Frequently Asked Questions on the Emergency Use Authorization of Casirivimab + 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 determination and declaration by the HHS Secretary, 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 of the product, when used to diagnose, treat, 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 coronavirus disease 2019 (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 drug products because they are still being studied for the uses authorized in the EUA.

Q: Casirivimab and imdevimab are authorized to be administered together for the treatment of mild to moderate coronavirus disease 2019 (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. 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 made by the immune system in response to the SARS-CoV-2 virus.

Q. How is high risk defined under the EUA?
A. High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
• Are ≥55 years of age AND have
  o cardiovascular disease, OR
  o hypertension, OR
  o chronic obstructive pulmonary disease/other chronic respiratory disease.
• Are 12 – 17 years of age AND have
  o BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
  o sickle cell disease, OR
  o congenital or acquired heart disease, OR
  o neurodevelopmental disorders, for example, cerebral palsy, OR
  o a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  o 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, is 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 cells. Casirivimab and imdevimab, administered together, are designed to block viral attachment and entry into human cells, thus neutralizing the virus. Administered together, these antibodies are designed to limit viral replication and may be effective for the treatment of COVID-19 in patients who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Q. Does the EUA permit the use of casirivimab and imdevimab as authorized in patients hospitalized for reasons other than COVID-19?
A: Yes, casirivimab and imdevimab, administered together, may be used in patients hospitalized for reasons other than COVID-19, so long as the terms and conditions of authorization are met. For example, a patient hospitalized for an elective orthopedic procedure who reports mild symptoms of COVID-19, confirmed with positive results of a direct SARS-CoV-2 viral test, may be appropriate for treatment with casirivimab and imdevimab if the patient is also at high risk for progressing to severe COVID-19 and/or hospitalization, as detailed in the Health Care Provider Fact Sheet.

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.

Casirivimab and imdevimab, administered together, is 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 (IV) 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 Health Care Provider Fact Sheet.

Q. Where are infusions of casirivimab and imdevimab available?
A. 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 (EMS), 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?

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. 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.

**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. Is there a requirement for providers to report side effects as part of the EUA?**
A. Yes. As part of the EUA, FDA is requiring health care providers who prescribe casirivimab and imdevimab 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 Health Care Provider Fact Sheet. FDA MedWatch forms should also be provided to Regeneron.

**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 also requires that healthcare facilities and/or healthcare providers make available the Fact Sheets 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. Casirivimab is also named REGN10933 and may be labeled with either name. Imdevimab is also named REGN10987 and may be labeled with either name.

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 has posted a Dear Health Care Provider Letter that 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.