Monoclonal Antibodies to Prevent Severe Disease from COVID-19

COVID-19 is caused by a virus called a coronavirus. People 'catch' COVID-19 through contact with another person who has the virus.

COVID-19 illnesses can be very mild (including some with no reported symptoms) or severe, including illness resulting in death. While most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. Older individuals, those with chronic medical conditions such as heart disease, lung disease, kidney disease, obesity, diabetes and those with a decreased immune system are at higher risk of being hospitalized for COVID-19. Drugs based on antibodies have been developed to help reduce the chance of COVID-19 worsening and requiring those infected to need hospitalization.

These drugs are designed to be outpatient therapies and contain antibodies similar to the antibodies found in patients who have recovered from COVID-19. *The goal of these therapies is to reduce the amount of COVID-19 virus in the body and give your body more time to produce your own antibodies, which could prevent you from getting sick enough to be hospitalized with COVID-19.*

The United States Food and Drug Administration (FDA) has issued Emergency Use Authorization (EUA) status for these therapies. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic. This medicine has not undergone the same type of review as an FDA-approved or cleared product. The FDA may issue a EUA when certain criteria are met, which include that there are no adequate, approved and available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is reasonable to believe that the product meets certain criteria for safety, performance and labeling, and may be effective in treatment of patients during the COVID-19 pandemic. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic. The EUA for infusion treatment is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the product may no longer be used).

<u>What are monoclonal antibodies?</u>

Bamlanivimab, casirivimab, and imdevimab are all monoclonal antibodies. An antibody is a protein that the body makes to fight off viruses and other foreign substances*. Monoclonal antibodies are man-made antibodies produced in a laboratory that can mimic the human immune system response to infection.* Each of these three drugs are designed to block viral attachment and entry into human cells, thus neutralizing the virus that causes COVID-19. Casirivimab and imdevimab must be given together, while bamlanivimab is given by itself. They are investigational drugs, meaning they are not currently FDA-approved, but are authorized for emergency use for the treatment of mild to moderate COVID-19. Bamlanivimab is produced by the pharmaceutical company Eli Lilly and

Company. Casirivimab/indevimab is produced by the pharmaceutical company Regeneron. The U.S. government is distributing supplies to states.

Who can receive monoclonal antibody therapy?

Under the terms of the EUAs, Monoclonal Antibodies may be used for the treatment of mild to moderate COVID-19 in adults and pediatric patients who meet all of the following:

- Have a positive test for SARS-CoV-2 (RT-PCR or antigen).
- Are within 10 days of the start of their symptoms.
- Are at least 12 years of age or older and weigh at least 40 kilograms (88 pounds).
- Are at high risk for progressing to severe COVID-19 and/or hospitalization.

How are these drugs given at UAMS?

Monoclonal Antibodies must be given by intravenous (IV) infusion in the Family Medical Center by appointment. Monoclonal Antibodies may be administered only in settings in which health care providers have immediate access to medications to treat severe infusion reactions, such as allergic reaction, and the ability to activate the emergency medical system, as necessary.

Are these medications effective?

Clinical trials are ongoing with these medications. Bamlanivimab was shown to decrease hospitalizations and ER visits and to decrease patients' viral load compared to those who got a placebo. Among patients who were at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of bamlanivimab-treated patients, compared to 10% in placebo-treated patients. For more information, see SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19.

Another clinical trial studied the combination of casirivimab and indevimab for the treatment of adult patients with mild to moderate COVID-19 who were not hospitalized. Similar to bamlanivimab, casirivimab/indevimab was also shown to decrease hospitalizations and ER visits and to decrease patients' viral load compared to placebo. In patients who were at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of casirivimab/indevimab-treated patients, compared to 9% in placebo-treated patients.

Which one will I receive?

At UAMS, you will be given either bamlanivimab or casivirimab/indevimab based on availability of the drug at the time of your infusion. At the current time, these drugs are considered equivalent with regard to outcome, safety, and efficacy.

Will my Insurance cover the cost of monoclonal antibodies?

The U.S. government has purchased a supply of monoclonal antibodies to distribute to states at no cost to patients, at least until the end of 2020. However, even though the therapies are provided at no cost, there will be other costs associated with the infusion, which will be charged to your insurance.

What are the risks of these medications?

In clinical trials of bamlanivimab and casirivimab/indevimab involving almost 3,000 people, two anaphylactic reactions (a severe allergic reaction) and five serious-infusion-related reactions have been reported. All reactions were treated and resolved.

For bamlanivimab, *the most commonly reported side effects (in 2% to 4% of people) were nausea, diarrhea, dizziness, headache, itchiness, and vomiting*. For casirivimab/indevimab, *the most commonly reported side effects (0.8-1.6% of people) were nausea and vomiting, hyperglycemia, and pneumonia*. Clinical studies evaluating the safety of monoclonal antibodies are ongoing, so it is possible all of the risks are not known at this time.

Because of the risk of allergic reaction, infusions may be administered only in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as allergic reactions, and the ability to activate the emergency medical system, as necessary.

Do I need to be NPO to receive the infusion?

No, you may eat up until the time of the infusion. Nausea is a commonly reported side effect, so eating immediately prior to your appointment is not recommended.

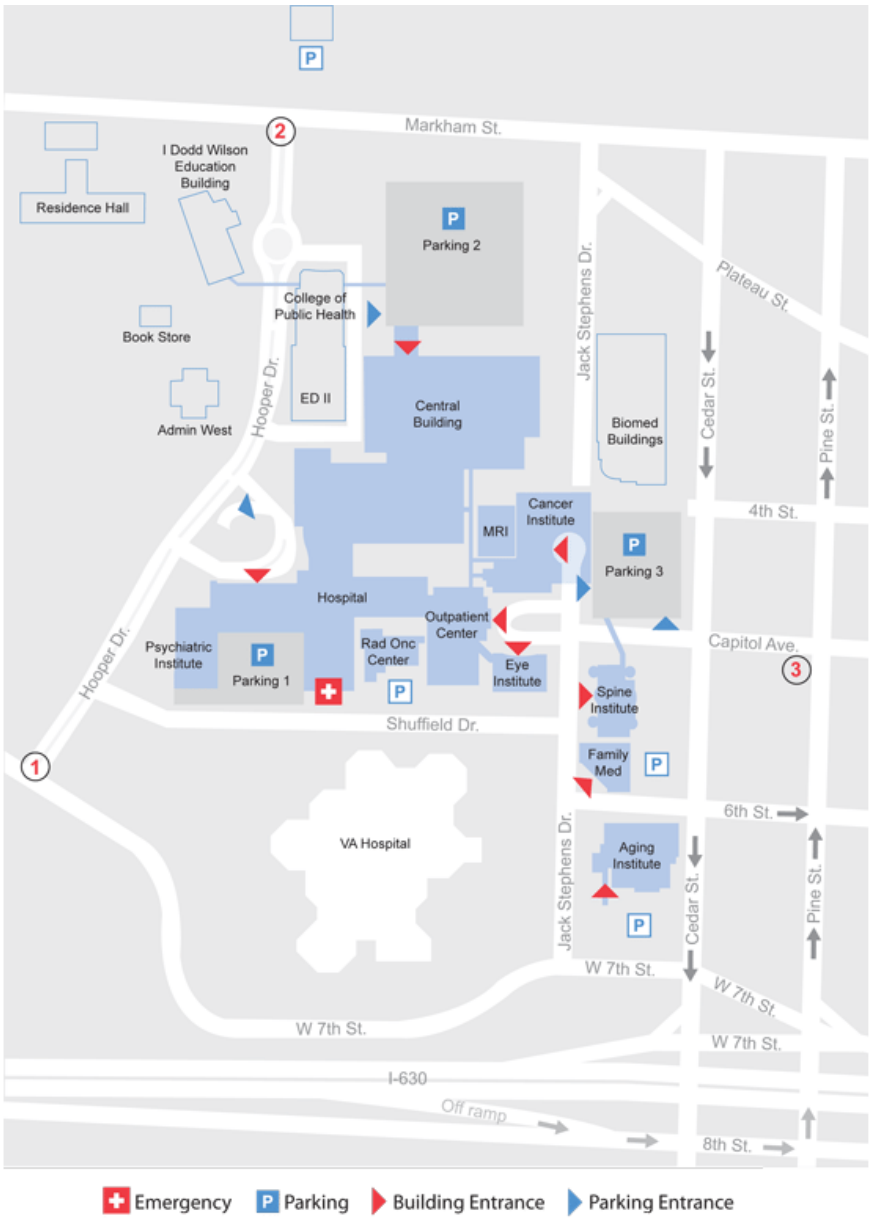
What do I need to know to be prepared for my appointment?

- You are the only one that is allowed in the building, family must either drop you off or wait in vehicle.
- Expect to be here approximately 2-3 hours
- Hydrate as much as possible the evening before and morning of infusion. We ask this because the nurse will have to start an IV and the more hydrated you are, the easier the IV placement will be.
- Bring whatever snacks and drinks you might want while you are getting your treatment as we do not have access to food in our clinic
- You will be sitting in a recliner so if you would like to bring a neck pillow or lap throw to make yourself comfortable, please do so
- You may bring whatever electronic devices you wish (ie: laptop, ipad, cell phone, portable dvd player) and charging cords needed. Or if you prefer to bring a book or whatever else you wish to keep you occupied during your treatment.
- If you have questions about scheduling or location, you can call Cynthia at 501-686-7104.

Where do I come for my appointment?

We are located at the UAMS Family Medical Center at 521 Jack Stephens Drive, Little Rock, AR 72205. Our building is the smaller building between the Jack T Stephens Spine center and the Center on Aging. The entry door faced the VA parking deck/lot. If you have handicapped parking there is parking in the front of our building. Otherwise you will need to park in our parking lot behind our building, on the corner of 6th and Jack Stephens Drive. When you pull up the arm will go up and we will give you parking card to get out. (Right now they are doing construction so arms will be up.) You can either come up the sidewalk on 6th street or there is a side walk in between the Spine center and Family Medical Center.

To reach the **Family Medical Center**, take the Pine/Cedar Street exit and go west on 7th street to Jack Stephens Drive, turn north. Turn east onto 6th street and enter the parking lot behind building.



Fact Sheet for Patients, Parents and Caregivers
Emergency Use Authorization (EUA) of Bamlanivimab for Coronavirus Disease 2019 (COVID-19)

You are being given a medicine called **bamlanivimab** for the treatment of coronavirus disease 2019 (COVID-19). This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking bamlanivimab, which you may receive.

Receiving bamlanivimab may benefit certain people with COVID-19.

Read this Fact Sheet for information about bamlanivimab. Talk to your healthcare provider if you have questions. It is your choice to receive bamlanivimab or stop it at any time.

What is COVID-19?
COVID-19 is caused by a virus called a coronavirus. People can get COVID-19 through contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. People of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

What are the symptoms of COVID-19?
The symptoms of COVID-19 include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure. Serious illness including breathing problems can occur and may cause your other medical conditions to become worse.

What is bamlanivimab?
Bamlanivimab is an investigational medicine used for the treatment of COVID-19 in non-hospitalized adults and adolescents 12 years of age and older with mild to moderate symptoms who weigh 88 pounds (40 kg) or more, and who are at high risk for developing severe COVID-19 symptoms or the need for hospitalization. Bamlanivimab is investigational because it is still being studied. There is limited information known about the safety or effectiveness of using bamlanivimab to treat people with COVID-19.

The FDA has authorized the emergency use of bamlanivimab for the treatment of COVID-19 under an Emergency Use Authorization (EUA). For more information on EUA, see the section "**What is an Emergency Use Authorization (EUA)?**" at the end of this Fact Sheet.

What should I tell my healthcare provider before I receive bamlanivimab?
Tell your healthcare provider about all of your medical conditions, including if you:
- Have any allergies
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illnesses
- Are taking any medications (prescription, over-the-counter, vitamins, and herbal products)

How will I receive bamlanivimab?
- Bamlanivimab is given to you through a vein (intravenous or IV) for at least 1 hour.
- You will receive one dose of bamlanivimab by IV infusion.

What are the important possible side effects of bamlanivimab?
Possible side effects of bamlanivimab are:
- Allergic reactions. Allergic reactions can happen during and after infusion with bamlanivimab. Tell your healthcare provider right away if you get any of the following signs and symptoms of allergic reactions: fever,

chills, nausea, headache, shortness of breath, low blood pressure, wheezing, swelling of your lips, face, or throat, rash including hives, itching, muscle aches, and dizziness.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

These are not all the possible side effects of bamlanivimab. Not a lot of people have been given bamlanivimab. Serious and unexpected side effects may happen. Bamlanivimab is still being studied so it is possible that all of the risks are not known at this time.

It is possible that bamlanivimab could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, bamlanivimab may reduce your body's immune response to a vaccine for SARS-CoV-2. Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

What other treatment choices are there?
Like bamlanivimab, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to https://www.covid19treatmentguidelines.nih.gov/ for information on the emergency use of other medicines that are not approved by FDA to treat people with COVID-19. Your healthcare provider may talk with you about clinical trials you may be eligible for.

It is your choice to be treated or not to be treated with bamlanivimab. Should you decide not to receive bamlanivimab or stop it at any time, it will not change your standard medical care.

What if I am pregnant or breastfeeding?
There is limited experience treating pregnant women or breastfeeding mothers with bamlanivimab. For a mother and unborn baby, the benefit of receiving bamlanivimab may be greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

How do I report side effects with bamlanivimab?
Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch, call 1-800-FDA-1088, or contact Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921).

How can I learn more?

- Ask your healthcare provider
- Visit www.bamlanivimab.com
- Visit https://www.covid19treatmentguidelines.nih.gov/
- Contact your local or state public health department

What is an Emergency Use Authorization (EUA)?
The United States FDA has made bamlanivimab available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Bamlanivimab has not undergone the same type of review as an FDA-approved or cleared product. The FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is reasonable to believe that the product meets certain criteria for safety, performance, and labeling and may be effective in treatment of patients during the COVID-19 pandemic. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for bamlanivimab is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the product may no longer be used).

Literature issued November 2020

Eli Lilly and Company, Indianapolis, IN 46285, USA

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FACT SHEET FOR PATIENTS, PARENTS AND CAREGIVERS
EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB FOR CORONAVIRUS DISEASE 2019
(COVID-19)

You are being given a medicine called **casirivimab** and **imdevimab** for the treatment of coronavirus disease 2019 (COVID-19). This Fact Sheet contains information to help you understand the potential risks and potential benefits of taking casirivimab and imdevimab, which you may receive.

Receiving casirivimab and imdevimab may benefit certain people with COVID-19.

Read this Fact Sheet for information about casirivimab and imdevimab. Talk to your healthcare provider if you have questions. It is your choice to receive casirivimab and imdevimab or stop at any time.

WHAT IS COVID-19?

COVID-19 is caused by a virus called a coronavirus. People can get COVID-19 through contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild (including some with no reported symptoms) to severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can occur and may cause some of your other medical conditions to become worse. People of all ages with severe, long-lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example, seem to be at higher risk of being hospitalized for COVID-19.

WHAT ARE THE SYMPTOMS OF COVID-19?

The symptoms of COVID-19 include fever, cough, and shortness of breath, which may appear 2 to 14 days after exposure. Serious illness including breathing problems can occur and may cause your other medical conditions to become worse.

WHAT IS CASIRIVIMAB AND IMDEVIMAB?

Casirivimab and imdevimab are investigational medicines used to treat mild to moderate symptoms of COVID-19 in non-hospitalized adults and adolescents (12 years of age and older who weigh at least 88 pounds (40 kg)), and who are at high risk for developing severe COVID-19 symptoms or the need for hospitalization. Casirivimab and imdevimab are investigational because they are still being studied. There is limited information known about the safety and effectiveness of using casirivimab and imdevimab to treat people with COVID-19.

The FDA has authorized the emergency use of casirivimab and imdevimab for the treatment of COVID-19 under an Emergency Use Authorization (EUA). For more information on EUA, see the **"What is an Emergency Use Authorization (EUA)?"** section at the end of this Fact Sheet.

WHAT SHOULD I TELL MY HEALTH CARE PROVIDER BEFORE I RECEIVE CASIRIVIMAB AND IMDEVIMAB?

Tell your healthcare provider about all of your medical conditions, including if you:

- Have any allergies

- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illnesses
- Are taking any medications (prescription, over-the-counter, vitamins, and herbal products)

HOW WILL I RECEIVE CASIRIVIMAB AND IMDEVIMAB?

- Casirivimab and imdevimab are two investigational medicines given together as a single intravenous infusion (through a vein) for at least 1 hour.
- You will receive one dose of casirivimab and imdevimab by intravenous infusion.

WHAT ARE THE IMPORTANT POSSIBLE SIDE EFFECTS OF CASIRIVIMAB AND IMDEVIMAB?

Possible side effects of casirivimab and imdevimab are:

- Allergic reactions. Allergic reactions can happen during and after infusion with casirivimab and imdevimab. Tell your healthcare provider or nurse, or get medical help right away if you get any of the following signs and symptoms of allergic reactions: fever, chills, low blood pressure, changes in your heartbeat, shortness of breath, wheezing, swelling of your lips, face, or throat, rash including hives, itching, headache, nausea, vomiting, sweating, muscle aches, dizziness and shivering.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

These are not all the possible side effects of casirivimab and imdevimab. Not a lot of people have been given casirivimab and imdevimab. Serious and unexpected side effects may happen. Casirivimab and imdevimab are still being studied so it is possible that all of the risks are not known at this time.

It is possible that casirivimab and imdevimab could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, casirivimab and imdevimab may reduce your body's immune response to a vaccine for SARS-CoV-2. Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

WHAT OTHER TREATMENT CHOICES ARE THERE?

Like casirivimab and imdevimab, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to https://www.covid19treatmentguidelines.nih.gov/ for information on other medicines used to treat people with COVID-19.

It is your choice to be treated or not to be treated with casirivimab and imdevimab. Should you decide not to receive casirivimab and imdevimab or stop it at any time, it will not change your standard medical care.

WHAT IF I AM PREGNANT OR BREASTFEEDING?

There is limited experience treating pregnant women or breastfeeding mothers with casirivimab and imdevimab. For a mother and unborn baby, the benefit of receiving casirivimab and imdevimab may be

greater than the risk from the treatment. If you are pregnant or breastfeeding, discuss your options and specific situation with your healthcare provider.

HOW DO I REPORT SIDE EFFECTS WITH CASIRIVIMAB AND IMDEVIMAB?

Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch or call 1-800-FDA-1088 or call 1-844-734-6643.

HOW CAN I LEARN MORE?

- Ask your health care provider.
- Visit www.REGENCOV2.com
- Visit https://www.covid19treatmentguidelines.nih.gov/
- Contact your local or state public health department.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?

The United States FDA has made casirivimab and imdevimab available under an emergency access mechanism called an EUA. The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

Casirivimab and imdevimab have not undergone the same type of review as an FDA-approved or cleared product. The FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives. In addition, the FDA decision is based on the totality of scientific evidence available showing that it is reasonable to believe that the product meets certain criteria for safety, performance, and labeling and may be effective in treatment of patients during the COVID-19 pandemic. All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic.

The EUA for casirivimab and imdevimab is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

REGENERON

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