WARNING: To be sold by retail on the prescription of medical specialist for use in hospital/ institutional set up only

ABRIDGED PRESCRIBING INFORMATION (RONAPREVE™)

SUMMARY OF PRESCRIBING INFORMATION

Generic name: Casirivimab 120mg/ml and Imdevimab 120mg/ml Injection **Brand Name:** RONAPREVE™

TREATMENT: The combination of Casirivimab and Imdevimab is indicated for restricted use in emergency situation, for the treatment of mild to moderate corona virus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with laboratory confirmed SARS-COV2 infection and who are at high risk of severe COVID-19 and do not require oxygen. **POST-EXPOSURE PROPHYLAXIS** Casirivimab in combination with Imdevimab is indicated in adult individuals (18 years) for postexposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are : not fully vaccinated (As per approved schedule) 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) and have been exposed to an individual infected with SARS-CoV-2 i.e. having direct physical contact with the person, sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person 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) Limitations of Authorized Use: Post-exposure prophylaxis with Casirivimab and Imdevimab is not a substitute for vaccination against COVID-19. Casirivimab and Imdevimab is not authorized for pre-exposure prophylaxis for prevention of COVID-19.High risk is defined as: Age 60 years 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 **WARNING:** To be sold by retail on the prescription of medical specialist for use in hospital/ institutional set up only Page 2 of 7 Immunosuppressed, based on investigator's assessment. Examples include: cancer treatment, bone marrow or organ transplantation, immune deficiencies, HIV (if poorly controlled or evidence of AIDS), sickle cell anemia, thalassemia, and prolonged use of immune-weakening medications. For patients hospitalised for Covid-19, there is no data showing benefit from treatment with casirivimab and imdevimab. Therefore, casirivimab and imdevimab should not be used in patients who: are hospitalised due to Covid-19, OR require oxygen therapy due to Covid-19, OR 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.Decisions regarding the use of Casirivimab and Imdevimab for treatment or prophylaxis should take intoconsideration what is known about the characteristics of the circulating SARS-CoV-2 viruses including regional or geographical differences and available information on Casirivimab and Imdevimab susceptibility patterns. **SARS-COV-2 VIRAL VARIANTS** Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Health care providers should review the Antiviral Resistance information in the full prescribing information for details regarding specific variants and resistance, as well as information from health authorities regarding reports of viral variants of importance in the country to guide treatment decisions. **ROUTE OF ADMINISTRATION** Casirivimab and Imdevimab may be administered by intravenous infusion or subcutaneous injection. **CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION AS A SINGLE INTRAVENOUS (IV) INFUSION** or **CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED CONSECUTIVELY BY SUBCUTANEOUS (SC) INJECTION. DOSAGE** Treatment Dosage:Casirivimab and Imdevimab is approved at combined dose of 1200 mg (600 mg of each drug) administered by intravenous infusion or subcutaneous route. Casirivimab and imdevimab should be given together as soon as possible after positive SARSCoV2 results of direct SARSCoV2 viral testing and within 10 days of symptom onset. Post-Exposure Prophylaxis **Dosage:** The authorized dosage is 600 mg of casirivimab and 600 mg of imdevimab administered by subcutaneous injection or together as a single intravenous infusion as soon as possible following exposure to SARS-CoV-2. 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 Page 3 of 7 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. The authorized dosage including dosage for repeat dosing is based on the totality of the scientific evidence including clinical pharmacology data and clinical trial data.Administration should be under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible. Individuals should be monitored post intravenous infusion according to local medical practice. Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS potentially related to Casirivimab and Imdevimab For intravenous administration, Casirivimab and Imdevimab solutions must be diluted prior to use. Patients treated with Casirivimab and Imdevimab 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 applicable guidelines. **Indications:** As mentioned above Type of Dosage form: Solution for Intravenous infusion or subcutaneous administration. Casirivimab and imdevimab are each supplied in individual single-dose or multi-dose vials for intravenous infusion or subcutaneous administration. **Dosage and Administration:** Administration should be under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible. Individuals should be monitored post intravenous infusion according to local medical practice. **Dosage:** Please refer to the dosage for the treatment and post-exposure prophylaxis as mentioned above. For patient selection for Treatment and Post-Exposure Prophylaxis, please refer to the High risk criteria defined above. **Dose Preparation and Administration** Casirivimab and imdevimab are for administration by intravenous infusion or subcutaneous injection. Intravenous administration: Preparation: Casirivimab and imdevimab solutions must be diluted prior to administration. Casirivimab and imdevimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique. If only an 11.1 mL vial of either casirivimab or imdevimab is available, you may prepare two IV bags simultaneously of 1,200 mg (600 mg casirivimab/600 mg imdevimab) each. Discard any product remaining in the vial. Administration: 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. Due to potential overfill of prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage. Page 4 of 7 The rate of infusion may be slowed or interrupted if the patient develops any signs of infusion-associated events or other adverse events. Patients should be monitored during the infusion and for at least one hour after the completion of the infusion Please refer to the full prescribing information for the complete instructions for preparation, administration (including recommended infusion rate and infusion time) and handling of infusion solution. **Subcutaneous administration:** Preparation: 600 mg of casirivimab and 600 mg of imdevimab should be prepared using 4 syringes. Obtain four 3 mL or 5 mL polypropylene Luer Lock syringes with luer connection and four 21-gauge 1½ inch transfer needles.Casirivimab and imdevimab should be prepared using the appropriate number of syringes (please refer to full prescribing information). Obtain 3 mL or 5 mL polypropylene Luer Lock syringes with luer connection and 21-gauge 1½ inch transfer needles.Withdraw the appropriate amount of solution into each syringe (please refer to full prescribing information). Prepare all syringes at the same time. If only an 11.1 mL vial of either casirivimab or imdevimab is available, you may prepare two doses simultaneously of 1,200 mg (600 mg casirivimab/600 mg imdevimab) each. Discard any product remaining in the vial. **Administration:** For the administration of 600 mg of casirivimab and 600 mg of imdevimab, gather 4 syringes and prepare for subcutaneous injections. For the administration of 300 mg of casirivimab and 300 mg of imdevimab, gather 2 syringes and prepare for subcutaneous injections. Administer the SC injections consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5 cm) around the navel. The waistline should be avoided. When administering the SC injections, it is recommended that providers use different quadrants of the abdomen or upper thighs to space apart each 2.5 mL SC injection of casirivimab and imdevimab. Do not inject into skin that is tender, damaged, bruised, or scarred. Clinically monitor patients after injections and observe patients for at least 15 to 30 minutes. Please refer to the full prescribing information for the complete instructions for preparation, administration and handling of prepared syringes for SC administration. Dose Adjustment in Special Populations Pediatric use: No dosage adjustment is recommended in children who weigh at least 40 kg and are older than 12 years of age. Pregnancy or Lactation: No dosage adjustment is recommended in pregnant or lactating women. Renal Impairment: No dosage adjustment is recommended in individuals with mild or moderate renal impairment. Hepatic Impairment: Page 5 of 7 No dosage adjustment is required in individuals with mild or moderate renal impairment, or in patients with creatinine clearance (CrCl) < 15 mL/min including those on dialysis. Limited data are available in individuals with severe renal impairment. **Contraindications:** Known hypersensitivity to casirivimab or imdevimab or to any of the excipients. **Warnings and Precautions:** There are limited clinical data available for Casirivimab and imdevimab. Serious and unexpected adverse events may occur that have not been previously reported with Casirivimab and imdevimab use. Hypersensitivity including Anaphylaxis and Infusion-Related Reactions: Serious hypersensitivity reactions, including anaphylaxis, have been reported with administration of casirivimab with imdevimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care. Infusion-related reactions have been observed with administration of casirivimab and imdevimab which may be severe or life threatening. Signs and symptoms of infusion related reactions may include: fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, fatigue, and diaphoresis. If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care. Hypersensitivity reactions occurring more than 24 hours after the infusion have also been reported with the use of Casirivimab and Imdevimab under Emergency Use Authorization. **Use in Special Populations:** Pediatric use: Casirivimab and Imdevimab is not recommended for pediatric patients weighing less than 40 kg or those less than 12 years of age. Pregnancy: Casirivimab and imdevimab should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus considering all associated health factors. Lactation: Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19. Geriatric Use: The difference in PK of casirivimab and imdevimab in geriatric patients compared to younger patients is unknown. Renal Impairment: Casirivimab and imdevimab are not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of casirivimab and imdevimab. Hepatic Impairment: The effect of hepatic impairment on PK of casirivimab and imdevimab is unknown Other Specific Populations: The effect of other covariates (e.g., sex, race, body weight, disease severity) on PK of casirivimab and imdevimab is unknown **Undesirable effects:** Clinical Trials: Overall, approximately 16,000 subjects have been exposed to casirivimab and imdevimab in clinical trials in hospitalized and non-hospitalized subjects. Overall, approximately 7116 subjects (approximately 4666 via IV administration and 2450 via subcutaneous administration) have been treated with casirivimab and imdevimab in clinical trials which support the treatment and prevention indication. Page 6 of 7 Reported adverse drug reactions (ADRs) identified from the clinical development programme relate to hypersensitivity reactions which include infusion related reactions (uncommon for IV) and injection site reactions (common for SC). ADRs with rare frequency include flushing (IV), urticaria (IV), pruritus (SC). ADRs with very rare frequency include anaphylaxis (IV) and ADRs with uncommon frequency include dizziness (IV and SC), nausea (IV), rash (IV), chills (IV) and Lymphadenopathy (SC). **Interactions with other Medicinal Products and other Forms of Interaction:** Casirivimab and imdevimab are not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely. **COVID-19 Vaccines:** Casirivimab and imdevimab bind to epitopes on spike protein used as immunogen in all COVID-19 vaccines, therefore it is possible that casirivimab and imdevimab may impact responses to COVID-19 vaccines. Refer to current vaccination guidelines with respect to timing of vaccination post treatment with anti-SARS-CoV-2 monoclonal antibodies. Limited safety data are available from the study HV 2093 where COVID-19 vaccine was permitted and no safety concerns identified. **Overdose:** Doses up to 8,000 mg (4,000 mg each of casirivimab and imdevimab, approximately 7-times the recommended dose) have been administered in clinical trials with no new safety concerns identified. There is no specific antidote for overdose with casirivimab with imdevimab. Treatment of overdose should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. **Storage Condition:** Store unopened casirivimab and imdevimab vials in a refrigerator at 2°C to 8°C in the original carton to protect from light. DO NOT FREEZE. DO NOT SHAKE. DO NOT EXPOSE TO DIRECT LIGHT. **Shelf life:** Unopened vials: 24 months when stored at recommended storage conditions Please refer to full prescribing information for instructions on allowing vials to equilibrate to room temperature after removing from refrigerated storage. Intravenous infusion: Storage condition for Co-packaged 20 mL multidose vials after initial puncture: If the vial is punctured to withdraw the first dose and if the second dose withdrawal is not required immediately, the product in the vial can be stored for 16 hours at room temperature up to 25°C or for 48 hours refrigerated between 2°C to 8°C. Other in-use storage times and conditions are the responsibility of the user. Co-packaged 6 mL single-use vials: After opening: Once opened, the medicinal product should be diluted and infused immediately Storage condition for the solution after dilution: The diluted solution may 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 if the dilution has taken place in controlled and validated aseptic conditions. If the dilution has not taken place under controlled and validated aseptic conditions, the product should be used immediately. Subcutaneous administration: Page 7 of 7 Storage condition for Co-packaged 20 mL multidose vials after initial puncture: If the vial is punctured to withdraw the first dose and if the second dose withdrawal is not required immediately, the product in the vial can be stored for 16 hours at room temperature up to 25°C or for 48 hours refrigerated between 2°C to 8°C. Other in-use storage times and conditions are the responsibility of the user. Co-packaged 6 mL single-use vials: After opening: Once opened, the medicinal product should be used immediately. Storage condition for the prepared syringes for Subcutaneous Injection: Once opened, the medicinal product should be used immediately. If immediate administration is not possible, store the prepared syringes of casirivimab and imdevimab in the refrigerator between 2ºC to 8ºC for no more than 24 hours or at room temperature up to 25ºC for no more than 4 total hours from vial puncture. **Packs:** Each carton contains 2 vials per package: Co-packaged 20 mL multidose vials 1 multi-dose vial of 1332 mg/11.1 mL of casirivimab and 1 multi-dose vial of 1332 mg/11.1 mL imdevimab. Each multidose vial contains two doses of 5 mL of casirivimab or imdevimab or Co-packaged 6 mL single-use vials 1 vial of 300 mg/2.5 mL of casirivimab and 1 vial of 300 mg/2.5 mL imdevimab. Please read the full prescribing information before usage.

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