

## Frequently Asked Questions on the Emergency Use Authorization of REGEN-COV (Casirivimab and Imdevimab)

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

A: Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), when the Secretary of Health and Human Services declares that an emergency use authorization is appropriate, FDA may authorize unapproved medical products or unapproved uses of approved medical products for emergency use. In issuing an EUA, the FDA must determine, among other things, that, based on all the scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe 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? What are the limitations of authorized use?

A. This [EUA](#) authorizes the emergency use of the investigational drug product REGEN-COV (casirivimab and imdevimab) for both treatment and as post-exposure prophylaxis:

#### *Treatment:*

Treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adult 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 progression to severe COVID-19, including hospitalization or death.

#### Limitations of Authorized Use for Treatment:

- REGEN-COV (casirivimab with imdevimab) 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.
- Monoclonal antibodies, such as REGEN-COV, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

#### *Post-Exposure Prophylaxis*

For use as post-exposure prophylaxis of COVID-19 in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:

- not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with

immunocompromising conditions including those taking immunosuppressive medications) **and**

- have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC) **or**
- who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing home or prisons).

In general, people are considered fully vaccinated two weeks after their second dose in a two-dose series (the [Pfizer](#) or [Moderna](#) vaccines) **OR** two weeks after a single-dose vaccine ([the Janssen vaccine](#)).

The CDC defines close contact as someone who has been within [six feet of an infected person](#) (laboratory-confirmed or a [clinically compatible illness](#)) for a cumulative total of 15 minutes or more over a 24-hour period.

Limitations of Authorized Use for Post-Exposure Prophylaxis:

- REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19.
- Post-exposure prophylaxis with REGEN-COV is not a substitute for vaccination against COVID-19.

FDA has authorized three vaccines to prevent COVID-19 and serious clinical outcomes caused by COVID-19, including hospitalization and death. FDA urges you to get vaccinated, if you are eligible. Learn more about FDA-authorized [COVID-19 vaccines](#).

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

A: REGEN-COV co-formulated product and REGEN-COV supplied as individual vials to be administered together is 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, including hospitalization or death.

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 treatment with REGEN-COV may be appropriate, if the patient is also at high risk for progressing to severe COVID-19, including hospitalization or death, and the terms and conditions of the authorization are met, as detailed in the [Fact Sheet for Health Care Providers](#).

REGEN-COV 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: 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 that the immune system makes in response to the SARS-CoV-2 virus.

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

A. The following medical conditions or other factors may place adults and pediatric patients (age 12-17 years and weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example age  $\geq 65$  years of age)
- Obesity or being overweight (for example, adults with BMI  $> 25$  kg/m<sup>2</sup>, or if age 12-17, have BMI  $\geq 85$ th percentile for their age and gender based on [CDC growth charts](#))
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19))

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19, and authorization of REGEN-COV under the EUA is not limited to the medical conditions or factors listed above. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: [People with Certain Medical Conditions](#). Healthcare providers should consider the benefit-risk for an individual patient.

**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. When, and how, should REGEN-COV be administered to a patient for its treatment use?**

A. The EUA authorizes REGEN-COV to be administered as soon as possible after a positive viral test for COVID-19 and within 10 days of symptom onset. REGEN-COV is authorized for intravenous infusion, and intravenous infusion is strongly recommended. Subcutaneous injection is authorized as an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

More information about dosage and administration is available in the [Fact Sheet for Health Care Providers](#).

**Q. Where are infusions of REGEN-COV 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 \(NICA\)](#)

REGEN-COV 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. Is REGEN-COV approved by the FDA to treat or prevent COVID-19?**

A. No. REGEN-COV is an investigational drug. It is not currently FDA-approved to treat or prevent any diseases or conditions, including COVID-19. REGEN-COV is only authorized under an EUA; it is not a replacement for vaccination against COVID-19.

**Q. Are there data showing REGEN-COV may provide benefit for the treatment of certain patients with COVID-19 or as post-exposure prophylaxis of COVID-19?**

A. Yes. The most important scientific evidence supporting the authorization for REGEN-COV for treatment of COVID-19 comes from the phase 3 portion of a randomized, double-blind, placebo-controlled clinical trial in 4,567 non-hospitalized adults with mild-to-moderate COVID-19 symptoms and at least one risk factor for severe COVID-19. Of these patients, 838 received a single intravenous infusion of 600 mg of casirivimab and 600 mg of imdevimab, 1,529 received 1,200 mg of casirivimab and 1,200 mg of imdevimab, 700 received 4,000 mg of casirivimab and 4,000 mg of imdevimab, and 1,500 received a placebo within three days of obtaining a positive SARS-CoV-2 viral test.

The data from this clinical trial showed that high risk outpatients with mild-to-moderate COVID-19 demonstrated a similar reduction in risk of hospitalization or death with either the lower doses or the higher doses of casirivimab and imdevimab, administered together, compared to placebo. In addition, patients that received either the lower doses or the higher doses of casirivimab and imdevimab administered together had a faster time to symptom resolution in the clinical trial.

The primary data supporting the post-exposure prophylaxis of COVID-19 are from a Phase 3 trial. The trial was a randomized, double-blind, placebo-controlled clinical trial studying a single dose of REGEN-COV for prevention of COVID-19 in household contacts of individuals infected with SARS-CoV-2. Cases

were confirmed using real-time reverse transcription–polymerase chain reaction (RT-PCR), one of the most accurate laboratory methods for detecting, tracking, and studying COVID-19. An 81% reduction in confirmed symptomatic COVID-19 cases was observed with REGEN-COV compared to placebo at day 29 in cases who were RT-PCR negative and seronegative at baseline (the primary analysis population). In the overall trial population, there was a 62% reduction in RT-PCR confirmed symptomatic COVID-19 cases in the REGEN-COV group compared to placebo at day 29.

Details on the clinical trial results can be found in section 18 of the authorized [Fact Sheet for Health Care Providers](#).

**Q. What is the authorized dose and route of administration for REGEN-COV?**

A. The authorized dose for REGEN-COV for both treatment and as post-exposure prophylaxis is 600 mg of casirivimab and 600 mg of imdevimab administered together.

- For *treatment*, intravenous infusion is strongly recommended; subcutaneous (under the skin) injection is authorized as an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.
- For *post-exposure prophylaxis*, either intravenous infusion or subcutaneous injection is appropriate. For individuals who remain at high risk of exposure to another individual with SARS-CoV-2 for longer than 4 weeks, and who are not expected to mount an adequate immune response to full SARS-CoV-2 vaccination, following an initial dose of 600 mg of casirivimab and 600 mg of imdevimab, repeat doses of 300 mg of casirivimab and 300 mg of imdevimab once every 4 weeks are appropriate for the duration of ongoing exposure.

**Q. Are there clinical trials underway evaluating REGEN-COV for COVID-19?**

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

**Q. Are there side effects (adverse events) of REGEN-COV?**

A. Approximately 16,000 non-hospitalized and hospitalized subjects with symptomatic COVID-19 received REGEN-COV intravenously in clinical trials at doses of 600 mg of casirivimab and 600 mg of imdevimab or higher doses. Approximately 2,500 subjects have received subcutaneous injections of 600 mg of casirivimab and 600 mg of imdevimab or higher doses.

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV. Infusion-related reactions have been observed with administration of REGEN-COV. In the clinical trial in non-hospitalized patients, these reactions have been rare [infusion-related reactions of at least moderate severity were observed in 10 subjects (0.2%) who received REGEN-COV intravenously at the authorized dose or a higher dose, but may be severe or life threatening.

Signs and symptoms of infusion-related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions (e.g., pre-syncope, syncope), dizziness.

Based on reporting of adverse events that occurred after administration of REGEN-COV, clinical worsening of COVID-19 after administration has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, sinus tachycardia,

bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to REGEN-COV use or were due to progression of COVID-19.

In a separate trial in healthy (non-hospitalized) adults, 600 mg of casirivimab and 600 mg of imdevimab were administered together subcutaneously in approximately 700 subjects. Injection site reactions were the most commonly reported adverse events after subcutaneous administration; and the remaining side effects with subcutaneous administration were similar to those observed with intravenous administration. Injection site reactions were the commonly reported side effects with repeat dosing every 4 weeks for six months.

These are not all the possible side effects of REGEN-COV, as not a lot of people have received REGEN-COV. Serious and unexpected side effects may happen. REGEN-COV is still being studied so it is possible that all of the risks are not known at this time. REGEN-COV is contraindicated in individuals with a previous severe hypersensitivity reaction, including anaphylaxis, to REGEN-COV.

**Q. Is there likely to be an increased risk of infusion-related reactions with shorter versus longer infusion times?**

A. FDA does not anticipate an increased risk of infusion-related reactions with the shorter infusion times or use of different size saline bags for dilution authorized. The preparation and administration instructions, including the shorter durations of infusion with smaller volumes of diluent were based on data evaluated by FDA including product quality data and data from clinical trials.

**Q. How can REGEN-COV be obtained for use under the EUA?**

A. Healthcare facilities or providers may request quantities of REGEN-COV via [direct ordering](#).

AmeriSource Bergen will distribute REGEN-COV 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 REGEN-COV to report all medication errors and serious adverse events considered to be potentially related to REGEN-COV 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 REGEN-COV is required.

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

A. The letter of authorization for REGEN-COV 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. How is REGEN-COV supplied?**

A. REGEN-COV is available in two distinct presentations:

*Dose pack bags:* Dose pack bags will include a sufficient number of vials of casirivimab and imdevimab to prepare up to two treatment doses or up to four doses for repeat dose prophylaxis, if appropriate. Casirivimab and imdevimab are each supplied in individual single use vials. Individual vials and carton container labeling for casirivimab and imdevimab included in dose pack bags are clearly marked "For Use under Emergency Use Authorization."

*Co-formulated solution of REGEN-COV:* The co-formulated solution of REGEN-COV contains two antibodies in a 1:1 ratio in a single dose vial consisting of 600 mg casirivimab and 600 mg of imdevimab per 10 mL (60 mg/60 mg per mL). Individual vials of co-formulated REGEN-COV are clearly marked "For Use under Emergency Use Authorization."

Individual vials of 1,200 mg of casirivimab and 1,200 mg of imdevimab distributed prior to the reissuance of [EUA letter of authorization](#) 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 by either intravenous infusion only or subcutaneous injection. Intravenous infusion is strongly recommended for treating infected symptomatic outpatients; and subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment. For post-exposure prophylaxis, casirivimab and imdevimab can be administered either by the subcutaneous or the intravenous route.

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 received a monoclonal antibody for COVID-19?**

A. Yes. Health care providers should refer to recommendations of the [Advisory Committee on Immunization Practices concerning the timing of vaccination](#).

**Q: How are the monoclonal antibody therapies affected by the SARS-CoV-2 viral variants in the United States?**

A. Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. The prevalence of these variants is being monitored by the FDA, Centers for Disease Control and Prevention (CDC), and other stakeholders. Health care providers should review the Antiviral Resistance information in Section 15 of the authorized Fact Sheets for each monoclonal antibody therapy available under an EUA for details regarding specific variants and resistance. Health care providers should also refer to the [CDC website](#) and information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.