

IMPORTANT PRESCRIBING INFORMATION

Subject: Important information on new co-formulated REGEN-COV™ (casirivimab and imdevimab) product, a lower authorized dose, an additional alternative route of administration (subcutaneous), and the updated treatment indication including expanded high-risk criteria for Regeneron COVID-19 Monoclonal Antibodies.

Dear Healthcare Provider:

The purpose of this notice is to make you aware of new information regarding REGEN-COV™ (casirivimab and imdevimab). The following chart highlights the pertinent new information, but is not inclusive of all changes to the Healthcare Providers (HCP) Fact Sheet.

CHART 1. SUMMARY OF RECENT MAJOR CHANGES

Section	Change	Further info located
Dosage and Administration (Box, and Section 2.2):	Updated authorized dosage to 600 mg of casirivimab and 600 mg of imdevimab.	Page 2
Dosage and Administration (Box, Section 2.2 and 2.4):	Addition of subcutaneous route of administration as an alternative route when intravenous infusion is not feasible and would lead to delay in treatment.	Page 2
Dosage and Administration (Box, Section 2.2 and 2.4)	Addition of new REGEN-COV co-formulated product in single vial.	Page 2
Authorized Use	Expanded the definition of progression of severe COVID-19 to include death.	Page 2
Dosage and Administration (Box, Section 2.1)	Expanded high-risk criteria for patient selection.	Page 3

REGEN-COV™ (casirivimab and imdevimab) co-formulated product and REGEN-COV (casirivimab and imdevimab to be administered together) are authorized for use under an Emergency Use Authorization (EUA) for treatment of SARS-CoV-2 infection.

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New Authorized Lower Dose of REGEN-COV

The Phase 3 clinical efficacy and safety endpoints from study COV-2067 in ambulatory patients with COVID-19 demonstrated consistent results across doses of 600 mg of casirivimab and 600 mg of imdevimab and 1,200 mg of casirivimab and 1,200 mg of imdevimab. Based on these data, the dose authorized for REGEN-COV(casirivimab and imdevimab) has been lowered.

The new recommended dosage in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is **600 mg of casirivimab and 600 mg of imdevimab, administered together.**

New Subcutaneous Route of Administration

REGEN-COV (casirivimab and imdevimab) may be administered by intravenous infusion or subcutaneous injection. **Intravenous infusion is strongly recommended. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.** Casirivimab and imdevimab should be given together as soon as possible after a positive viral test for SARS-CoV-2 and within 10 days of symptom onset.

New REGEN-COV Co-formulated Product in Single Vial

REGEN-COV (casirivimab and imdevimab) co-formulated product, NDC 61755-039-01, containing two antibodies in a 1:1 ratio of casirivimab and imdevimab in a **single vial** is now authorized. Each 10 mL vial includes 600 mg of casirivimab and 600 mg of imdevimab. The REGEN-COV co-formulated product may be used to prepare a single treatment dose to be administered by intravenous infusion or subcutaneous injection. Images of the product packaging for REGEN-COV co-formulated product are provided as [Attachment 1](#) at the end of the document.

Authorized Use

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, REGEN-COV (casirivimab and imdevimab) co-formulated product and REGEN-COV (casirivimab and imdevimab 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 progression to severe COVID-19, including hospitalization or death.

LIMITATIONS FOR AUTHORIZED USE

- REGEN-COV (casirivimab and 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

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- 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.
- Benefit of treatment with REGEN-COV has not been observed in patients hospitalized due to COVID-19. 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.

Expanded High-risk Criteria for Patient Selection

Treatment is now authorized in anyone with onset within the past 10 days of symptomatic COVID-19 who is deemed by the HCP as being at increased risk of severe COVID-19, including having an increased risk of hospitalization or death due to COVID-19. To assist in this determination, patient selection criteria were expanded to reference the known information identified by the Centers for Disease Control on factors that put individuals at higher risk for progressing to severe COVID-19. The selection criteria are provided as [Attachment 2](#) at the end of the letter and in the HCP fact sheet Section 2.1.

HCP Action when Using REGEN-COV

In light of these updates and additions to the authorized dosage and route of administration, healthcare providers should update their Electronic Health Records (EHRs) with the new product information including the new authorized dosage to guide the prescribing of REGEN-COV and to allow for the use of current supplies to appropriately treat patients.

Preparation and administration instructions in the HCP Fact Sheet have been updated to reflect the new authorized dosage and route of administration. **Stay current with the latest Fact Sheet for Health Care Providers by visiting** (<https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf>)

All existing REGEN-COV vials may be used to prepare doses for intravenous infusion as well as subcutaneous injection. Although some REGEN-COV cartons and vial labels may have statements such as “Solution for Intravenous Administration” or “For Intravenous Infusion after Dilution” without language that states the subcutaneous route is appropriate, any of these vials may be used to prepare and administer intravenous infusions as well as subcutaneous injections.

Preparation of the 600 mg of casirivimab and 600 mg of imdevimab dose can be prepared with the individual casirivimab vials and imdevimab vials or the REGEN-COV dose packs currently in distribution or the co-formulated product once that product becomes available. If you have REGEN-COV dose packs, it is important to note that the material in each dose pack is sufficient to make **two** 600 mg of casirivimab and 600 mg of imdevimab doses.¹

¹As a reminder, casirivimab and imdevimab are packaged and have been made available to the marketplace in various sizes and configurations. Pharmacists are urged to carefully review the labeling for each carton or package and properly combine the appropriate quantity of vials to obtain the authorized dose (See Section 19 HOW

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- If desired, two doses may be prepared simultaneously according to the direction provided in the HCP Fact Sheet.
- Keep any unused, unopened vials of casirivimab and imdevimab together in the refrigerator to avoid medication errors.
- All REGEN-COV vials are preservative-free. **Once punctured, the vials should be discarded after 4 hours.**

Resources to help clarify dose preparation can be found on www.REGENCOV.com.

Considerations specific to administration of REGEN-COV by intravenous infusion

- For intravenous infusion, consider enabling EHR alerts to remind providers that casirivimab and imdevimab must be diluted prior to intravenous infusion and infused together using a single intravenous bag.
- Have the intravenous dose preparation information for casirivimab and imdevimab available to those preparing the medication.
- If preparing two intravenous bags simultaneously from a dose pack, it is recommended to have an independent double check of the drawn up medications in the syringes prior to injecting into the intravenous bags to prevent medication errors.
- The intravenous bag may be stored under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 36 hours or at room temperature up to 25°C (77°F) for no more than 4 hours.

Considerations specific to administration of REGEN-COV by subcutaneous injection

- Intravenous administration is strongly recommended. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.
- Have the subcutaneous dose preparation information for casirivimab and imdevimab available to those preparing the medication.
- If preparing two subcutaneous treatment doses simultaneously from a dose pack for a total eight prefilled syringes, it is recommended to have an independent double check of the drawn up medications in the syringes and clearly labeled syringe contents at the time of preparation.
- The prepared syringes for subcutaneous administration may be stored under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 4 hours or at room temperature up to 25°C (77°F) for no more than 4 hours.

Patient Counseling Information

- Instruct patients to review the Fact Sheet for Patients, Parents, & Caregivers.

SUPPLIED/STORAGE AND HANDLING in the HCP Fact Sheet). Information and images of variations of individual carton and vial labeling can be found at <https://www.regencov.com/content/pdf/treatment-covid19-packaging-flashcard.pdf>

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- Patients who are treated with REGEN-COV should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.
- If medically appropriate for the patient to receive a COVID-19 vaccine, providers should counsel patients that REGEN-COV does not replace vaccination against COVID-19.
 - Counsel patients to record the date of REGEN-COV administration.
 - Providers may consider recommending that patients schedule COVID-19 vaccination as soon as they are eligible according to local/state public health guidelines but no earlier than 90 days² after REGEN-COV administration.

Reporting Adverse Events and Medication Errors

Healthcare providers should direct questions about REGEN-COV (casirivimab with imdevimab) packaging or use to the Regeneron Medical Information Department at 1-844-734-6643 or to medical.information@regeneron.com.

Under the EUA, all serious adverse events and medication errors potentially related to casirivimab and imdevimab must be reported within 7 calendar days from the onset of the event. Serious adverse event reports and medication error reports should be submitted to FDA’s MedWatch program using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Complete and submit a postage-paid Form FDA 3500 (<https://www.fda.gov/media/76299/download>) and return by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form.

Please provide a copy of all FDA MedWatch forms to Regeneron via fax (1-888-876-2736) or email (medical.information@regeneron.com).

The EUA Fact Sheet for Healthcare Providers is included with this notice, available at www.REGENCOV.com, or available by scanning the QR Code below:



² There are currently no data on the safety and effectiveness of the Pfizer-BioNTech, Moderna, or Janssen COVID-19 vaccines in people who received REGEN-COV. Based upon the low risk of reinfection and the estimated half-life of the monoclonal antibodies to treat COVID-19, the Centers for Disease Control and Prevention’s 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. Updates to the ACIP recommendation may be made as additional information on the interaction between prior monoclonal antibody treatment and vaccine response becomes available.

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Enclosure: EUA Fact Sheet for Healthcare Providers

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1. Images of the REGEN-COV Coformulation Presentation Packaging



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2. High-risk patient criteria

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

- Older age (for example, age ≥ 65 years of age)
- Obesity or being overweight (for example, BMI > 25 kg/m², or if age 12-17, have BMI ≥ 85 th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- 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, see the CDC website: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>. Healthcare providers should consider the benefit-risk for an individual patient.