

## Frequently Asked Questions on the Emergency Use Authorization of Casirivimab and Imdevimab

### Q. What is an Emergency Use Authorization (EUA)?

A: Under section 564 of the Federal Food, Drug & Cosmetic Act, the FDA may, pursuant to a declaration by the HHS Secretary based on one of four types of determinations, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, the FDA must determine, among other things, that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

### Q. What does this EUA authorize?

A. [This EUA authorizes the emergency use of the investigational drug products casirivimab and imdevimab](#), manufactured by Regeneron Pharmaceuticals, Inc., to be administered together for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Casirivimab and imdevimab are investigational drugs because they are being studied for the uses authorized in the EUA.

### Q: What does direct SARS-CoV-2 viral testing mean?

A: Direct SARS-CoV-2 viral tests diagnose active COVID-19 infection. Direct SARS-CoV-2 viral tests include two types of diagnostic tests for COVID-19:

- Molecular tests, such as reverse transcription polymerase chain reaction (RT-PCR) tests, that detect the virus's genetic material.
- Antigen tests that detect specific proteins from the virus.

Antibody tests should not be used to diagnose COVID-19 and are not direct SARS-CoV-2 viral tests. Antibody tests look for antibodies the immune system makes in response to the SARS-CoV-2 virus.

### Q. How is high risk defined under the EUA?

A. High risk for progressing to severe COVID-19 and/or hospitalization is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI)  $\geq 35$
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are  $\geq 65$  years of age
- Are  $\geq 55$  years of age AND have
  - cardiovascular disease, or
  - hypertension, or

- chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, [https://www.cdc.gov/growthcharts/clinical\\_charts.htm](https://www.cdc.gov/growthcharts/clinical_charts.htm), or
  - sickle cell disease, or
  - congenital or acquired heart disease, or
  - neurodevelopmental disorders, for example, cerebral palsy, or
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID19), or
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

**Q. Are there limitations of the authorized use under this EUA?**

A. Yes, casirivimab and imdevimab, administered together, are not authorized for use in patients:

- who are hospitalized due to COVID-19, or
- who require oxygen therapy due to COVID-19, or
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

**Q. Are casirivimab and imdevimab monoclonal antibodies? What are monoclonal antibodies?**

A. Yes, casirivimab and imdevimab are monoclonal antibodies. Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that can restore, enhance or mimic the immune system's attack on pathogens. Casirivimab and imdevimab, administered together, are designed to block viral attachment and entry into human cells, thus neutralizing the virus.

**Q. Does the EUA permit the use of casirivimab and imdevimab as authorized in patients hospitalized for reasons other than COVID-19?**

A: Specifically, casirivimab and imdevimab, administered together, are authorized for emergency use, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

If a patient is hospitalized *for reasons other than COVID-19*, such as for an elective orthopedic procedure, and the patient reports mild to moderate symptoms of COVID-19, confirmed with positive results of a direct SARS-CoV-2 viral test, then it may be appropriate for treatment with casirivimab and imdevimab, administered together, if the patient is also at high risk for progressing to severe COVID-19 and/or hospitalization and the terms and conditions of the authorization are met, as detailed in the [Fact Sheet for Health Care Providers](#).

Casirivimab and imdevimab, administered together, are not authorized for use in patients:

- who are hospitalized *due to* COVID-19, or
- who require oxygen therapy *due to* COVID-19, or
- who require an increase in baseline oxygen flow rate *due to* COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

**Q. When should casirivimab and imdevimab be administered to a patient?**

A. The EUA authorizes casirivimab and imdevimab, administered together, as a single intravenous infusion as soon as possible after positive viral test for COVID-19 and within 10 days of symptom onset. More information about administration is available in the [Fact Sheet for Health Care Providers](#).

**Q. Where are infusions of casirivimab and imdevimab available?**

A. The following websites contain information regarding access to monoclonal antibody treatments for COVID-19:

- HHS Protect Public Data Hub – [Therapeutics Distribution](#)
- [National Infusion Center Association \(NICA\)](#)

Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and have the ability to activate the emergency medical system, if necessary. Please speak with your doctor or contact your local or state public health department for more information.

**Q. Are casirivimab and imdevimab approved by the FDA to treat COVID-19?**

A. No. Casirivimab and imdevimab are investigational drugs. They are not currently FDA-approved to treat any diseases or conditions, including COVID-19.

**Q. Are there data showing casirivimab and imdevimab might benefit patients with COVID-19?**

A. The data supporting benefit for casirivimab and imdevimab are based on a randomized, double-blind, placebo-controlled clinical trial in 799 non-hospitalized adults with mild-to-moderate COVID-19 symptoms. Of these patients, 266 received a single intravenous infusion of 2,400 milligrams casirivimab and imdevimab (1,200 mg of each), 267 received 8,000 mg casirivimab and imdevimab (4,000 mg of each), and 266 received a placebo within three days of obtaining a positive SARS-CoV-2 viral test.

The prespecified primary endpoint for the trial was time-weighted average change in viral load from baseline. Viral load reduction in patients treated with casirivimab and imdevimab was larger than in patients treated with placebo at day 7.

However, the most important evidence that casirivimab and imdevimab, administered together, may be effective came from the predefined secondary endpoint of medically attended visits related to COVID-19, particularly hospitalizations and emergency room visits for COVID-19 within 28 days after treatment. For patients at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of casirivimab and imdevimab-treated patients, on average, compared to 9% in placebo-treated patients. The effects on viral load, reduction in hospitalizations and ER visits, and safety, were similar in patients receiving either of the two casirivimab and imdevimab doses.

**Q. Are there clinical trials underway evaluating casirivimab and imdevimab for COVID-19?**

A. Yes. [Clinical trials](#) remain ongoing to study casirivimab and imdevimab for treatment and prevention of COVID-19.

**Q. Are there side effects (adverse events) of casirivimab and imdevimab?**

A. There is a potential for serious hypersensitivity reactions, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or

anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related reactions have been observed with administration of casirivimab and imdevimab.

Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, or dizziness.

These are not all the possible side effects of casirivimab and imdevimab, as not a lot of people have received 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.

**Q. How can casirivimab and imdevimab be obtained for use under the EUA?**

A. HHS will review case counts and severity of outbreaks across the U.S. and make allocations accordingly to state and territorial health departments. State and territorial health departments will allocate to healthcare facilities. AmeriSource Bergen will distribute casirivimab and imdevimab for the U.S. Government.

**Q. Are there reporting requirements for healthcare facilities and providers as part of the EUA?**

A. Yes. As part of the EUA, FDA requires health care providers who prescribe casirivimab and imdevimab together to report all medication errors and serious adverse events considered to be potentially related to casirivimab and imdevimab through FDA's [MedWatch Adverse Event Reporting](#) program. Providers can complete and submit the report [online](#); or download and complete the [form](#), then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's [Fact Sheet for Health Care Providers](#). FDA MedWatch forms should also be provided to Regeneron.

Healthcare facilities and providers must report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services. Such information and data should be reported through HHS Protect, Teletracking or National Healthcare Safety Network.

**Q. Do patient outcomes need to be reported under the EUA?**

A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to casirivimab and imdevimab is required.

**Q. Does the EUA authorize casirivimab and imdevimab to be used to prevent COVID-19?**

A. No. Casirivimab and imdevimab are not authorized for the prevention of COVID-19.

**Q. Can health care providers share the patient/caregiver Fact Sheet electronically?**

A. The letter of authorization for casirivimab and imdevimab requires that Regeneron and its authorized distributors make the Fact Sheets available to healthcare facilities and health care providers through Regeneron's [website](#).

The [letter of authorization \(LOA\)](#) requires that healthcare facilities and healthcare providers ensure that they are aware of the LOA. The Fact Sheets must be made available to healthcare providers and to patients and caregivers, respectively, through "appropriate means", prior to the administration of the

authorized product. Electronic delivery of the Fact Sheet is an appropriate means. For example, Fact Sheets can be delivered to a patient, parent or caregiver as a PDF electronically prior to medication administration. Health care providers should confirm receipt of the Fact Sheet with the patient.

**Q. Are there differences in vial labels for casirivimab and imdevimab available under the EUA?**

A. REGEN-COV is distributed as dose pack bags, which contain a sufficient number of vials of casirivimab and imdevimab to prepare one treatment dose. Casirivimab and imdevimab included in dose pack bags are clearly marked “For Use Under Emergency Use Authorization.”

Individual vials of casirivimab and imdevimab distributed prior to the reissuance of [EUA letter of authorization](#) on February 3, 2021 remain authorized for emergency use. FDA is not requiring that such product be repackaged given the public health need for the product. The use of the individual vials of casirivimab and imdevimab must be consistent with the terms and conditions of the reissued authorization. Individual vial labels for casirivimab and imdevimab and carton labeling may be clearly marked with either “Caution: New Drug - Limited by Federal (or United States) law to investigational use” or with “For use under Emergency Use Authorization (EUA)”. Some vial labels and carton labeling of casirivimab and imdevimab may be instead labeled with the Investigational New Drug (IND) clinical trial code name as “REGN10933” and “REGN10987”, respectively.

Casirivimab and imdevimab must be administered together after dilution **by intravenous infusion only**.

See the [Health Care Provider Fact Sheet](#) for dose preparation and administration. Regeneron’s [Dear Health Care Provider Letter](#) also provides additional information for health care providers regarding vial and carton labeling, as well as contact information for healthcare providers and patients who may have questions.

**Q. Can I be vaccinated for COVID-19 if I was treated with a monoclonal antibody for COVID-19?**

A. Currently, there are no data on the safety and effectiveness of either the Pfizer-BioNTech or Moderna COVID-19 vaccine in people who received monoclonal antibodies authorized by FDA for emergency use as part of COVID-19 treatment (casirivimab and imdevimab, or bamlanivimab, or bamlanivimab and eteseivmab). Under the conditions of the emergency use authorization for each monoclonal antibody product, patients treated should have had a documented positive test for COVID-19 infection. Data available to the agency suggests that reinfection with SARS-CoV-2 is uncommon in the 90 days after initial infection. Based upon this low risk of reinfection and the estimated half-life of the monoclonal antibodies, the Advisory Committee on Immunization Practices (ACIP) recommends COVID-19 vaccination be deferred for at least 90 days after treatment with a monoclonal antibody for COVID-19. This is a precautionary measure to avoid interference of monoclonal antibody treatment specifically with vaccine-induced immune responses. Updates to this recommendation may be made as additional information on the interaction between prior monoclonal antibody treatment and vaccine response becomes available.