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**IMPORTANT PRESCRIBING INFORMATION**

**Subject: Important information on new authorized use (post-exposure prophylaxis of COVID-19) for REGEN-COV™ (casirivimab and imdevimab) including Dosage and Administration information.**

Dear Healthcare Provider:

The purpose of this notice is to make you aware of new information regarding REGEN-COV™ (casirivimab and imdevimab).

The following chart highlights the pertinent new information but is not inclusive of all changes to the Fact Sheet for Health Care Providers.

**CHART 1**. SUMMARY OF RECENT MAJOR CHANGES

| **Section** | **Change** | **Further info located** |
|---|---|---|
| Authorized Use | Additional authorized use for post-exposure prophylaxis of COVID-19 | Page 2 |
| Dosage and Administration (Box, and Section 2.2): | Added authorized dosage for post-exposure prophylaxis of COVID-19 | Page 2 |

REGEN-COV™ (casirivimab and imdevimab) co-formulated product and REGEN-COV (casirivimab and imdevimab to be administered together) are authorized for use under an Emergency Use Authorization (EUA) for treatment of mild to moderate COVID-19 or for post-exposure prophylaxis of COVID-19 in patients who are at high risk for progression to severe COVID-19[1], including hospitalization or death.

The Healthcare Provider Fact Sheet is enclosed with this letter for reference to the full prescribing information. Stay current with the latest Fact Sheet for Health Care Providers by visiting (https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf).

[1] Please see the Healthcare Provider Fact Sheet for information on high risk criteria.

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**New Authorized Post-Exposure Prophylaxis Indication for COVID-19**

FDA has authorized REGEN-COV for use in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) for post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19[1], including hospitalization or death, and are:

- not fully vaccinated[2] or who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications[3]) and
  - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Center for Disease Control and Prevention (CDC)[4] 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)*.

*Limitations of Authorized Use (Post-exposure prophylaxis)*

- Post-exposure prophylaxis with REGEN-COV (casirivimab and imdevimab) is not a substitute for vaccination against COVID-19.
- REGEN-COV (casirivimab and imdevimab) is not authorized for pre-exposure prophylaxis for prevention of COVID-19.

**Dosage for Post-Exposure Prophylaxis of COVID-19**

The dosage in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) 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 be administered by subcutaneous injections given consecutively or together as a single intravenous infusions as soon as possible following exposure to SARS-CoV-2.

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[2] 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

[3] See this website for more details: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

[4] 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

For individuals 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.

**Preparation & Administration for Post-Exposure Prophylaxis of COVID-19**

REGEN-COV (casirivimab and imdevimab) is available as:

1. A single vial which contains two antibodies co-formulated in a 1:1 ratio of casirivimab and imdevimab or
2. Individual antibody solutions in separate vials, which may be supplied in separate cartons or in a dose pack.

All existing REGEN-COV vials[5] may be used to prepare doses for intravenous infusion as well as subcutaneous injection for post-exposure prophylaxis.

- Preparation of the 600 mg of casirivimab and 600 mg of imdevimab dose can be prepared with the REGEN-COV dose packs currently in distribution or the co-formulated product. If you have REGEN-COV dose packs, it is important to note that the material in each dose pack is sufficient to make two doses each of casirivimab and imdevimab.
- Preparation of subsequent doses for post-exposure prophylaxis for the 300 mg of casirivimab and 300 mg of imdevimab dose can be prepared with the REGEN-COV dose packs currently in distribution or the co-formulated product. If you have REGEN-COV dose packs, it is important to note that the material in each dose pack is sufficient to make four doses each of 300 mg of casirivimab and 300 mg of imdevimab. The co-formulated vial may be used to make two doses of 300 mg of casirivimab and 300 mg of imdevimab.

If desired, multiple doses may be prepared simultaneously as appropriate, according to the direction provided in the EUA HCP Fact Sheet. However, all REGEN-COV vials are preservative-free, and any unused portion in the vial should be discarded. Store unopened casirivimab and imdevimab vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

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

[5] As a reminder, casirivimab and imdevimab are packaged and have been made available to the marketplace in various sizes and configurations. Pharmacists are urged to carefully review the labeling for each carton or package and properly combine the appropriate quantity of vials to obtain the authorized dose (See Section 19 HOW SUPPLIED/STORAGE AND HANDLING in the HCP Fact Sheet). Information and images of variations of individual carton and vial labeling can be found at https://www.regencov.com/content/pdf/treatment-covid19-packaging-flashcard.pdf

For Subcutaneous Injection:

- Administer casirivimab and imdevimab using the co-formulated vial or using the individual vials by subcutaneous injection according to the instructions provided in the Health Care Provider Fact Sheet.
- Clinically monitor patients after injections and observe patients for at least 1 hour.

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 casirivimab and imdevimab together as a single intravenous infusion via pump or gravity according to the instructions provided in the Health Care Provider Fact Sheet.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

## HCP Action when Using REGEN-COV for Post-Exposure Prophylaxis of COVID-19

In light of the addition of a new authorized use and new dosage for that use, healthcare providers should update their Electronic Health Records (EHRs) with the new product information including the new use and authorized dosage to guide the prescribing of REGEN-COV and to allow for the use of current supplies to prepare doses for treatment or prophylaxis.

Healthcare providers are advised to stay current with the latest Fact Sheet for Health Care Providers by visiting (https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf)

Preparation and administration instructions in the HCP Fact Sheet have been updated to reflect the new authorized post-exposure prophylaxis use and corresponding dosage and administration.

**For post-exposure prophylaxis, either subcutaneous injection or intravenous infusion can be used.**

All existing REGEN-COV vials may be used to prepare doses for intravenous infusion as well as subcutaneous injection for post-exposure prophylaxis. Although some REGEN-COV cartons and vial labels may have statements such as “Solution for Intravenous Administration” or “For Intravenous Infusion after Dilution” without language that states the subcutaneous route is appropriate, any of these vials may be used to prepare and administer intravenous infusions as well as subcutaneous injections.

Preparation of the 600 mg of casirivimab and 600 mg of imdevimab dose or the 300 mg of casirivimab and 300 mg of imdevimab dose can be prepared with the REGEN-COV dose packs currently in distribution or the co-formulated product.

Healthcare providers are advised to take care when preparing the appropriate dose. If you have REGEN-COV dose packs, it is important to note that the material in each dose pack is sufficient to make **two** doses each of 600 mg of casirivimab and 600 mg of imdevimab or **four** doses each of 300 mg of casirivimab and 300 mg of imdevimab.[6]

There are differences in the way the two formulations are prepared. Carefully follow the preparation procedures described in Section 2.4 of the Healthcare Provider Fact Sheet and refer to those instructions for detail on administration.

- 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 to prepare multiple doses simultaneously as appropriate, either in intravenous bags or 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 the refrigerator.

Resources to help clarify dose preparation can be found on www.REGENCOV.com.

***Patient Counseling Information***

- Instruct patients to review the Fact Sheet for Patients, Parents, & Caregivers.
- Instruct individuals who are given REGEN-COV for the post-exposure prevention of COVID-19 that they 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.
- Providers should inform individuals that REGEN-COV does not replace vaccination against COVID-19.

***Reporting Adverse Events and Medication Errors***

Healthcare providers should direct questions about REGEN-COV (casirivimab with imdevimab) packaging or use to the Regeneron Medical Information Department at 1-844-734-6643 or to medical.information@regeneron.com.

Under the EUA, all serious adverse events and all medication errors potentially related to casirivimab and imdevimab must be reported within 7 calendar days from the onset of the event. Serious adverse event reports and medication error reports should be submitted to FDA's MedWatch program using one of the following methods:

[6] As a reminder, casirivimab and imdevimab are packaged and have been made available to the marketplace in various sizes and configurations. Pharmacists are urged to carefully review the labeling for each carton or package and properly combine the appropriate quantity of vials to obtain the authorized dose (See Section 19 HOW SUPPLIED/STORAGE AND HANDLING in the HCP Fact Sheet). Information and images of variations of individual carton and vial labeling can be found at https://www.regencov.com/content/pdf/treatment-covid19-packaging-flashcard.pdf

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- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Complete and submit a postage-paid Form FDA 3500 (https://www.fda.gov/media/76299/download) and return by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 208529787, or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form.

Please provide a copy of all FDA MedWatch forms to Regeneron via fax (1-888-876-2736) or email (medical.information@regeneron.com).

The EUA Fact Sheet for Healthcare Providers is included with this notice, available at www.REGENCOV.com, or available by scanning the QR Code below:

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**Enclosure:** EUA Fact Sheet for Healthcare Providers