

# Going Viral: Testing, Diagnosis and Treatment of COVID-19

with

**Angela Leclerc, MSPA, PA-C**

**Stephanie Podolski, MPH, MSPA, PA-C**

**Sampath Wijesinghe, DHSC, AAHIVS, PA-C**

## ***EPISODE 4: TREATMENT OPTIONS: MONOCLONAL ANTIBODIES***

**ANGELA LECLERC:** Hello and thank you for joining us today. My name is Angela Leclerc, I'm a PA working in Critical Care in Portland, Maine. You are tuning into the Going Viral: Testing, Diagnosis, and Treatment of COVID-19 podcast series, developed by the American Academy of Physician Associates and supported by an independent education grant from Pfizer. The goal of this series is to provide education and tools to assist PAs and other clinicians in providing patient-centered care in the early recognition, diagnosis, and management of patients presenting in the outpatient setting with symptoms of COVID-19.

The COVID-19 pandemic is now entering its third year, and while cases are abating, new variants continue to emerge along with the threat of new surges in infections. In addition to having three effective and approved vaccines in the United States, new therapeutics have arrived in the clinic that have the goal of preventing serious illness, hospitalization, and death.

Throughout the pandemic, PAs have played a critical role in helping combat COVID-19. As diagnosis and treatment shift to the outpatient setting, PAs are ready to meet the challenge on the frontlines. This is the fourth episode in a five-part podcast series focused on monoclonal antibodies. I'm proud to be joined by Steph Podolski, who is a PA working in Hospital Medicine in Augusta, Maine, with a Master's of Public Health, and Dr. Sam Wijesinghe, who is a PA and Clinical Assistant Professor of Medicine at Stanford University with a Doctorate in Health Sciences.

Before we get started, to recap our last three episodes, we have reviewed testing and diagnosis, risk stratification, addressed some social determinants of access to testing and treatment, as well as antivirals. Today's episode will focus on monoclonal antibodies, which have shown promise in the outpatient setting. It has been important to note that with the rapidly-changing information and data for treatment, many of us have felt at times that we may be behind in understanding certain treatment options for acute COVID-19 infections. Additionally, we have seen higher rates of provider and healthcare worker burnout than ever before. Our hope in this podcast is to provide some additional resources for frontline healthcare providers that are treating COVID-19 patients.

I am anxious to hear about the recommendations for monoclonal antibodies. Simply put, monoclonal antibodies are antibodies that are made in a laboratory,



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The Testing, Diagnosis  
& Treatment of COVID-19



administered intravenously or in some cases intramuscularly, and designed to fight off a particular infection, in this case, COVID-19. They target the spike protein and have variable efficacy, depending on the strain of COVID-19. Sam, what are our options for monoclonal antibodies?

**DR. SAM WIJESINGHE:** Yeah, please allow me to share a few highlights about monoclonal antibody. In 2020, the FDA issued an emergency use authorization to allow monoclonal antibodies as a treatment option for COVID-19. So Angie already touched on this a little bit, the monoclonal antibody can block the virus that causes COVID-19 from entering cells in your body and limit the amount of the virus within your body, so this means you may have milder symptoms and may decrease the likelihood of you needing to stay in the hospital. One other thing I really like to highlight, the monoclonal antibody for COVID-19 is different from COVID-19 vaccine. The vaccine triggers your body's natural immune response, but this can take a few weeks to develop enough antibodies against the virus, so if you have the virus right now and happening acutely, monoclonal antibodies give your body the antibodies it needs to protect itself and help you, if you are sick from developing serious COVID-19.

So as far as the options, according to the literature I have reviewed, there are five monoclonal antibodies available. Let me try to pronounce them all correctly as best as I can. Bamlanivimab plus etesevimab, that is one; then bebtelovimab is another one; and then casirivimab plus imdevimab; sotrovimab is another one; and then tixagevimab plus cilgavimab is the other one. So those are the five different monoclonal antibodies available, from my most recent reading.

**ANGELA LECLERC:** Great, thank you for that. Who is eligible and ineligible for these monoclonal antibodies?

**DR. SAM WIJESINGHE:** Yeah, this treatment is for if other COVID-19 treatment options approved or authorized by the FDA are unavailable or not clinically appropriate. So when I recommend monoclonal antibody, I consider the following: A patient should have a positive COVID-19 result. It can be done by a PCR or antigen. Then they should have mild to moderate symptoms for 7 days or less I would say, and then other conditions, ineligible for other antiviral, like nirmatrelvir and ritonavir. For example, nirmatrelvir/ritonavir should be prescribed within five days of symptoms, so if you are treating a patient on their sixth or seventh day of symptoms, then monoclonal is recommended. Then also there are some other things that we can consider, you know, if someone has poor renal function, let's say GFR is less than 30, then monoclonals should be considered; and then if there is a drug interaction with nirmatrelvir and ritonavir, monoclonal antibody is recommended; and the other conditions are patients 65 years or older, and then immunocompromised, and then pregnant patients are eligible.



As far as not eligible, there are four conditions come to my mind. If they have a negative COVID-19 test, we don't do a monoclonal antibody; and then test positive for COVID-19 but asymptomatic, then you don't recommend monoclonal antibody; and then patient has been sick for five days or less, and eligible for other treatment options, like I mentioned, nirmatrelvir and ritonavir, then that is my preferred option, I would prescribe that first; and then if someone is symptomatic and needs a new or increased oxygen requirement, then I think this patient needs an inpatient comprehensive evaluation at the emergency medicine setting then hospital medicine setting, then I refer them to inpatient setting.

**ANGELA LECLERC:** Oh, thanks, Sam. Does vaccination status matter?

**DR. SAM WIJESINGHE:** That's an excellent question, Angie, and no, it does not. If you get COVID-19 and meet criteria for monoclonal antibody treatment, you can receive the treatment regardless of COVID-19 vaccination status. Also, I should emphasize that this is not a replacement for the vaccine, but rather it is given to treat your current COVID-19 infection, so if someone was not vaccinated, getting the vaccine later is recommended. I should add that in the past, there was a recommendation from CDC, you had to wait 90 days to get the vaccine after you had monoclonal antibody, but there is no actually waiting period like that anymore. Having said that, I was wondering whether, Steph, Angie, you have anything to add?

**STEPHANIE PODOLSKI:** That's a great point, Sam. You know, the only thing I found for drug-drug interactions for monoclonal antibodies are that drug-drug interactions are unlikely, but the one time that vaccination status does matter, if a clinician is considering administering monoclonal antibodies, is if someone received the COVID-19 vaccine within two weeks of an acute COVID-19 illness. So for example, if someone received a booster vaccination and then one week later developed an acute COVID-19 infection, and they otherwise met all criteria for monoclonal antibodies, they would not be eligible to receive monoclonal antibodies because they received the vaccine within two weeks.

**DR. SAM WIJESINGHE:** Great, thank you so much.

**ANGELA LECLERC:** Sam, another question about monoclonal antibodies, what is your practice like in prescribing these in the outpatient setting?

**DR. SAM WIJESINGHE:** Yeah, that's a very good question, Angie, thank you, and this is what I generally recommend. So we have to make sure it's available first, and then I will see if the available option is recommended for the circulating variants and subvariants. I think I should share an example here to make it clear, let me take Omicron variant as an example. While some monoclonal antibodies have reduced against Omicron, sotrovimab is active against Omicron BA.1 and BA.1.1 subvariants, but it has substantially decreased in vitro actually against Omicron BA.2 subvariant, so it is important to look at all those information when



we are choosing the monoclonal antibody option. There is another thing I should mention, bebtelovimab retains in vitro activity against circulating Omicron subvariants. So, these recommendations remain very fluid and depend on the prevalence of resistant variants, so at this time, recommendations are for the treatment of non-hospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. So to summarize, please look at what monoclonal antibodies are available in your area, and then know the variants and subvariants circulating, and then choose the best available monoclonal antibody option for your patients.

**ANGELA LECLERC:** That's very helpful, Sam, thank you. On that same note, Steph, how can patients access monoclonal antibodies?

**DR. SAM WIJESINGHE:** And Steph, while you're thinking about it, I just wanted to share something what I did recently, I visited this website, Office of Assistant Secretary for Preparedness and Response, and I chose monoclonal antibody as the treatment option, then I used my zip code, then I was able to see like six locations with the addresses and if they have monoclonal antibodies available or not, and then if they did, they even have the number of monoclonal antibodies available, so that was really, really helpful information for me, and I recommend our listeners, primary care providers and other clinicians who are looking for this information, please visit that website: Office of the Assistant Secretary for Preparedness and Response, and then you will be able to get very up-to-date information there as far as access.

**STEPHANIE PODOLSKI:** You know, Sam, I found that same website as you, and we actually use it regularly in our health system. As we've talked about before, monoclonal antibodies are only used for folks in the outpatient setting. I think one of the things that everybody could do, the first thing they should do if they're wondering if they're a candidate for monoclonal antibodies, is to call your healthcare provider or your primary care provider after you've been exposed or you have a positive test for COVID-19, within 7 days of symptom onset, and I mention if you've been exposed too because there is one monoclonal antibody option that is a preexposure prophylaxis for folks who, for example, are severely immunocompromised and are at high risk for developing severe disease requiring hospitalization.

Another thing that folks could do is if they have symptoms, but they don't have a healthcare provider, is to call the Combat COVID Monoclonal Antibody Call Center. That phone number is 1-877-332-6585. And lastly, as Sam mentioned, you know, healthcare providers or even folks at home, if they have access to the internet, can use that therapeutics locator link. What I found interesting about that website is that that therapeutics locator link was not specific just to monoclonal antibodies, but also would tell you what oral antiviral treatments are available near you and what the supply is like in your area, how many are actually available for distribution in your state.



**ANGELA LECLERC:** Awesome. Thank you both, Sam and Steph, that's all incredibly useful information. To round out this discussion, Steph, could you share what the special considerations are when it comes to monoclonal antibodies?

**STEPHANIE PODOLSKI:** Yeah, that's a great question, Angie. I'm sure a lot of folks who are listening to this are wondering - they've heard various things about monoclonal antibodies being pulled off the market, and that's in fact true, and I think one of the things that all healthcare clinicians need to remember is that the FDA did revoke the Emergency Use Authorization for some monoclonal antibody treatments that originally came out earlier on in the pandemic, and that a lot of the monoclonal antibody specific treatments are not currently working against the Omicron variant.

With that said, I think it's really important to highlight that there are current studies going on, multiple of them, about whether or not one or two of the five different monoclonal treatments that Sam mentioned earlier would be helpful down the road, as the COVID-19 virus continues to mutate over time. So I do recommend that outpatient providers review the available FDA fact sheets for more information, use PubMed or other resources they have to follow those studies to see which specific monoclonal antibodies receive potential Emergency Use Authorization again in the future.

Some additional special considerations are antiviral resistance, so the development of the SARS-CoV-2 variants has reduced susceptibility to specific types of monoclonal antibodies, which in fact increases the risk of treatment failure, and so as Sam mentioned, you need to consider the local prevalence of the SARS-CoV-2 variant, what is circulating in your area, what's the incidence and prevalence of the certain viral strains in your area.

Something else to consider is clinical worsening of COVID-19, including signs or symptoms of worsening mental status, heart arrhythmias such as bradycardia, tachycardia, fatigue, fever, hypoxia, increased respiratory difficulty. All of these specific clinical exam findings have been reported after administration of some of the monoclonal antibodies, and it's not known if it's related, if these physical exam findings were related to the monoclonal antibodies themselves, or if they were due to COVID-19 progression, and with that said, I just want to highlight again that if you have a patient who is in fact displaying signs and symptoms of exam progression, the monoclonal antibody treatment is not meant for folks who are getting worse. If you have a patient who's getting worse, I recommend that you send them to a higher level of care.

There are some limitations of use for the monoclonal antibodies, some of which include age. Specifically, the preexposure prophylaxis medication should be used for pediatric patients at least 12 years or older and weighing at least 40



kilograms. The bebtelovimab that Sam mentioned is actually eligible for pediatric patients under age 12, but those pediatric patients should be greater than or equal to 2 years of age when monoclonal antibodies are being considered for use. I think it's really important to highlight that there is a preexposure prophylaxis monoclonal antibody as I mentioned, for folks who are high risk for developing severe disease, and these aren't used very often, but are used in the special populations that we highlighted previously for you, so folks who are severely immunocompromised, or have progressive cancer, who may be transplant patients, etcetera, who are high risk for being hospitalized from COVID-19, and this formulation is an IM injection that can be administered outpatient, and it can be administered to folks regardless of whether or not they may be pregnant or considering planning a family. There are no significant contraindications to the medication, unless there's been a hypersensitivity reaction or anaphylaxis to any component of the preexposure prophylaxis, and this medication is to be used, again, within a similar timeframe. If exposed to a known positive COVID-19 patient, the same timeframe applies, it can be used within 7 days.

By comparison, Sam mentioned when somebody has a known positive COVID-19 result, the bebtelovimab is the monoclonal antibody of choice currently that's used via IV injection route. This medication can also be safely used in pregnancy or lactation, and there's no dose adjustment needed. Additionally, for special populations, for both the IM injection preexposure prophylaxis medication or the bebtelovimab, which is the IV injection monoclonal antibody treatment, there's no dosing adjustment needed for renal disease, for hepatic disease, or for folks who are over the age of 65, so your geriatric population.

And again, we talked previously about oral antivirals not being able to be safely used for patients who are pregnant. Monoclonal antibodies can be safely used for both prophylaxis for pregnant patients as well as for treatment of acute COVID-19 in pregnant patients. The only contraindication to the medication is, again, that hypersensitivity reaction. There's no other major contraindication on file, which I think is actually a benefit of monoclonal antibodies as compared to other therapies.

**ANGELA LECLERC:** Steph, finally, the one thing that we're all wondering about is the challenges of logistics in providing monoclonal antibodies as a therapeutic option for patients. Would you comment on this?

**STEPHANIE PODOLSKI:** Yes, I'm happy to, so similarly to what I mentioned previously, there's only so much of monoclonal antibody product available and dispensed to each state across the country, and this is all federally determined based on population size, etcetera, and a healthcare provider could look at the local supply in order to determine how much would be available in their geographic area. So in addition to there being variable supply, based on jurisdiction or even healthcare facility, there's some cost barriers specific to the



healthcare facility or even the healthcare provider individually. The insurers – Medicare, Medicaid, private insurers – are all currently paying for these treatments, so the cost to the patient is zero, as long as the patient is insured, however depending on the treatment, the monoclonal antibodies are actually hundreds of dollars per administration and can be quite costly to the facility.

The additional barriers to treatment include having trained healthcare providers who can actually administer and also legally prescribe these medications, so all healthcare clinicians are able to prescribe them, but the staff needs to be trained to monitor for those side effects after IM or IV administration, and then in addition, there needs to be infusion supplies available, the ability to obtain IV access, immediate access to resuscitation medication, and the ability to contact emergency medical services if need be. The supplies for monoclonal antibodies are mostly located at healthcare facilities, and it's harder to reach to rural health clinics or under-served health clinics across the country.

**DR. SAM WIJESINGHE:** Those are excellent points, Steph. I would like to add that when we compare antiviral versus monoclonal antibodies, getting antiviral for our patients is much, much easier and easy access. For example, we might have like six locations for monoclonal antibody in our area, and then there are many more available places for antiviral, you know, many pharmacies carry that, so it is very easy. In general, what I do is I use monoclonal antibody only if I cannot use antiviral as the option. For example, if they're having very poor renal function, GFR being less than 30, then I consider monoclonal antibody for those patients, and then, like I mentioned earlier, if this is their sixth or seventh day onset of their symptoms, then we cannot use antiviral, the nirmatrelvir and ritonavir available, so because I cannot use that then I talk to patients about monoclonal antibody as the option at that time. So it is not the easiest thing to access, but we do that for patients who really need at that point.

**ANGELA LECLERC:** Great, thank you, Sam and Steph. This pandemic has really highlighted the barriers to healthcare that have been percolating for many, many years pre-pandemic, but the need for ubiquitous care for all in the setting of a pandemic has led to these issues really exploding.

Well, this concludes our episode about monoclonal antibodies. I want to thank our listeners for joining us, and thank you again, Sam and Steph, for joining the discussion, and we look forward to hearing from you both on our next and final episode on special populations.

## **RESOURCES**

### **For Providers**

- [COVID-19 Treatment Guidelines: Anti-SARS-CoV-2 Antibody Products \(NIH\)](#)
- [COVID-19 Therapeutics Locator \(HHS\)](#)



## For Patients

- [COVID-19 Test to Treat Initiative](#) (HHS)
- [What are Monoclonal Antibodies?](#) (HHS)

