

Clinical Management of COVID-19

CASIRIVIMAB AND IMDEVIMAB FOR COVID-19

Learning objectives

At the end of this module, you will be able to:

- Describe what monoclonal antibodies are and how they work.
- Describe the role of casirivimab and imdevimab in the management of patients with COVID-19.
- Describe key casirivimab and imdevimab dosing and administration considerations for patients with COVID-19.

Special note

Drugs and doses stated here are for illustrative purposes only.

Decisions regarding the use of any medication must be made by a licensed provider and take into account each patient's specific clinical history and other circumstances, and be in accordance with relevant local management and prescribing guidelines.

casirivimab and imdevimab in COVID-19: summary of recommendations

In September 2021, the following WHO recommendations regarding casirivimab and imdevimab for patients with COVID-19 were released:

Conditional recommendation: We recommend treatment with casirivimab and imdevimab for patients with non-severe COVID-19 at highest risk for hospitalization and those with severe and critical COVID-19 who are seronegative for SARS-CoV-2.

Oxygen, corticosteroids and IL-6 receptor blockers have previously been recommended in patients with severe and critical COVID-19. We recommend severe and critical patients with seronegative status should now also receive casirivimab and imdevimab.

casirivimab and imdevimab in COVID-19: recommendation

Population

This recommendation applies only to people with these characteristics:



Interventions

Casirivimab and imdevimab

Neutralising monoclonal antibodies

Disease severity

Non-severe

Absence of signs of severe or critical disease

Severe

Oxygen saturation <90% on room air

Signs of pneumonia

Signs of severe respiratory distress ⁱ

Critical

Requires life sustaining treatment

Acute respiratory distress syndrome

Sepsis

Septic shock



Recommendation in favour (conditional) ⁱ

For those with highest risk of hospitalisation



Recommendation in favour (conditional) ⁱ

For those with seronegative status
Assessed by accurate and rapid testing

Review of monoclonal antibodies and their function

Monoclonal antibodies: overview

- **Antibodies**, or immunoglobulins, are protein molecules that serve as a core component of the immune system.
- Antibodies are produced by **B cells**, a type of white blood cell that originate from stem cells in the bone marrow.
- Antibodies bind to proteins on the surface of bacteria, viruses or other cells (**antigens**), to trigger immune an immune response that clears infections.

Monoclonal Antibodies: overview (continued)

- Monoclonal antibodies (mAbs) have been developed for various pathogens, including RSV, MERS-CoV, Ebola and Zika virus.
- They are typically created by identifying pathogen specific B cells in patients recently recovered from an infection or by immunizing genetically modified mice and harvesting effective antibodies from them.
- Once B cells are identified the genes of immune globulin heavy and light chains are recovered and expressed to produce mAbs which have activity against a predetermined target.



Monoclonal Antibodies for COVID-19

- Most monoclonal antibody's being developed for SARS-CoV-2 target the **spike protein**, which the virus utilizes to enter the host cells via the ACE-2 receptor.
- Casirivimab and imdevimab are two recombinant human monoclonal antibodies developed and studied for patients with COVID-19.
- Both antibodies targets a different part of the SARS-CoV-2 **spike protein** receptor binding domain.
- By binding to the SARS-CoV-2 spike protein, the virus is unable to attach to the human ACE-2 receptor and infection of the host cell is prevented.
- The half-life for both monoclonal antibodies ranges from 27 to 32 days.

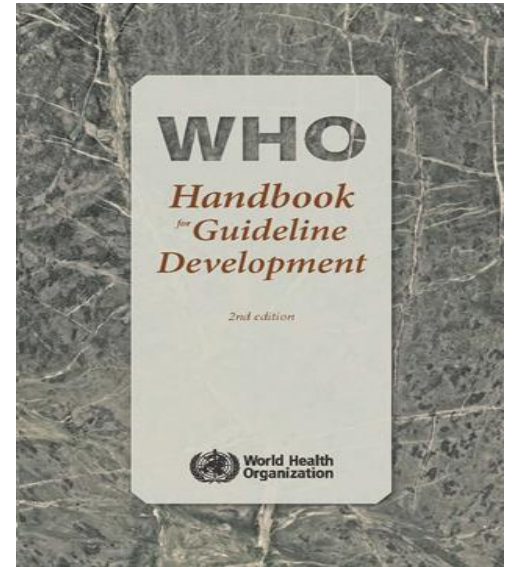
Reviewing process of developing recommendations for casirivimab and imdevimab

casirivimab and imdevimab in COVID-19: guideline development process

- The WHO Therapeutics and COVID-19 Guideline Development Group (GDG), a group of international content experts, patients, clinicians, and methodologists with no conflicts of interest and balanced in terms of gender, geography, expertise, and patient representation met in July 2021.
- The GDG produced recommendations following standards for trustworthy guideline development using the **GRADE approach** (Grading of Recommendations Assessment, Development and Evaluation) in full compliance with the WHO Handbook for guideline development, 2nd edition.
- The GDG took an **individual patient perspective to values and preferences**.

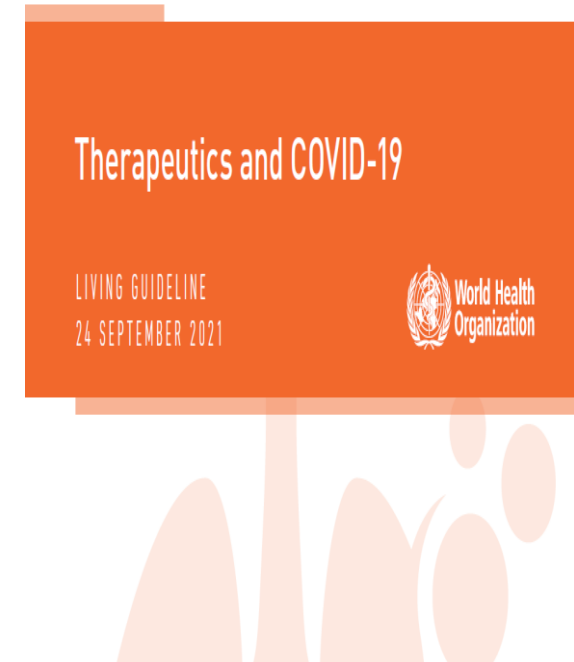
A high value was placed on resource allocation, given the burden of pandemic for healthcare systems globally. Values considered include

- **Applicability**
- **Balance of benefits and harms**
- **Resource implications, feasibility, equity and human rights**
- **Acceptability**



casirivimab and imdevimab in COVID-19: guideline development process

- Since 2020, WHO has worked with COVID- living network meta-analysis (COVID-LNMA), an international research initiative.
- The COVID-LNMA keeps a live mapping of registered trials and a living systematic review of trial results.
- Analysis of therapies such as casirivimab and imdevimab for COVID-19 were conducted and presented to the WHO guideline development group (GDG).



<https://covid-nma.com/>

casirivimab and imdevimab for COVID-19:

Conditional recommendation for use of monoclonal antibody

The GDG made a **conditional recommendation** for casirivimab and imdevimab in selected patients **with COVID-19** based on **moderate** certainty of evidence in patients with **non-severe disease** and **low** certainty of evidence in patients with **severe or critical disease**.

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casirivimab and imdevimab for COVID-19: understanding the strength of recommendations

Conditional

- **For patients:** The majority of individuals would want the suggested course of action, but many would not.
- **For clinicians:** Different choices are likely to be appropriate for different patients and therapy should be tailored to the individual patient circumstances.
- **For policymakers:** Policy making will require substantial debates and involvement of many stakeholders. Policies are also likely to vary between regions.

Evidence for Casirivimab and Imdevimab

casirivimab and imdevimab for COVID-19: summary of evidence for non-severe disease

- Analysis of **four trials** that enrolled total of 4722 participants with **non-severe COVID-19** revealed that casirivimab and imdevimab:
 - probably reduces admission to hospital (moderate certainty evidence)
 - probably reduce duration of hospitalization (best estimate of a reduction from 9.6 to 8.2 days; moderate certainty evidence)
 - probably reduces time to symptom improvement (moderate certainty evidence)
 - have trivial or no effect on mortality (moderate certainty evidence)
 - have trivial or no effect on mechanical ventilation (moderate certainty evidence)

casirivimab and imdevimab for COVID-19: Evidence in non-severe disease

Among a 1000 patients like you, on average with Casirivimab and imdevimab

Admission to hospital		Time to symptom improvement	
↓ 29 fewer		↓ 4.1 lower	
No casirivimab and imdevimab	Casirivimab and imdevimab	No casirivimab and imdevimab	Casirivimab and imdevimab
42 per 1000	13 per 1000	14	9.9
Certainty ○○○○ MODERATE		Certainty ○○○○ MODERATE	

The GDG made a conditional recommendation for casirivimab and imdevimab in patients with non-severe COVID-19 at highest risk for hospitalization.

Outcome Timeframe	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Plain language summary
No casirivimab and imdevimab	Casirivimab and imdevimab				
Mortality	Odds Ratio 0.57 (CI 95% 0.28 – 1.20) Based on data from 4722 patients in 4 studies	2 per 1000	1 per 1000	Moderate Due to serious indirectness	Casirivimab and imdevimab do not have an important effect on mortality. No impact
Mechanical ventilation	Odds Ratio 0.22 (CI 95% 0.03 – 1.21) Based on data from 3403 patients in 2 studies	4 per 1000	1 per 1000	Moderate Due to serious indirectness	Casirivimab and imdevimab probably do not have an important effect on mechanical ventilation. No impact
Admission to hospital	Odds Ratio 0.29 (CI 95% 0.17 – 0.48) Based on data from 4722 patients in 4 studies	42 per 1000	13 per 1000	Moderate Due to serious indirectness	Casirivimab and imdevimab probably reduce admission to hospital. Benefit
Allergic reactions	Based on data from 15406 patients in 4 studies	3 per 1000	9 per 1000	Moderate Due to serious imprecision	Casirivimab and imdevimab probably do not result in an important increase in allergic reactions. No impact
Adverse effects leading to drug discontinuation	Based on data from 5284 patients in 4 studies	2 per 1000	1 per 1000	High	Casirivimab and imdevimab do not result in an important increase in adverse effects leading to drug discontinuation. No impact
Time to symptom improvement	Lower better Based on data from 3284 patients in 2 studies	14 (Mean)	9.9 (Mean)	Moderate Due to serious indirectness	Casirivimab and imdevimab probably reduce time to symptom improvement. Benefit
Duration of hospitalization (not in hospital at baseline)	Lower better Based on data from 111 patients in 2 studies	9.6 (Mean)	8.2 (Mean)	Low Due to very serious imprecision	Casirivimab and imdevimab may not have an important impact on duration of hospitalization. No impact



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casirivimab and imdevimab for COVID-19: summary of evidence for severe and critical disease (seronegative)

- Analysis of evidence in patients with **severe and critical COVID-19** from one trial of 9785 patients (RECOVERY) revealed that casirivimab and imdevimab:
 - Reduces mortality risk in seronegative patients (moderate certainty of evidence, based on 3153 patients).
 - Have very uncertain impact on mechanical ventilation and duration of hospitalization
 - In patients who are seronegative, risk for mechanical ventilation reduces 13% (low certainty evidence).

casirivimab and imdevimab for COVID-19: evidence for severe and critical disease (seronegative)

Among a 1000 patients like you, on average with Casirivimab and imdevimab

Mortality		Mortality		Mechanical ventilation	
 39 fewer Severe disease		 69 fewer Critical disease		 42 fewer	
No casirivimab and imdevimab	Casirivimab and imdevimab	No casirivimab and imdevimab	Casirivimab and imdevimab	No casirivimab and imdevimab	Casirivimab and imdevimab
260 per 1000	221 per 1000	460 per 1000	391 per 1000	320 per 1000	278 per 1000
Certainty  MODERATE		Certainty  MODERATE		Certainty  LOW	

The GDG made a conditional recommendation for casirivimab and imdevimab in patients with severe and critical COVID-19 who are seronegative for SARS-CoV-2.

Outcome Timeframe	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Plain language summary
		No casirivimab and imdevimab	Casirivimab and imdevimab		
Mortality Severe disease	Relative risk 0.85 (CI 95% 0.76 – 0.95) Based on data from 2823 patients in 1 study	260 per 1000	221 per 1000 Difference: 39 fewer per 1000 (CI 95% 62 fewer – 13 fewer)	Moderate Due to concerns with imprecision and indirectness	Casirivimab and imdevimab probably reduce mortality.
Mortality Critical disease	Relative risk 0.85 (CI 95% 0.76 – 0.95) Based on data from 2823 patients in 1 study	460 per 1000	391 per 1000 Difference: 69 fewer per 1000 (CI 95% 110 fewer – 23 fewer)	Moderate Due to concerns with imprecision and indirectness	Casirivimab and imdevimab probably reduce mortality.
Mechanical ventilation	Relative risk 0.87 (CI 95% 0.77 – 0.98) Based on data from 2410 patients in 1 study	320 per 1000	278 per 1000 Difference: 42 fewer per 1000 (CI 95% 74 fewer – 6 fewer)	Low Due to concerns with risk of bias, imprecision, and indirectness	Casirivimab and imdevimab may reduce mechanical ventilation.
Duration of hospitalization	Based on data from 3153 patients in 1 study	The median duration of hospital stay was 4 days shorter with casirivimab and imdevimab (13 days vs. 17 days).		Very low Due to serious risk of bias, serious indirectness, and very serious imprecision	The impact on duration of hospitalization is very uncertain.



casirivimab and imdevimab for COVID-19: hypothesis and evidence about seronegative serostatus

- Casirivimab and imdevimab are antibodies that target SARS-CoV-2 spike protein.
- People who have been exposed to SARS-CoV-2 may produce their own anti-SARS-CoV-2 spike protein antibodies. If they have produced antibodies, the hypothesis is that they would be seropositive.
 - It was postulated that administration might have differential effects in patients who have produced their own anti-SARS-CoV-2 spike protein antibodies (seropositive) compared with those who have not (seronegative).
- In the RECOVERY trial, analysis showed that administration of casirivimab and imdevimab had more benefit in patients who were seronegative. This was a credible subgroup effect.

Clinical considerations when administering casirivimab and imdevimab

Who should get casirivimab and imdevimab: summary of recommendations

Patients with confirmed non-severe COVID-19 at greater than 10% risk for progression of infection and hospitalization*

Those at highest risk typically are:

1. Older
2. Have an immunodeficiency and/or chronic disease
3. Unvaccinated

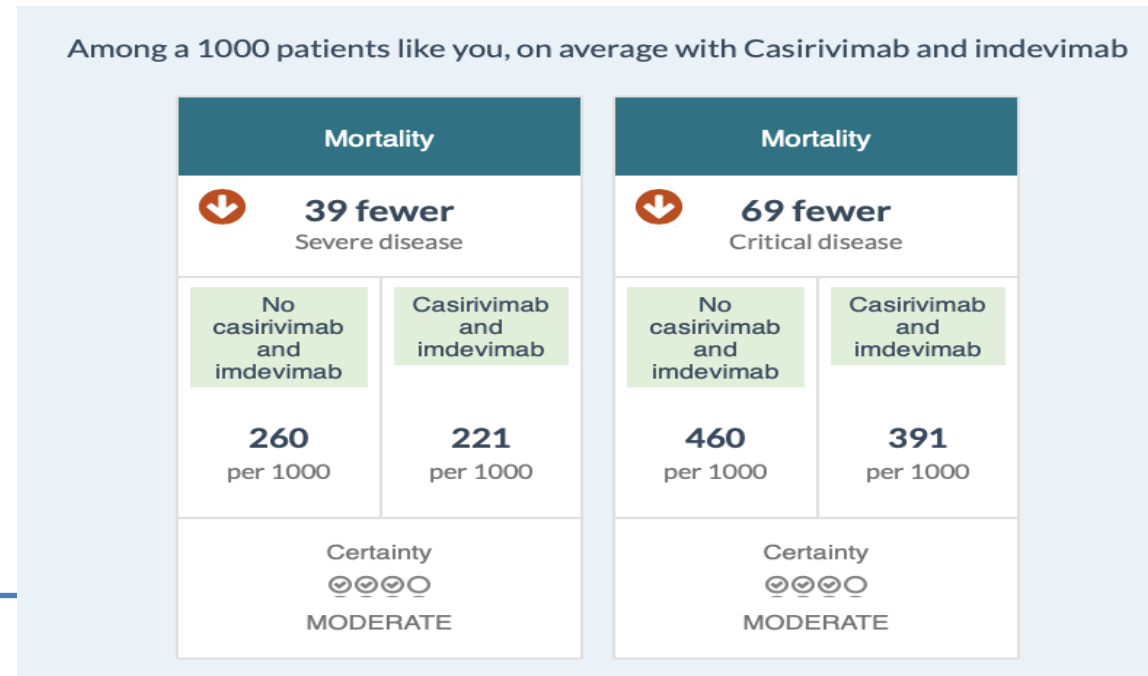
Patients with confirmed severe or critical COVID-19 seronegative for SARS-CoV-2

*Serologic testing should be conducted with tests that detect the presence of the SARS-CoV-2 spike protein antibodies and have performance characteristics similar to the reference standard test used to characterize seronegative patients in the RECOVERY trial

- Risk factors include: > 60 years old, hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression (including HIV), obesity, cancer.
- In pregnancy risk factors include: advanced maternal age, high BMI, and chronic medical conditions.

casirivimab and imdevimab for COVID-19: summary of recommendations (continued)

- At a time of drug shortage, it may be necessary to prioritize use of casirivimab and imdevimab.
- One possibility is to prioritize patients with the highest baseline risk for mortality (e.g. those with critical disease over those with severe disease).



casirivimab and imdevimab for COVID-19:

Why must patients with severe or critical disease be seronegative?

- Casirivimab and imdevimab are antibodies that target SARS-CoV-2 spike protein.
- People who have been exposed to SARS-CoV-2 may produce their own antibodies against the SARS-CoV-2 spike protein antibodies and may be seropositive.
- Casirivimab and imdevimab might have differential effects in patients who have produced their own anti-SARS-CoV-2 spike protein antibodies (seropositive) compared with those who have not (seronegative).
- It is hypothesized the effect of casirivimab and imdevimab might be greater, or restricted to, seronegative individuals who have not yet mounted an effective antibody response.

casirivimab and imdevimab for COVID-19: serologic testing considerations

- Use a test with performance characteristics similar to the reference standard test used to characterize seronegative patients in the RECOVERY trial
 - i.e. the Oxford fluorescent-based ELISA assay for serum IgG against the SARS-CoV- 2 spike protein, with an arbitrary cut-off determined by a panel of positive controls
- Some lateral flow assays may be suitable and can usually be performed in several minutes (36)(37)(38).
- Choose the most applicable test for your setting.

casirivimab and imdevimab in COVID-19: contraindications

- Allergy to casirivimab and imdevimab or components: L-Histidine, L-Histidine monohydrochloride monohydrate, polysorbate 80, sucrose
- Prior hypersensitivity to casirivimab or imdevimab

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casirivimab and imdevimab for COVID-19: dosing

- Casirivimab and Imdevimab can be administered as 1200– 8000 mg
 - (600 – 4000 mg of each antibody) demonstrating efficacy at all doses.
- Doses apply to individuals $\geq$ 12 years of age and weighing $\geq$ 40 kg.

Drug	Dose (Non-Severe COVID-19)	Dose (Severe and Critical COVID-19)
Casirivimab	600 mg IV infusion or subcutaneous OR 1200 mg IV infusion	1200 mg or 4000 mg IV infusion
Imdevimab	600 mg IV infusion or subcutaneous OR 1200 mg IV infusion	1200 mg or 4000 mg IV infusion
Total	1200-2400 mg IV infusion OR 1200 mg subcutaneous * If administered subcutaneously, the maximum dose is 1200 mg (600 mg each drug)	2400 mg or 8000 mg IV infusion

The drugs and doses stated here are for illustrative purposes only. Decisions regarding the use of any medication must be made by a licensed provider and take into account each patient's specific clinical history and other circumstances, and be in accordance with relevant local management and prescribing guidelines.

casirivimab and imdevimab for COVID-19: choosing a dose and administration route (1/2)

- Four clinical trials that were used to make the WHO recommendation used IV administration route.
 - Subcutaneous dose has been studied in prophylactic studies.
- Total doses ranged between 1200 mg to 8000 mg among the trials.
- Efficacy found at all tested doses.
- If priority is to ensure maximum effectiveness in every individual who receives treatment, one might choose the higher total dose and IV administrations.
- If priority is to ensure giving as many people as possible the opportunity to benefit from treatment (in the face of difficulties in widespread IV administration in the community for example), one might choose the lower total dose and ensure the availability of SQ administration as an alternative.

casirivimab and imdevimab for COVID-19: choosing a dose and administration route (2/2)

- One trial (RECOVERY) used to make the WHO recommendation used IV administration at total dose 8000mg.
 - This trial was in patients with severe or critical COVID-19.
- Pharmacokinetic data from patients with non-severe COVID-19 demonstrate therapeutics thresholds can be reached at total dose of 1200 mg and above.
- If priority is to ensure maximum effectiveness in every individual who receives treatment, and minimize risk of emergence of resistance, one might choose the higher IV total dose (8000 mg).
- If one's priority is to ensure giving as many people as possible the opportunity to benefit from treatment (in the face of difficulties in widespread IV administration in the community for example), one might choose the lower IV total dose (2400 mg).

casirivimab and imdevimab in COVID-19: route of delivery

- For COVID-19, casirivimab and imdevimab should be given together.
- The medication can be given **intravenously (IV)** or **subcutaneously (SC)**.

Preferred: Casirivimab and imdevimab intravenous single infusion should be administered using a dedicated IV line with a sterile low protein binding in-line or add-on 0.2 micron filter via pump (preferred) or gravity.

Alternative: Casirivimab and imdevimab may be administered by subcutaneous injection via syringes when it is unable to be given by intravenous infusion and would lead to a delay in treatment.

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casirivimab and imdevimab for COVID-19: Preparation (Intravenous)

1. Remove casirivimab and imdevimab vials from refrigerator and allow to equilibrate to room temperature for 20 minutes prior to preparation.

- Ensure there is no discoloration or particulate matter of the product prior to administration. If observed then discard.

2. Obtain a prefilled intravenous infusion bag of sodium chloride or dextrose solution. *

3. To allow for space in the infusion bag for the addition of the casirivimab and imdevimab, use a syringe and aseptic non-touch technique to withdraw the total volume dose equivalent from the infusion bag and discard.

- For example, if preparing a total dose of casirivimab and imdevimab of 1200 mg infusion, remove 10 mL of fluid from the infusion bag prior to injecting the monoclonal antibody

4. Using a separate syringe for each vial of casirivimab and imdevimab, withdraw the appropriate amount of each product from the respective vial and inject into the prefilled infusion bag.

5. Gently invert infusion bag by hand ten times to mix and then immediately administer.

- If unable to immediately administer infusion solution, then store in refrigerator at 2-8° C for up to 36 hours**
- May also store at room temperature (25° C) for no more than 4 hours

* Infusion bag may be 50mL, 100 mL, 150 mL, or 200 mL of 0.9% sodium chloride or 5% dextrose injection

** If refrigerated, remove 30 minutes prior to patient infusion to allow for equilibration to room temperature

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casirivimab and imdevimab for COVID-19: preparation (intravenous – dilution instructions)

Table 1: Dilution instructions for casirivimab 600 mg + imdevimab 600 mg for intravenous infusion (Total Dose 1200 mg)

Size of prefilled infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL	Into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag inject • 5 mL of casirivimab (Use two 6-mL single use vials OR one 20-mL multidose vial) PLUS • 5 mL of imdevimab (Use two 6-mL single use vials OR one 20-mL multidose vial)
100 mL	
150 mL	
200 mL	

Table 2: Dilution instructions for casirivimab 1200 mg + imdevimab 1200 mg for intravenous infusion (Total Dose 2400 mg)

Size of prefilled infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL	Into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag inject • 10 mL of casirivimab (Use four 6-mL single use vials OR one 20-mL multidose vial) PLUS • 10 mL of imdevimab (Use four 6-mL single use vials OR one 20-mL multidose vial)
100 mL	
150 mL	
200 mL	

Table 3: Dilution instructions for casirivimab 4000 mg + imdevimab 4000 mg for intravenous infusion (Total Dose 8000 mg)

Size of prefilled infusion bag	Preparing casirivimab and imdevimab using individual vials
150 mL	Into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag inject • 33.3 mL of casirivimab (Use three 20-mL multidose vial) PLUS • 33.3 mL of imdevimab (Use three 20-mL multidose vial)
250 mL	
500 mL	

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casirivimab and imdevimab for COVID-19: preparation (subcutaneous)

1. Remove casirivimab and imdevimab vials from the refrigerator and allow to equilibrate to room temperature for 20 minutes prior to preparation.

- Ensure there is no discoloration or particulate matter of the product prior to administration. If observed then discard.

2. Subcutaneous injection of casirivimab and imdevimab should be administered consecutively using the appropriate number of syringes.*

3. Withdraw the appropriate amount of casirivimab and imdevimab into each syringe and then replace the transfer needle with a 25- gauge to 27-gauge needle for subcutaneous injection.

4. Immediately administer the product

- If unable to immediately administer, the prepared syringes can be stored at room temperature for up to 4 hours.

* Use 3-mL or 5-mL polypropylene luer lock syringes with a luer connection and a 21 gauge 1 ½ inch transfer needle

* A maximum dose of casirivimab 600 mg + imdevimab 600 mg (Total dose 1200 mg subcutaneous)

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casirivimab and imdevimab for COVID-19: administration (intravenous)

Casirivimab and imdevimab should be administered by a qualified healthcare professional in a monitored setting using septic non touch technique.

Materials needed

- Polyvinyl chloride or polyurethane infusion set
- In-line or add-on low protein binding 0.2 micron polyethersulfone (PES) filter

1. Attach the infusion set to the infusion bag

2. Prime the infusion set

3. Administer the entire infusion solution in the infusion bag via pump or gravity through an intravenous line containing a sterile in-line or add-on 0.2 micron filter

4. Do NOT administer the infusion solution with another medication

5. Once the infusion is complete, flush the line with 0.9% sodium chloride or 5% dextrose injection

6. Clinically monitor patient during and for one hour post infusion

- BP, HR, RR, Temp, Oxygen Saturation
- 15 min, 30 min, and one hour after injection

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casirivimab and imdevimab for COVID-19: administration (intravenous)

Table 1: Administration rate for casirivimab 600 mg + Imdevimab 600 mg for intravenous infusion (total dose 1200 mg)

Size of Prefilled Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
50 mL	150 mL/hour	20 minutes
100 mL	300 mL/hour	20 minutes
150 mL	450 mL/hour	20 minutes
200 mL	500 mL/hour	30 minutes

Table 2: Administration rate for casirivimab 1200 mg + imdevimab 1200 mg for intravenous infusion (total dose 2400 mg)

Size of Prefilled Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
50 mL	150 mL/hour	20 minutes
100 mL	300 mL/hour	20 minutes
150 mL	450 mL/hour	20 minutes
200 mL	500 mL/hour	30 minutes

Infusion should **NOT**
be administered > 4 hours

Table 3: Administration rate for casirivimab 4000 mg + imdevimab 4000 mg for intravenous infusion (total dose 8000 mg)

Size of Prefilled Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
150 mL	350 mL/hour	60 minutes
250 mL	250 mL/hour	60 minutes
500 mL	500 mL/hour	60 minutes

The information stated here are for illustrative purposes only. Decisions regarding the use of any medication must be made by a licensed provider and take into account each patient's specific clinical history and other circumstances, and be in accordance with relevant local management and prescribing guidelines. <https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf>

casirivimab and imdevimab for COVID-19: administration (subcutaneous)

1. Administer subcutaneous injection of casirivimab and imdevimab consecutively and at a different injection site in the

- Thigh
- Abdomen
- Upper Arm

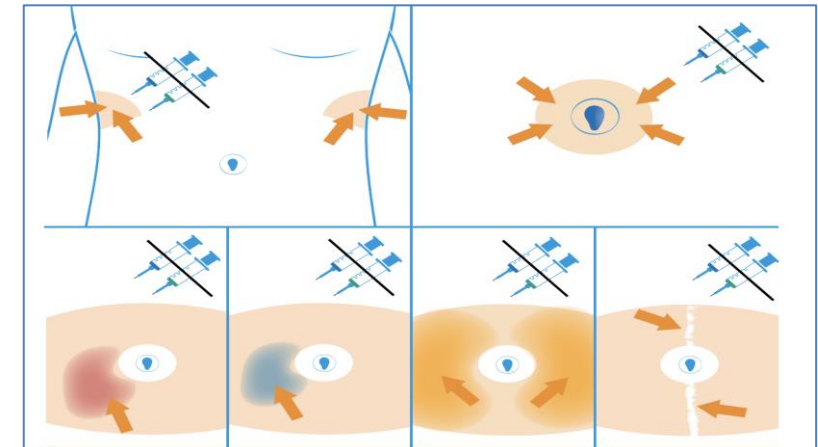
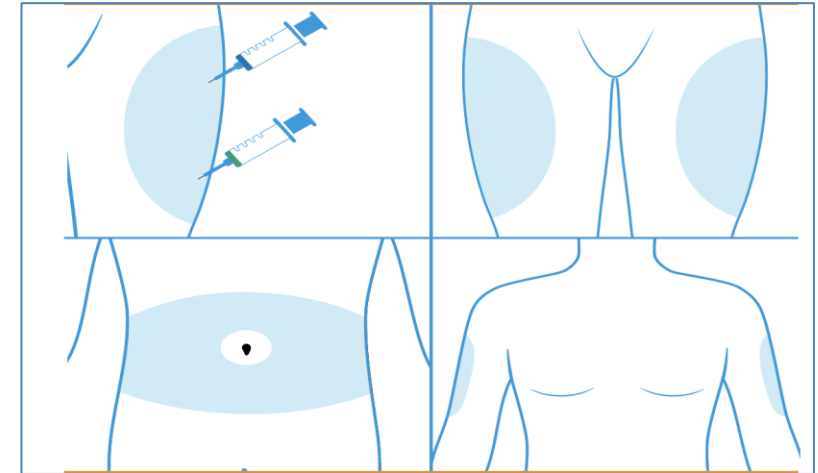
Maximum total dose is 1200 mg

2. Areas to avoid include

- Waistline
- Two inches around the navel
- Skin that is tender, tender, damaged, bruised, or scarred

3. Monitor patient for 1 hour after injection

- Blood pressure, heart rate, respiratory rate, temperature, oxygen saturation
- 15 min, 30 min, and one hour after injection



casirivimab and imdevimab for COVID-19: patient monitoring

Monitor patients during infusion and for one hour once completed.

They should have blood pressure, heart rate, respiratory rate, temperature and oxygen saturation checked at 15 minutes, 30 minutes, and one hour post –infusion.

Hypersensitivity

- Serious hypersensitivity reactions, including anaphylaxis has been reported with casirivimab and imdevimab
- Hypersensitivity reactions occurring > 24 hours after administration of casirivimab and imdevimab have been reported
- If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occurs, immediately discontinue the infusion and initiate appropriate medications, supportive therapy, and airway management

Management of anaphylaxis

- Severe allergic reactions can cause swelling of the airway and lead to obstruction.
- Give intramuscular adrenaline for airway obstruction, severe wheezing, or shock (Since adrenaline can wear off in minutes be prepared to administer additional doses).
- Make sure the patient as a IV and administer intravenous fluids while continuing to reassess the airway and administering oxygen as needed
- If patient has severe anaphylaxis or is not improving, consider transferring to a higher level of care for further management.
- Further details on basic emergency care can be accessed at <https://www.who.int/publications/i/item/basic-emergency-care-approach-to-the-acutely-ill-and-injured>

Infusion related reactions

- Infusion related reactions occurring during infusion and up to 24 hours post infusion have been observed.
- They may be severe or life-threatening and you should consider slowing or stopping the infusion and providing appropriate medications and/or supportive care.
- These reactions may include
 - Fever
 - Angioedema
 - Dizziness
 - Chest Pain or Discomfort
 - Reduced Oxygenation
 - Chills
 - Diaphoresis
 - Hypotension
 - Difficulty Breathing
 - Throat Irritation
 - Irregular Heart Beat
 - Weakness
 - Headache
 - Fatigue
 - Hypertension
 - Rash/Pruritis
 - Nausea
 - Bronchospasm
 - Pre-Syncope and Syncope
 - Muscle Aches

casirivimab and imdevimab for COVID-19: post-marketing surveillance and other considerations

Reporting of adverse events

- Report all adverse events to WHO via medsafe application
- Report all adverse events to the manufacturer: www.roche.com/products/local_safety_reporting/htm



Special populations to monitor

- Limited data regarding the use of casirivimab and imdevimab in pregnant women with COVID-19.
- The use of casirivimab and imdevimab should be used in pregnancy only if the potential benefit justifies the potential risk to the mother and fetus.
- There is no available data on the presence of casirivimab and imdevimab in human or animal milk, the effects on the breastfed infant, or the effect of the drug on milk production.

COVID-19 vaccine administration

- As a precautionary measure, vaccination for SARS-CoV-2 should be deferred for ≥ 90 days in people who have received casirivimab and imdevimab. The antibody treatment may interfere with vaccine-induced immune responses.

Summary



World Health
Organization

HEALTH
EMERGENCIES
programme

casirivimab and imdevimab for COVID-19:

Summary

- Give casirivimab and imdevimab to patients with confirmed non-severe COVID-19 at risk for progression of infection and hospitalization
- Give casirivimab and imdevimab along with oxygen, systemic corticosteroids and IL-6RB for patients who are seronegative and have severe and critical COVID-19.

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Acknowledgements

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