



EMERGENCY USE AUTHORIZATION  
**EUA GUIDEBOOK**

**REGENERON | MARCH 2021**

REGEN-COV, (casirivimab with imdevimab to be administered together) is authorized 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. [see Limitations of Authorized Use]

- REGEN-COV has not been approved, but has been authorized for emergency use by FDA
- This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner
- Healthcare providers should review the [Fact Sheet for Healthcare Providers](#) for information on the authorized use of REGEN-COV and mandatory requirements of the EUA and must comply with the requirements of the EUA. The [FDA Letter of Authorization](#) is available for reference, as well as the [Dear Healthcare Provider Letter](#) and [Patient Fact Sheet](#)

**Limitations of Authorized Use**

- 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
- 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

**Be sure to check [regencov.com](https://www.regencov.com) for periodic updates to the information contained in this guidebook.**

## TABLE OF CONTENTS

|  |           |
|--|-----------|
| <b>EXECUTIVE SUMMARY</b>   | <b>3</b>  |
| <b>SECTION 1: Population for Antibody Treatment and Important Information for Healthcare Providers</b> | <b>5</b>  |
| Authorized Use and Important Safety Information  | 6         |
| <b>SECTION 2: Current Supply and Ongoing Manufacturing Effort</b>                                      | <b>12</b> |
| <b>SECTION 3: Allocation, Ordering, and Administration Sites</b>                                       | <b>14</b> |
| Dual Antibody Therapy: Allocation Flow in the US   | 18        |
| <b>SECTION 4: Coding and Reimbursement</b>   | <b>19</b> |
| <b>SECTION 5: Product Packaging</b>  | <b>24</b> |
| <b>SECTION 6: Preparation and Administration Instructions</b>  | <b>30</b> |
| Dosing and Administration  | 31        |
| Preparation and Administration   | 33        |
| <b>SECTION 7: Education and Awareness</b>  | <b>36</b> |
| Passive Immunity   | 41        |
| Active Immunity  | 43        |
| <b>SECTION 8: Clinical Data</b>  | <b>46</b> |
| <b>APPENDIX A: Dear Healthcare Provider Letter: Important Information for Healthcare Providers</b>     | <b>55</b> |
| <b>APPENDIX B: Overview of Direct Order System</b>   | <b>66</b> |
| <b>APPENDIX C: Clinical Trial Modeling Information</b>   | <b>68</b> |
| <b>APPENDIX D: Ongoing Clinical Trials</b>   | <b>70</b> |
| <b>APPENDIX E: FAQs</b>  | <b>72</b> |
| <b>APPENDIX F: Basic Equipment Recommendations</b>   | <b>81</b> |

# EXECUTIVE SUMMARY

The COVID-19 pandemic is a global health crisis unlike any experienced in our lifetime. Regeneron has risen to this challenge with our 30 years of biotechnology expertise and deep experience in rapid response against global infectious diseases. Our science-driven culture and sense of responsibility to communities around the world galvanize us as we join in the fight against COVID-19.

## **About REGEN-COV™ (casirivimab with imdevimab)**

REGEN-COV consists of casirivimab and imdevimab, which are administered together by intravenous (IV) infusion. Casirivimab and imdevimab, also known as REGN10933 and REGN10987, respectively, form a dual monoclonal antibody (mAb) therapy designed specifically to block infectivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19.

To develop REGEN-COV, Regeneron scientists evaluated thousands of fully human antibodies produced by the company's *VelocImmune*® mice, which have been genetically modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19. The 2 virus-neutralizing mAb that form REGEN-COV bind noncompetitively to the critical receptor-binding domain of the virus' spike protein. In preclinical studies, each variant of the virus showing reduced susceptibility to one mAb retained susceptibility to the other, and all variants retained susceptibility to the casirivimab and imdevimab combination. Circulating SARS-CoV-2 viral variants may be associated with resistance to mAbs. Health care providers should review the Antiviral Resistance information in Section 15 of the Fact Sheet for Healthcare Providers for details regarding specific variants and resistance, and refer to the [CDC website](#) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

The development and manufacturing of REGEN-COV have been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the US Department of Health and Human Services under OT number: HHSO100201700020C.

# EXECUTIVE SUMMARY (CONT'D)

## About REGEN-COV™ (casirivimab with imdevimab) (cont'd)

The REGEN-COV antibody combination continues to be evaluated in Phase 2/3 clinical trials for the treatment of COVID-19 in certain hospitalized and nonhospitalized patients, the Phase 3 open-label RECOVERY trial of hospitalized patients in the UK, and a Phase 3 trial for the prevention of COVID-19 in household contacts of infected individuals. To date, approximately 23,000 people have participated in REGEN-COV clinical trials. For information on these ongoing trials, visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov). REGEN-COV does not have FDA Emergency Use Authorizations in these populations described and is not FDA approved for these uses.

This **REGEN-COV EUA Guidebook** compiles critical information, including Regeneron's clinical trial experience with REGEN-COV, guidance from the National Infusion Center Association (NICA), and links to available resources, to assist health authorities and healthcare providers in planning and implementing treatment efforts against COVID-19. This guidebook should not supersede local requirements for sites of care or substitute for the medical judgment of treating healthcare professionals.

Healthcare providers should review the [Fact Sheet for Healthcare Providers](#) for information on the authorized use of REGEN-COV and mandatory requirements of the EUA. The [FDA Letter of Authorization](#) is available for reference, as well as the [Dear Healthcare Provider Letter](#) and [Patient Fact Sheet](#).

*SECTION 1:*

**POPULATION FOR  
ANTIBODY TREATMENT  
AND IMPORTANT  
INFORMATION FOR  
HEALTHCARE PROVIDERS**

# POPULATION FOR ANTIBODY TREATMENT

## Authorized Use and Important Safety Information

REGEN-COV™, (casirivimab with imdevimab to be administered together) is authorized 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. [see Limitations of Authorized Use]

- REGEN-COV has not been approved, but has been authorized for emergency use by FDA
- This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner
- Healthcare providers should review the [Fact Sheet for Healthcare Providers](#) for information on the authorized use of REGEN-COV and mandatory requirements of the EUA and must comply with the requirements of the EUA. The [FDA Letter of Authorization](#) is available for reference, as well as the [Dear Healthcare Provider Letter](#) and [Patient Fact Sheet](#)

## Limitations of Authorized Use

- 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
- 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

# POPULATION FOR ANTIBODY TREATMENT (CONT'D)

**This EUA is for the use of the unapproved product, REGEN-COV™, (casirivimab with imdevimab 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 [see *Limitations of Authorized Use*].**

## **Definition of High Risk Patients**

High risk 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  $\geq 85$ th 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 COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control

Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Healthcare providers should review the Antiviral Resistance information in Section 15 of the [Fact Sheet for Healthcare Providers](#) for details regarding specific variants and resistance, and refer to the [CDC website](#) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

## POPULATION FOR ANTIBODY TREATMENT (CONT'D)

### **CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.**

REGEN-COV™ (casirivimab with 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 the ability to activate the emergency medical system (EMS), as necessary.

Healthcare providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to REGEN-COV. See sections 8 and 9 of the Full EUA Prescribing Information for reporting requirements.

- The authorized dosage is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous (IV) infusion as soon as possible after a positive viral test for SARS-CoV-2 and within 10 days of symptom onset
- Casirivimab and imdevimab solutions must be diluted prior to administration
- Administer 1,200 mg of casirivimab and 1,200 mg of imdevimab together as a single IV infusion via pump or gravity (see Table 1)
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete
- Patients treated with REGEN-COV should continue to self-isolate and use infection control measures (eg, wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines

The authorized dosage may be updated as additional data from clinical trials become available.

For information on clinical trials that are testing the use of REGEN-COV in COVID-19, please see [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **Additional Information for Healthcare Providers:**

- Casirivimab and imdevimab are each provided in a separate carton and vial. **Casirivimab** and **imdevimab** vial labels and carton labeling may instead be labeled **REGN10933** and **REGN10987**, respectively.
- Each REGEN-COV dose pack contains sufficient number of vials of casirivimab (REGN10933) and imdevimab (REGN10987) to prepare one treatment dose.



## POPULATION FOR ANTIBODY TREATMENT (CONT'D)

- You may receive cartons and vials of casirivimab and imdevimab that are labeled “for intravenous infusion or subcutaneous injection.” **However, casirivimab and imdevimab must be administered together (although packaged separately) after dilution by intravenous (IV) infusion only**
- Store casirivimab and imdevimab together in inventory. See [regencov.com/hcp/dosing/packaging](https://regencov.com/hcp/dosing/packaging) for images of packaging
- REGEN-COV™ (casirivimab with imdevimab) may only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary
- **The authorized dosage is 1200 mg of casirivimab with 1200 mg of imdevimab administered together as a single intravenous (IV) infusion as soon as possible after a positive viral test for SARS-CoV-2 and within 10 days of symptom onset.** Since the optimal dosing regimen has not yet been established, it might be updated as data become available. See the [Fact Sheet for Healthcare Providers](#) for complete dosage, preparation, and administration instructions

- The prescribing healthcare provider and/or the provider’s designee are responsible for mandatory reporting of all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to REGEN-COV. These adverse events must be reported within 7 calendar days from the onset of the event
- Healthcare facilities and providers must report therapeutics information and demonstrate adequate utilization via data reported through HHS Protect, Teletracking or National Healthcare Safety Network (NHSN) as directed by the U.S. Department of Health and Human Services
- **MedWatch adverse event reports can be submitted to the FDA [here](#), by using a postage-paid Form FDA 3500 and returning by mail/fax, or by calling 1-800-FDA-1088 to request a reporting form.** In addition, please provide a copy of all FDA MedWatch forms to Regeneron Pharmaceuticals, Inc via fax (1-888-876-2736) or email ([medical.information@regeneron.com](mailto:medical.information@regeneron.com))

# IMPORTANT SAFETY INFORMATION

REGEN-COV™ (casirivimab with imdevimab) is an unapproved investigational therapy, and there are limited clinical data available. Serious and unexpected adverse events may occur that have not been previously reported with REGEN-COV use.

- **Warnings and Precautions:**

- **Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions:** Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV (casirivimab with 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 REGEN-COV. These reactions may be severe or life threatening.
  - **Signs and symptoms of infusion-related reactions may include:** fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, fatigue and diaphoresis. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care
- **Clinical Worsening After REGEN-COV Administration:** Clinical worsening of COVID-19 after administration of REGEN-COV has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, 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
- **Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19:** 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. Therefore, 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

- **Adverse Reactions:**

- Serious adverse events (SAEs) were reported in 4 (1.6%) patients in the REGEN-COV 2,400-mg group, 2 (0.8%) patients in the REGEN-COV 8,000-mg group, and 6 (2.3%) patients in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg REGEN-COV), intestinal obstruction and dyspnea (8,000 mg REGEN-COV) and COVID-19, pneumonia and hypoxia (placebo). REGEN-COV **is not authorized at the 8,000-mg dose (4,000 mg casirivimab and 4,000 mg imdevimab)**

## IMPORTANT SAFETY INFORMATION (CONT'D)

- **Adverse Reactions (cont'd):**

- One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of Grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000-mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and included pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm, and none were reported in the 2,400-mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm. In two subjects receiving the 8,000-mg dose of REGEN-COV, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved

- **Patient Monitoring Recommendations:** Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete

- **Use in Specific Populations:**

- **Pregnancy:** There is currently limited clinical experience in the use of REGEN-COV in COVID-19 patients who are pregnant. REGEN-COV therapy should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus
- **Lactation:** There is currently no clinical experience in the use of REGEN-COV in COVID-19 patients who are breastfeeding. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for REGEN-COV and any potential adverse effects on the breastfed child from REGEN-COV or from the underlying maternal condition

*SECTION 2:*

**CURRENT SUPPLY  
AND ONGOING  
MANUFACTURING EFFORT**

# CURRENT SUPPLY AND ONGOING MANUFACTURING EFFORT

Production of monoclonal antibodies is a complex, time- and labor-intensive process that requires deep expertise. Utilizing production and manufacturing platforms developed over decades, Regeneron rapidly scaled up REGEN-COV™ (casirivimab with imdevimab) production, beginning in the early days of the pandemic with support from the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the US Department of Health and Human Services.

All treatment sites meeting EUA requirements can order REGEN-COV directly from AmerisourceBergen Corporation, the drug's sole distributor. The product is free of charge to requesting sites.

Regeneron continues to increase in-house production of REGEN-COV, and the company has partnered with Roche to increase the global supply beginning in 2021. If the therapy proves effective in clinical trials and regulatory approvals are granted, Regeneron will manufacture and distribute it in the



## 1.5M+ DOSES

**The government has committed to providing more than 1.5 million doses at no cost to patients** although healthcare facilities may charge fees related to infusion administration.

US and Roche will develop, manufacture, and distribute it outside the US. Once both companies are at full manufacturing capacity in 2021, at least 2 million treatment doses are expected to be available annually.

Be sure to visit [regencov.com](https://regencov.com) for periodic updates.

*SECTION 3:*

**ALLOCATION, ORDERING,  
AND ADMINISTRATION SITES**

# ALLOCATION, ORDERING, AND ADMINISTRATION SITES

## Access

All treatment sites meeting EUA requirements must order REGEN-COV™ (casirivimab with imdevimab) directly from AmerisourceBergen Corporation, the drug's sole distributor. The product is free of charge to requesting sites.

Treatment sites should review the [ASPR direct ordering process guide](#) and place orders directly with AmerisourceBergen Corporation [here](#).

## Find Infusion Sites Near You

US states and territories are partnering with the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR) and the National Infusion Center Association (NICA)\* to provide a list of infusion site locations by state.

To find infusion centers where REGEN-COV and other antibody therapies for COVID-19 may be available, use the following infusion center locators:

### [Locate Infusion Centers \(NICA\)](#)

### [Locate Infusion Centers \(ASPR\)](#)

\*IMPORTANT INFORMATION: Infusion sites displayed in this tool have been authorized to administer antibody treatments for COVID-positive patients under Emergency Use Authorization. These antibody therapies are restricted to certain high-risk patients and require a drug order (similar to a prescription) from a healthcare provider (HCP) for eligible patients. HCPs must verify eligibility of their patients and verify the availability of doses at an authorized infusion site before they refer an eligible patient to schedule an appointment to receive treatment at an authorized infusion site. Please note that the inclusion of a site does not imply current availability of doses. More states and locations are regularly being added to both resources. Any questions related to distribution should be directed to AmerisourceBergen Corporation.

# ALLOCATION, ORDERING, AND ADMINISTRATION SITES (CONT'D)

## FAQs

? Is there a list of centers where REGEN-COV™ (casirivimab with imdevimab) is available?

Details on infusion centers where antibody therapies, including REGEN-COV, may be available can be found on the [HHS Office of the Assistant Secretary for Preparedness and Response \(ASPR\)](#) and the [National Infusion Center Association \(NICA\)\\*](#) site locators.

\*IMPORTANT INFORMATION: Infusion sites displayed in this tool have been authorized to administer antibody treatments for COVID-positive patients under Emergency Use Authorization. These antibody therapies are restricted to certain high-risk patients and require a drug order (similar to a prescription) from a healthcare provider (HCP) for eligible patients. HCPs must verify eligibility of their patients and verify the availability of doses at an authorized infusion site before they refer an eligible patient to schedule an appointment to receive treatment at an authorized infusion site. Please note that the inclusion of a site does not imply current availability of doses. More states and locations are regularly being added. If not yet listed, ambulatory centers or other administration sites should contact their state health departments.

? How can treatment sites order/reorder REGEN-COV?

To order REGEN-COV, treatment sites should contact AmerisourceBergen Corporation directly at [c19therapies@amerisourcebergen.com](mailto:c19therapies@amerisourcebergen.com). Treatment sites should also review the ASPR direct ordering process guide found in **Appendix B** of this guidebook, and can fill out a C19 Therapies Direct Order Request [here](#).

? What is the coverage and reimbursement for REGEN-COV?

REGEN-COV is free of charge to requesting treatment sites, as the United States government is paying for the product. The combination therapy must be administered via a single intravenous infusion. Therefore, claims may be submitted for the reimbursement of the drug administration only.

Coverage and reimbursement of COVID-19-related treatments and procedures may vary from payer to payer; therefore, it is important that providers clarify and confirm any coding/billing requirements with respective payers.



# ALLOCATION, ORDERING, AND ADMINISTRATION SITES (CONT'D)

## FAQs (cont'd)



Who determines which infusion sites receive REGEN-COV™ (casirivimab with imdevimab)?

Treatment sites must order REGEN-COV directly from AmerisourceBergen Corporation, the drug's sole distributor. Approval of sites to receive product will be determined by AmerisourceBergen Corporation in conjunction with the United States government.



How is REGEN-COV supplied?

Casirivimab and imdevimab are both sterile, preservative-free, clear to slightly opalescent and colorless to pale yellow solutions to be administered together in a single intravenous infusion after dilution. Product is shipped refrigerated (2-8 °C) to the administration site by AmerisourceBergen Corporation. As of February 2021, AmerisourceBergen Corporation is shipping REGEN-COV Dose Packs providing one treatment dose of 2,400 mg (1,200 mg of casirivimab and 1,200 mg of imdevimab).

**For important packaging information, see Section 5 of this guidebook.**

# ALLOCATION, ORDERING, AND ADMINISTRATION SITES (CONT'D)

## Dual Antibody Therapy: Allocation Flow in the US



Treatment sites can review the [ASPR direct ordering process guide](#) and place orders directly with AmerisourceBergen [here](#).

*SECTION 4:*

# **CODING AND REIMBURSEMENT**

# CODING AND REIMBURSEMENT

**The following information is presented for informational purposes only and is not intended to guarantee or provide reimbursement or legal advice. Regeneron and its agents make no warranties or guarantees concerning the accuracy or appropriateness of this information for your particular use. The information in this guidebook is gathered from various resources and subject to change without notice. Payer coding requirements may vary or change over time, so it is important to regularly check with each payer to confirm payer-specific requirements.**

**The following information pertains to REGEN-COV™ (casirivimab with imdevimab) therapy and administration:**

- Review of relevant codes
  - International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes
  - Level I Healthcare Common Procedure Coding System (HCPCS) Current Procedural Terminology (CPT) Codes
  - Level II Healthcare Common Procedure Coding System (HCPCS) Product Codes
  - National Drug Code (NDC)
- Additional considerations

## **Review of Relevant Codes**

The following codes should be confirmed with each respective payer, as there may be variability in both coding and documentation requirements.

# CODING AND REIMBURSEMENT (CONT'D)

## International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes

A COVID-19 diagnosis code was implemented for services on or after April 2, 2020. This code should be designated as the primary diagnosis. Providers will select secondary diagnoses based on the patient presentation of further complications from COVID-19. These complications require appropriate documentation in the patient's medical record.

| Code <sup>1</sup> | Description | Notes   |
|-------------------|-------------|---|
| U07.1             | COVID-19    | For discharges on or after April 1, 2020, through the duration of the COVID-19 public health emergency period |

## Level I Healthcare Common Procedure Coding System (HCPCS) Current Procedural Terminology (CPT) Codes

REGEN-COV™ (casirivimab with imdevimab) will be administered via a single intravenous (IV) infusion. Please check with the payer to determine the appropriate administration code.

| Code <sup>2</sup> | Description   |
|-------------------|---|
| M0243             | IV infusion, casirivimab and imdevimab includes infusion and post administration monitoring |

# CODING AND REIMBURSEMENT (CONT'D)

## Level II Healthcare Common Procedure Coding System (HCPCS) Product Coding

The following HCPCS code may be used to identify REGEN-COV™ (casirivimab with imdevimab). Please check with the payer to determine the appropriate drug code.

| Code <sup>2</sup> | Description                                   |
|-------------------|---|
| <b>Q0243</b>      | Injection, casirivimab and imdevimab, 2400 mg |

Select payers may require further claims documentation to better identify both casirivimab (REGN10933) and imdevimab (REGN10987), which could include but not be limited to:

- Treatment National Drug Codes (NDCs)
- Descriptor of monoclonal antibody name(s)
- Mode of administration

## Casirivimab and Imdevimab NDC<sup>3</sup>

| Antibody           | Concentration               | Package size      | NDC number <sup>a</sup> |
|--------------------|-----------------------------|-------------------|-------------------------|
| <b>Casirivimab</b> | 1332 mg/11.1 mL (120 mg/mL) | 1 vial per carton | 61755- <b>00</b> 24-01  |
|                    | 300 mg/2.5 mL (120 mg/mL)   | 1 vial per carton | 61755- <b>00</b> 26-01  |
| <b>Imdevimab</b>   | 1332 mg/11.1 mL (120 mg/mL) | 1 vial per carton | 61755- <b>00</b> 25-01  |
|                    | 300 mg/2.5 mL (120 mg/mL)   | 1 vial per carton | 61755- <b>00</b> 27-01  |

Note: casirivimab=REGN10933; imdevimab=REGN10987.

<sup>a</sup>Note that each NDC code has been “zero-filled” to ensure creation of an 11-digit code that meets HIPAA compliant standards. The zero-fill location is indicated in bold. HIPAA (Health Insurance Portability and Accountability Act); NDC (National Drug Code).<sup>4</sup>

# CODING AND REIMBURSEMENT (CONT'D)

## Dose Pack Providing 1 Treatment Dose of 2,400 mg (1,200 mg Casirivimab and 1,200 mg Imdevimab)<sup>3</sup>

| Dose-Pack Size | Dose-Pack Components                          | Concentration                | Dose-Pack National Drug Code (NDC) Number |
|----------------|---|------------------------------|---|
| 2 Cartons      | 1 casirivimab REGN10933<br>(NDC 61755-024-01) | 1,332 mg/11.1 mL (120 mg/mL) | 61755-035-02                              |
|                | 1 imdevimab REGN10987<br>(NDC 61755-025-01)   | 1,332 mg/11.1 mL (120 mg/mL) |   |
| 8 Cartons      | 4 casirivimab REGN10933<br>(NDC 61755-026-01) | 300 mg/2.5 mL (120 mg/mL)    | 61755-036-08                              |
|                | 4 imdevimab REGN10987<br>(NDC 61755-027-01)   | 300 mg/2.5 mL (120 mg/mL)    |   |
| 5 Cartons      | 1 casirivimab REGN10933<br>(NDC 61755-024-01) | 1,332 mg/11.1 mL (120 mg/mL) | 61755-037-05                              |
|                | 4 imdevimab REGN10987<br>(NDC 61755-027-01)   | 300 mg/2.5 mL (120 mg/mL)    |   |
| 5 Cartons      | 4 casirivimab REGN10933<br>(NDC 61755-026-01) | 300 mg/2.5 mL (120 mg/mL)    | 61755-038-05                              |
|                | 1 imdevimab REGN10987<br>(NDC 61755-025-01)   | 1,332 mg/11.1 mL (120 mg/mL) |   |

## Additional Considerations

Since REGEN-COV™ (casirivimab with imdevimab) will be made available by the government to providers at no cost during the initial EUA period, providers may not receive third-party payer reimbursement for the therapy when delivered in the hospital outpatient setting of care. However, providers MAY be able to obtain payment for the drug administration service. Providers should clarify claim submission requirements by payer, as the documentation may vary.

For Medicare beneficiaries, providers must report the applicable drug Healthcare Common Procedure Coding System (HCPCS) code and appropriate units with a token charge of less than \$1.01 for the item in the covered charge field and mirror this less than \$1.01 amount reported in the noncovered charge field. Providers must also bill the corresponding drug administration charge with the appropriate drug administration Current Procedural Terminology (CPT) code.<sup>5</sup>

### References:

- Centers for Disease Control and Prevention. ICD-10-CM Official Guidelines for Coding and Reporting FY 2021 (October 1, 2020 - September 30, 2021). Chapter 1: Certain Infectious and Parasitic Diseases, U07.1. [https://www.cdc.gov/nchs/data/icd/10cmguidelines-FY2021.pdf?fbclid=IwAR34L5vPlwhbRYv6AgCFxpZX\\_Gt42jgLAeMncAraBPEpaW8lcVEDPbH3uVw](https://www.cdc.gov/nchs/data/icd/10cmguidelines-FY2021.pdf?fbclid=IwAR34L5vPlwhbRYv6AgCFxpZX_Gt42jgLAeMncAraBPEpaW8lcVEDPbH3uVw). Accessed January 29, 2021.
- Centers for Medicare & Medicaid Services. Medicare monoclonal antibody COVID-19 infusion program instruction. <https://www.cms.gov/files/document/covid-medicare-monoclonal-antibody-infusion-program-instruction.pdf>. Updated December 3, 2020. Accessed January 29, 2021.
- Fact Sheet For Health Care Providers. Emergency Use Authorization (EUA) Of REGEN-COV™ (casirivimab with imdevimab). Regeneron Pharmaceuticals, Inc. March 2021. <https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf>. Accessed March 22, 2021.
- US Food and Drug Administration. National Drug Code Background Information. <https://www.fda.gov/drugs/development-approval-process-drugs/national-drug-code-database-background-information>. Accessed January 29, 2021.
- Centers for Medicare & Medicaid Services. Medicare Claims Processing Manual Chapter 32 - Billing Requirements for Special Services 67.2 – Institutional Billing for No Cost Items. <https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM10521.pdf>. Accessed January 31, 2021.

*SECTION 5:*

# **PRODUCT PACKAGING**



# PRODUCT PACKAGING

## IMPORTANT PACKAGING INFORMATION

**Casirivimab** and **imdevimab** vial labels and carton labeling may instead be labeled **REGN10933** and **REGN10987**, respectively.

You may receive cartons and vials of casirivimab and imdevimab that are labeled “for intravenous infusion or subcutaneous injection.” **However, casirivimab and imdevimab must be administered together after dilution by intravenous (IV) infusion only.**

- **REGN10933 or casirivimab**; these refer to the same monoclonal antibody
- **REGN10987 or imdevimab**; these refer to the same monoclonal antibody

# REGEN-COV™ (casirivimab with imdevimab) DOSE PACKS

## REGEN-COV Dose Packs: Casirivimab and Imdevimab Now Packaged Together

REGEN-COV Dose Packs are now available.

Each REGEN-COV Dose Pack is delivered in a sealed plastic bag and contains:

- **Sufficient number of vials of casirivimab (REGN10933) and imdevimab (REGN10987) to prepare one treatment dose**
  - Since casirivimab and imdevimab are both available in different vial sizes (see Table 1 on the next page for all dose pack vial combinations), REGEN-COV Dose Packs may contain 2, 5, or 8 vials
- A 1-page **Information Sheet**; please read this information carefully
- A sticker on the bag with the name REGEN-COV and the National Drug Code (NDC) based on the combination of cartons contained within the dose pack

# REGEN-COV™ (casirivimab with imdevimab) DOSE PACKS (CONT'D)

**Table 1: Dose Pack Providing 1 Treatment Dose of 2,400 mg REGEN-COV  
(1,200 mg Casirivimab and 1,200 mg Imdevimab)**

The cartons depicted in these dose packs may vary in appearance. See next 2 pages for all carton labeling variations.



NDC 61755-**035**-02  
**Combination of 2 vials**



1 vial of  
casirivimab  
11.1 mL

AND



1 vial of  
imdevimab  
11.1 mL



NDC 61755-**037**-05  
**Combination of 5 vials**



1 vial of  
casirivimab  
11.1 mL

AND



4 vials of  
imdevimab  
2.5 mL



NDC 61755-**036**-08  
**Combination of 8 vials**

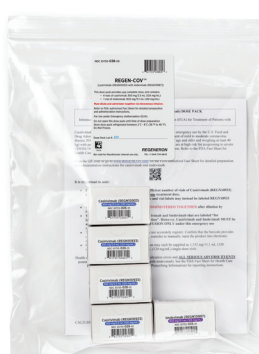


4 vials of  
casirivimab  
2.5 mL

AND



4 vials of  
imdevimab  
2.5 mL



NDC 61755-**038**-05  
**Combination of 5 vials**



4 vials of  
casirivimab  
2.5 mL

AND



1 vial of  
imdevimab  
11.1 mL

The dose packs' expiry is based on the expiration dating of the vials included in the dose pack, and none will expire any earlier than May 31, 2022. If you are uncertain of when the products expire, you may call Regeneron Medical Information at 1-844-734-6643. Expiration dates for dose packs can be found on the packing slip within a shipment of material. Cartons in the dose pack may have different labeling, lot numbers, and expiration dates but none will expire any earlier than May 31, 2022.

**CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER  
AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.**


# REGEN-COV™ (casirivimab with imdevimab) PACKAGING

In addition to REGEN-COV Dose Packs, single cartons of casirivimab and imdevimab will still be in distribution and you may encounter variations in carton and vial labeling. This is because some clinical trial supply is being made available to fulfill need during this public health emergency. Please see below for the two variations of carton and vial labeling for each antibody vial size.


## Casirivimab REGN10933

2.5 mL

Carton




Vial

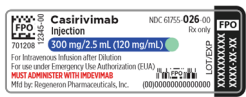


Reverse side of carton

Carton




Vial




11.1 mL

Carton




Vial

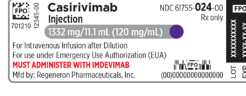


Reverse side of carton

Carton



Vial



Some cartons do not include expiration. To obtain expiration dating, contact Regeneron Medical Information at [medical.information@regeneron.com](mailto:medical.information@regeneron.com)

**FOR INFORMATION ABOUT THE DOSING AND ADMINISTRATION OF REGEN-COV,  
SEE SECTION 6 AND APPENDIX A OF THIS GUIDEBOOK.**

**REGENERON** | 28

# REGEN-COV™ (casirivimab with imdevimab) PACKAGING (CONT'D)

## Imdevimab REGN10987

2.5 mL

Carton

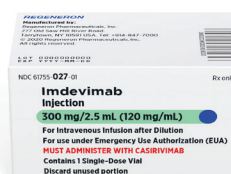


Vial

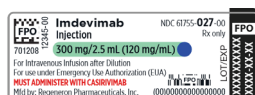


Reverse side of carton

Carton



Vial

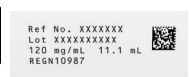


11.1 mL

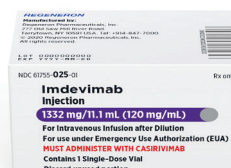
Carton



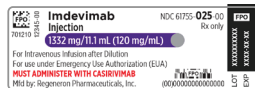
Vial



Carton



Vial



**FOR INFORMATION ABOUT THE DOSING AND ADMINISTRATION OF REGEN-COV,  
SEE SECTION 6 AND APPENDIX A OF THIS GUIDEBOOK.**

*SECTION 6:*

**PREPARATION  
AND ADMINISTRATION  
INSTRUCTIONS**

# PREPARATION AND ADMINISTRATION INSTRUCTIONS

## DOSING AND ADMINISTRATION

- **CASIRIVIMAB WITH IMDEVIMAB MUST BE ADMINISTERED TOGETHER (ALTHOUGH PACKAGED SEPARATELY) AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY**
- REGEN-COV™ (casirivimab with imdevimab) may only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary
- The dosage in adults and in pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion via pump or gravity (see Table 1 below)
- Casirivimab and imdevimab solutions must be diluted prior to administration
- Casirivimab and imdevimab should be given together as soon as possible after positive SARS-CoV-2 results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset. Since the optimal dosing regimen has not yet been established, it might be updated as data become available
- No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment
- See the [Fact Sheet for Healthcare Providers](#) for complete dosage, preparation, and administration instructions, as well as for use in specific populations (Section 11)

# PREPARATION AND ADMINISTRATION INSTRUCTIONS (CONT'D)



## Storage and Handling

Casirivimab is preservative-free. Discard any unused portion.

Imdevimab is preservative-free. Discard any unused portion.

Store unopened casirivimab and imdevimab vials in a refrigerator at 2-8 °C (36-46 °F) in the original carton to protect from light.

**DO NOT FREEZE. DO NOT SHAKE.  
DO NOT EXPOSE TO DIRECT LIGHT  
OR HEAT.**

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted casirivimab and imdevimab solution in the refrigerator at 2-8 °C (36-46 °F) for no more than 36 hours or at room temperature up to 25 °C (77 °F) for no more than 4 hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.\*

\*These times were based on preparation in an environment with at least ISO Class 5 air quality in accordance with United States Pharmacopeia (USP) General Chapter <797> Pharmaceutical Compounding–Sterile Preparations. If extenuating circumstances preclude immediate administration, manufacturer guidelines and National Infusion Center Association standards regarding stability, storage and preparation must be followed.

**CARTONS AND VIALS FOR CASIRIVIMAB AND IMDEVIMAB MAY BE LABELED  
REGN10933 AND REGN10987, RESPECTIVELY.**



# PREPARATION AND ADMINISTRATION INSTRUCTIONS (CONT'D)



## PARENTERAL MEDICATION PREPARATION GUIDELINES

According to the National Infusion Center Association Standards, prepared product is intended for immediate administration to an individual patient. Administration of parenteral medications should begin immediately, ideally within 1 hour of beginning preparation. If extenuating circumstances preclude immediate administration, manufacturer guidelines and National Infusion Center Association standards regarding stability, storage and preparation must be followed.

## PREPARATION AND ADMINISTRATION

### Preparation

Casirivimab and imdevimab are each supplied in individual single-dose vials. Casirivimab with imdevimab infusion solution must be diluted prior to administration.

Casirivimab with imdevimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique:

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation.  
**Do not expose to direct heat. Do not shake the vials.**
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and fresh solution prepared.
  - The solution for each vial should be clear to slightly opalescent, colorless to pale yellow
3. Obtain a prefilled IV infusion bag containing either 50 mL, 100 mL, 150 mL, or 250 mL of 0.9% Sodium Chloride Injection.
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial\* using 2 separate syringes (see **Table 1**) and inject all 20 mL into a prefilled infusion bag containing 0.9% Sodium Chloride Injection (see **Table 1**). Discard any product remaining in the vial.
5. Gently invert infusion bag by hand approximately 10 times to mix. **Do not shake.**
6. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately.
  - If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 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. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration†

Each REGEN-COV Dose Pack contains sufficient number of vials of casirivimab and imdevimab to prepare one treatment dose. Vials should remain in the dose pack until time of preparation of the IV solution. See **Table 2**.

\*Multiple vials may be needed to obtain 10 mL. See preparation and administration instructions on the next page.

†These times were based on preparation in an environment with at least ISO Class 5 air quality in accordance with United States Pharmacopeia (USP) General Chapter <797> Pharmaceutical Compounding—Sterile Preparations.

# PREPARATION AND ADMINISTRATION INSTRUCTIONS (CONT'D)







**Table 1: Recommended Dosing, Dilution, and Administration Instructions for Casirivimab with Imdevimab for Intravenous (IV) Infusion**

| Size of Prefilled 0.9% Sodium Chloride Infusion Bag | Maximum Infusion Rate | Concentration |
|---|-----------------------|---------------|
| 50 mL <sup>a</sup>                                  | 210 mL/hr             | 20 minutes    |
| 100 mL  | 310 mL/hr             | 23 minutes    |
| 150 mL  | 310 mL/hr             | 33 minutes    |
| 250 mL  | 310 mL/hr             | 52 minutes    |

<sup>a</sup>The minimum infusion time for patients administered casirivimab with imdevimab together using the 50-mL prefilled 0.9% Sodium Chloride infusion bag must be at least 20 minutes to ensure safe use.

1,200 mg casirivimab and 1,200 mg imdevimab are added to the same infusion bag and administered together as a single IV infusion. After infusion is complete, flush with 0.9% Sodium Chloride Injection.

**Table 2: Casirivimab with Imdevimab for IV Infusion (to be administered together as a 2,400-mg dose)<sup>a</sup>**

| Antibody dose                               | Volume to withdraw from vial(s)   | Number of vials needed <sup>b</sup>   |
|---|---|---|
| <b>Casirivimab</b><br>REGN10933<br>1,200 mg |  10 mL |  1 vial of 11.1 mL<br><b>OR</b><br> 4 vials of 2.5 mL |
| <b>Imdevimab</b><br>REGN10987<br>1,200 mg   |  10 mL |  1 vial of 11.1 mL<br><b>OR</b><br> 4 vials of 2.5 mL |

<sup>a</sup>1,200 mg casirivimab and 1,200 mg imdevimab are added to the same infusion bag and administered together as a single IV infusion.

<sup>b</sup>One 11.1-mL vial of one antibody may be prepared with four 2.5-mL vials of the other antibody to create one treatment course.

# PREPARATION AND ADMINISTRATION INSTRUCTIONS (CONT'D)

## Administration

Casirivimab with imdevimab infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, or polyurethane (PU) infusion set
  - In-line or add-on 0.2 micron polyethersulfone (PES)\* filter
- Attach the infusion set to the intravenous bag
- Prime the infusion set
- Administer the entire infusion solution in the bag via pump or gravity through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see **Table 1**). Due to potential overfill of prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known
- After infusion is complete, flush the tubing with 0.9% Sodium Chloride Injection to ensure delivery of the required dose
- Discard unused product
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete

\*If alternate materials are used, the compatibility of these materials should be confirmed with that vendor. Casirivimab and imdevimab have no known incompatibilities with conventional medical supplies and equipment.

**Table 3: Gravity Drip Rate<sup>1</sup>**

**Drip rates for 10-drops/mL administration sets**

| VTBI (mL) | Duration (min) | Rate (mL/hr) | Drops per minute | Drops per 15 seconds |
|-----------|----------------|--------------|------------------|----------------------|
| 70        | 20             | 210          | 35               | 9                    |
| 120       | 23             | 310          | 52               | 13                   |
| 170       | 33             |              |                  |                      |
| 270       | 52             |              |                  |                      |

**Drip rates for 15-drops/mL administration sets**

| VTBI (mL) | Duration (min) | Rate (mL/hr) | Drops per minute | Drops per 15 seconds |
|-----------|----------------|--------------|------------------|----------------------|
| 70        | 20             | 210          | 53               | 13                   |
| 120       | 23             | 310          | 77               | 19                   |
| 170       | 33             |              |                  |                      |
| 270       | 52             |              |                  |                      |

**Drip rates for 20-drops/mL administration sets**

| VTBI (mL) | Duration (min) | Rate (mL/hr) | Drops per minute | Drops per 15 seconds |
|-----------|----------------|--------------|------------------|----------------------|
| 70        | 20             | 210          | 70               | 18                   |
| 120       | 23             | 310          | 103              | 26                   |
| 170       | 33             |              |                  |                      |
| 270       | 52             |              |                  |                      |

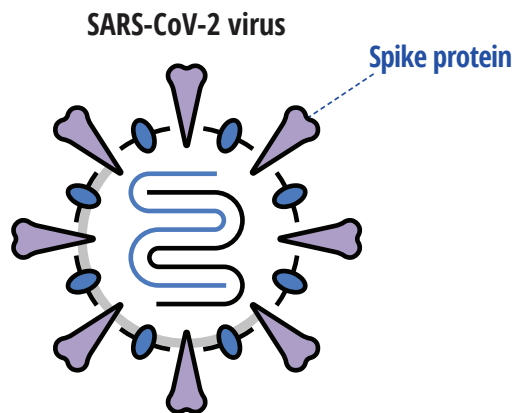
VTBI=volume to be infused over time.

**Reference: 1.** Data on file. National Infusion Center Association.

*SECTION 7:*

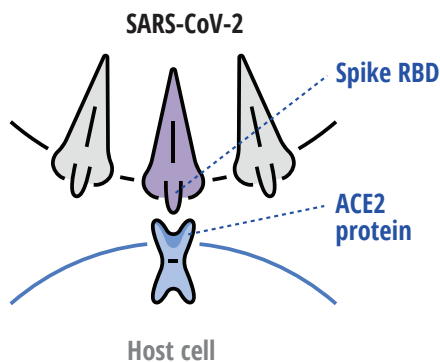
# **EDUCATION AND AWARENESS**

# EDUCATION AND AWARENESS



## How SARS-CoV-2 infection starts

SARS-CoV-2 enters host cells by binding to the ACE2 receptor on the cell surface<sup>1</sup>



## SARS-CoV-2 interacts with ACE2 through the receptor-binding domain

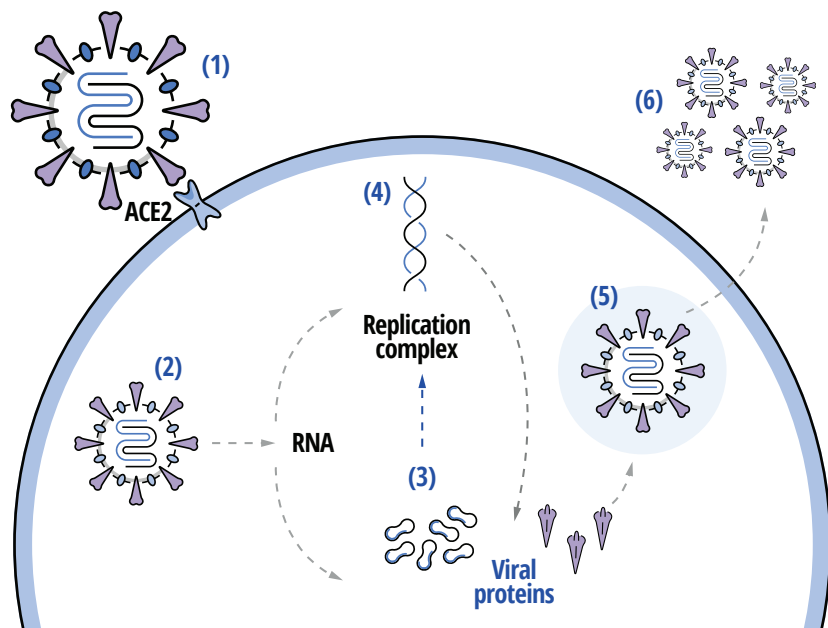
- The spike protein is a trimeric protein composed of a “head” and “stem”<sup>2,3</sup>
- The “head” of the spike protein contains the recognition and attachment site for ACE2, known as the RBD<sup>4</sup>
- The spike RBD has an “up” and “down” conformation, binding to ACE2 only in the “up” conformation<sup>5</sup>

ACE2, angiotensin-converting enzyme 2.  
RBD, receptor-binding domain.

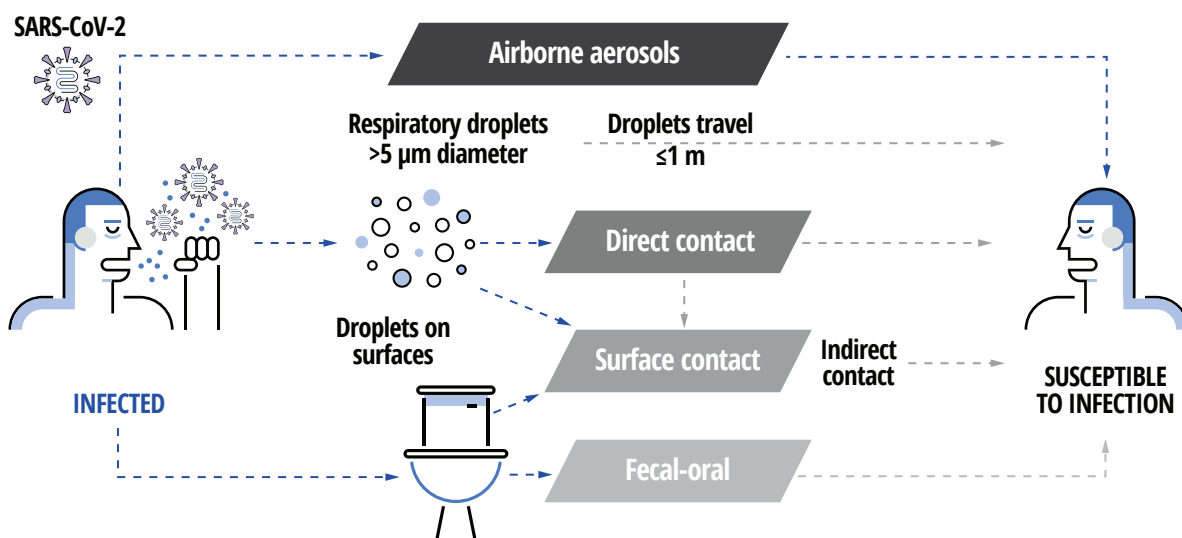
# EDUCATION AND AWARENESS (CONT'D)

**SARS-CoV-2 replicates within host cells to form new virus particles<sup>6,7</sup>**

- 1 The virus enters the host by first binding to ACE2 on the cell surface
- 2 Once inside the cell, the virus releases its RNA
- 3 Viral RNA is translated into proteins
- 4 Some of these proteins form a replication complex to make more viral RNA
- 5 Viral proteins and viral RNA are assembled into new virus particles
- 6 New virus particles are released from the cell and proceed to infect other cells



**There are multiple routes of transmission<sup>8</sup>**

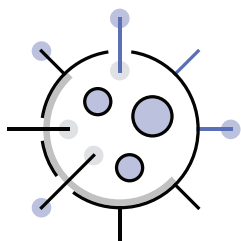


FOR MORE INFORMATION ABOUT SARS-CoV-2, VISIT [regencov.com](https://www.regencov.com)

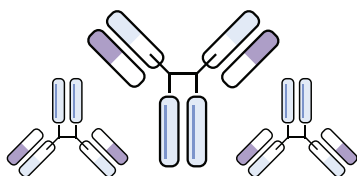
## EDUCATION AND AWARENESS (CONT'D)

### Vaccines and antiviral monoclonal antibodies may help people with SARS-CoV-2

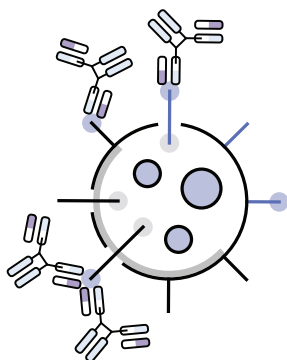
Antiviral monoclonal antibodies and vaccines are different, and both may help against COVID-19<sup>9-11</sup>



**Pathogens** are harmful organisms that can invade the body, such as viruses or bacteria. Some molecules from these pathogens, called **antigens**, are recognized by B cells and prompt them to produce antibodies by the billions.<sup>9</sup>



**Antibodies** are Y-shaped proteins produced by the human body as part of a normal immune response to foreign molecules. Antibodies help fight off foreign substances before they can cause sickness. Monoclonal antibodies can be made in the laboratory and given to someone whose immune system response may not be adequate or fast enough to fight an infection.<sup>10,11</sup>



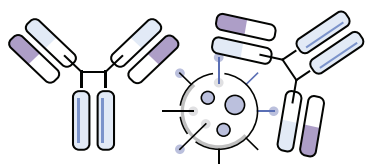
When the human body encounters **pathogens** like SARS-CoV-2, the virus that causes COVID-19, the body's immune system naturally produces **antibodies** to recognize and kill or neutralize the dangerous invaders.<sup>9</sup>

The immune system typically remembers its reaction to a pathogen and can produce the same protective antibodies again in the future. This is called **immunological memory**.<sup>9</sup>

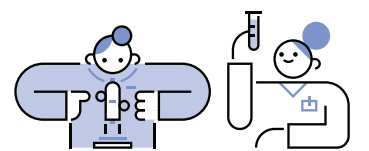
## EDUCATION AND AWARENESS (CONT'D)

As the COVID-19 pandemic continues to threaten the health of people across the globe, everyone wants to know:

### How can widespread immunity against this virus be achieved more quickly?



**Innate immunity** is the immunity you're born with. But the immunity you gain during your lifetime is called **adaptive immunity**, and it has 2 types: active and passive. **Active immunity** is conferred through endogenous antibodies, or antibodies found within the body whether through a previous infection or vaccination. **Passive immunity** is conferred through exogenous antibodies, or antibodies found outside of the body, such as in convalescent plasma or created in a laboratory.<sup>9,10</sup> There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to reinfection.<sup>12</sup>



The biopharmaceutical industry is researching ways to provide people with passive immunity through the use of antiviral monoclonal antibodies. Passive immunity can be achieved without infection and can be achieved faster than active immunity.<sup>11</sup>



## PASSIVE IMMUNITY

Occurs immediately after receiving exogenous antibodies from an injection, infusion, or blood transfer.<sup>13</sup>

### ANTIBODY MEDICINES

Based on key principles of biology, these mimic the natural defenses and pathways of the immune system. Regeneron's core technologies allow for rapid and efficient generation of antiviral monoclonal antibodies outside of the body—corresponding to specific virus-neutralizing monoclonal antibodies.<sup>9</sup>

#### EXOGENOUS MONOCLONAL ANTIBODIES ARE<sup>9</sup>:

Derived from patients who have recovered from a particular virus



OR



Laboratory engineered

#### These monoclonal antibodies are then<sup>14</sup>:



Put into a cell line that can produce the desired monoclonal antibody at scale.



Grown at larger and larger quantities in bioreactors.



Purified and packaged into vials.

For infectious diseases, Regeneron typically pursues a **combination antibody approach** of at least 2 monoclonal antibodies against a pathogen combined in a single medicine. The different monoclonal antibodies in a combination therapy work in slightly different ways to better neutralize the virus and to reduce the virus' ability to mutate.

#### THIS ANTIVIRAL MONOCLONAL ANTIBODY COMBINATION MEDICINE IS GIVEN:

As treatment: For sick patients through IV to block active infection.

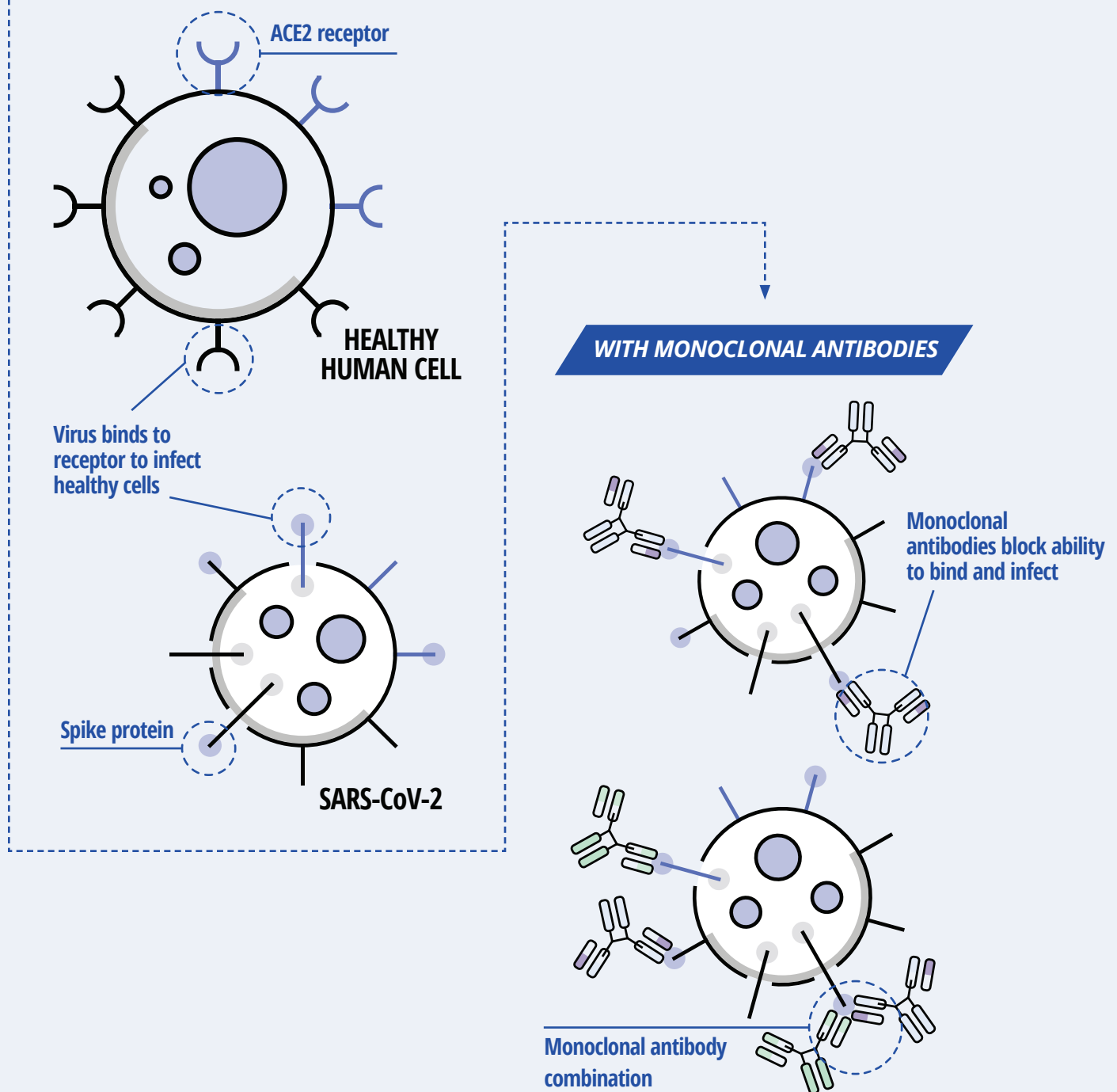


With this approach, immunity is provided immediately but is temporary.<sup>11</sup>



# HOW

## MONOCLONAL ANTIBODIES NEUTRALIZE THE SARS-CoV-2 VIRUS<sup>2</sup>



## ACTIVE IMMUNITY

**Develops over time in response to an infection or vaccination.<sup>10</sup>**

### VACCINES

Used to induce the body's active immune response in order to protect from an infectious viral disease in the future, such as measles, the flu, or coronaviruses like SARS-CoV-2.<sup>15-17</sup>



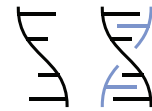
A weakened, or attenuated, virus.



A dead, or inactivated, form of the virus.



A fragment of the virus.\*



The virus' RNA or DNA.\*

\*These 2 approaches are primarily being explored for vaccines to prevent COVID-19.<sup>15</sup>

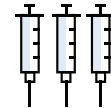
### To make many doses of vaccines, manufacturers<sup>18</sup>:



Gather needed key ingredients.



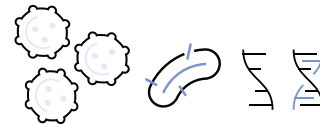
Produce the antigen in large quantities.



Package the antigen into an injection-ready form.



### VACCINES WORK BY:



Exposing healthy individuals to one of the items above via injection, which tricks the immune system into thinking the body is infected and generating a response.<sup>16,17</sup>



B cells in the vaccinated person's body begin producing protective antiviral antibodies in response.<sup>15</sup>



With time, active immunity is acquired.<sup>19</sup>

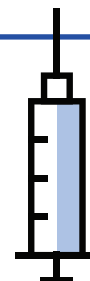


Developing active immunity takes time (days to weeks), but usually lasts longer (months to years). Experts don't yet know how long active immunity will last against COVID-19. Since it takes time to develop immunity from vaccines, they are not intended to treat patients with active infections.<sup>19,20</sup>

Extensive testing for safety and efficacy, as well as quality control through good manufacturing practices, is critical to both the development of vaccines and monoclonal antibodies.<sup>18</sup>

***ANTIVIRAL MONOCLONAL ANTIBODIES could serve as an important option. They may have utility for certain people, such as those who are immunocompromised, those with active infections, or those who do not respond to a vaccine. These different approaches are important to address the COVID-19 pandemic.<sup>21</sup>***

Learn more about Regeneron's combination of antiviral monoclonal antibodies, technologies, and COVID-19 research at [regeneron.com/covid19](https://regeneron.com/covid19).



## **PASSIVE vs ACTIVE IMMUNITY:**

### **Key takeaways<sup>9,19</sup>**

- Passive immunity and active immunity are both pathogen specific
- The duration of active immunity is longer than that of passive immunity, but it takes longer to develop
- Passive immunity is conferred through exogenous antibodies, or antibodies found outside of the body, such as in convalescent plasma or created in a laboratory
- Active immunity is developed by the host antibodies in response to natural infection or administration of a vaccine
- There are also risks to both approaches, and healthcare providers and patients should weigh the benefits and risks to each individual and public health

**TO LEARN MORE ABOUT PASSIVE vs ACTIVE IMMUNITY, VISIT [regencov.com](https://regencov.com)**

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*SECTION 8:*

# CLINICAL DATA

# CLINICAL DATA

## **Clinical Trial Results and Supporting Data for REGEN-COV™ (casirivimab with imdevimab) EUA**

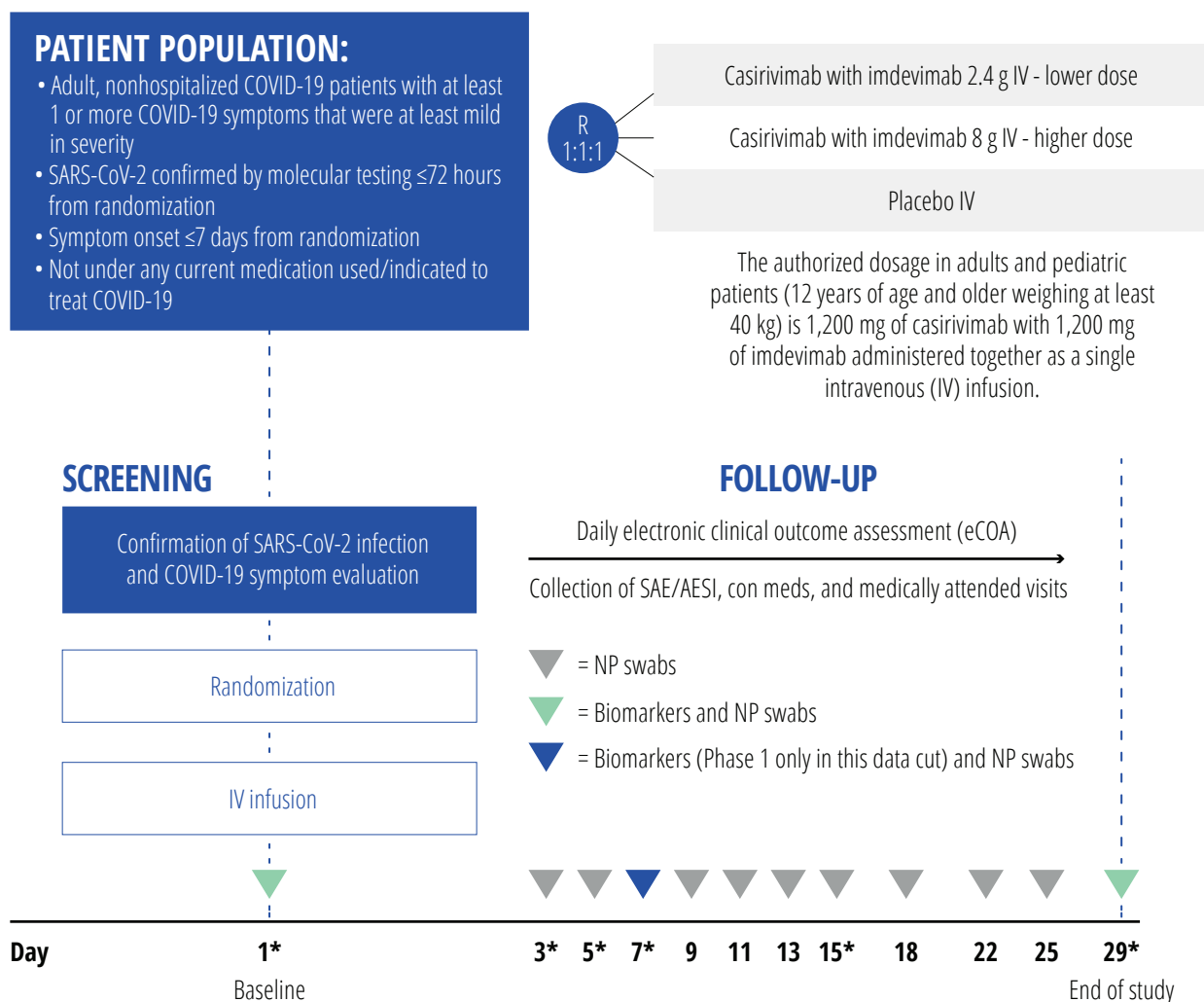
The data supporting this EUA are based on the analysis of Phase 1/2 data from trial R10933-10987-COV-2067 that occurred after 799 enrolled subjects had completed at least 28 days of study duration. R10933-10987-COV-2067 is a randomized, double-blinded, placebo-controlled clinical trial studying REGEN-COV for the treatment of adult subjects with mild to moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized).

Treatment was initiated within 3 days of obtaining a positive SARS-CoV-2 viral infection determination. Subjects were randomized in a 1:1:1 manner to receive a single intravenous (IV) infusion of 2,400 mg of REGEN-COV (1,200 mg casirivimab and 1,200 mg imdevimab) (n=266), or 8,000 mg of REGEN-COV (4,000 mg casirivimab and 4,000 mg imdevimab) (n=267), or placebo (n=266).

# CLINICAL DATA (CONT'D)

## Nonhospitalized seamless study design for 2 analysis sets in Phases 1/2/3 of trial 2067

View Publication: [Outpatient ambulatory adult patients](#)



\*Serum for PK (Day 3, 5, 7, 15 included in Phase 1 only).



## CLINICAL DATA (CONT'D)

### **BASELINE CHARACTERISTICS:**

- Median age was 42 years (with 7% of subjects ages 65 years or older)
- 53% of subjects were female
- 85% white
- 50% Hispanic or Latino
- 9% Black
- 34% were considered high risk
- Approximately 31% of subjects reported at least 1 severe symptom at baseline
- 36% reported at least 1 moderate symptom and no severe symptoms
- 13% reported only mild symptoms
- Median duration of symptoms was 3 days
- Mean viral load was 5.8 log<sub>10</sub> copies/mL at baseline

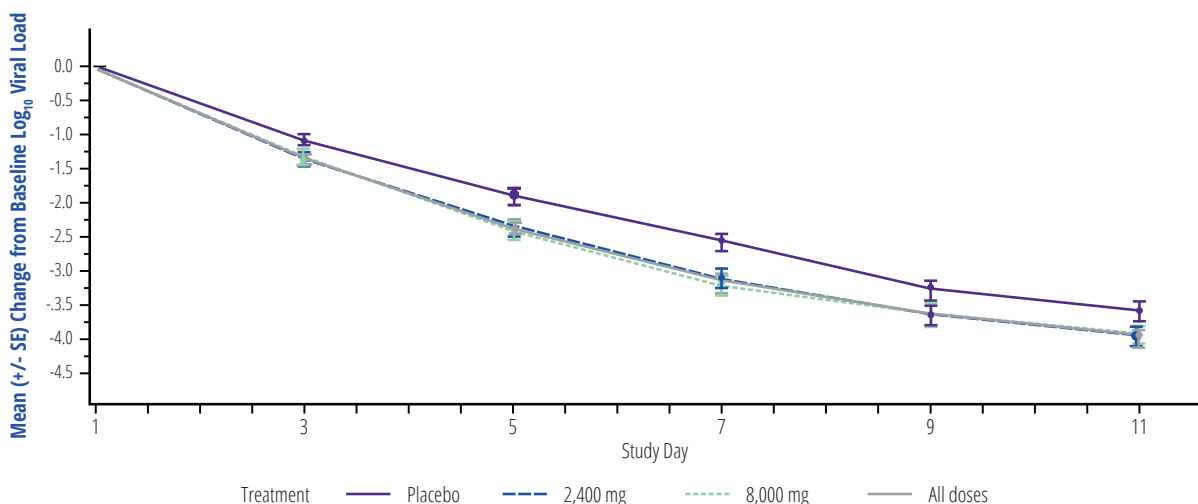
The baseline demographics and disease characteristics were well balanced across the REGEN-COV™ (casirivimab with imdevimab) and placebo treatment groups.

The prespecified primary endpoint in Phase 1/2 of trial R10933-10987-COV-2067 was the time-weighted average (TWA) change from baseline in viral load (log<sub>10</sub> copies/mL), as measured by RT-qPCR in nasopharyngeal swab samples, in subjects with a positive baseline RT-qPCR value, ie, the modified full analysis set (mFAS).

In the mFAS (n=665) for the Phase 1/2 analysis, the difference in TWA from Day 1 through Day 7 for the pooled doses of REGEN-COV compared with placebo was -0.36 log<sub>10</sub> copies/mL ( $P<0.0001$ ). The largest reductions in viral load relative to placebo occurred in patients with high viral load (-0.78 log<sub>10</sub> copies/mL) or who were seronegative (-0.69 log<sub>10</sub> copies/mL) at baseline. Reductions occurring from Day 1 through Day 11 were similar to those for Day 1 through Day 7. Figure 1 shows the mean change from baseline in SARS-CoV-2 viral load over time.

## CLINICAL DATA (CONT'D)

**Figure 1: Mean Change from Baseline in SARS-CoV-2 Viral Load Over Time**



While viral load was used to define the primary endpoint in the Phase 1/2 analysis, clinical evidence demonstrating that REGEN-COV™ (casirivimab with imdevimab) may be effective came from the predefined secondary endpoint, medically attended visits (MAV) related to COVID-19. Medically attended visits comprised hospitalizations, emergency room visits, urgent care visits, or physician office/telemedicine visits for COVID-19. A lower proportion of subjects treated with REGEN-COV had COVID-19-related MAVs (2.8% for combined treatment arms vs 6.5% placebo).

In post-hoc analyses, a lower proportion of subjects treated with REGEN-COV had COVID-19-related hospitalizations or emergency room visits compared to placebo, see Table 1. Results for this secondary endpoint (COVID-19-related hospitalizations or emergency room visits compared to placebo) were suggestive of a relatively flat dose-response relationship. The absolute risk reduction for REGEN-COV compared to placebo was greater in subjects at high risk for progression to severe COVID-19 and/or hospitalization, according to the criteria outlined (Table 2).

**The dosage in adults and in pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion via pump or gravity.**

## CLINICAL DATA (CONT'D)

**Table 1: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment<sup>a</sup>**

| Treatment  | N <sup>b</sup> | Events | Proportion of subjects |
|--|----------------|--------|------------------------|
| Placebo  | 231            | 10     | 4%                     |
| 2,400 mg <sup>c</sup> REGEN-COV™<br>(casirivimab with imdevimab) | 215            | 4      | 2%                     |
| 8,000 mg <sup>d</sup> REGEN-COV                                  | 219            | 4      | 2%                     |
| All doses REGEN-COV  | 434            | 8      | 2%                     |

<sup>a</sup>Hospitalization and emergency room visits were a subset of a key secondary endpoint, medically attended visits, which also included urgent care visits, physician's office visits, and telemedicine visits.

<sup>b</sup>N=number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization.

<sup>c</sup>2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab).

<sup>d</sup>8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab).

**Table 2: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits Within 28 Days After Treatment for Subjects at Higher Risk of Hospitalization<sup>a</sup>**

| Treatment                       | N <sup>b</sup> | Events | Proportion of subjects |
|---------------------------------|----------------|--------|------------------------|
| Placebo                         | 78             | 7      | 9%                     |
| 2,400 mg <sup>c</sup> REGEN-COV | 70             | 2      | 3%                     |
| 8,000 mg <sup>d</sup> REGEN-COV | 81             | 2      | 2%                     |
| All doses REGEN-COV             | 151            | 4      | 3%                     |

<sup>a</sup>Hospitalization and emergency room visits were a subset of a key secondary endpoint, medically attended visits, which also included urgent care visits, physician's office visits, and telemedicine visits.

<sup>b</sup>N=number of randomized subjects with a positive central-lab determined RT-qPCR from nasopharyngeal swab samples at randomization.

<sup>c</sup>2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab).

<sup>d</sup>8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab).

The median time to symptom improvement, as recorded in a trial-specific daily symptom diary, was 5 days for REGEN-COV-treated subjects, as compared with 6 days for placebo-treated subjects. Symptoms assessed were shortness of breath or difficulty breathing, chills, feverish, sore throat, cough, nausea, vomiting, diarrhea, headache, red or watery eyes, body and muscle aches, loss of taste or smell, fatigue, loss of appetite, confusion, dizziness, pressure or tight chest, chest pain, stomach ache, rash, sneezing, sputum/phlegm, runny nose. Symptom improvement was defined as symptoms scored as moderate or severe at baseline being scored as mild or absent, and symptoms scored as mild at baseline being scored as absent.

## CLINICAL DATA (CONT'D)

### Incidence of Key Safety Events for the 3 Treatment Groups

| Patients with:                                     | Placebo<br>(n=93) | Casirivimab and Imdevimab<br>Low Dose (2.4 g IV)<br>(n=88) | Casirivimab and Imdevimab<br>High Dose (8.0 g IV)<br>(n=88) |
|--|-------------------|--|---|
| Treatment TEAE                                     | 4 (4.3%)          | 1 (1.1%)   | 2 (2.3%)  |
| SAE  | 2 (2.2%)          | 1 (1.1%)   | 0   |
| Infusion-related reactions Grade ≥2<br>thru Day 4  | 1 (1.1%)          | 0  | 2 (2.3%)  |
| Hypersensitivity reactions Grade ≥2<br>thru Day 29 | 2 (2.2%)          | 0  | 1 (1.1%)  |
| Deaths   | 0                 | 0  | 0   |
| TEAE leading to study infusion<br>interruption     | 1 (1.1%)          | 0  | 1 (1.1%)  |

IV=intravenous; TEAE=treatment-emergent adverse events; SAE=serious adverse events.

### Important Safety Information

#### • **Adverse Reactions:**

- Serious adverse events (SAEs) were reported in 4 (1.6%) patients in the REGEN-COV™ (casirivimab with imdevimab) 2,400-mg group, 2 (0.8%) patients in the REGEN-COV 8,000-mg group, and 6 (2.3%) patients in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg REGEN-COV), intestinal obstruction and dyspnea (8,000 mg REGEN-COV) and COVID-19, pneumonia and hypoxia (placebo). **REGEN-COV is not authorized at the 8,000-mg dose (4,000 mg casirivimab and 4,000 mg imdevimab)**
- One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of Grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000-mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and included pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm, and none were reported in the 2,400-mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm. In two subjects receiving the 8,000-mg dose of REGEN-COV, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved

**The dosage in adults and in pediatric patients (12 years of age and older weighing at least 40 kg) is 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as a single intravenous infusion via pump or gravity.**

# CLINICAL DATA (CONT'D)

## Important Safety Information (cont'd)

REGEN-COV (casirivimab with imdevimab) is an unapproved investigational therapy, and there are limited clinical data available. Serious and unexpected adverse events may occur that have not been previously reported with REGEN-COV use.

- **Warnings and Precautions:**

- **Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions:** Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV (casirivimab with 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 REGEN-COV. These reactions may be severe or life threatening.
    - **Signs and symptoms of infusion-related reactions may include:** fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, fatigue and diaphoresis. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care
  - **Clinical Worsening After REGEN-COV Administration:** Clinical worsening of COVID-19 after administration of REGEN-COV has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, 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
  - **Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19:** 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. Therefore, 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
- **Patient Monitoring Recommendations:** Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete

# CLINICAL DATA (CONT'D)

## Important Safety Information (cont'd)

- **Use in Specific Populations:**

- **Pregnancy:** There is currently limited clinical experience in the use of REGEN-COV in COVID-19 patients who are pregnant. REGEN-COV therapy should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus
- **Lactation:** There is currently no clinical experience in the use of REGEN-COV in COVID-19 patients who are breastfeeding. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for REGEN-COV and any potential adverse effects on the breastfed child from REGEN-COV or from the underlying maternal condition

*FOR MORE CLINICAL DATA, VISIT [regencov.com](https://regencov.com) TO VIEW THE ANTIVIRAL AND CLINICAL PROFILE OF REGEN-COV (CASIRIVIMAB WITH IMDEVIMAB).*

***APPENDIX A:***

**DEAR HEALTHCARE PROVIDER LETTER:**

**IMPORTANT INFORMATION  
FOR HEALTHCARE PROVIDERS**

## IMPORTANT PRESCRIBING INFORMATION

**Subject: New Name and Packaging for Regeneron COVID-19 Monoclonal Antibodies (casirivimab with imdevimab) to be administered together: REGEN-COV™**

Dear Healthcare Provider:

The purpose of this notice is to make you aware of the proprietary name (REGEN-COV™) and new packaging (dose packs) for casirivimab with imdevimab.

REGEN-COV™, (casirivimab with imdevimab) to be administered together is authorized<sup>[1]</sup> for use under an emergency use authorization (EUA) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older and 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. Healthcare Providers should administer REGEN-COV™ (casirivimab with imdevimab) per the full Fact Sheet for Healthcare Providers available at [www.REGENCOV.com](http://www.REGENCOV.com).<sup>1</sup> Healthcare providers should review the enclosed Fact Sheet for instructions on dosing, preparation and administration of REGEN-COV™ (casirivimab with imdevimab).

### New REGEN-COV Dose Pack

Starting on about February 15, 2021, Regeneron will start shipping dose packs, a new packaging presentation of REGEN-COV (casirivimab with imdevimab). **The REGEN-COV dose pack is a plastic bag that contains cartons of casirivimab and imdevimab to make one 2,400 mg dose (1,200 mg of casirivimab and 1,200 mg of imdevimab) and a one-page informational document.**

The cartons in the REGEN-COV dose pack may vary in appearance; and the number of cartons in each dose pack may vary. The REGEN-COV dose pack could contain 2, 5, or 8 cartons, each containing vials of casirivimab and imdevimab, to make a single treatment dose (see page 2 for dose pack presentations). Regardless of the carton appearance, all of the combinations of casirivimab and imdevimab found in the dose pack make up **1 complete treatment dose** of REGEN-COV. Each dose pack will be labeled with the name REGEN-COV and the NDC based on the combination of cartons in the dose pack (see images starting on page 4).

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<sup>1</sup> Casirivimab and imdevimab are not approved, but The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products 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 and 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 only for the duration of the declaration.



# REGENERON

## Labeling of Individual Cartons in REGEN-COV Dose Packs

There are three versions of casirivimab and imdevimab carton packaging, which are reproduced in the enclosure. Please note:

- Casirivimab and imdevimab may each be supplied as two different strengths: 1,332 mg/11.1 mL (120 mg/mL) single-dose vials and 300 mg/2.5 mL (120 mg/mL) single-dose vials.
- One treatment dose (2,400 mg consisting of 1,200 mg of casirivimab and 1,200 mg of imdevimab) can consist of 4 different dose pack presentations:
  - One 11.1 mL vial of casirivimab and one 11.1 mL vial of imdevimab
  - Four 2.5 mL vials of casirivimab and four 2.5 mL vials of imdevimab
  - One 11.1 mL vial of casirivimab and four 2.5 mL vials of imdevimab
  - Four 2.5 mL vials of casirivimab and one 11.1 mL vial of imdevimab
- Some vials and cartons of casirivimab and imdevimab may be instead labeled REGN10933 and REGN10987, respectively (see pages 8 and 9 below). The cartons of these vials will also have a sticker affixed that includes the nonproprietary name of the product (“casirivimab” or “imdevimab”), the product strength and NDC number, along with a linear barcode that can be scanned by healthcare facilities.

## Expiration Dates

The dose packs will expire no earlier than May 31, 2022. If you are uncertain of when the products expire, you may call Regeneron Medical Information at 1-844-734-6643. Expiration dates for dose packs can be found on the packing slip within a shipment of material and reflects the earliest expiration date of the enclosed material. Cartons in the dose pack may have different lot numbers and expiration dates but none will expire any earlier than May 31, 2022.

## Inventory Management

The linear barcodes on cartons, dose packs, and shipper labels are functional and can be used to obtain the NDC of either the dose pack(s) or the carton. Please ensure proper rotation of stock by utilizing current inventory. Be aware that there are 4 new NDCs assigned for the 4 different dose pack presentations of REGEN-COV (casirivimab with imdevimab) and update your systems accordingly to capture these new NDCs and the brand name, REGEN-COV.

For previously distributed EUA casirivimab and imdevimab products (not in the new dose pack presentations), the cartons have no NDCs or functional barcodes.

## Healthcare Provider Action

- Stay current with the latest Fact Sheets for Health Care Providers (<https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf>)
- Use the brand name along with the nonproprietary name in prescribing (“REGEN-COV (casirivimab with imdevimab)”)
- Create alerts in the electronic health record (EHR) systems for healthcare providers that casirivimab and imdevimab must be administered together after dilution by intravenous infusion.

# REGENERON

- Store REGEN-COV (casirivimab with imdevimab) dose packs in the refrigerator in the original dose pack container together and away from other COVID-19 vaccines and drug products. **Do not open dose pack until the time at which the infusion is to be compounded.**
- Store individual cartons of casirivimab and imdevimab separately from COVID-19 vaccines and other drug products.
- Have the dosing information for casirivimab and imdevimab, that visually displays the 4 possible unique vial combinations that can be used to prepare the IV solution, available to those preparing the medication.

## **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](mailto: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](http://www.fda.gov/medwatch/report.htm), or
- Use a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) 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 at [medical.information@regeneron.com](mailto:medical.information@regeneron.com).

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



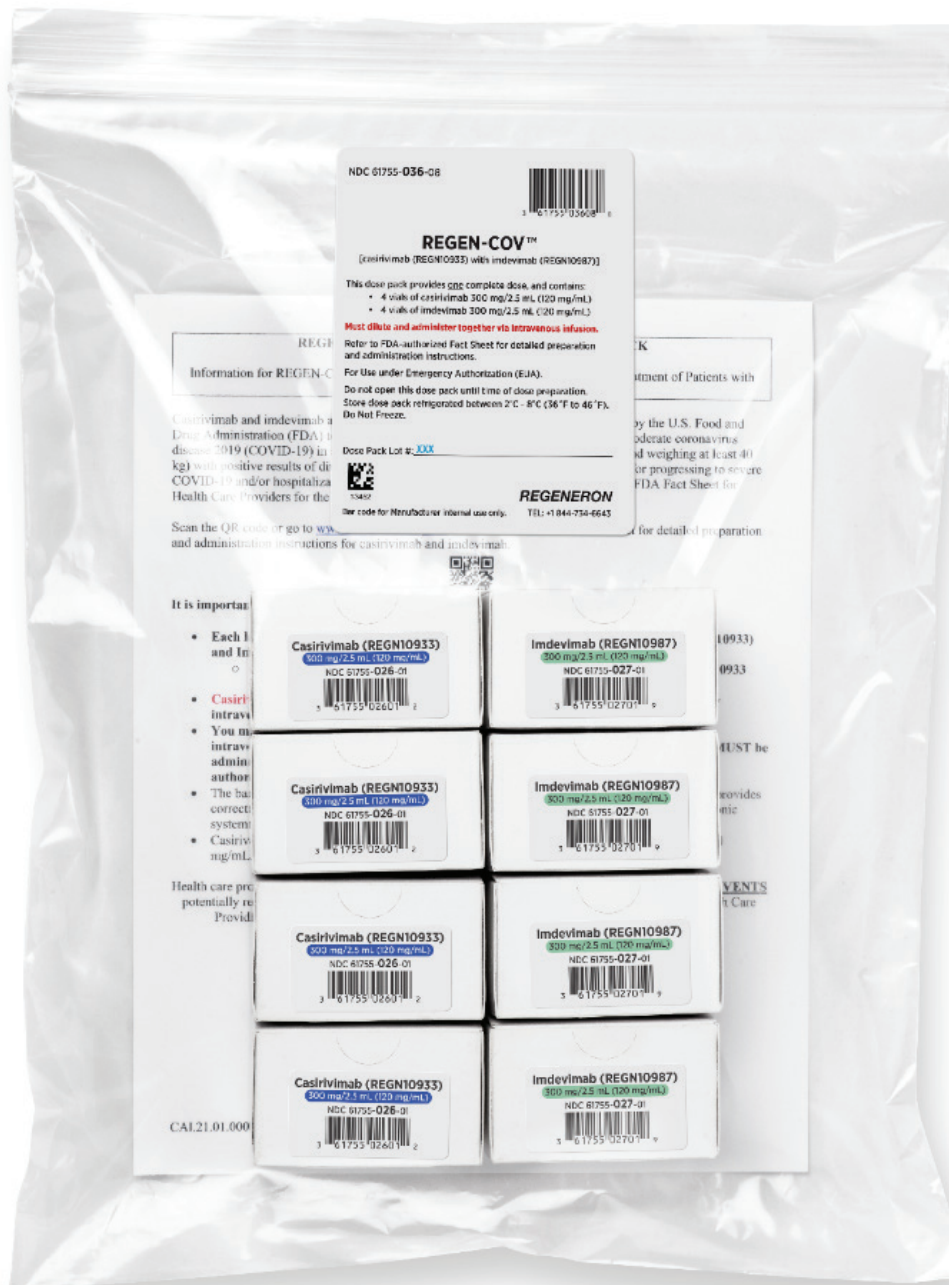
Johnathan Lancaster, MD, PhD

Senior Vice President, Global Medical Affairs

**Enclosure:** EUA Fact Sheet for Healthcare Providers for REGEN-COV Dose Pack

## Images of the REGEN-COV 4 Dose Pack Presentations<sup>2</sup>

### 1. 8 carton Dose Pack (4 casirivimab: 4 imdevimab)



<sup>2</sup> The cartons in the REGEN-COV dose pack may vary in appearance, see page 8-10 for images. Regardless of the carton appearance, all of the combinations of casirivimab and imdevimab found in the dose pack make up **1 complete treatment dose** of REGEN-COV.

# REGENERON

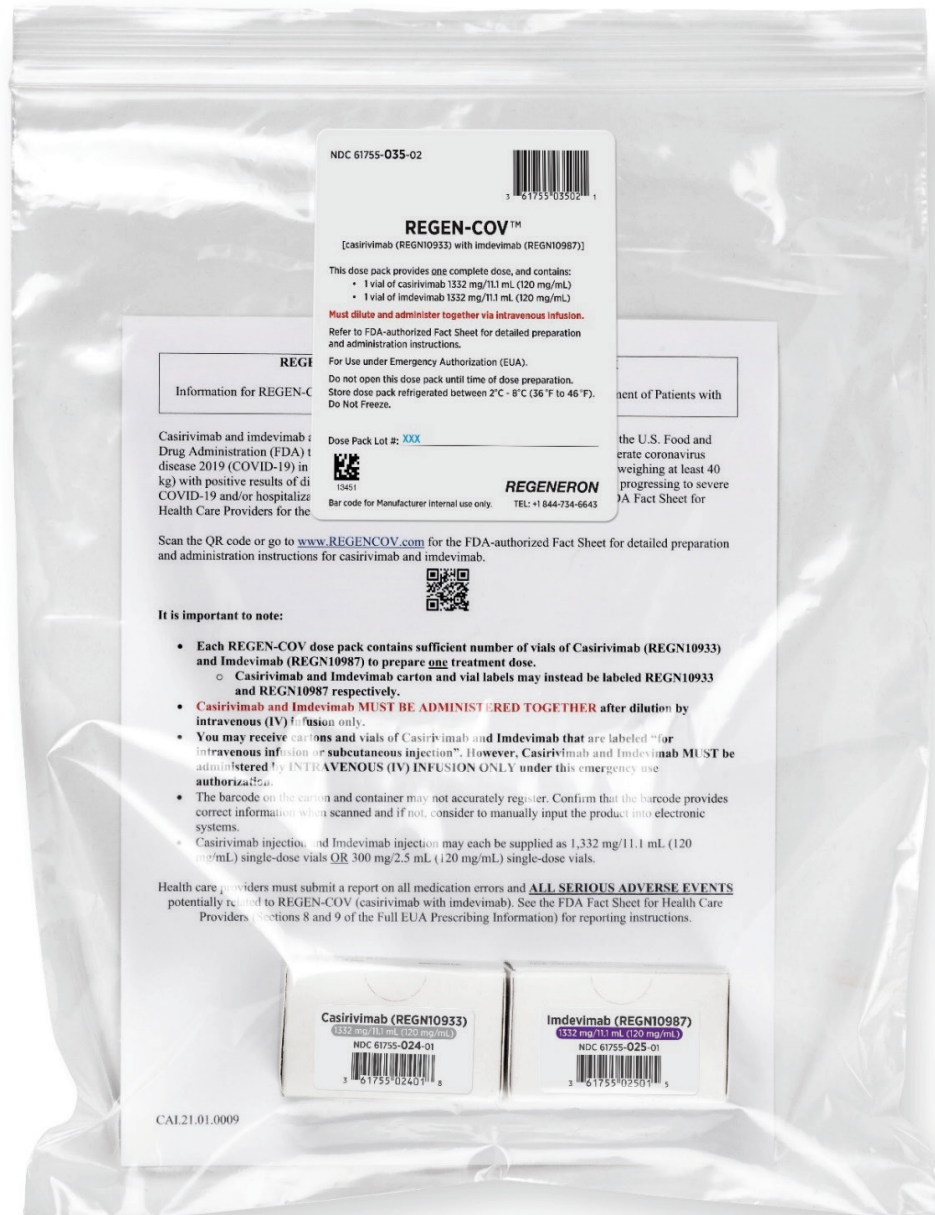
## 2. 5 carton Dose Pack (1 casirivimab: 4 imdevimab)





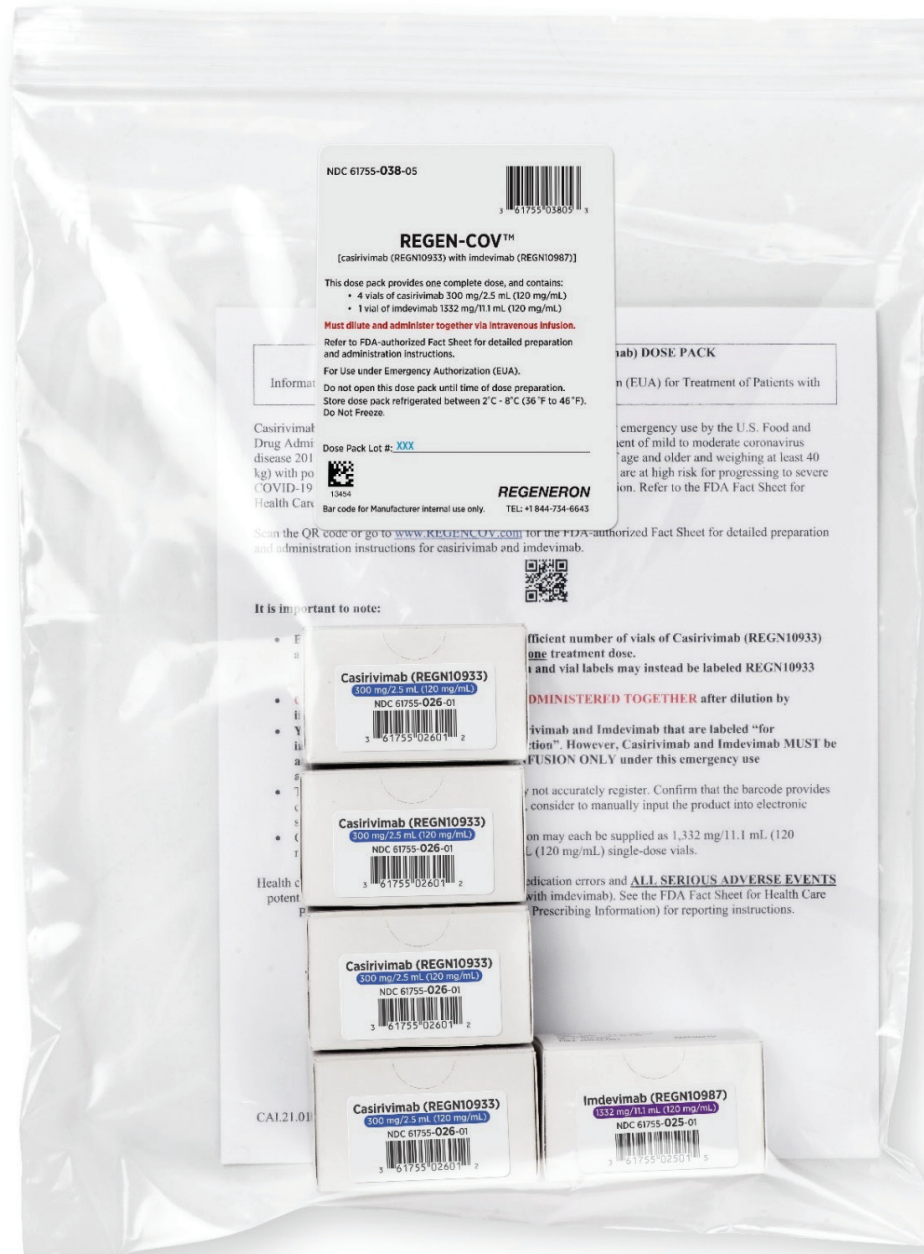
# REGENERON

## 3. 2 carton Dose Pack (1 casirivimab: 1 imdevimab)



# REGENERON

## 4. 5 carton Dose Pack (4 casirivimab: 1 imdevimab)

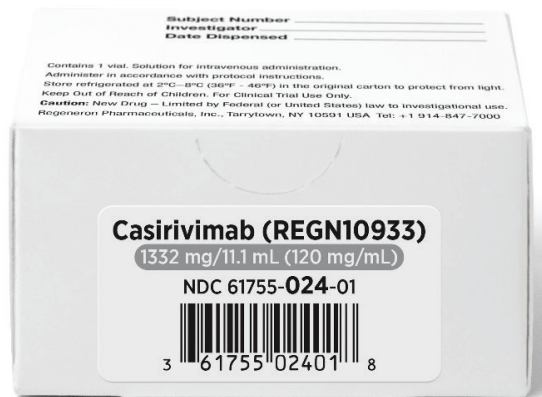


# REGENERON

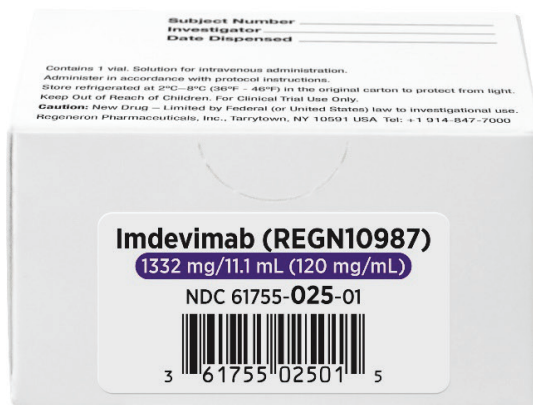
## Variations of the packaging and labeling of casirivimab and imdevimab

### VERSION 1

**1a: casirivimab (also referred to as REGN10933) – 1,332 mg/11.1 mL (120 mg/mL solution)**

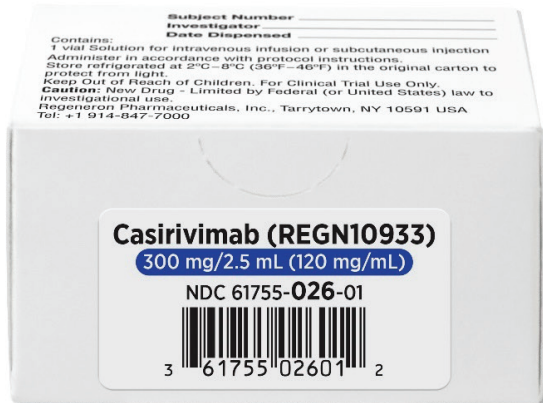


**1b: imdevimab (also referred to as REGN10987) – 1,332 mg/11.1 mL (120 mg/mL solution)**

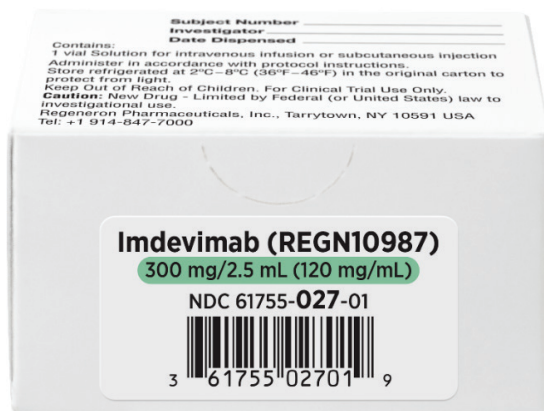


### VERSION 2\*

**2a: casirivimab (also referred to as REGN10933) – 300 mg/2.5 mL (120 mg/mL solution)**



**2b: imdevimab (also referred to as REGN10987) – 300 mg/2.5 mL (120 mg/mL solution)**



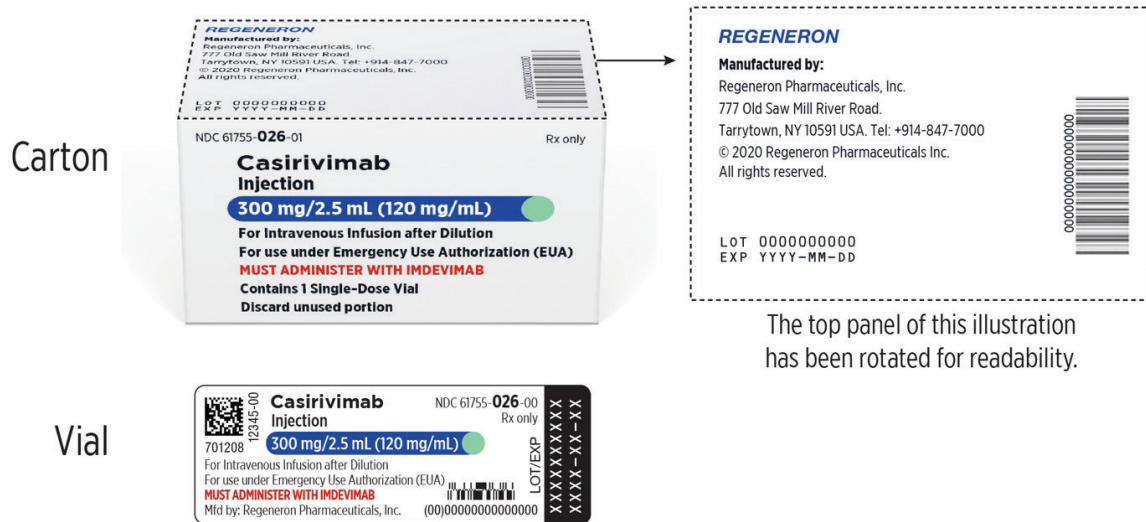
\*The packaging for casirivimab and imdevimab is labeled “for intravenous infusion or subcutaneous injection.” However, casirivimab and imdevimab **MUST** be administered by **INTRAVENOUS (IV) INFUSION ONLY** under the emergency use authorization.



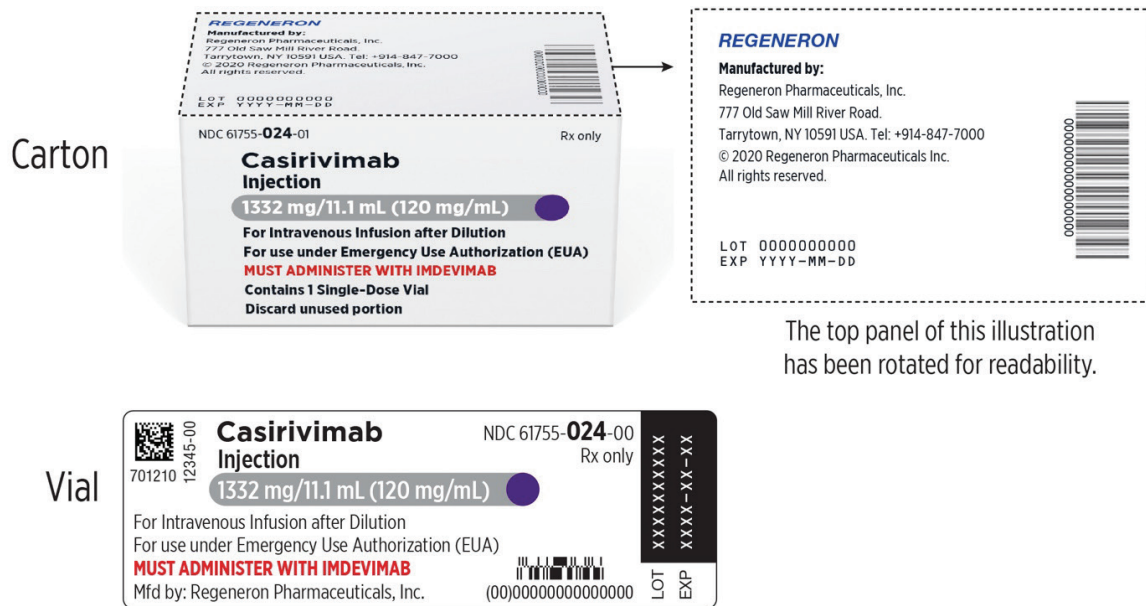
# REGENERON

VERSION 3 (expected to be available mid-February 2021)

3a: casirivimab (also referred to as REGN10933) – 300 mg/2.5 mL (120 mg/mL solution)



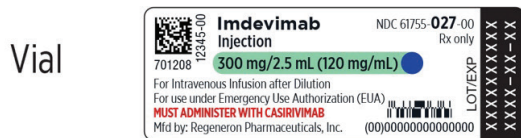
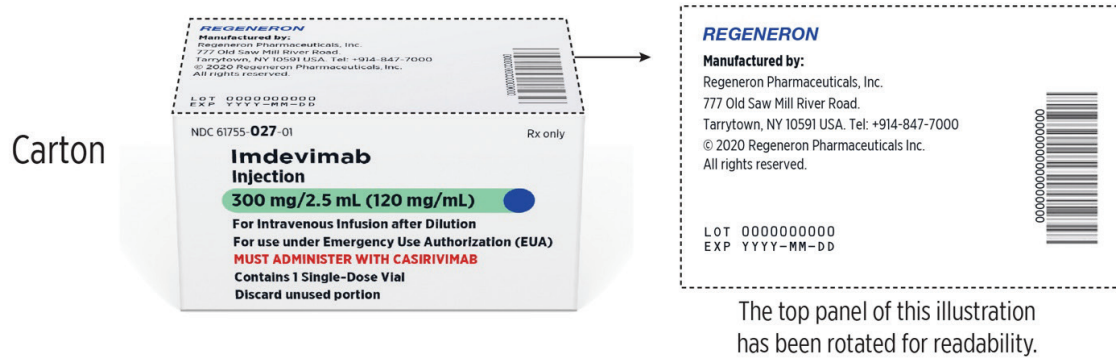
3b: casirivimab (also referred to as REGN10933) – 1332 mg/11.1 mL (120 mg/mL solution)



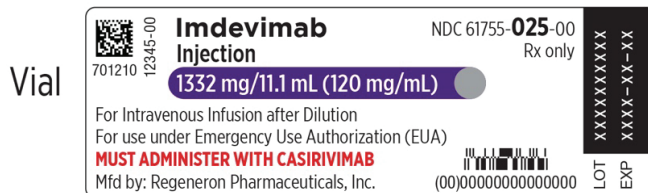
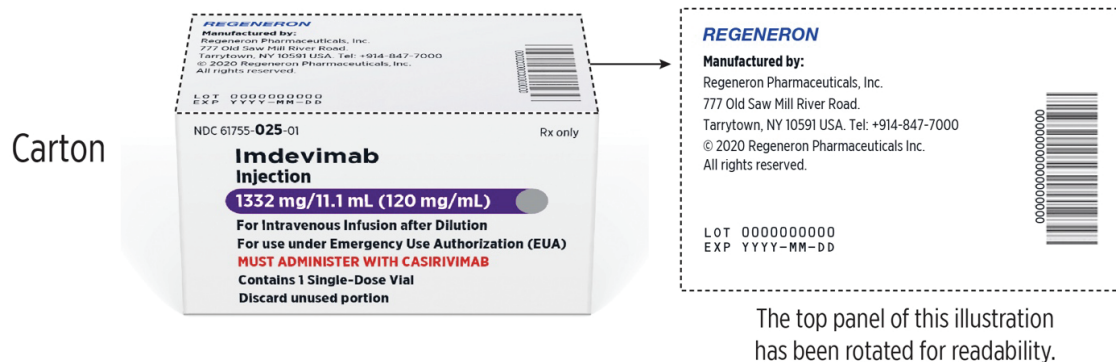


# REGENERON

## 3c: imdevimab (also referred to as REGN10987) – 300 mg/2.5 mL (120 mg/mL solution)



## 3d: imdevimab (also referred to as REGN10987) – 1,332 mg/11.1 mL (120 mg/mL solution)



*APPENDIX B:*

# OVERVIEW OF DIRECT ORDER SYSTEM



# Overview of Direct Order Process for COVID-19 Therapeutics

## Purpose:

The United States Government (USG) is responsible for the allocation and distribution of monoclonal antibody (mAb) therapeutics for the treatment of COVID-19 as per the Emergency Use Authorizations (EUA) issued by the U.S. Food and Drug Administration (FDA). The USG has developed a process for sites to directly order from the distributor, AmerisourceBergen (ABC).

## Process overview:

- Sites (based on classes of trade), are able to order bamlanivimab (Lilly) and/or casirivimab/imdevimab (Regeneron) monoclonal antibodies for their facilities at the link listed below
- Sites will be required to:
  - Provide ABC with a board of pharmacy license or physician letter of authorization
  - Attest to their designated class of trade and that they will administer the authorized product according to the terms of the FDA issued EUA
  - Provide utilization data via either TeleTracking or NHSN
- Sites can order product based on established minimum amounts; subsequent orders are subject to a maximum amount based on previous orders and utilization
- State departments of health will be informed of therapies ordered within their jurisdictions for awareness.

**Link to order:** <https://app.smartsheet.com/b/form/255d164d67834793b4ab549e160941e8>

## Required utilization reporting:

- Weekly reporting on these therapeutics is **required every Wednesday** through HHS Protect, TeleTracking, or CDC's National Healthcare Safety Network (NHSN) depending on facility type
- Instructions are included at the bottom of the ABC order form, and included here for reference
  - To improve availability of treatments for Monoclonal Antibody (mAb) therapies for COVID patients across the nation, the federal government requires entities receiving shipments of mAb treatments to provide weekly reports of mAb treatments administered and stocks on hand through one of the following reporting mechanisms:
    - For Hospitals, mAb therapeutic data reporting is included in the [COVID-19 hospital data reporting](https://www.hhs.gov/sites/default/files/covid-19-faqs-hospitals-hospital-laboratory-acute-care-facility-data-reporting.pdf) as described in US Dept. of Health and Human Services FAQ/Guidance on linked here: <https://www.hhs.gov/sites/default/files/covid-19-faqs-hospitals-hospital-laboratory-acute-care-facility-data-reporting.pdf>
    - Skilled Nursing Facilities / Long Term Care Facilities are requested to provide data through the CDC's NHSN data system at a future date (**Guidance forthcoming**)
    - All Additional Facilities such as Dialysis Centers, Home Health Services, Oncology, and Infusion Centers, are required to [provide the requested data](#) through the following portal: <https://teletracking.protect.hhs.gov/>
- First-time users will receive enrollment and reporting instructions in an e-mail from [protect-noreply@hhs.gov](mailto:protect-noreply@hhs.gov) with the subject line of "Invitation: HHS TeleTracking COVID-19 Portal." This email provides step-by-step instructions to access the Portal for the first time. If you do not receive an email in the next 48 hours, please [contact TeleTracking's Technical Support at \[hhs-protect@teletracking.com\]\(mailto:hhs-protect@teletracking.com\)](#)

*APPENDIX C:*

# **CLINICAL TRIAL MODELING INFORMATION**

# CLINICAL TRIAL MODELING INFORMATION

Assuming the infusion site of care setup details provided below, this information can be used to model the estimated number of infusions (patients) an infusion site of care can serve, depending on its capacity.

Each infusion site of care will vary in terms of the number of chairs for infusion, staffing considerations, work-day length, and more. The information provided here is meant as a general guide based upon Regeneron's clinical trial experience. In some cases, ideal criteria are included, such as for observation time. In other instances, such as the consent and intake time, there are estimated ranges shown, with "+" or "-" conditions in parentheses.

**Casirivimab and imdevimab must be administered together. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted casirivimab and imdevimab solution in the refrigerator 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. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.**

## Estimated Infusion Timing\*

| Criteria                | Details   | Additional Notes  |
|-------------------------|---|---|
| Consent and intake time | 30 min (+/- 15 min)   | Consent and intake may occur outside of the infusion chair, such as at the prescriber's location, and consent and intake time may vary per patient.   |
| IV prep time            | 60 min  | Review the Fact Sheet for Healthcare Providers for instructions on preparation and administration.  |
| Infusion time           | 20-52 min (see <b>Table 1</b> in <b>Section 6</b> of this guidebook for infusion times) | Infusion time will range from 20-52 minutes, depending on size of prefilled 0.9% Sodium Chloride infusion bag (see <b>Table 1</b> in <b>Section 6</b> of this guidebook for infusion times).  |
| Observation time        | 60 min  | It is clinically recommended to monitor patients during infusion and observe patients for at least 1 hour after infusion is complete, although more time may be necessary. Sites of care should follow local requirements when determining appropriate observation periods. |
| <b>TOTAL TIME</b>       | 155-187 min<br>(~2.75 to 3.25 hours)  | This represents the estimated total time from consent through observation of the patient.   |

\*The infusion times above have been updated on March 18, 2021.

*APPENDIX D:*

# ONGOING CLINICAL TRIALS

# ONGOING CLINICAL TRIALS

REGEN-COV™ (casirivimab with imdevimab) is currently being studied in **2 ongoing** Phase 2/3 clinical trials for the treatment of COVID-19 in certain hospitalized and outpatient ambulatory patients, a Phase 3 trial for the prevention of COVID-19 in household contacts of infected individuals and the Phase 3 open-label RECOVERY trial of hospitalized patients in the UK. **Use of REGEN-COV in certain hospitalized patients or in household contacts of infected individuals has not been granted an EUA; these uses are not approved by any regulatory authority.**

For more information on clinical trials testing the use of REGEN-COV, see the following table:

## Current Clinical Trials Testing the Use of REGEN-COV

| Trial Focus | Phase     | Patient Population  | Link  |
|-------------|-----------|---|---|
| Treatment   | Phase 2/3 | Outpatient ambulatory adult and pediatric patients*   | <a href="#">NCT04425629</a>   |
| Treatment   | Phase 2/3 | Certain hospitalized adult patients   | <a href="#">NCT04426695</a>   |
| Prevention  | Phase 3   | Healthy adults and children who are household contacts to an individual with a positive SARS-CoV-2 RT-PCR assay | <a href="#">NCT04452318</a>   |
| Treatment   | Phase 3   | Hospitalized patients (RECOVERY trial)  | <a href="#">NCT04381936</a><br>Not currently recruiting US patients |
| Treatment   | Phase 2   | Outpatient ambulatory adult patients  | <a href="#">NCT04666441</a><br>Active, not currently recruiting     |
| Treatment   | Phase 1   | Healthy adults  | <a href="#">NCT04519437</a><br>Active, not currently recruiting     |

\*Due to recommendation from IDMC (independent data monitoring committee), enrollment of placebo patients has been halted.

**FOR MORE CLINICAL TRIAL SITES, VISIT [CLINICALTRIALS.GOV](#)**

***APPENDIX E:***

**FAQs**



# FAQs

## FREQUENTLY ASKED QUESTIONS

### ACCESS AND REIMBURSEMENT



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

An EUA allows the U.S. Food and Drug Administration (FDA) to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) defense threats by facilitating the availability and use of therapies needed during public health emergencies.

Under section 564 of the Federal Food, Drug, and Cosmetic Act, the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents when there are no adequate, approved, and available alternatives.



#### Is there a list of centers where REGEN-COV™ (casirivimab with imdevimab) is available?

Details on infusion centers where antibody therapies, including REGEN-COV, may be available can be found on the [HHS Office of the Assistant Secretary for Preparedness and Response \(ASPR\)](#) and the [National Infusion Center Association \(NICA\)](#)\* site locators.

\*IMPORTANT INFORMATION: Infusion sites displayed in this tool have been authorized to administer antibody treatments for COVID-positive patients under Emergency Use Authorization. These antibody therapies are restricted to certain high-risk patients and require a drug order (similar to a prescription) from a healthcare provider (HCP) for eligible patients. HCPs must verify eligibility of their patients and verify the availability of doses at an authorized infusion site before they refer an eligible patient to schedule an appointment to receive treatment at an authorized infusion site. Please note that the inclusion of a site does not imply current availability of doses. More states and locations are regularly being added. If not yet listed, ambulatory centers or other administration sites should contact their state health departments.

## FAQs (CONT'D)



How can treatment sites order/re-order REGEN-COV™ (casirivimab with imdevimab)?

To order REGEN-COV, treatment sites should contact AmerisourceBergen Corporation directly at [c19therapies@amerisourcebergen.com](mailto:c19therapies@amerisourcebergen.com). Treatment sites should also review the [ASPR direct ordering process guide](#) and can fill out a [C19 Therapies Direct Order Request](#).



What is the coverage and reimbursement for REGEN-COV?

REGEN-COV is free of charge to requesting treatment sites, as the United States government is paying for the product. The combination therapy must be administered via a single intravenous infusion. Therefore, claims may be submitted for the reimbursement of the drug administration only.

Coverage and reimbursement of COVID-19–related treatments and procedures may vary from payer to payer; therefore, it is important that providers clarify and confirm any coding/billing requirements with respective payers.



Who determines which treatment sites receive REGEN-COV?

Treatment sites must order REGEN-COV directly from AmerisourceBergen Corporation, the drug's sole distributor. Approval of sites to receive product will be determined by AmerisourceBergen Corporation in conjunction with the United States government.

### PACKAGING AND PREPARATION



Why are there different types of packages for REGEN-COV?

New REGEN-COV Dose Packs are now available. Each REGEN-COV Dose Pack contains sufficient number of vials of casirivimab and imdevimab to prepare one treatment dose.

Previously, because of the rapid timing of the EUA and to meet the needs of the public health emergency, we were using the same vials and packaging used as part of the clinical trial. These vials and packaging may still be in circulation.



There is no expiration dating on the dose pack. What is the product expiration date?

As of March 2021, all distributed lots of REGEN-COV have an expiry date that is **no earlier than** 2022. The expiration date for the material shipped from the distributor can be found on the packing list. For the specific expiration dating for a lot, please reach out to the distributor or to Regeneron medical information at 1-844-734-6643 or to [medical.information@regeneron.com](mailto:medical.information@regeneron.com).

## FAQs (CONT'D)



**Does casirivimab or imdevimab packaging include latex?**

The vial and vial stopper for casirivimab and imdevimab are not made with natural latex rubber.



**Does the prepared intravenous (IV) bag need to be protected from light?**

Prepared IV bags of casirivimab and imdevimab do not require protection from ambient light.



**What are my options if I can't start the IV infusion immediately?**

If immediate administration is not possible, store the diluted REGEN-COV™ (casirivimab with imdevimab) infusion solution in the refrigerator between 2 °C to 8 °C (36 °F to 45 °F) for no more than 36 hours or at room temperature up to 25 °C (77 °F) for no more than 4 hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

### CLINICAL DATA



**How does REGEN-COV work?**

The combination of casirivimab and imdevimab makes up REGEN-COV, Regeneron's investigational anti-viral antibody cocktail being studied in COVID-19. It consists of two noncompeting, virus-neutralizing monoclonal antibodies.

Casirivimab and imdevimab bind simultaneously to different, non-overlapping epitopes on the SARS-CoV-2 spike (S) glycoprotein.



**Can patients who have already been vaccinated for COVID-19 still receive REGEN-COV?**

Those who have received a COVID-19 vaccine can still receive monoclonal antibody therapy if they meet the authorized use criteria for REGEN-COV. Please consider the proximate risk for each patient when considering REGEN-COV use. Please consult the latest guidelines from the CDC at: <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>.

## FAQs (CONT'D)



**Does REGEN-COV™ (casirivimab with imdevimab) protect against viral variants that have emerged?**

There is a potential risk of treatment failure due to the development of viral variants that are resistant to casirivimab and imdevimab administered together. Prescribing healthcare providers should consider the prevalence of SARS-CoV-2 variants in their area, where data are available, when considering treatment options.

REGEN-COV has been tested against, and was found to retain neutralization activity against, pseudoviruses expressing the spike protein substitution(s) identified in the below COVID-19 variants.<sup>a</sup> It is not known how pseudovirus data correlate with clinical outcomes.

- B.1.1.7 (United Kingdom origin). REGEN-COV retained neutralization activity against all spike protein substitutions.<sup>b</sup>
- B.1.351 (South Africa origin). REGEN-COV retained neutralization activity against all spike protein substitutions.<sup>c,d</sup>
- B.1.427/B.1.429 (California origin). REGEN-COV retained neutralization activity against the L452R spike protein substitution.
- P.1 (Brazil origin). REGEN-COV retained neutralization activity against the K417T + E484K spike protein substitution.<sup>e</sup>
- B.1.526 (New York origin). REGEN-COV retained neutralization activity against the E484K spike protein substitution.<sup>f,g</sup>

Healthcare providers should review the Antiviral Resistance information in Section 15 of the Fact Sheet for Healthcare Providers for details regarding specific variants and resistance, and refer to the [CDC website](#) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

<sup>a</sup>As of March 18, 2021.

<sup>b</sup>Pseudovirus expressing the entire variant spike protein was tested. The following changes from wild-type spike protein are found in the variant: del69-70, del145, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H.

<sup>c</sup>Pseudovirus expressing the entire variant spike protein was tested. The following changes from wild-type spike protein are found in the variant: D80Y, D215Y, del241-243, K417N, E484K, N501Y, D614G, A701V.

<sup>d</sup>Casirivimab alone, but not imdevimab, had reduced activity against pseudovirus expressing K417N or E484K (which are found in this variant).

<sup>e</sup>Casirivimab alone, but not imdevimab, had reduced activity against pseudovirus expressing K417N or E484K.

<sup>f</sup>Casirivimab alone, but not imdevimab, had reduced activity against pseudovirus expressing E484K.

<sup>g</sup>Not all isolates of the New York lineage harbor E484K substitution (as of February 2021).

# FAQs (CONT'D)

## SAFETY INFORMATION AND REPORTING

### ? What are my requirements for reporting medication errors and serious adverse events?

Prescribing healthcare professionals and/or the provider's designee are responsible for mandatory reporting of all medication errors and all serious adverse events potentially related to REGEN-COV™ (casirivimab with imdevimab). These adverse events must be reported within 7 calendar days from the onset of the event. MedWatch adverse event reports can be submitted to the FDA online [here](#) by using a postage-paid Form FDA 3500 and returning by mail/fax, or by calling 1-800-FDA-1088 to request a reporting form. In addition, please provide a copy of all FDA MedWatch forms to Regeneron Pharmaceuticals, Inc via fax (1-888-876-2736) or email ([medical.information@regeneron.com](mailto:medical.information@regeneron.com)). See the [Fact Sheet for Healthcare Providers](#) for detailed information about the obligation to report medication errors and serious adverse events.

### ? Are there any warnings associated with use of this combination therapy?

REGEN-COV (casirivimab with imdevimab) is an unapproved investigational therapy, and there are limited clinical data available. Serious and unexpected adverse events may occur that have not been previously reported with REGEN-COV use.

#### • **Warnings and Precautions**

- Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions: Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV (casirivimab with imdevimab). If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy. Infusion-related reactions have been observed with administration of REGEN-COV. These reactions may be severe or life threatening.
  - Signs and symptoms of infusion-related reactions may include: fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (eg, atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, and diaphoresis. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.
- Clinical Worsening After REGEN-COV Administration: Clinical worsening of COVID-19 after administration of REGEN-COV has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (eg, atrial fibrillation, 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.

## FAQs (CONT'D)



Are there any warnings associated with use of this combination therapy? (cont'd)

- **Warnings and Precautions (cont'd)**

- Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19: Benefit of treatment with REGEN-COV™ (casirivimab with imdevimab) 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 requiring high-flow oxygen or mechanical ventilation with COVID-19. Therefore, 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.



What adverse reactions have been identified thus far in the randomized trials?

The safety of REGEN-COV is based on analysis from one phase 1/2 trial of 799 ambulatory (non-hospitalized) patients with COVID-19.

- Serious adverse events (SAEs) were reported in 4 (1.6%) patients in the REGEN-COV 2,400-mg group, 2 (0.8%) patients in the REGEN-COV 8,000-mg group, and 6 (2.3%) patients in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea, and vomiting (2,400 mg REGEN-COV), intestinal obstruction and dyspnea (8,000 mg REGEN-COV) and COVID-19, pneumonia and hypoxia (placebo). **REGEN-COV is not authorized at the 8,000-mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).**
- One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of Grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000-mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and included pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm, and none were reported in the 2,400-mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm. In two subjects receiving the 8,000-mg dose of REGEN-COV, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved.

## FAQs (CONT'D)



### Who is eligible for REGEN-COV™ (casirivimab with imdevimab) under the EUA?

REGEN-COV is authorized 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. [see Limitations of Authorized Use]

REGEN-COV has not been approved, but has been authorized for emergency use by FDA.

This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

- Healthcare providers should review the [Fact Sheet for Healthcare Providers](#) for information on the authorized use of REGEN-COV and mandatory requirements of the EUA and must comply with the requirements of the EUA. The [FDA Letter of Authorization](#) is available for reference, as well as the [Dear Healthcare Provider Letter](#) and [Patient Fact Sheet](#).

#### **Limitations of Authorized Use**

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
- 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.

## FAQs (CONT'D)



Who is eligible for REGEN-COV™ (casirivimab with imdevimab) under the EUA? (cont'd)

### Definition of High Risk Patients

High risk 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  $\geq 85$ th 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 (e.g., cerebral palsy), OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control

## CLINICAL TRIALS



How can I register my patients for a clinical trial with REGEN-COV for COVID-19?

For more information on [clinical trials](#) that are testing the use of REGEN-COV in COVID-19, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).



Is REGEN-COV being studied in ongoing clinical trials?

Please refer to Appendix D of this guidebook for more information. Clinical investigators, hospitals, or clinical sites interested in joining the REGEN-COV clinical program can email Regeneron at [COVID19SiteInterest@regeneron.com](mailto:COVID19SiteInterest@regeneron.com).



*APPENDIX F:*

# **BASIC EQUIPMENT RECOMMENDATIONS**

# BASIC EQUIPMENT RECOMMENDATIONS

Equipment requirements may vary by state. Follow your local requirements when determining the equipment needed for your infusion center. Based on Regeneron's clinical trial experience, the following equipment should be considered to ensure the most optimal care environment for patients receiving REGEN-COV™ (casirivimab with imdevimab). This list is not intended to substitute for your independent medical judgment.

Additional information on administration sets can be found in **Section 6** of this guidebook.

## BASIC EQUIPMENT RECOMMENDATIONS

### PPE

- Gloves
- Gowns
- Eye and face protection (eg goggles, safety glasses, face shields)
- NIOSH-certified, disposable N95 filter facepiece respirators or better

### Infusion supplies

- Infusion chairs – recommended only
- IV pole
- Administration set
  - Sterile in-line 0.2/0.22 micron filter (may be integrated into administration set or separate add-on device)
- IV and catheters
- Infusion pumps (if available)
- Infusion pump bracket for IV pole (if available)
- 3-mL saline syringes
- Appropriately sized syringes
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Occlusive dressing
- Absorbent underpads (blue pads)
- Extension set tubing
- 18-gauge stainless steel needles
- Sharps containers
- Tape
- Transilluminator (vein finder)

### General supplies

- Infusion Reaction Kit
- Vital signs equipment
- Reaction management kit
  - IV diphenhydramine, IV corticosteroid (eg, methylprednisolone 125 mg), epinephrine (auto-injector preferred), CPR barrier mask and bag valve mask, oxygen and delivery devices (nasal cannula and non-rebreather mask)
- Locking refrigerator with temperature monitoring capability
- Privacy screens
- Biohazard disposal bag
- Disposable disinfecting wipes
- Thermometer probe covers (if required)
- 70% alcohol wipes
- Paper towels
- Trash bins and liners