Louisiana Department of Health
Protocol- Monoclonal Antibodies for Treatment of COVID-19
REGEN-COV™ (casirivimab and imdevimab)
Revised 10/01/2021

GENERAL REQUIREMENTS

1. Review and be familiar with the most current revision of the **Fact Sheet for Health Care Providers for the EUA of REGEN-COV™ (casirivimab and imdevimab)**, available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf.
2. Verify that the individual meets the FDA EUA criteria for administration of REGEN-COV™ (casirivimab and imdevimab).
3. Review and be familiar with personal protective equipment (PPE) required for providing Casirivimab and Imdevimab to qualifying patients.
4. Review and follow the "Intravenous Infusion Preparation and Administration Instructions" outlined in this Protocol for qualifying patients receiving intravenous infusion.
5. Review and follow the "Subcutaneous Injection Preparation and Administration Instructions" outlined in this Protocol for qualifying patients receiving subcutaneous injections.
6. Inform each patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting, that REGEN-COV™ (casirivimab and imdevimab) is not approved by the FDA but has received emergency use authorization from the FDA for (1) the treatment of mild to moderate COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death and (2) for post-exposure prophylaxis of COVID-19 in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death. Provide to the patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting, the most current revision of the **Fact Sheet for Patients, Parents and Caregivers for the EUA of REGEN-COV™ (casirivimab and imdevimab)**, available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-patient.pdf, prior to administering the drug.
7. Receive informed written consent for use of REGEN-COV™ (casirivimab and imdevimab) for treatment of COVID-19 or post-exposure prophylaxis from the patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting.
8. Submit a report on all medication errors and all serious adverse events potentially related to REGEN-COV™ (casirivimab and imdevimab).
9. Advise all patients, or parents or legal guardians if the patient is under 18 years of age or incapable of consenting, to continue to self-isolate and use infection control measures.

Patient Selection for Treatment and Post-Exposure Prophylaxis

This section provides essential information on the unapproved product, REGEN-COV (casirivimab and imdevimab) co-formulated product and REGEN-COV (casirivimab andimdevimab) supplied in individual vials to be administered together in adult and pediatricpatients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death for:

- Treatment of mild to moderate COVID-19 in adult and pediatric patients with positiveresults of direct SARS-CoV-2 viral testing *[see Limitations of Authorized Use (1.1)]*.
- Post-exposure prophylaxis of COVID-19 in high risk individuals who are:
    - not fully vaccinated[1] **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals withimmunocompromising conditions including those taking immunosuppressive medications[2]**) and**
        - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Controland Prevention (CDC)[3] **or**
        - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes, prisons) *[see Limitations of Authorized Use (1.2)]*.

Criteria for Identifying High Risk Individuals

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

- Older age (for example, age ≥65 years of age)
- Obesity or being overweight (for example, BMI >25 kg/m^2, or if age 12-17, have BMI
  ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma[moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions thatconfer medical complexity (for example, genetic or metabolic syndromes and severecongenital anomalies)
- Having a medical-related technological dependence (for example,

tracheostomy,gastrostomy, or positive pressure ventilation (not related to COVID-19))

Other medical conditions or factors (for example, race or ethnicity) may also place individualpatients at high risk for progression to severe COVID-19 and authorization of REGEN-COV under the EUA is not limited to the medical conditions or factors listed above. For additionalinformation on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: https://www.cdc.gov/coronavirus/2019- ncov/need-extra-precautions/people-with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.

Dosage

Treatment:
The dosage in adult and pediatric patients (12 years of age and older weighing at least 40 kg) is 600 mg of casirivimab and 600 mg of imdevimab administered together as a single intravenous infusion or by subcutaneous injection. Casirivimab and imdevimab should be given together as soon as possible after positive results of direct SARS-CoV-2 viral testing andwithin 10 days of symptom onset.

Post-Exposure Prophylaxis:
The dosage in adult and pediatric individuals (12 years of age and older weighing at least 40kg) is 600 mg of casirivimab and 600 mg of imdevimab administered by subcutaneous injection or together as a single intravenous infusion. Casirivimab and imdevimab should begiven together as soon as possible following exposure to SARS-CoV-2.

For individuals in whom repeat dosing is determined to be appropriate for ongoing exposure toSARS-CoV-2 for longer than 4 weeks and who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination, the initial dose is 600 mg of casirivimab and 600 mg of imdevimab by subcutaneous injection or intravenous infusion followed by subsequent repeat dosing of 300 mg of casirivimab and 300 mg of imdevimab bysubcutaneous injection or intravenous infusion once every 4 weeks for the duration of ongoing exposure.

For Intravenous Infusion:
- Casirivimab and imdevimab solution co-formulated in a vial and in individual vials,including co-packaged carton and dose pack, must be diluted prior to intravenous administration.
- Administer casirivimab and imdevimab together as a single intravenous infusion viapump or gravity (see Table 1, Table 2, Table 3 and Table 4).
- Clinically monitor patients during infusion and observe patients for at least 1 hourafter infusion is complete.

For Subcutaneous Injection:
- Administer casirivimab and imdevimab using the co-formulated vial or using theindividual vials by subcutaneous injection (see Table 5 and Table 6).
- Clinically monitor patients after injections and observe patients for at least 1 hour.

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

There are TWO different formulations of REGEN-COV:

- Casirivimab and imdevimab co-formulated solution containing two antibodies in a 1:1ratio in a vial.
- Casirivimab and imdevimab available as individual antibody solutions in separatevials supplied as follows:
  - Individual vials in individual cartons, or
  - together in a single carton (as referred to as a co-packaged carton), or
  - in a dose pack. The dose pack contains individual vials of casirivimab and imdevimab, configurations that may vary in vial size, strength and appearance andare available in dose pack configurations that include 2, 5, and 8 cartons *[see Full EUA Prescribing Information, How Supplied/Storage and Handling (19)]*.

For treatment, intravenous infusion is strongly recommended. Subcutaneous injection isan alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

For post-exposure prophylaxis, either subcutaneous injection or intravenous infusioncan be used.

There are differences in the way the two formulations are prepared. Carefully follow thepreparation procedures below.

- Casirivimab and imdevimab co-formulated solution in a vial and casirivimab or imdevimab as individual antibody solutions in separate 11.1 mL vials may be used toprepare more than one dose simultaneously as appropriate, either in intravenous bagsor in syringes for subcutaneous injection. Discard any product remaining in the vial.
- Keep any unopened vials of casirivimab and imdevimab in their original carton in therefrigerator.

Under the EUA, a single-dose vial may be used to prepare more than one

dose.Preparation for Intravenous Infusion

For treatment, the preferred route of administration for casirivimab and imdevimab is byintravenous infusion after dilution.

Casirivimab and imdevimab solution for intravenous infusion should be prepared by aqualified 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. **Donot 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 vial must bediscarded and replaced with a new vial.
   - The solution for each vial should be clear to slightly opalescent, colorless to paleyellow.
3. Obtain a prefilled intravenous infusion bag containing either 50 mL, 100 mL, 150 mL,or 250 mL of either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP.
4. Withdraw the appropriate amount of casirivimab and imdevimab from each respectivevial(s) and inject into a prefilled infusion bag containing either 0.9% Sodium ChlorideInjection, USP or 5% Dextrose Injection, USP (see Table 1 and Table 2). If using one vial to prepare more than one infusion bag, then prepare all infusion bags at the same time. The product is preservative-free, therefore do not store unused solution in vial(s).
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 beadministered immediately (see Table 3 and Table 4).
   - 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 nomore than 4 hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Table 1: Recommended Dilution Instructions for 600 mg of Casirivimab and 600mg of Imdevimab for Intravenous Infusion

Size of Prefilled 0.9% Sodium Chloride or 5% Dextrose InfusionBag	**Preparing Using Co-Formulated Casirivimab andImdevimab Vial**	**Preparing Casirivimab and Imdevimab Using IndividualVials**[a]
50 mL	Add 10 mL of co-formulated casirivimab and imdevimab (1 vial) into a prefilled 0.9% Sodium Chloride or 5% Dextroseinfusion bag and administer as instructed below	Add: • 5 mL of casirivimab (may use2 vials of 2.5 mL OR 1 vial of 11.1 mL) and • 5 mL of imdevimab (may use2 vials of 2.5 mL OR 1 vial of 11.1 mL)
100 mL		
150 mL		

250 mL		and inject into a prefilled 0.9% Sodium Chloride or 5% Dextroseinfusion bag and administer as instructed below

[a] 600 mg of casirivimab and 600 mg of imdevimab are added to the same infusion bag and administeredtogether as a single intravenous infusion.

Table 2: Recommended Dilution Instructions for 300 mg of Casirivimab and 300mg of Imdevimab for Intravenous Infusion for Repeat Dosing[a]

Size of Prefilled 0.9% Sodium Chloride or 5% Dextrose InfusionBag	**Preparing Using Co-Formulated Casirivimab andImdevimab Vial**	**Preparing Casirivimab and Imdevimab Using IndividualVials[b]**
50 mL	Add 5 mL of co-formulated casirivimab and imdevimab into a prefilled 0.9% Sodium Chlorideor 5% Dextrose infusion bag and administer as instructed below	Add: • 2.5 mL of casirivimab (mayuse 1 vial of 2.5 mL OR 1 vial of 11.1 mL) and • 2.5 mL of imdevimab (mayuse 1 vial of 2.5 mL OR 1 vial of 11.1 mL)
100 mL		
150 mL		
250 mL		and inject into a prefilled 0.9% Sodium Chloride or 5% Dextroseinfusion bag and administer as instructed below

[a] Subsequent repeat dosing every 4 weeks after initial 600 mg casirivimab and 600 mg imdevimab dosing forthe duration of ongoing exposure.
[b] 300 mg of casirivimab and 300 mg of imdevimab are added to the same infusion bag and administeredtogether as a single intravenous infusion.

Administration by Intravenous Infusion

Casirivimab and imdevimab infusion solution should be administered by a qualifiedhealthcare 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 3 and Table 4). 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 anyother medication. The compatibility of casirivimab and imdevimab injection with intravenous solutions and medications other than 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP is not known.
- After infusion is complete, flush the tubing with either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to ensure delivery of the required dose.
- Discard unused product.
- Clinically monitor patients during administration and observe patients for at least 1hour after infusion is complete.

Table 3: Recommended Administration Rate for 600 mg of Casirivimab and 600mg of Imdevimab for Intravenous Infusion

Size of Prefilled 0.9% SodiumChloride or 5% Dextrose Infusion Bag used	Maximum Infusion Rate	Minimum Infusion Time
50 mL[a]	180 mL/hr	20 minutes
100 mL	310 mL/hr	21 minutes
150 mL	310 mL/hr	31 minutes
250 mL	310 mL/hr	50 minutes

[a] The minimum infusion time for patients administered casirivimab and imdevimab together using the 50 mL prefilled 0.9% Sodium Chloride or 5% Dextrose infusion bag must be at least 20 minutes to ensure safe use.

Table 4: Recommended Administration Rate for 300 mg of Casirivimab and 300mg of Imdevimab for Intravenous Infusion for Repeat Dosing[a]

Size of Prefilled 0.9% SodiumChloride or 5% Dextrose Infusion Bag used	Maximum Infusion Rate	Minimum Infusion Time
50 mL[b]	165 mL/hr	20 minutes
100 mL	310 mL/hr	20 minutes
150 mL	310 mL/hr	30 minutes
250 mL	310 mL/hr	49 minutes

[a] Subsequent repeat dosing every 4 weeks after initial 600 mg casirivimab and 600 mg imdevimab dosing for theduration of ongoing exposure.
[b] The minimum infusion time for patients administered casirivimab and imdevimab together using the 50 mL prefilled 0.9% Sodium Chloride or 5% Dextrose infusion bag must be at least 20 minutes to ensure safe use.

Preparation for Subcutaneous Injection

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do notexpose to direct heat. Do not shake the vials.**

Inspect casirivimab and imdevimab vial(s) visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded and replaced with a new vial. The solution for each vial should be clear to slightly opalescent, colorless topale yellow.

1. Casirivimab and imdevimab should be prepared using the appropriate number of syringes (see Table 5 and Table 6). Obtain 3 mL or 5 mL polypropylene Luer Locksyringes with luer connection and 21-gauge 1½ inch transfer needles.
2. Withdraw the appropriate amount of solution into each syringe (see Table 5 and Table6). Prepare all syringes at the same time.
3. Replace the 21-gauge transfer needle with a 25-gauge or 27-gauge needle forsubcutaneous injection.
4. This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes in the refrigerator between 2ºC to 8ºC(36ºF to 46ºF) for no more than 4 hours or at room temperature up to 25ºC (77ºF) forno more than 4 total hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 20 minutes prior to administration.

Table 5: Preparation of 600 mg of Casirivimab and 600 mg of Imdevimab forSubcutaneous Injections

Prepare 600 mg of Casirivimaband 600 mg of Imdevimab	**Preparation of 4 Syringes**
Using Casirivimab and Imdevimab Co-formulatedVial	Withdraw 2.5 mL solution per syringe into FOURseparate syringes.
Using Casirivimab and Imdevimab Individual Vials	• **Casirivimab:** Withdraw 2.5 mL solution persyringe into TWO separate syringes. • **Imdevimab:** Withdraw 2.5 mL solution persyringe into TWO separate syringes. For total of 4 syringes.

Table 6: Preparation of 300 mg of Casirivimab and 300 mg of Imdevimab forSubcutaneous Injections for Repeat Dosing[a]

Prepare 300 mg of Casirivimaband 300 mg of Imdevimab	Preparation of 2 Syringes
Using Casirivimab and Imdevimab Co-formulatedVial	Withdraw 2.5 mL solution per syringe into TWOseparate syringes.
Using Casirivimab and Imdevimab Individual Vials	• **Casirivimab:** Withdraw 2.5 mL solution intoONE syringe. • **Imdevimab:** Withdraw 2.5 mL solution intoONE syringe. For total of 2 syringes.

[a] Subsequent repeat dosing every 4 weeks after initial 600 mg casirivimab and 600 mg imdevimab dosing for theduration of ongoing exposure.

Administration for Subcutaneous Injection

- For the administration of 600 mg of casirivimab and 600 mg of imdevimab, gather 4syringes (see Table 5) and prepare for subcutaneous injections.
- For the administration of 300 mg of casirivimab and 300 mg of imdevimab, gather 2syringes (see Table 6) and prepare for subcutaneous injections.
- Administer the subcutaneous injections consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5 cm) around thenavel. The waistline should be avoided.
- When administering the subcutaneous injections, it is recommended that providers use different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL subcutaneous injection of casirivimab and imdevimab. DO NOT injectinto skin that is tender, damaged, bruised, or scarred.
- Clinically monitor patients after injections and observe patients for at least 1 hour.

Storage

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

Warnings

There are limited clinical data available for REGEN-COV (casirivimab and imdevimab).Serious and unexpected adverse events may occur that have not

been previously reportedwith REGEN-COV use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV (casirivimab and imdevimab). If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinueadministration and initiate appropriate medications and/or supportive therapy.

Infusion-related reactions, occurring during the infusion and up to 24 hours after the infusion,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 (e.g.,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, vasovagal reactions (e.g., pre-syncope, syncope), dizziness, and diaphoresis.

Consider slowing or stopping the infusion and administer appropriate medications and/orsupportive care if an infusion-related reaction occurs.

Hypersensitivity reactions occurring more than 24 hours after the infusion have also beenreported with the use of REGEN-COV under Emergency Use Authorization.

Clinical Worsening After REGEN-COV Administration

Clinical worsening of COVID-19 after administration of REGEN-COV has been reportedand 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

Monoclonal antibodies, such as REGEN-COV, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flowoxygen or mechanical ventilation. Therefore, REGEN-COV is not authorized for use in patients *[see Limitations of Authorized Use (1.1)]*:

- 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 relatedcomorbidity.

Side Effects

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

Additional adverse events associated with REGEN-COV, some of which may be serious,may become apparent with more widespread use.