Indian Health Service
National Pharmacy and Therapeutics Committee

COVID-19 Emerging Treatments Update

November 23, 2020

Casirivimab & Imdevimab (REGN-COV2)

EMERGENCY USE AUTHORIZATION

Mechanism of action[1]: Casirivimab (REGN10933) and imdevimab (REGN10987) are recombinant, human, neutralizing monoclonal antibodies that bind to the receptor binding domain of the SARS-CoV-2 spike protein.

Current Status[1,2]: Casirivimab & imdevimab are not FDA approved, they are an investigational drug combination and are not currently approved for any indication. On November 21, 2020, the FDA issued an Emergency Use Authorization (EUA) for casirivimab & imdevimab to be administered together to treat mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

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, OR sickle cell disease, OR congenital or acquired heart disease, OR neurodevelopmental disorders, OR a medical-related technological dependence or positive pressure ventilation (not related to COVID-19), OR asthma, reactive airway or chronic respiratory disease requiring daily medication.

Benefit 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.**

Therefore, casirivimab & imdevimab are not authorized for use in the following patient populations:

- Adults or pediatric patients who are *hospitalized* due to COVID-19, or
- Adults or pediatric patients who *require oxygen therapy* due to COVID-19, or
- Adults or pediatric patients who *require an increase in baseline oxygen flow rate* due to COVID-19 in those patients on chronic oxygen therapy due to underlying non-COVID-19-related comorbidity.

Availability[1,3]: Distribution of the authorized casirivimab & imdevimab will be controlled by the United States Government for use consistent with the terms and conditions of the EUA. More information can be found here.

Efficacy[2,4]: Unpublished interim analysis (N=799 of 2104) of R10933-10987-COV-2067 Trial (NCT04425629)
"Safety, Tolerability, & Efficacy of Anti-Spike SARS-CoV-2 Monoclonal Antibodies for the Treatment of Ambulatory Adult Patients with COVID-19" – *Full Results Not Currently Published/Available for Review*
Design: Double-blind RCT of casirivimab/imdevimab 2400mg (N=238), 8000mg (N=267) or placebo (N=262)
Patients: 2104 outpatients with recently diagnosed, mild-to-moderate COVID-19 at 96 sites in US & Romania
1º endpoint: Reductions in viral load (baseline to Day 7) were noted for both doses vs. placebo (p<0.0001)
2º endpoint: Reduction in Medically-Attended Visits @ 28 days for both doses (2.8%) vs. placebo (6.5%)

Safety / Adverse Drug Events[1,2]: All safety data derived from analysis of phase 1/2 trial of 799 ambulatory subjects with COVID-19. Serious adverse events (SAEs) reported in:

- 4 subjects (1.6%) in the casirivimab & imdevimab 2,400 mg group
- 2 subjects (0.8%) in the casirivimab & imdevimab 8,000 mg group
- 6 subjects (2.3%) in the placebo group

None of the SAEs were considered to be related to the study drug. One anaphylactic reaction was reported in the clinical program. Infusion-related reactions, of grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000 mg arm. These infusion-related reactions events were moderate in severity; and include fever, chills, urticaria, pruritis, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm and none were reported in the 2,400 mg arm. *If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.*

Dosing & Administration[2]: Casirivimab & imdevimab **may only be administered together** by IV infusion and may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system, as necessary.

- A single IV infusion of 1,200 mg of casirivimab and 1,200 mg of imdevimab administered together as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.
- Casirivimab & imdevimab are available as concentrated solutions and must be diluted prior to administration. DO NOT SHAKE. Administer casirivimab 1,200 mg & imdevimab 1,200 mg together via IV infusion over at least 60 minutes via pump or gravity.
- Monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

Product Administration Logistics[2]: Staffing requirements may vary by state. Follow your local requirements when determining the staff needed for your infusion site of care. Infusion sites of care should have appropriately trained medical staff to administer infusion treatments and identify and manage potential adverse reactions. To ensure the safest care environment for patients receiving casirivimab & imdevimab:

- Healthcare staff should utilize proper PPE in accordance with current CDC guidance.
- Drug infusion should be prepared by a healthcare professional trained in IV admixture preparation.
- Infusion administration/monitoring should be performed by properly trained healthcare professionals
- Infusion monitoring and post-infusion observation should include vital sign monitoring as well as assessment for and treatment of infusion-related reactions.
- COVID-19 cleaning and disinfection should be performed by appropriately trained staff.

Mandatory Requirements under the EUA[1,2]:

- Use casirivimab & imdevimab only in authorized patient populations described above
- Communicate to patients or parents/caregivers, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to 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:**
  - *Given the "Fact Sheet for Patients, Parents and Caregivers",*
  - *Informed of alternatives to receiving authorized casirivimab & imdevimab, and*
  - *Informed that casirivimab & imdevimab are unapproved drugs authorized for use under this EUA.*
- Patients with known hypersensitivity to any ingredient of casirivimab & imdevimab must not receive casirivimab & imdevimab.
- The prescriber is responsible for mandatory reporting of all drug errors and SAEs potentially related to casirivimab/imdevimab treatment within 7 calendar days from onset of event.
  - *Should include the words "use of casirivimab & imdevimab was under EUA" in the "Describe Event" section*
  - *Should include the words "Indian Health Service" or "IHS" on the form in the reporter section (section G).*
  - Information on the FDA MedWatch program can be found on the IHS Pharmacovigilance website.

References:

1. U.S. Food and Drug Administration. Letter of Authorization. Emergency Use Authorization (EUA) of casirivimab & imdevimab.
2. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. Emergency Use Authorization (EUA) of casirivimab & imdevimab.
3. U.S. Department of Health & Human Services. ASPR. Public Health Emergency: Casirivimab and imdevimab. Accessed Nov 23, 2020.
4. U.S. National Library of Medicine. Clinicaltrials.gov. NCT04425629. Accessed Nov 23, 2020.
5. U.S. Food and Drug Administration. Fact Sheet for Patients, Parents and Caregivers. Emergency Use Authorization of casirivimab & imdevimab.