Casirivimab and imdevimab are investigational therapies and have been authorized by FDA for the emergency use described below. Casirivimab and imdevimab must be administered together. Casirivimab and imdevimab are not FDA approved for any use. Safety and effectiveness of casirivimab and imdevimab have not been fully established for the treatment of COVID-19.

The Secretary of the Department of Health and Human Services has declared a public health emergency that justifies the emergency use of the unapproved products, casirivimab and imdevimab, to be administered together, for the treatment of mild to moderate coronavirus disease 2019 (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 progressing to severe COVID-19 and/or hospitalization. In response, the U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for casirivimab and imdevimab in the treatment of COVID-19.

This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Limitations of Authorized Use:

- Casirivimab and imdevimab are not authorized for use in patients:
  - 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 related comorbidity.

- Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19.

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 for reference, as well as the Dear Healthcare Provider Letter and Patient Fact Sheet.
**Definition of High Risk Patients**

High risk is defined as patients who meet at least one of the following criteria: Have a body mass index (BMI) ≥35, chronic kidney disease, diabetes, immunosuppressive disease [immunocompromised], 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 a 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 (e.g. cerebral palsy) or a medical-related technological dependence (e.g. tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)), or asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

**Additional Information for Healthcare Providers:**

- **Casirivimab and imdevimab** carton and vial labels may instead be labeled REGN10933 and REGN10987, respectively.

- You may receive cartons and vials of casirivimab and imdevimab that are labeled “for intravenous infusion or subcutaneous injection.” **However, casirivimab and imdevimab must be administered together (although packaged separately) after dilution by intravenous infusion only.**

- Store casirivimab and imdevimab together in inventory. See www.regeneroneua.com/access for images of packaging.

- Casirivimab and imdevimab may only be administered in settings in which healthcare 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.

- **The recommended dose is 1200 mg of casirivimab and 1200 mg of imdevimab administered as a single intravenous infusion over at least 60 minutes as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.** Since the optimal dosing regimen has not yet been established, it might be updated as new data becomes available. See the HCP Fact Sheet for complete dosage, preparation and administration instructions.

Distribution of casirivimab and imdevimab is controlled by the United States (U.S.) Government for use consistent with the terms and conditions of the EUA. Regeneron will supply casirivimab and imdevimab to AmerisourceBergen, who will distribute to infusion sites as directed by the U.S. Government, in collaboration with state and local government authorities. Providers should contact their state health departments to discuss any allocation of casirivimab and imdevimab for their site(s).

This resource provides an overview of the relevant codes, current as of November 2020, that may support reimbursement of the administration of casirivimab and imdevimab in the outpatient setting in which healthcare providers have immediate access to medications to treat a severe infusion reaction. The Centers for Medicare and Medicaid Services (CMS) has issued specific coding guidance for casirivimab and imdevimab and its administration. In addition, please note that there is comprehensive documentation and guidance, as published by the CMS for other aspects of COVID-19-diagnostic laboratory services and treatment, which is not outlined in this information.

The following information is presented for informational purposes only and is not intended to guarantee or provide reimbursement or legal advice. Regeneron and its agents make no warranties or guarantees concerning the accuracy or appropriateness of this information for your particular use. The information in this Resource Tool is gathered from various resources and subject to change without notice. Payer coding requirements may vary or change over time, so it is important to regularly check with each payer to confirm payer specific requirements.

The following information pertains to casirivimab and imdevimab Therapy and Administration:

- **Review of Relevant Codes**
  - ICD-10-CM Diagnosis Codes
  - Level I HCPCS CPT Codes
  - Level II HCPCS Product Code
  - NDC
- **Additional Considerations**
REVIEW OF RELEVANT CODES

The following codes should be confirmed with each respective payer, as there may be variability in both coding and documentation requirements.

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes

A COVID-19 diagnosis code was implemented for services on or after April 1, 2020. This code should be designated as the primary diagnosis. Providers will select secondary diagnoses based on the patient presentation of further complications from COVID-19. These complications require appropriate documentation in the patient’s medical record.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>U07.1</td>
<td>COVID-19</td>
<td>For discharges on or after April 1, 2020, through the duration of the COVID-19 public health emergency period</td>
</tr>
</tbody>
</table>


Casirivimab and imdevimab will be administered via a single intravenous infusion. CMS recently assigned M0243 to describe casirivimab and imdevimab administration.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0243</td>
<td>Intravenous infusion, casirivimab and imdevimab, includes infusion and post administration monitoring</td>
</tr>
</tbody>
</table>

Level II Healthcare Common Procedure Coding System (HCPCS) Drug Coding

CMS recently assigned the unique HCPCS code Q0243, injection casirivimab and imdevimab.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q0243</td>
<td>Injection, casirivimab and imdevimab 2400 mg</td>
</tr>
</tbody>
</table>

Centers for Medicare & Medicaid Services. Medicare Monoclonal Antibody COVID-19 Infusion Program Instruction. COVID-19 Vaccines and Monoclonal Antibodies | CMS

Select payers may require further claims documentation to better identify both casirivimab (REGN10933) and imdevimab (REGN10987), which could include but not be limited to:

- Treatment NDCs
- Descriptor of antibody name(s)
- Mode of administration

Casirivimab and Imdevimab National Drug Codes (NDC)

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Concentration</th>
<th>Package Size</th>
<th>NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>casirivimab</td>
<td>1332 mg/11.1 mL (120 mg/mL)</td>
<td>1 vial per carton</td>
<td>61755-0024-01*</td>
</tr>
<tr>
<td>casirivimab</td>
<td>300 mg/2.5 mL (120 mg/mL)</td>
<td>1 vial per carton</td>
<td>61755-0026-01*</td>
</tr>
<tr>
<td>imdevimab</td>
<td>1332 mg/11.1 mL (120 mg/mL)</td>
<td>1 vial per carton</td>
<td>61755-0025-01*</td>
</tr>
<tr>
<td>imdevimab</td>
<td>300 mg/2.5 mL (120 mg/mL)</td>
<td>1 vial per carton</td>
<td>61755-0027-01*</td>
</tr>
</tbody>
</table>

Note: casirivimab = REGN10933; imdevimab = REGN10987

*Note that each NDC code has been “zero-filled” to ensure creation of an 11-digit code that meets HIPAA compliant standards. The zero-fill location is indicated in bold. HIPAA (Health Insurance Portability and Accountability Act); NDC (National Drug Code).
ADDITIONAL CONSIDERATIONS

Since casirivimab and imdevimab will be made available by the government to providers at no cost during the initial EUA period, providers may not receive third party payer reimbursement for the therapy when delivered in the outpatient setting of care. However, providers MAY be able to obtain payment for the drug administration service. Providers should clarify claim submission requirements by payer, as the documentation may vary.

For Medicare beneficiaries, providers must report the applicable drug HCPCS code and appropriate units with a token charge of less than $1.01 for the item in the covered charge field and mirror this less than $1.01 amount reported in the noncovered charge field. Providers must also bill the corresponding drug administration charge with the appropriate drug administration CPT code.

Additional Information for Healthcare Providers:

The prescribing healthcare provider and/or the provider’s designee are responsible for mandatory reporting of all medication errors and ALL SERIOUS ADVERSE EVENTS potentially related to casirivimab and imdevimab. These adverse events must be reported within 7 calendar days from the onset of the event.

MedWatch adverse event reports can be submitted to the FDA online here, by using a postage-paid Form FDA 3500 and returning by mail/fax or by calling 1-800-FDA-1088 to request a reporting form. In addition, please provide a copy of all FDA MedWatch forms to Regeneron Pharmaceuticals, Inc via fax or email. See the Fact Sheet for Healthcare Providers for additional information about this mandatory reporting obligation.

IMPORTANT SAFETY INFORMATION

Casirivimab and imdevimab are unapproved investigational therapies, and there are limited clinical data available. Serious and unexpected adverse events may occur that have not been previously reported with casirivimab and imdevimab use.

Warnings and Precautions:

• **Hypersensitivity Reactions Including Anaphylaxis and Infusion-Related Reactions**: There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of casirivimab and imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy. Infusion-related reactions have been observed with administration of casirivimab and imdevimab. Signs and symptoms of infusion related reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and/or dizziness. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

• **Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19**: Benefit of treatment with casirivimab and imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab and imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow oxygen or mechanical ventilation with COVID-19. Therefore, casirivimab and imdevimab is not authorized for use in patients 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 related comorbidity.
Adverse Reactions:

- Serious adverse events (SAEs) were reported in 4 (1.6%) patients in the casirivimab and imdevimab 2,400 mg group, 2 (0.8%) patients in casirivimab and imdevimab 8,000 mg group and 6 (2.3%) patients in the placebo group. None of the SAEs were considered to be related to study drug. SAEs that were reported as Grade 3 or 4 adverse events were pneumonia, hyperglycemia, nausea and vomiting (2,400 mg casirivimab and imdevimab), intestinal obstruction and dyspnea (8,000 mg casirivimab and imdevimab) and COVID-19, pneumonia and hypoxia (placebo). Casirivimab and imdevimab are not authorized at the 8,000 mg dose (4,000 mg casirivimab and 4,000 mg imdevimab).

- One anaphylactic reaction was reported in the clinical program. The event began within 1 hour of completion of the infusion, and required treatment including epinephrine. The event resolved. Infusion-related reactions, of grade 2 or higher severity, were reported in 4 subjects (1.5%) in the 8,000 mg (4,000 mg casirivimab and 4,000 mg imdevimab) arm. These infusion-related reactions events were moderate in severity; and include pyrexia, chills, urticaria, pruritus, abdominal pain, and flushing. One infusion-related reaction (nausea) was reported in the placebo arm and none were reported in the 2,400 mg (1,200 mg casirivimab and 1,200 mg imdevimab) arm. In two subjects receiving the 8,000 mg dose of casirivimab and imdevimab, the infusion-related reactions (urticaria, pruritus, flushing, pyrexia, shortness of breath, chest tightness, nausea, vomiting) resulted in permanent discontinuation of the infusion. All events resolved.

Patient Monitoring Recommendations:

- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

Use in Specific Populations:

- Pregnancy: There is currently limited clinical experience in the use of casirivimab and imdevimab in COVID-19 patients who are pregnant. Casirivimab and imdevimab therapy should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

- Nursing Mothers: There is currently no clinical experience in the use of casirivimab and imdevimab in COVID-19 patients who are breastfeeding. The development and health benefits of breastfeeding should be considered along with the mother’s clinical need for casirivimab and imdevimab and any potential adverse effects on the breastfed child from casirivimab and imdevimab injection or from the underlying maternal condition.