B. PACKAGE LEAFLET

Package leaflet: Information for the patient
INTERIM AUTHORISATION

Casirivimab and Imdevimab 120 mg/mL concentrate for solution for infusion
casirivimab and imdevimab

The HSA has granted interim authorisation of casirivimab and imdevimab to treat confirmed COVID-19 in certain at-risk individuals 18 years of age and older under the Pandemic Special Access Route (PSAR).

For more information about Interim Authorisation under PSAR, visit HSA at: https://www.hsa.gov.sg/therapeutic-products/register/special-access-routes/psar-emergency-therapeutic-product.

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 casirivimab and imdevimab are and what they are used for

What casirivimab and imdevimab are

Casirivimab and imdevimab are a type of protein called ‘monoclonal antibodies’.

What casirivimab and imdevimab are used for

Casirivimab and imdevimab are used to treat patients with confirmed COVID-19. These patients are infected with COVID-19 and who:
- do not require oxygen treatment for COVID-19 or
- are at high risk of progressing to severe COVID-19.

Some of the risk factors that put patients at high risk are:
- old age
- being overweight
- heart disease, including high blood pressure
- lung disease, including asthma
- diabetes
- long-term kidney disease, including when dialysis is needed
- long-term liver disease
- weak immune system due to certain illnesses or using certain medicines

This medicine is used in patients aged 18 years and older.

What is COVID-19?

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

COVID-19 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 COVID-19 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 COVID-19.

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

How casirivimab and imdevimab work

Casirivimab and imdevimab attach to something called the 'spike protein' of the coronavirus. 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 casirivimab and imdevimab

You must not be given casirivimab and imdevimab

- 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 starting on casirivimab and imdevimab.

Reactions following the infusion

This medicine can cause allergic reactions or reactions following the infusion. 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

Do not give this medicine to children under 18 years of age or children that weigh less than 40 kg. This is because not enough is known for it to be given to these children.

Other medicines and casirivimab and imdevimab

Before you have casirivimab and imdevimab, tell the doctor or nurse who is giving it to you about any other medicines you are taking, or have recently taken.

After you have had casirivimab and imdevimab:

- tell any other doctors you see that you have had this medicine to treat COVID-19
- tell other doctors or nurses you have had this medicine, if you are getting a COVID-19 vaccine.

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 or the COVID-19 virus pass 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 casirivimab and imdevimab are given to you

Casirivimab and imdevimab 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, the infusion lasts for 20 to 30 mintues. You will be monitored for an hour after you are given the medicine. This is in case you have any side effects such as infusion-related reactions.

How much is given?
The recommended dose is 600 mg of casirivimab and 600 mg of imdevimab - given as a single infusion.

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.

Reactions following the infusion
Tell your doctor straight away if you get any of these signs of an allergic reaction or reaction following the infusion. These infusion-related reactions are uncommon (may affect up to 1 in 100 patients). The signs or symptoms of allergic reaction or infusion-related reactions may include:

- fever or chills
- headache or feeling light-headed
- feeling weak or tired
- altered mental status
- muscle pain
- stomach pain or feeling sick
- difficulty breathing
- red face or swelling of the face
- itching or an itchy rash
- throat irritation
- uneven heart-beat
- fall or increase in blood pressure
- chest pain or tight chest
- low oxygen in the blood
- increased sweating

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 to Roche via their website www.roche.com/products/local_safety_reporting.htm. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store casirivimab and imdevimab

Casirivimab and imdevimab will be stored by the healthcare professionals at the hospital or clinic under the following conditions:

- **Before use,** store unopened casirivimab and imdevimab 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,** casirivimab and imdevimab should be used immediately. If necessary, bags of diluted solution can be stored for up to 4 hours at room temperature (up to 25°C), or refrigerated between 2°C to 8°C for up to 36 hours.

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. These measures will help protect the environment.

6. Contents of the pack and other information

What casirivimab and imdevimab contains

- The active substances are casirivimab or imdevimab. Each 20 mL multidose vial contains 1332 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 casirivimab and imdevimab looks like and contents of the pack
Casirivimab and imdevimab are available in cartons that contain 2 vials per package, one vial for each molecule.

Product Owner

F. Hoffmann-La Roche Ltd
Wurmisweg
4303 Kaiseraugst
Switzerland

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

Instructions for healthcare professionals
INTERIM AUTHORISATION
Casirivimab and Imdevimab 120 mg/mL concentrate for solution for infusion

Casirivimab and imdevimab must be administered together after dilution by intravenous infusion

Casirivimab:
Each multidose 20 mL vial contains 1332 mg of casirivimab per 11.1 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution. Each multidose vial contains two doses of 5 mL of casirivimab.

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 1332 mg of imdevimab per 11.1 mL (120 mg/mL) as a clear to slightly opalescent and colourless to pale yellow solution. Each multidose vial contains two doses of 5 mL of imdevimab.

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.

Summary of Treatment
Casirivimab and imdevimab are medicines for the treatment of confirmed COVID-19 in patients aged 18 years and older that do not require supplemental oxygen for COVID-19 and who are at high risk of progressing to severe COVID-19.

Risk factors may include, but are not limited to:

- Advanced age
- Obesity
- Cardiovascular disease, including hypertension
- Chronic lung disease, including asthma
- Type 1 or type 2 diabetes mellitus
- Chronic kidney disease, including those on dialysis
- Chronic liver disease
- Immunosuppressed, based on prescriber's assessment. Examples include: cancer treatment, bone marrow or organ transplantation, immune deficiencies, HIV (if poorly controlled or evidence of AIDS), sickle cell anaemia, thalassaemia, and prolonged use of immune-weakening medications.

Limitation in Patients with Severe 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.

The recommended dose is 600 mg of casirivimab and 600 mg of imdevimab administered as a single intravenous infusion.

The concentrated solution must be diluted with sodium chloride solution 9 mg/mL (0.9%) under aseptic conditions. Administer the diluted solution immediately.

Monitor the patient for side effects during and after the infusion. See below for details on reporting of side effects.

Dilute the concentrate with sodium chloride solution

Casirivimab and imdevimab concentrated solution must be diluted with sodium chloride 9 mg/mL (0.9%) solution 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 discolouration prior to administration. Should either be observed, the concentrates must be discarded, and new vials used.
   - The concentrates in each vial should be clear to slightly opalescent, colourless to pale yellow.
3. Obtain a prefilled IV infusion bag containing either 50 mL, 100 mL, 150 mL, or 250 mL of 0.9% Sodium Chloride Injection.
4. Withdraw 5 mL of casirivimab and 5 mL of imdevimab from each respective vial(s) using separate syringes for each withdrawal (see Table 1) and inject all 10 mL into a prefilled infusion bag containing 0.9% Sodium Chloride Injection (see Table 1).
5. Gently invert infusion bag by hand approximately 10 times to mix. Do not shake.
6. This product is preservative-free and therefore, the diluted infusion solution should be administered immediately.
   - If immediate administration is not possible, store the diluted casirivimab and imdevimab infusion solution in the refrigerator between 2°C to 8°C (36°F to 46°F) for no more than 36 hours or at room temperature up to 25°C (77°F) for no more than 4 hours. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 30 minutes prior to administration.

Table 1: Recommended Dosing, Dilution and Administration Instructions for 600 mg Casirivimab with 600 mg Imdevimab for IV Infusion

Casirivimab with Imdevimab 1,200 mg Dose[a]. Add: • **5 mL of casirivimab (use 1 vial of 11.1 mL OR 2 vials of 2.5 mL) and** • **5 mL of imdevimab (use 1 vial of 11.1 mL OR 2 vials of 2.5 mL)** **for a total of 10 mL into a prefilled 0.9% sodium chloride infusion bag and administer as instructed below[b]**		
Size of Prefilled 0.9% Sodium Chloride Infusion Bag	**Maximum Infusion Rate**	**Minimum Infusion Time**
50 mL	180 mL/hr	20 minutes
100 mL	330 mL/hr	20 minutes
150 mL	480 mL/hr	20 minutes
250 mL	520 mL/hr	30 minutes

[a] 600 mg casirivimab and 600 mg imdevimab are added to the same infusion bag and administered together as a single intravenous infusion.

[b] After infusion is complete, flush with 0.9% Sodium Chloride Injection

Administration

Casirivimab with imdevimab 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 micron polyethersulfone (PES) filter

- 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-micron polyethersulfone (PES) filter (see Table 1). Due to potential overfill of prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
- 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 is not known.
- After infusion is complete, flush the tubing with 0.9% Sodium Chloride Injection to ensure delivery of the required dose.
- Discard unused product.

Monitor and report side effects

- Monitor the patient for side effects during and at least one hour after the infusion. 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 to Roche via their website www.roche.com/products/local_safety_reporting.htm.

Storage

- **Before use,** store casirivimab and imdevimab vials in a fridge between 2°C to 8°C (36°F to 46°F) until they are required. Do not use after expiry date, marked on the vials/cartons after the letters EXP.
- Casirivimab and imdevimab concentrate is a clear to slightly opalescent and colourless to pale yellow solution.
- **Before dilution,** allow casirivimab and imdevimab vials to warm up to room temperature (up to 25°C/77°F).
- **After initial puncture of the 20 mL vial**, if not used immediately, the medicinal product in the vial can be stored for 16 hours at room temperature up to 25°C (77°F) or for 48 hours refrigerated between 2°C to 8°C (36°F to 46°F). Other in-use storage times and conditions are the responsibility of the user.
- **After initial puncture of the 6 mL vial**, the medicinal product should be diluted and infused immediately.
- **Once diluted,** casirivimab and imdevimab should be administered immediately. If necessary, bags of diluted solution can be stored for up to 4 hours at room temperature (up to 25°C), or for up to 36 hours in a fridge (2°C to 8°C). From a microbiological point of view, the prepared infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C (36°F to 46°F), unless dilution has taken place in controlled and validated aseptic conditions.