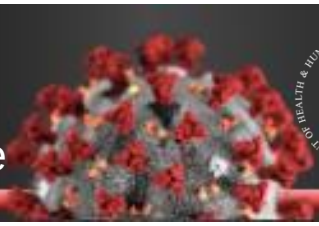
Indian Health Service
National Pharmacy and Therapeutics Committee

COVID-19 Emerging Treatments Update



June 30, 2021

Casirivimab & Imdevimab (REGEN-COV™)

- UPDATES to the Emergency Use Authorization -

On November 21, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of REGEN-COV (casirivimab and imdevimab, 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 SARSCoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Casirivimab and imdevimab are recombinant human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2. They are investigational drugs and are not approved for any indication.[1]

On June 3, 2021, the FDA authorized revisions to the EUA for REGEN-COV, noting the following items:

- ***a change in dosing of REGEN-COV from 2400 mg (1200 mg casirivimab and 1200 mg imdevimab) to 1200 mg (600 mg casirivimab and 600 mg imdevimab),***
- *the expansion of the definition of progression of severe COVID-19 to include death,*
- *the addition of a new presentation consisting of a single vial containing casirivimab and imdevimab co-formulated in a 1:1 ratio for either intravenous infusion or subcutaneous injection,*
- *the addition of Phase 3 results and safety with subcutaneous dosing.*

Based on review of the analysis of phase 3 data from COV-20677 (NCT04425629), a phase 1/2/3 randomized, double-blind, placebo-controlled trial evaluating the safety and efficacy of a single intravenous infusion of 600 mg casirivimab and 600 mg imdevimab in outpatients (nonhospitalized) with SARS-CoV-2 infection, it is reasonable to believe that REGEN-COV may be effective 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 progression to severe COVID-19, including hospitalization or death, and that, when used under the conditions described in this authorization, the known and potential benefits of REGEN-COV outweigh the known and potential risks of such product.

As a reminder, the following guidance remains in place with the current EUA (June 3, 2021).

1. REGEN-COV is 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 COVID19, 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

2. REGEN-COV 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.

3. REGEN-COV is authorized for intravenous infusion. **Subcutaneous injection is authorized as an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.**

Updated Dosage & Formulations[2]:

1. For Intravenous Infusion:
   - Casirivimab and imdevimab solution co-formulated in a vial and in individual vials, including dose pack, must be diluted prior to intravenous administration.
   - Administer 600 mg of casirivimab and 600 mg of imdevimab together as a single intravenous infusion via pump or gravity (see Table 1 and Table 2 in HCP Fact Sheet).
   - Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

2. For Subcutaneous Injection:
   - Administer 600 mg of casirivimab and 600 mg of imdevimab using the co-formulated vial or using the individual vials by subcutaneous injection (see Table 3 in HCP Fact Sheet).
   - Clinically monitor patients after injections and observe patients for at least 1 hour.

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.

Other Medical Conditions or Factors[2,3]:

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients 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. ***Importantly, comparative data on Risk for COVID-19 Infection, Hospitalization, and Death by Race/Ethnicity (including American Indians or Alaskan Natives) can be viewed here:*** https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html.

For additional information on medical conditions and factors associated with increased risk for progression to severe COVID, 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.

As a convenience, the accompanying **EUA Fact Sheets** are accessible immediately below.

1. Fact Sheet – For Health Care Providers (HCP)
2. Fact Sheet – Patients, Parents, and Caregivers

Mandatory Requirements under the EUA[2]:

- Use casirivimab & imdevimab only in authorized patient populations described in Fact Sheet (HCP)
- 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 REGEN-COV™. June 3, 2021.
2. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. Emergency Use Authorization (EUA) of REGEN-COV™. June 3, 2021.
3. Centers for Disease Control and Prevention. COVID-19: Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity. Accessed June 30, 2021.