Package leaflet: Information for the patient

Ronapreve 120 mg/mL solution for injection or infusion
casirivimab and imdevimab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ronapreve is and what it is used for
2. What you need to know before you are given Ronapreve
3. How Ronapreve is given to you
4. Possible side effects
5. How to store Ronapreve
6. Contents of the pack and other information

1. What Ronapreve is and what it is used for

What Ronapreve is

Ronapreve contains the active substances ‘casirivimab’ and ‘imdevimab’. Casirivimab and imdevimab are a type of protein called ‘monoclonal antibodies’.

What Ronapreve is used for

Ronapreve is used to treat patients with confirmed acute covid-19 infection.

Ronapreve is used to prevent acute covid-19 infection.

Clinical trial experience of use is limited to individuals aged 12 years and older and weighing at least 35.5 kg.

Ronapreve is not a vaccine, it treats or prevents acute covid-19 infection.

What is acute COVID-19 infection?

Acute covid-19 infection is caused by a virus called a coronavirus. People can get COVID-19 through contact with another person who has the virus.

Acute covid-19 infection illnesses can be very mild (sometimes with no symptoms). However, the symptoms can also be severe - including illness resulting in going to the hospital or illness causing death.

- Although most acute covid-19 infection illness is mild, it can be serious - and may make some of your other illnesses worse.
- People of all ages with severe, long-lasting illness like heart disease, lung disease, and diabetes, seem to be more likely to have to go into the hospital for management of acute covid-19 infection.

The symptoms of acute covid-19 infection include fever, cough, and shortness of breath. These may appear 2 to 14 days after exposure. Serious illness can include breathing problems.

How Ronapreve works

Ronapreve attaches to a protein on the surface of the coronavirus called the 'spike protein'. This stops the virus from getting into your cells and causing an infection. This can help your body to overcome the virus infection and may help you get better faster.

2. What you need to know before you are given Ronapreve

You must not be given Ronapreve

- if you are allergic to casirivimab, imdevimab, or any of the other ingredients of this medicine (listed in section 6).

Talk to your doctor or nurse as soon as possible, if this applies to you.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given Ronapreve:

Reactions following the infusion or injection

This medicine can cause allergic reactions or reactions following the infusion or injection. The signs of these reactions are listed in Section 4. Tell your doctor straight away if you get any of these signs or symptoms.

Children and adolescents

Clinical trial experience has been limited thus far to individuals aged 12 years and older and weighing at least 35.5 kg.

Other medicines and Ronapreve

Before you have Ronapreve, tell the doctor or nurse who is giving it to you about any other medicines you are taking, or have recently taken – this includes if you have been vaccinated against covid.

After you have had Ronapreve:

- tell any other doctors you see that you have had this medicine to treat or prevent acute covid-19 infection
- tell other doctors or nurses you have had this medicine, if you are getting a vaccine for acute covid-19 infection

Pregnancy and breast-feeding

Tell your doctor or nurse if you are pregnant, or if you might be pregnant.

- This is because there is not enough information to be sure that this medicine is safe for use in pregnancy.

- This medicine will only be given if the potential benefits of treatment outweigh the potential risks to the mother and the unborn child.

Tell your doctor or nurse if you are breast-feeding.
- This is because it is not yet known whether this medicine passes into human breast milk - or what the effects might be on the baby or milk production.
- Your doctor will help you decide whether to keep breast-feeding or to start treatment with this medicine.
- You will need to consider the potential benefits of treatment for you - compared with the health benefits and risks of breast-feeding for your baby.

Driving and using machines
This medicine is not expected to have any effect on your ability to drive.

3. How Ronapreve is given to you

Ronapreve will be given to you by a doctor or nurse who is experienced in the use of this type of treatment. They will watch you closely while you are being given this medicine. This is in case you get any side effects.

How is this medicine given?
The medicine is given as an infusion into your vein, that lasts for 20 to 30 minutes. Or you can be given this medicine as subcutaneous (under the skin) injections into your thigh, upper arm, or abdomen. Your doctor or nurse will decide how long you will be monitored after you are given the medicine. This is in case you have any side effects.

How much is given?
The recommended dose for treatment and prevention of acute covid-19 infection is 600 mg of casirivimab and 600 mg of imdevimab given as an infusion or injections.

The recommended dose for continuous prevention of acute covid-19 infection is 300 mg of casirivimab and 300 mg of imdevimab given every four weeks given as an infusion or injections.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects have been reported with Ronapreve.

Reactions following the infusion
Tell your doctor straight away if you get any of these signs of an allergic reaction or reaction listed below during or following the infusion. The infusion may need to be slowed down, interrupted or stopped and you may need other medicines to treat the symptoms. The signs or symptoms of allergic reaction or infusion-related reactions may include:

Uncommon: may affect up to 1 in 100 people
- Feeling sick (nausea)
- chills
- dizziness (fainting)
- rash
- itchy rash
- hot flushes

Very rare: may affect up to 1 in 10 000 people
- severe allergic reaction (anaphylaxis)

Reactions following the subcutaneous (under the skin) injection
Tell your doctor straight away if you get any of these signs of a reaction following the injections.

Common: may affect up to 1 in 10 people
- redness, itching, bruising, swelling, pain or itchy rash at the injection site

Uncommon: may affect up to 1 in 100 people
- dizziness
- swollen lymph nodes close to injection site

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Ronapreve

Ronapreve will be stored by the healthcare professionals at the hospital or clinic under the following conditions:
- **Before use,** store unopened Ronapreve concentrated solution in a refrigerator until the day it is needed. Before diluting it, allow the concentrated solution to come up to room temperature.
- **Once diluted,** Ronapreve should be used immediately. If necessary, bags of diluted solution can be stored at 2°C to 8°C for no more than 24 hours and at room temperature up to 25ºC for no more than 6 hours. Allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.
- Prepared syringes should be used immediately. If necessary, store the prepared syringes at 2ºC to 8ºC for no more than 24 hours and at room temperature up to 25ºC for no more than 4 hours. Allow the syringes to equilibrate to room temperature for approximately 10-15 minutes prior to administration.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after EXP. The expiry date refers to the last day of that month.

Do not use this medicine if you notice particulate matter or discolouration.

Do not throw away any medicines via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What Ronapreve contains
- The active substances are casirivimab or imdevimab. Each 20 mL multidose vial contains 1 332 mg of casirivimab or imdevimab, i.e. two doses of 5 mL of casirivimab or imdevimab. Each single-use 6 mL vial contains 300 mg of casirivimab or imdevimab.
- The other ingredients are L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose, and water for injection.

What Ronapreve looks like and contents of the pack
Ronapreve is available in cartons that contain 2 vials per package, one vial for each molecule.

Marketing Authorisation Holder
Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

Manufacturer
Roche Pharma AG
Emil-Barell-Strasse 1
79639 Grenzach-Wyhlen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Roche Products Ltd.
Tel: +44 (0) 1707 366000

This leaflet was last revised in July 2021.

The following information is intended for healthcare professionals only. Please refer to the Summary of Product Characteristics for further information.

Instructions for healthcare professionals

Ronapreve 120 mg/mL solution for injection or infusion

Casirivimab and imdevimab must be administered together by intravenous infusion (after dilution) or subcutaneous injection

Casirivimab:
Each multidose 20 mL vial contains 1 332 mg of casirivimab per 11.1 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution.

Each single-use 6 mL vial contains 300 mg of casirivimab per 2.5 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution.

Imdevimab:
Each multidose 20 mL vial contains 1 332 mg of imdevimab per 11.1 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution.

Each single-use 6 mL vial contains 300 mg of imdevimab per 2.5 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution.
Please refer to the Summary of Product Characteristics for further information on clinical trial experience of use of Ronapreve in the context of acute covid-19 infection.

Indication
Ronapreve is indicated for the treatment of acute covid-19 infection.

Ronapreve is indicated for the prevention of acute covid-19 infection.

Ronapreve is not intended to be used as a substitute for vaccination against COVID-19.

The recommended dose is:

- 600 mg of casirivimab and 600 mg of imdevimab, or
- 300 mg of casirivimab and 300 mg of imdevimab

Preparation for Intravenous Infusion Administration

Ronapreve concentrated solution must be diluted with sodium chloride 9 mg/mL (0.9%) solution or 5% dextrose injection for infusion under aseptic conditions. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

1. Remove the casirivimab and imdevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat. Do not shake the vials.
2. Inspect casirivimab and imdevimab vials visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded and replaced with a new vial.
   - The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.
3. Obtain a prefilled IV infusion bag (PVC or PO) containing either 50 mL , 100 mL , 150 mL , or 250 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
4. Withdraw the appropriate volume of casirivimab and imdevimab from each respective vial and inject into a prefilled infusion bag containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection (see Table 1).
5. Gently mix infusion bag by inversion. Do not shake.
6. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately (see Table 2).
   - If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution at 2 °C to 8 °C for no more than 24 hours and at room temperature up to 25°C for no more than 6 hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Table 1: Recommended Dilution Instructions for Ronapreve (casirivimab and imdevimab) for IV Infusion

Indication	Ronapreve Dose (Total)	Total Volume for 1 Dose	Volume to be withdrawn from each respective vial and inject into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag
Treatment and Prevention – single dose	600 mg casirivimab and 600 mg imdevimab (1 200 mg dose)	10 mL	2.5 mL from two 6 mL single-use vials of casirivimab 2.5 mL from-two 6 mL single-use vials of imdevimab
			5.0 mL from one 20 mL multidose vial of casirivimab 5.0 mL from one 20 mL multidose vial of imdevimab
			2.5 mL from two 6 mL single-use vials of casirivimab 5.0 mL from one 20 mL multidose vial of imdevimab

			5.0 mL from one 20 mL multidose vial of casirivimab 2.5 mL from two 6 mL single-use vials of imdevimab
Prevention – repeat dose	300 mg casirivimab and 300 mg imdevimab (600 mg dose)	5 mL	2.5 mL from one 6 mL single-use vial of casirivimab 2.5 mL from one 6 mL single-use vial of imdevimab
			2.5 mL from one 20 mL multidose vial of casirivimab 2.5 mL from one 20 mL multidose vial of imdevimab
			2.5 mL from one 6 mL single-use vial of casirivimab 2.5 mL from one 20 mL multidose vial of imdevimab
			2.5 mL from one 20 mL multidose vial of casirivimab 2.5 mL from one 6 mL single-use vial of imdevimab

Table 2: Minimum Infusion Time for IV Infusion Bag Volumes for diluted Ronapreve - 600 mg of Casirivimab and 600 mg of Imdevimab (1 200 mg dose) or 300 mg of Casirivimab and 300 mg of Imdevimab (600 mg dose)

Size of Prefilled 0.9% Sodium Chloride or 5% Dextrose Infusion Bag	**Minimum Infusion Time Ronapreve 600 mg casirivimab and 600 mg imdevimab (1 200 mg)**	**Minimum Infusion Time Ronapreve 300 mg casirivimab and 300 mg imdevimab (600 mg)**
50 mL	20 minutes	20 minutes
100 mL	20 minutes	20 minutes
150 mL	20 minutes	20 minutes
250 mL	30 minutes	30 minutes

Administration

Ronapreve infusion solution should be administered by a qualified healthcare professional using aseptic technique.

- Gather the recommended materials for infusion:
  - Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, or polyurethane (PU) infusion set
  - In-line or add-on 0.2 μm to 5 μm polyethersulfone, polysulfone, or polyamide end filter for IV administration
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the entire infusion solution in the bag via pump or gravity through an intravenous line containing a sterile, in-line or add-on 0.2 μm to 5 μm polyethersulfone, polysulfone, or polyamide end filter for IV administration (see Table 2).
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of casirivimab and imdevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection or 5% Dextrose Injection is not known.
- After infusion is complete, flush the tubing with 0.9% Sodium Chloride Injection or 5% Dextrose Injection to ensure delivery of the required dose.

Preparation for Subcutaneous Injection

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat. Do not shake the vials**.**

Inspect casirivimab and imdevimab vial(s) visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded and replaced with a new vial. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.

1. Ronapreve should be prepared using the appropriate number of syringes (see Table 3). Obtain 3 mL or 5 mL polypropylene syringes with luer connection and 21-gauge transfer needles.
2. Withdraw the appropriate volume of casirivimab and imdevimab from each respective vial into each syringe (see Table 3) for a total of 4 syringes for the 1 200 mg combined total dose and a total of 2 syringes for the 600 mg combined total dose. Store any remaining product as directed.
3. Replace the 21-gauge transfer needle with a 25-gauge or 27-gauge needle for subcutaneous injection.
4. This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes at 2ºC to 8ºC for no more than 24 hours and at room temperature up to 25ºC for no more than 4 hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 10-15 minutes prior to administration.

Table 3 Preparation of Ronapreve (casirivimab and imdevimab) for Subcutaneous Injection

Indication	**Ronapreve Dose (Total)**	**Total Volume for 1 Dose**	**Volume to be withdrawn to prepare 4 syringes**
Treatment and Prevention – single dose	600 mg casirivimab and 600 mg imdevimab (1 200 mg dose)	10 mL	2.5 mL from two 6 mL single-use vials of casirivimab 2.5 mL from two 6 mL single-use vials of imdevimab
			2.5 mL (2x) from one-20 mL multidose vial of casirivimab 2.5 mL (2x) from one 20 mL multidose vial of imdevimab
			2.5 mL from two 6 mL single-use vials of casirivimab 2.5 mL (2x) from one 20 mL multidose vial of imdevimab
			2.5 mL (2x) from one 20 mL multidose vial of casirivimab 2.5 mL from two 6 mL single-use vials of imdevimab
Indication	**Ronapreve Dose (Total)**	**Total Volume for 1 Dose**	**Volume to be withdrawn to prepare 2 syringes**
Prevention – repeat dose	300 mg casirivimab and 300 mg imdevimab (600 mg dose)	5 mL	2.5 mL from one 6 mL single-use vial of casirivimab 2.5 mL from one 6 mL single-use vial of imdevimab
			2.5 mL from one 20 mL multidose vial of casirivimab 2.5 mL from one 20 mL multidose vial of imdevimab

			2.5 mL from one 6 mL single-use vial of casirivimab 2.5 mL from one 20 mL multidose vial of imdevimab
			2.5 mL from one 20 mL multidose vial of casirivimab 2.5 mL from one 6 mL single-use vial of imdevimab

Administration for Subcutaneous Injection

- For the administration of Ronapreve 1 200 mg dose (600 mg of casirivimab and 600 mg of imdevimab), gather 4 syringes (Table 3) and prepare for subcutaneous injections.
- For the administration of Ronapreve 600 mg dose (300 mg of casirivimab and 300 mg of imdevimab), gather 2 syringes (Table 3) and prepare for subcutaneous injections.
- Administer the subcutaneous injections consecutively, each at a different injection site, into the upper thigh, back of the upper outer arm, or abdomen, except for 5 cm around the navel. The waistline should be avoided.
- When administering the subcutaneous injections, it is recommended that providers use different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL subcutaneous injection of casirivimab and imdevimab. DO NOT inject into skin that is tender, damaged, bruised, or scarred.

Monitor and report side effects

- Monitor the patient for side effects during and after the infusion or injection according to current medical practice. The rate of infusion may be slowed or interrupted if the patient develops any signs of infusion-associated events or other adverse events. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.
- Report side effects via (see details below)

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Storage

- **Before use,** store casirivimab and imdevimab vials in a fridge between 2 °C to 8 °C until they are required. Do not use after expiry date, marked on the vials/cartons after the letters EXP.
- Casirivimab and imdevimab concentrates are clear to slightly opalescent and colourless to pale yellow solutions.
- **Before dilution,** allow casirivimab and imdevimab vials to warm up to room temperature (up to 25 °C).
- **After initial puncture of the 20 mL vial**, if not used immediately, the medicinal product in the vial can be stored for 6 hours at room temperature up to 25 °C or for 24 hours refrigerated between 2 °C to 8 °C. Beyond these times and conditions, in-use storage is the responsibility of the user.
- **After initial puncture of the 6 mL vial**, the medicinal product should be used immediately, and any remaining product should be discarded.
- **Once diluted,** Ronapreve should be administered immediately. If necessary, bags of diluted solution can be stored for up to 6 hours at room temperature (up to 25 °C) and 2 °C to 8 °C for no more than 24 hours. Beyond these times and conditions, in-use storage is the responsibility of the user. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.
- This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and

imdevimab syringes at 2 ºC to 8 ºC for no more than 24 hours and at room temperature up to 25ºC for no more than 4 hours. Beyond these times and conditions, in-use storage is the responsibility of the user. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 10-15 minutes prior to administration.