos, made this vaccine available for commercial purchase. So, this is readily available on commercial market right now. And we are hearing that this commercial workflow is going well.

On April 30th, we at HHS started to wind down our distribution of Jynneos from our strategic national stockpile. And on August 1st, we plan on making a full transition of Jynneos to the commercial workflow, meaning we will no longer be distributing Jynneos. And you can access that product, again, through your usual commercial channels. Next slide. So, I just want to discuss sustained access for various populations as we are now transitioned to commercial availability.

So, I just want to remind everyone, for Medicaid and Medicare, because this is within the ACIP recommended immunizations, there is full coverage for all beneficiaries, Medicare and Medicaid beneficiaries, that fall within the ACIP recommended populations. For commercial insurance, so for those who have private insurance, we do expect, and we are hearing, that private insurance plans do intend to fully cover this product. Again, likely within the ACIP recommendations. And just a reminder that these private insurance plans are obligated to cover the first plan year that begins one year after the ACIP recommendation. So, while they're not fully obligated right now, we are hearing that they do intend to cover, and we are hearing that there is coverage.

Next. So, for those who are underinsured, or uninsured, for under or uninsured individuals, we rely on some of the programs, the immunization programs we rely on for other immunizations, such as the 3, CDC 317 & Vaccine for Children Programs. And those will be available. So, this

vaccine will be available under those programs. Of course, for Vaccines for Children, that provides vaccines for uninsured and underinsured, when served in certain clinical sites, such as FQHCs and rural health clinics.

That, of course, in this particular case, only applies to 18-year-olds, because, again, of the ACIP recommendation being for 18 years and above. For those 19 years and above, the 317 program can be used by jurisdictional partners to serve some of those adults. And we do expect the ordering through those programs to open on or near August 1st of this year, so just a few in about a month or so. Next. Of course, Ryan White and other HRSA supported clinics are also important engagement points for the populations that are at risk.

And those can also provide access for under and uninsured populations. HRSA grant and Ryan White HIV/AIDS Program funding may be used to purchase and administer Jynneos vaccine. And there's more information around that, at that link, that hrsa. gov link that's on this slide. We'll also mention that there's 340B Prime Vendor Programs that are up and running that can offer reduced price to eligible provider sites, again, such as FQHCs and others.

Next. And just want to let you know that retail pharmacies, we know that there are appointments available at several pharmacy chains, and certainly other pharmacies are also making this, again, available, such as CVS, Rite Aid, and Walgreens. We know those are accepting appointments now in states that allow pharmacist administration of this vaccine. So, not all states necessarily. Next slide.

And that is it for this section. So, we'll just wrap up with a self-knowledge check. And we'll give everyone a minute just to think about the answer here. Which statement best describes insurance coverage for the commercially available Jynneos vaccine? A, since the product is only available under emergency use authorization, there is currently no insurance coverage expected. B, as an FDA approved and ACIP recommended vaccine, both Medicare and Medicaid provide full coverage for at risk beneficiaries aged 18 years and older. C, the product is not expected to be covered by commercial insurance plans for any age group. Or D, insurance plans are expected to cover only one dose of the two-dose series, with additional doses paid out of pocket. And I think we can go to the answer on the next slide. So, the correct answer is, of course, B, Medicare and Medicare, sorry, Medicaid, and Medicare, fully cover Jynneos to those individuals, again, within the ACIP recommended populations. As a reminder, private insurance plans are also expected to fully cover this vaccine.

And I can hand it over now to Dr. Yu to take you through the next section.

Thank you, Dr. Pennini. Good afternoon. I am the Team Lead for Medical Countermeasures Regulatory Support Team within the Office of Readiness and Response at CDC. I will be highlighting the recently updated Tecovirimat Expanded Access Investigational New Drug Protocol that further specifies the eligibility criteria for treatment of mpox.

Next slide, please. Let's start with a brief background on Tecovirimat for some context and perspective. Tecovirimat, also known as TPOXX, is a novel antiviral drug that was developed and stockpiled by U. S. governments for smallpox preparedness.

It is FDA approved, only for the treatment of smallpox based on animal efficacy data that showed survival benefit over placebo, and human safety data from 359 healthy adult volunteers. While there are ongoing randomized clinical trials to evaluate efficacy and safety of Tecovirimat in people with Mpox, its efficacy and safety in treating any human orthopoxvirus infections have not yet been determined. Also, Tecovirimat use for treatment of mpox's investigation since it is not FDA approved for mpox indication. For all these reasons, Tecovirimat access is through the clinical trials sponsored by the National Institutes of Health, known as Study of Tecovirimat for mpox, or STOMP, or CDC's expanded access IND protocol, which is for compassionate use. CDC's expanded access IND protocol that existed prior to the 2022 clade II mpox outbreak was to allow direct use in rare occasions of occupational exposure in laboratorians or traveler associated cases.

However, it provided a regulatory means to make stockpiled Tecovirimat available at the start of the mpox outbreak, including the subsequent prepositioned managed deployment of positioning supplies, while getting the randomized clinical trial up and running. NIH's STOMP launched in September 2022 and continues to actively recruit patients with mpox for voluntary participation. Next slide, please. Per FDA regulations, the expanded access IND use must be for treatment of serious or life-threatening disease, or condition when there is no comparable or satisfactory alternative therapy. It is, it also requires that expanded access IND use not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use.

For additional context with more than 32,000 cases that were reported in the U.S. from the 2002 outbreak, there were only 58 deaths reported. So, fortunately, the mortality has been low, mpox less than 02%. Under the expanded access IND, there have been more than 79,000 patients prescribed with Tecovirimat.

Starting September 2022, CDC's interim clinical guidance, and EA IND protocol, recommended that Tecovirimat used to be in patients who have or are at high risk for severe disease due to severe immunocompromise, such as advanced or poorly controlled HIV. However, based on the returned IND forms, most patients were treated as outpatients for mild to moderate illness that included patients with controlled HIV, as well as HIV negative patients. Most commonly reported reasons by providers for having prescribed Tecovirimat were lesions in sensitive anatomic areas, and pain including where pain was the only reported reasons for some patients. These characteristics alone, without immunocompromising conditions, or other underlying conditions, were not part of the recommended use per CDC's interim guidance, or EA IND eligible patients for Tecovirimat. Expanded access IND use is not adequate to determine efficacy, given the inherent limitations and highly variable nature of data collection and reporting.

So, even with nearly 8,000 patient uses, which probably underreporting, we still don't know whether Tecovirimat provides clinical benefit, which it may very well do so, in whom it benefits, and what those clinical benefits are exactly. And this cannot be answered without randomized clinical trial data. Again, for these reasons, oral Tecovirimat access for treatment of mpox is primarily through the enrollment in NIH's STOMP clinical trial, which has a placebo controlled randomized arm, and an open label Tecovirimat treatment arm. Remote enrollment is also

available Monday through Friday. CDC's expanded access IND protocol remains available for IV and oral Tecovirimat for patients who meet the EA IND eligibility criteria.

Next slide, please. Next slide, please. Last week, I'm sorry, could you go back one slide? The one that's titled, I'm sorry, 46? Thank you. Last week on June 18th, CDC posted and sent out an e mail notification on the revised expanded access IND protocols that updated the eligibility criteria. So, what are the changes? Listed on this slide are the patient groups who can receive Tecovirimat under the current version of the protocol, which is Version 6. 4, dated June 5th, 2024. Please refer to the protocol for details, which is posted on the CDC website. And the link is included in my last slide. The same three primary patient groups eligible for Tecovirimat under the EA IND protocol, as before, are retained. However, those with severe immunocompromise is listed first, since this group is known to be at high risk for protracted or life-threatening manifestations of mpox.

Also, so severe immunocompromise, compromising conditions are now better defined in the protocol, which also aligns with STOMP's definition of immunocompromising conditions for their open label arm. Only difference between STOMP's definition and CDC's for immunocompromising conditions in the list under number one is regarding HIV, where STOMP defines and controls HIV for their open label arm, as either CD4 count less than 200, or HIV RNA greater than 1,000 copies per ml, where CDC uses CD4 count only, and we have included the last bullet under number one, other comparable immunocompromising condition. Patient categories under number two stay pretty much the same as before. The active skin conditions that are defined as listed here on this slide have replaced what was previously listed as conditions affecting skin integrity. The revision now is exactly the same as the active skin condition for STOMP's open label arm criteria.

Pregnant or lactating persons and children have always been eligible for treatment under the EA IND protocol and are retained with just the clarification that their eligibility is irrespective of illness severity or underlying conditions at presentation. Lastly, what was previously referred to as severe disease has been revised to patients with protracted or life-threatening manifestations of mpox as listed under number three on the slide. The use of protracted or life threatening is intentional to underscore the life-threatening disease that the EA IND use must be for per the earlier of FDA regulatory requirements, and to differentiate from STOMP's severe disease definition, which is less strict. The involvement of anatomic areas which might result in fewer sequelae, have been removed completely. This was associated much subjective interpretation and reported reason for prescribing Tecovirimat, even in those individuals without any immunocompromising or active skin conditions.

Next slide, please. The reason for revised EA IND eligibility criteria are to ensure Tecovirimat access for patients with mpox through STOMP and EA IND that will help facilitate appropriate drug use while allowing for evaluation of Tecovirimat efficacy through STOMP, which also includes evaluating pharmacokinetics to determine the correct clinical dose and duration. The critical questions on whether Tecovirimat helps, does nothing, or possibly harms in treating human mpox cannot be answered without clinical trial data. And lack of clinical trial data hampers making informed policy clinical and regulatory decisions regarding Tecovirimat use and access. Furthermore, indiscriminate use of Tecovirimat have the risk of developing

resistance, since it has a low barrier to viral resistance, which prompted FDA's notice for judicious use of Tecovirimat.

Resistance has been identified in over 50 patients with mpox, including those who developed treatment resistance to Tecovirimat, 11 in Tecovirimat naive individuals, and most recent new cluster of Tecovirimat resistant mpox virus variant detected in 18 patients from 5 states. Next slide, please. The VENN diagram also posted on the CDC's website summarizes the oral Tecovirimat access via STOMP versus IND protocol. Between these two routes, it provides Tecovirimat treatment option for virtually anyone with mpox. And the left blue circle is STOMP information, starting with the inclusion criteria, which includes illness onset less than 14 days, that's one active lesion, or proctitis, and no prior or concomitant Tecovirimat receipt qualify individuals for STOMP.

Pregnant or lactating persons and children are allowed up to three days of STOMP's prior to enrollment. STOMP's placebo controlled randomized arm is for non-pregnant or non-lactating adults with mild illness who do not have severe immunocompromised or active skin conditions. Two thirds of participants in the randomized arm of STOMP received Tecovirimat. If participants in the randomized arm develop severe disease or have persistent severe pain, they are moved to the open label arm of Tecovirimat where they receive Tecovirimat. In the middle are the patient groups that would have treatment options, either through STOMP or EA IND protocol.

On the right tan color circle, the EA IND eligibility groups that were just previously described. Next slide, please. I won't typically have walked through the algorithm here, but it is provided as an example algorithm in case helpful in determining STOMP versus EA IND for Tecovirimat access. However, I do want to note that for STOMP eligible patients, providers help departments and/or patients to call or can call the STOMP call center to be connected to a study site that can help the quickest, rather than to directly contacting each individual study site. This is per the NIH's study, study team's recommendation.

For patients not STOMP eligible but meets EA IND eligibility providers to contact their local health departments to see if any remaining supply from prior pre-positioning of oral Tecovirimat still are available. We recognize that large scale pre-positioning has stopped, since it doesn't justify with the sustained locations of mpox. However, any unexpired local supply that may remain can be used for patients who meet EA IND eligibility, without contacting CDC or getting CDC's prior approval. If no local supply remains available, health departments should contact the CDC Emergency Operation Center to request Tecovirimat on behalf of the providers. Next slide, please.

The next two slides are a quick reminder on additional stockpiled therapeutics available for treatment of mpox. Oral Brincidofovir, also known as Tembexa, is a prodrug of Cidofovir. It is FDA approved, only for treatment of smallpox based on animal efficacy data, and is not approved, FDA approved from mpox, similarly as Tecovirimat. Therefore, it is available from the stockpile to clinicians who request and obtain an SBA authorized single patient's emergency IND use, or patients who meet FDA's EA IND criteria, which was recently updated. The yellow highlights reflect FDA's recent revisions, which defines severe disease.

And they've added two additional bullets to include open label participants as being eligible for Brincidofovir treatment, and to initiate Brincidofovir simultaneously with Tecovirimat in severely immunocompromised patients. This is, again, a reminder for clinicians that Brincidofovir EA IND request is directly to FDA, and the information on how to submit the EA IND request FDA are posted on FDA and CDC websites, the links that I'll, again, include in my last slide. Next slide, please. Vaccinia immune globulin intravenous is FDA approved for treatment of complications due to vaccinia virus vaccination. This product VIGIV, is available for treatment of mpox under CDC's IND protocol for VIGIV, again, since it doesn't have mpox indication as part of FDA approved use.

The considerations for VIGIV are for patients with protracted or life-threatening manifestations of mpox, patients with clinically significant disease progression while receiving Tecovirimat, such as initial improvement, followed by worsening signs and symptoms, for patients who may be clinically suspected of having Tecovirimat resistance, and/or patients allergic to, allergic to components of Tecovirimat. Or requesting VIGIV, providers and health departments can contact CDC clinical consultation team by e mail listed there during business hours, or CDC Emergency Operations Centers. Next slide, please. These are the references mentioned. Next slide, please.

I'll be concluding with a self-knowledge check question. Which statement regarding Tecovirimat for treatment of mpox is false? Tecovirimat is not FDA approved for treatment of mpox. The oral Tecovirimat for treatment of mpox is primarily available for the NIH's STOMP clinical study. Tecovirimat for treatment of mpox under CDC's expanded access IND protocol must be for those who meet eligibility as defined in the CDC’s expanded access of the IND protocol. Those who are EA IND eligible for oral Tecovirimat can also receive the drug through enrollment in the open label arm of STOMP.

E, patient, a patient with HIV CD4 count of 400 who has proctitis and pain due to mpox for the last two days, can be treated with Tecovirimat under the EA IND protocol. And we'll go to the next slide for the answer. The correct answer is C, the rationale being that this patient does not meet the EA IND eligibility. However, the patient has the option of enrolling in the placebo controlled randomized arm of STOMP where two thirds of participants are randomized to the Tecovirimat treatment arm. Those who have persistent severe pain will be moved to the open label arm of STOMP.

And I believe that concludes my slides. And then I'll turn it back over to Marcy. Thank you.

Presenters, thank you for providing this timely information with our audience. And we will now go into our question-and-answer session. Please remember that to ask a question, click the Q&A button at the bottom of your screen. Then type your question. Joining our presenters today for the Q&A session are Dr.

Christina Hutson, Senior Science Advisor for the CDC Clade I Mpox Response, and the Chief of the Poxvirus and Rabies Branch at CDC. And Timothy McLeod, the Syndemic Partnerships Coordinator on the Strategic Partnerships Team in the Office of Policy, Planning, Partnerships, and Communication, in the Division of HIV Prevention, in the National Center for HIV, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention. Our first

question, for providers with patients who are ineligible for STOMP's open label arm, but meet EA IND eligibility for Tecovirimat treatment, who should they contact to see if any oral Tpox remains available within their jurisdiction from the prior pre-positioned supply? Yon, do you want to take that question? I'm not hearing Yon. Is anyone else hearing Yon?

No, I can't hear her either. I think I can take it. Oh, there she is. There she is.

Oh, sorry. Oh, go ahead. I just realized I was on mute. Go ahead, Meghan, if you would like to take that question.

Oh, well, actually, Yon, I was going to add that…people should call their public health, public health departments to see if there is any Tecovirimat that is, that is still in place that is not expired and that is pre-positioned, and that if there is no product that is pre-positioned, that they can contact CDC through either a pox virus at cdc.gov, or through the Emergency Operations Center number, but it really is the state, the health department that our Emergency Operations Center is expecting to hear from, and not from individual clinicians. And so that's why we ask that clinicians reach out directly to their health department first. Meghan, were you going to add anything to that?

No, I think that covers it.

Okay, thank you.

Could I just? I'd just…is correct. I just need to add that many of the health departments also have the practice in sending out notifications to their jurisdictional or health providers in clinical facilities on whether they still have any remaining oral Tecovirimat from prior preposition that remains available or not. So, we also wanted to just note that, that health departments also take that proactive action.

Thank you. Is it possible for those who were vaccinated and are still getting, is it possible that those who have been vaccinated are still getting infected, but are asymptomatic?

I can take that question. I think that there are people who are probably having very mild cases after vaccination, so they might not personally recognize that they have an infection, that they have a single lesion if they have two lesions. And so there might be those subclinical cases. As far as completely asymptomatic, I don't know. I think some clinical cases are probably indeed occurring that that might, that that might occur, and that might lead to some spread.

Thank you. Our next question asks, can you address ventilation considerations in terms of infection, prevention, and control practices?

You know, we don't have any of the experts from the Division of Healthcare Quality and Promotion on this call, and so I think we should probably come back with this answer, and not try, not try for those of us on this call to answer that question. But, Nikki, if I can, is it all right, I noticed there were a couple questions about the ACIP recommendations. Is it okay with you if I try to, try to address those?

Sure, go ahead.

So, there were some questions about why it is that a booster dose is recommended for some laboratorians who are at risk for exposure to, occupational exposure to Orthopoxviruses, but not the people involved in this current outbreak, including the laboratorians who might process specimens and test those for mpox. And the reason for that is that there's a different level of risk associated with people who are working directly with monkeypox virus, and directly with variola virus. That ACIP recommendation that calls for a booster, boaster dose every two years, was intended for those individuals who were working directly with the virus. And they have a higher-level exposure. That's a different level of risk than what the patients who were being exposed to mpox have.

And also the clinical laboratorians who are working with specimens that might contain monkeypox virus. And that's the reason that the vaccine booster doses are different. You know, if things change, I mean, things do change, things are evolving. If there is any indication that there are breakthrough infections occurring, then, of course, the recommendations for a booster dose would change. But at this time, that's what they are.

And then someone else had made a comment asking why it is that people who might not know the sexual and might not know whether they are having sex with someone who has multiple sexual partners, can get vaccinated. And the current wording of the ACIP recommendations actually should allow for someone like that to be vaccinated. That's what we have that if someone anticipates these risks, that they anticipate that they may have or may be having sex with someone who meets that criteria, who is having sex with multiple sexual partners, and they can be vaccinated. So, our so that the necessary people would get vaccinated. And then back to you, Nikki.

Thank you so much. We have time for one more question. And there were actually several questions related to this, so we'll try to condense it into just one kind of general question. But talking about travel and the vaccine, should Jynneos be considered in individuals traveling to areas with local mpox outbreaks?

Yeah, so at this time, there is no recommendation, travel associated recommendation, but the 2022 ACIP recommendations do say that for those who are part of mpox response teams, and by that we mean someone who might be traveling to DRC as part of Doctors Without Borders, for example, or providing care to patients with mpox, then those individuals should be vaccinated, because they don't have access to the PPE that we have here in the United States. As far as people who are working in DRC, it's still a rare disease in most parts of the country. I think there was something in the chat about South Kivu. And the state department really isn't allowing people to travel to South Kivu for work, because it is a conflict region, so I don't think that in the high concentration regions where there is mpox, people would be traveling for work. If there is such a situation that arises for someone who is traveling for other reasons, then please do reach out to us at poxvirus@cdc.gov, and we can handle those situations on a case-by-case basis. But we're just not aware of this happening much, if at all, and want to keep the recommendation as simple as possible at this time.

Great. Thank you very much. And, again, thank you to all of our presenters for answering these questions, and for sharing your expertise with us today. This year, CDC is moving from the training and continuing education online, TCEO system, that provides access to CDC educational activities for continuing education to CDC TRAIN. If you do not already have a TRAIN account, please create one at https colon forward slash forward slash www. train. org forward slash cdctrain. All new activities that offer continuing education from CDC will only be listed in CDC TRAIN. CDC TRAIN is a gateway into the TRAIN learning network, and it is the most comprehensive catalog of shared public health training opportunities. This transition will allow you to access noncredit and for credit educational activities and track your learning, including CE, in one place.

Many CDC accredited activities are listed in CDC TRAIN. The move to one system approves efficiency and makes it easier for learners, CDC staff, and partners to offer and earn continuing education in one place. You can continue to use TCEO for existing activities that have CE, which are set to expire in 2024, since these courses will not move to CDC TRAIN. You may also use TCEO for existing activities with CE that are set to expire in 2025 before the courses transition to CDC TRAIN next year. If you begin one of these courses in TCEO, we will let you know when the course will move to CDC TRAIN.

You can access and download CE transcripts and certificates in TCEO through the end of 2025. Instructions will be available on both platforms, and a learner support team will be available to answer questions. All continuing education for COCA calls are now issued through CDC TRAIN. Those who participate in today's live COCA call and wish to receive continuing education, please complete the online evaluation and posttest before July 29th, 2024, with the course code WC4520R 062724. The registration code is COCA062724.

Again, that's COCA062724. Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between July 30th, 2024, and July 30th, 2026, and use course code WD4520R 062724. Today's COCA call will be available to view on demand a few hours after the live call ends at emergency.cdc.gov forward slash coca.

A transcript and closed-captioned video will be available on demand on this call page about a week after the live session. You can also visit emergency.cdc.gov forward slash coca for more details about this COCA call and other upcoming calls. We invite you to subscribe to receive announcements for reach COCA calls by visiting emergency. cdc.gov forward slash coca forward slash subscribe.asp. You will also receive other COCA products to help keep you informed.