

10.18 Administration of Casirivimab/Imdevimab	Revision Dates June 2021, 8/2/21
Application Licensed Nurses Providing Infusion Therapy in the LTC Facility	Original Date December 2020

THE FACILITY MUST ENSURE THAT ALL NURSES RESPONSIBLE FOR THE CARE AND MANAGEMENT OF PATIENTS RECEIVING MONOCLONAL ANTIBODY INFUSIONS ARE KNOWLEDGEABLE AND COMPETENT IN THE ADMINISTRATION PROCEDURES AND THE POTENTIAL COMPLICATIONS ASSOCIATED WITH THIS THERAPY.

To Be Performed By:

Licensed nurses in accordance with state law and facility policy. The nurse shall be competent in the safe delivery of infusion therapy within his or her scope of practice. Competency validation is documented in accordance with organizational policy.

Considerations:

1. Casirivimab/imdevimab is a monoclonal antibody for the treatment of mild to moderate COVID-19. These medications are specifically directed against the spike protein of SARS-CoV-2 and are designed to block the virus' attachment and entry into human cells, thus neutralizing the virus.
2. Casirivimab and imdevimab must be administered together by IV infusion, or 4 subcutaneous injection to equal one dose. **Note: IV administration is strongly recommended. Subcutaneous injection is an alternative route of administration when iv route is not feasible and would lead to delay in treatment.**
3. The FDA has issued an Emergency Use Authorization (EUA) to treat adults and pediatric patients who are 12 years of age and older weighing at least 40 kg with high risk for progressing to severe COVID-19 and/or hospitalization that have:
 - 3.1 Mild to moderate COVID-19 (positive results of direct SARS-CoV-2 viral testing)
 - 3.2 Exposure to COVID-19 (Prophylaxis Use) in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:
 - 3.2.1 not fully vaccinated¹ **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination² (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications) **and**
 - 3.2.1.1 have been exposed to an individual infected with SARS-CoV-2 consistent with close contact³ criteria per Centers for Disease Control and Prevention (CDC) **or**
 - 3.2.1.2 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)

¹ Individuals are considered to be fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series (such as the Pfizer or Moderna vaccines), or 2 weeks after a single-dose vaccine (such as Johnson & Johnson's Janssen vaccine). See this website for more details: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html#vaccinated>

² See this website for more details: <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html>

³ Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). See this website for additional details: <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html>

- 3.3 **Limitations of Authorized Use**
 - 3.3.1 Post-exposure prophylaxis with REGEN-COV (casirivimab and imdevimab) is not a substitute for vaccination against COVID-19.
 - 3.3.2 REGEN-COV (casirivimab and imdevimab) is not authorized for pre-exposure prophylaxis for prevention of COVID-19.
4. Casirivimab/Imdevimab is not authorized for use in patients:
 - 4.1 Who are hospitalized due to COVID-19, **OR**
 - 4.2 Who require oxygen therapy due to COVID-19, **OR**
 - 4.3 Oxygen dependent patients who require an increase in oxygen flow rate due to COVID-19 complications
5. Benefit of treatment with casirivimab/imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab/imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.
6. Monoclonal Antibodies and COVID-19 Vaccines¹:
 - 6.1 Currently, there is no data on the safety and efficacy of Pfizer-BioNTech COVID-19 vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment.
 - 6.2 Based on the estimated half-life of such therapies, as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days, as a precautionary measure, until additional information becomes available, to avoid interference of the antibody treatment with vaccine-induced immune responses. Healthcare providers should review the **Fact Sheet for Healthcare Providers** for information on the authorized use of casirivimab and imdevimab and mandatory requirements of the EUA and must comply with the requirements of the EUA. The **FDA Letter of Authorization** is available here for reference, as well as the **Dear Healthcare Provider Letter** and **Patient Fact Sheet**.
7. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and adverse events (death, serious adverse events) potentially related to casirivimab/imdevimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words **"Casirivimab and imdevimab under Emergency Use Authorization (EUA)" in the description section of the report.**
 - 7.1 Submit adverse event reports to FDA MedWatch using one of the following methods:
 - 7.1.1 Complete and submit the report online: www.fda.gov/medwatch/report.htm
 - 7.1.2 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 (1-277 800-FDA-0178)
 - 7.1.3 Call 1-800-FDA-1088 to request a reporting form
 - 7.1.4 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)."
 - 7.1.5 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.

1 https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/clinical-considerations.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2F covid-19%2Finfo-by-manufacturer%2Fpfizer%2Fclinical-considerations.html

- 7.2 Serious Adverse Events are defined as:
 - 7.2.1 Death
 - 7.2.2 A life-threatening adverse event
 - 7.2.3 Inpatient hospitalization or prolongation of existing hospitalization
 - 7.2.4 A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
 - 7.2.5 A congenital anomaly/birth defect
 - 7.2.6 A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly
8. Licensed nurses caring for patients receiving infusion therapies are expected to follow infection prevention procedures.

Guidance

1. Casirivimab/Imdevimab is administered as a single intravenous infusion of 600 mg of casirivimab AND 600 mg of imdevimab over a minimum of 30 minutes, as soon as possible after a positive COVID-19 test and within 10 days of symptom onset, or post-exposure. **IV administration is strongly recommended. Subcutaneous injection is an alternative route of administration when iv route is not feasible and would lead to delay in treatment.**
 - 1.1 Consider slower infusion rate for patients with CHF, chronic kidney disease, and Systemic Inflammatory Response Syndrome (SIRS)
 - 1.2 Casirivimab and imdevimab solutions must be diluted prior to IV administration
2. Subsequent dosing for ongoing exposure: For patients with in whom repeat dosing is determined to be appropriate for ongoing exposure to SARS-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 by subcutaneous injection or intravenous infusion once every 4 weeks for the duration of ongoing exposure.
3. There is a potential for serious hypersensitivity reaction, including anaphylaxis with the administration of casirivimab/imdevimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive therapy.
 - 3.1 Anaphylaxis and infusion-related orders must be obtained prior to administration
 - 3.2 Anaphylaxis kit/medications must be readily available
4. The casirivimab/imdevimab infusion should be followed by administration of **25** mL 0.9% Sodium Chloride to clear the medication from the administration set, ensuring the complete dose is administered. A prescriber order must be obtained for this solution, at the same rate as the medication.
5. Casirivimab/imdevimab is available as concentrated solution and must be diluted prior to IV administration.
6. Casirivimab/imdevimab vial(s) or compounded medications must be removed from the refrigerator approximately 20-30 minutes prior to admixing or administration to bring to room temperature. Do not expose to direct heat and do not shake the vials.
 - 6.1 **If IV, prior to admixing or removing from refrigerator, confirm the presence of a patent vascular access device**
7. Inspect for particulate matter and discoloration. Solution is slightly opalescent and colorless to pale yellow. Do not use if particulate matter identified.
8. Do not freeze, shake or expose to direct light.

9. Monitor patient during administration and for at least one hour post administration. Signs and symptoms of adverse reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticarial, pruritus, myalgia, and dizziness.
10. Monitor vital signs:
 - 10.1 Prior to initiating administration
 - 10.2 Every 15 minutes during infusion, if applicable
 - 10.3 Every 15 minutes for 1 hour post administration
11. If an adverse reaction occurs, consider slowing or stopping the infusion, if applicable, and administer appropriate medications and supportive care per prescriber's orders. Stop administration for signs and symptoms of clinically significant hypersensitivity reaction or if anaphylaxis occurs. Note: If administering monoclonal antibody subcutaneously and patient exhibits an adverse reaction, a short peripheral IV catheter may need to be placed to administer anaphylaxis medications.
12. If infusion, administration set with 0.2 or 0.22 micron in-line filter provided by the pharmacy must be used. Use of electronic infusion device for medication administration is recommended.
13. No dosage adjustment is recommended in pregnant or lactating women and in patients with renal impairment.
14. Patients treated with casirivimab/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.
15. Use strict aseptic technique/precautions, when admixing and during administration of this medication as there are no preservatives or any bacteriostatic agents in the products.
16. Patient with known hypersensitivity to any ingredient of casirivimab/imdevimab must not receive casirivimab/imdevimab.
17. As the healthcare 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/imdevimab. Healthcare 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:
 - 17.1 Provided the "Fact Sheet for Patients, Parents and Caregivers"
 - 17.2 Informed of alternatives to receiving authorized casirivimab/imdevimab
 - 17.3 Informed that casirivimab/imdevimab is an unapproved drug that is authorized for use under this Emergency Use Authorization

Equipment if administering intravenously*:

- Compounded medication bag
- 50-100 mL minibag of 0.9% sodium chloride for clearing medication from administration set
- Alcohol pads
- Prescribed flushing/locking agent(s) in 10 mL barrel diameter or larger syringe, if appropriate
- Electronic infusion device
- Administration set with 0.2 or 0.22 micron filter
- Clean gloves

* Also gather supplies for short peripheral IV catheter insertion, if applicable (see procedure 4.1 Short Peripheral Catheter Insertion)

Equipment if administering by subcutaneous injection*:

- Medication vial(s)
- (4) 3 mL syringes
- (4) 24 or 27 gauge subcutaneous needles
- (4) 21 gauge needles for withdrawing medication from vial(s)
- Alcohol wipes
- Clean gloves

Procedure:

1. Verify prescriber order. Perform pre-administration vital sign assessment.
2. Assemble equipment and supplies on clean work surface.
3. Perform hand hygiene. Don clean gloves.
4. If infusion, prior to removing medication from the refrigerator, establish vascular access or verify patency of vascular access device. (Refer to procedure 4.1 Short Peripheral Catheter Insertion)
5. **Remove medication bag, or vial(s), from refrigerator and allow to reach room temperature for approximately 30 minutes.**
6. If subcutaneous injection, proceed to step # 16.
7. 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.
8. Attach admixed medication bag to filtered administration set and administer immediately. Program infusion pump to infuse over a minimum of 30 minutes. Program in BASIC mode when using SIGMA Spectrum™ infusion pump. (Refer to procedure 3.6, Administration of an Intermittent Infusion for administration steps.)
9. Monitor patient during administration and for at least one hour post administration performing patient assessment/vital signs every 15 minutes. Signs and symptoms of adverse reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticarial, pruritus, myalgia, and dizziness.
10. If an adverse reaction occurs, consider slowing or stopping the infusion, if applicable, and administer appropriate medications and/or supportive care. Stop administration for signs and symptoms of clinically significant hypersensitivity reaction or if anaphylaxis occurs.
11. Upon completion of casirivimab/imdevimab infusion, replace empty medication bag with a 50 - 100 mL 0.9% Sodium Chloride minibag. This will be used to clear administration set of medication ensuring the complete dose has been administered. Administer 0.9% Sodium Chloride at same rate as infusion for a volume of **25 mL** (reset the volume to be infused on the infusion pump at 25 mL). Continue infusion.
12. Upon completion of administration, perform hand hygiene.
13. Don gloves.
14. Close the clamp and disconnect the administration set from needleless connector.
15. Perform a vigorous mechanical scrub to manually disinfect the needleless connector. Allow to air dry. Follow with prescribed flushing/locking solution, if vascular access device is to remain intact.

* Also gather supplies for short peripheral IV catheter insertion, if applicable (see procedure 4.1 Short Peripheral Catheter Insertion)

16. If subcutaneous injection,
 - 16.1 Prepare casirivimab 600 mg and imdevimab 600 mg using 4 syringes (either 3 or 5 mL) and 21 gauge transfer needle.
 - 16.2 Withdraw 2.5 mL into each syringe (total of 4 syringes).
 - 16.3 Replace 21 gauge transfer needle with a 25-27 gauge needle for subcutaneous injection.
 - 16.4 Administer immediately after preparation. Administer all four syringes consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5cm) around the navel. the waistline should be avoided. When administering, it is recommended to 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 inject into skin that is tender, damaged, bruised, or scarred.
 - 16.5 Remain with patient for 15 minutes post administration. Monitor patient for adverse reactions as in steps # 9-10 above for one hour post administration.
17. Dispose of used supplies per facility policy.
18. Remove gloves.
19. Perform hand hygiene.
20. Documentation in the medical record includes, but is not limited to:
 - 20.1 Date and time
 - 20.2 Medications/solution
 - 20.3 Rate and method of administration
 - 20.4 Prescribed flushing/locking agent(s), if applicable
 - 20.5 Site assessment(s)
 - 20.6 Complications and interventions
 - 20.7 Patient response to procedure and/or medication
 - 20.8 Patient/significant other teaching

References:

1. Regeneron webpage for casirivimab/imdevimab: <https://investor.regeneron.com/index.php/news-releases/news-release-details/fda-authorizes-lower-1200-mg-intravenous-and-subcutaneous-dose> (accessed 8/2/21)
2. Casirivimab/imdevimab Fact Sheet for Healthcare Providers: <https://c212.net/c/link/?t=0&l=en&o=3182647-1&h=3528456854&u=https%3A%2F%2Fwww.regeneron.com%2Fsites%2Fdefault%2Ffiles%2Ftreatment-covid19-eua-fact-sheet-for-hcp.pdf&a=Fact+Sheet+for+Healthcare+Providers> (accessed 8/2/21)
3. https://www.cdc.gov/growthcharts/clinical_charts.htm (accessed 6/8/21)
4. FDA.gov website. Casirivimab Imdevimab treatment-covid19-eua-fact-sheet-for-patient. <https://c212.net/c/link/?t=0&l=en&o=3182647-1&h=628731868&u=https%3A%2F%2Fwww.regeneron.com%2Fsites%2Fdefault%2Ffiles%2Ftreatment-covid19-eua-fact-sheet-for-patient.pdf&a=Patient+Fact+Sheet> (accessed 8/2/21)