

FACT SHEET FOR HEALTH CARE PROVIDERS EMERGENCY USE AUTHORIZATION (EUA) OF CASIRIVIMAB AND IMDEVIMAB

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved 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 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.

LIMITATIONS OF AUTHORIZED USE

- Casirivimab and imdevimab are not authorized for use in patients:
 - who are hospitalized due to COVID-19, OR
 - who require oxygen therapy due to COVID-19, OR
 - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

Casirivimab and imdevimab have been authorized by FDA for the emergency uses described above.

Casirivimab and imdevimab are not FDA-approved for these uses.

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

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

This EUA is for the use of the unapproved products, casirivimab and 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*].

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age

- Are ≥55 years of age AND have
 - cardiovascular disease, OR
 - hypertension, OR
 - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
 - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, 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.

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

Casirivimab and imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to casirivimab and imdevimab. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

- 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 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 over at least 60 minutes via pump or gravity.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

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

For information on clinical trials that are testing the use of casirivimab and imdevimab in COVID-19, please see www.clinicaltrials.gov.

Contraindications

None.

Dosing

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

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved products, casirivimab and imdevimab, 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*].

High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age
- Are ≥ 55 years of age AND have
 - cardiovascular disease, OR
 - hypertension, OR
 - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
 - BMI ≥ 85 th percentile for their age and gender based on CDC growth charts, 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.

Dosage

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 over at least 60 minutes. Casirivimab and imdevimab solutions must be diluted prior to administration. Casirivimab and imdevimab should be given together as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Dosage Adjustment in Specific Populations

No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment [*see Full EUA Prescribing Information, Use in Specific Populations (11)*].

Preparation and Administration

Preparation

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

Casirivimab and imdevimab solution for infusion 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 an IV infusion bag containing 250 mL of 0.9% Sodium Chloride Injection. Withdraw and discard 20 mL of 0.9% Sodium Chloride Injection from the infusion bag prior to adding casirivimab and imdevimab solutions according to [Table 1](#).
4. Withdraw 10 mL of casirivimab and 10 mL of imdevimab from each respective vial using two separate syringes and dilute together in the 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.** 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 and at room temperature up to 25°C (77°F) for no more than 4 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

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

Table 1: Recommended Dilution Instructions for Casirivimab and Imdevimab for IV Infusion

	Antibody Dose	Volume to Withdraw from Vial	Number of Vials Needed ^b	Volume of 0.9% Sodium Chloride to Discard from a 250 mL Infusion Bag	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Casirivimab and Imdevimab 2,400 mg Dose ^a	Casirivimab REGN10933 1,200 mg	10 mL	1 vial of 11.1 mL OR 4 vials of 2.5 mL	20 mL	250 mL	250 mL/hr	60 minutes
	Imdevimab REGN10987 1,200 mg	10 mL	1 vial of 11.1 mL OR 4 vials of 2.5 mL				

NOTE: casirivimab = REGN10933; imdevimab = REGN10987

^a 1,200 mg of Casirivimab and 1,200 mg of Imdevimab are to be administered together as a single intravenous infusion for a combined 2,400 mg dose.

^b 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.

Administration

Casirivimab and 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 IV bag.
- Prime the infusion set.
- Administer as an IV infusion via pump or gravity over at least 60 minutes through an intravenous line containing a sterile, in-line or add-on 0.2-micron polyethersulfone (PES) filter (see [Table 1](#)).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.
- After infusion is complete, flush with 0.9% Sodium Chloride Injection.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.

Storage

Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the individual original carton to protect from light. Do NOT freeze, shake, or expose to direct light.

Warnings

There are limited clinical data available for casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

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

Signs and symptoms of infusion-related reactions may include:

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

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients

requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab are not authorized for use in patients *[see Limitations of Authorized Use]*:

- 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.

Side Effects

Adverse events have been reported with casirivimab and imdevimab *[see Full EUA Prescribing Information, Clinical Trials Experience (6.1)]*.

Additional adverse events associated with casirivimab and imdevimab, some of which may be serious, may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the health care provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” (and provide a copy of the Fact Sheet) prior to the patient receiving casirivimab and imdevimab, including:

- FDA has authorized the emergency use of casirivimab and 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]*.
- The patient or parent/caregiver has the option to accept or refuse casirivimab and imdevimab.
- The significant known and potential risks and benefits of casirivimab and imdevimab, and the extent to which such risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with casirivimab and imdevimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

For information on clinical trials that are testing the use of casirivimab and imdevimab related to COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR CASIRIVIMAB AND IMDEVIMAB UNDER EMERGENCY USE AUTHORIZATION:

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of casirivimab and imdevimab to be administered together, the following items are required. Use of casirivimab and imdevimab under this EUA is limited to the following (all requirements **must** be met):

1. 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*].
2. As the health care provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” prior to the patient receiving casirivimab and imdevimab. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient’s medical record that the patient/caregiver has been:
 - a. Given the “Fact Sheet for Patients, Parents and Caregivers”,
 - b. Informed of alternatives to receiving casirivimab and imdevimab, and
 - c. Informed that casirivimab and imdevimab are unapproved drugs that are authorized for use under this Emergency Use Authorization.
3. Patients with known hypersensitivity to any ingredient of casirivimab and imdevimab must not receive casirivimab and imdevimab.
4. The prescribing health care provider and/or the provider’s designee are/is responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of casirivimab and imdevimab.
5. The prescribing health care provider and/or the provider’s designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to casirivimab and imdevimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words “Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)” in the description section of the report.
 - Submit adverse event reports to FDA MedWatch using one of the following methods:
 - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
 - By using a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning 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
 - Submitted reports should include in the field name, “Describe Event, Problem, or Product Use/Medication Error” a statement “Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA).”

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

6. OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:

Regeneron Pharmaceuticals, Inc

Fax: 1-888-876-2736

E-mail: medical.information@regeneron.com

Or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved and available alternatives to casirivimab and imdevimab to be administered together for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. The health care provider should visit <https://clinicaltrials.gov/> to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Regeneron Pharmaceuticals, Inc. for the unapproved products, casirivimab and 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.¹ As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

¹ The health care provider should visit <https://clinicaltrials.gov/> to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that casirivimab and imdevimab, administered together, may be effective for the treatment of COVID-19 in patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for casirivimab and imdevimab will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

CONTACT INFORMATION

For additional information visit www.REGENCOV2.com

If you have questions, please contact Regeneron at 1-844-734-6643.

END SHORT VERSION FACT SHEET

Long Version Begins on Next Page
