



The Antibody Cocktail, Ronapreve Approved for Additional Indication as a Preventive Treatment of Symptomatic COVID-19

- Ronapreve is approved as the first antibody therapy to prevent development of symptomatic COVID-19 in individuals who have been in close contact with COVID-19 patients; and individuals who have tested positive for asymptomatic COVID-19.
- Global phase III study confirmed a reduced risk of disease in non-infected and asymptomatic COVID-19 positive individuals who were in close contact with infected individuals.
- Subcutaneous administration can be used in addition to the initially approved administration of intravenous infusion.

TOKYO, November 5, 2021 -- [Chugai Pharmaceutical Co., Ltd.](#) (TOKYO: 4519) announced that it obtained approval from the Ministry of Health, Labour and Welfare (MHLW) for the anti-SARS-CoV-2 monoclonal antibody RONAPREVE® [generic name: casirivimab (genetical recombination) /imdevimab (genetical recombination)] for the additional indication of the prevention of symptomatic SARS-CoV-2 infection (COVID-19). The Special Approval for Emergency under article 14-3 of the Pharmaceuticals and Medical Devices Act was applied to this approval. This approval allows intravenous or subcutaneous administration of Ronapreve to treat unvaccinated or inadequately vaccinated individuals who have been in close contact with COVID-19 patients or have tested positive for asymptomatic COVID-19, and are at high risk for progression to severe COVID-19. When intravenous administration is not feasible due to unavoidable circumstances, subcutaneous administration can be used for the treatment of SARS-CoV-2 infection, the indication which has been previously approved.

“We are very pleased that Ronapreve can further contribute to COVID-19 control in Japan as the first antibody therapy for the prevention of symptomatic COVID-19. Vaccines are the main way to prevent COVID-19. However, some people should not get vaccines or may not fully respond to vaccination, due to underlying diseases or medications they take. Ronapreve is an important option when such people have close contact with infected people or have tested positive for an asymptomatic COVID-19,” said Chugai’s President and CEO, Dr. Osamu Okuda. “With an additional subcutaneous dosing regimen, Ronapreve is expected to provide new treatment opportunities for patients with mild to moderate COVID-19 who have difficulty with intravenous administration, as well as contribute to reducing the burden in home treatment.”

This approval is based on the results from the global phase III clinical study (REGN-COV 2069 study) in individuals, non-infected or infected without developing symptoms, who have been in close contact with COVID-19 patients, global phase II study (REGN-COV 20145 study) to examine the dosage and dosage regimen and a phase I clinical study to examine the safety, tolerability, and pharmacokinetics in Japanese.

The antibody cocktail combining two virus-neutralizing antibodies, casirivimab and imdevimab, is

developed by U.S.-based Regeneron and Roche for the potential treatment and prevention of COVID-19. In August 2020, both companies announced a collaboration to develop, manufacture and distribute the antibody cocktail. In December of the same year, Chugai obtained development and exclusive commercialization rights in Japan from Roche. Chugai obtained regulatory approval in July 2021 for the indication of SARS-CoV-2 infection, subject to the Special Approval for Emergency.

Approval Information *The underlined parts were changed.

Indications:	SARS-CoV-2 infection <u>and prevention of symptomatic SARS-CoV-2 infection</u>
Dosage and administration:	The usual dose for adults and children aged 12 years and older and weighing 40 kg or more is 600 mg casirivimab (genetical recombination) and 600 mg imdevimab (genetical recombination) given as a single intravenous dose <u>or a single subcutaneous dose.</u>

<Reference>

The Antibody Cocktail, RONAPREVE for Intravenous Infusion Set Receives the World's First Regulatory Approval from MHLW for COVID-19 (Press release by Chugai issued on July 19, 2021)

https://www.chugai-pharm.co.jp/english/news/detail/20210719220000_843.html

Chugai Reached Agreement with Japanese Government regarding Investigational Antibody Cocktail (casirivimab and imdevimab) for COVID-19 (Press release by Chugai issued on May 10, 2021)

https://www.chugai-pharm.co.jp/english/news/detail/20210510150000_821.html

Phase III prevention trial showed subcutaneous administration of investigational antibody cocktail casirivimab and imdevimab reduced risk of symptomatic COVID-19 infections by 81% (Press release by Roche issued on April 12, 2021)

<https://www.roche.com/media/releases/med-cor-2021-04-12.htm>

New phase III data shows investigational antibody cocktail casirivimab and imdevimab reduced hospitalisation or death by 70% in non-hospitalised patients with COVID-19 (Press release by Roche issued on March 23, 2021)

<https://www.roche.com/media/releases/med-cor-2021-03-23.htm>

Chugai in-licenses Antibody Cocktail for COVID-19 from Roche (Press release by Chugai issued on December 10, 2020)

https://www.chugai-pharm.co.jp/english/news/detail/20201210170001_785.html

About Ronapreve

Ronapreve was designed specifically by Regeneron scientists to block the infectivity of SARS-CoV-2, the virus that causes COVID-19. They evaluated thousands of fully-human antibodies produced by the company's proprietary VelocImmune[®] mice, which have been genetically-modified to have a human immune system, as well as antibodies identified from humans who have recovered from COVID-19. The two potent, virus-neutralizing antibodies that form casirivimab and imdevimab are believed to bind non-competitively to the critical receptor binding domain of the virus's spike protein, which may help diminish the ability of all of the

concerned and noteworthy mutants (as of October 2021)^{1,2} Including the delta strain based on the *in vitro* study. They also may help suppress the occurrence of escape mutation based on the *in vitro* study³.

About the Special Approval for Emergency

Under article 14-3, Paragraph 1 of the Act on Quality, Efficacy and Safety of Pharmaceuticals and Medical Devices, the Minister of Health, Labour and Welfare may approve a certain medical product that meets the following criteria, upon discussion with the Pharmaceutical Affairs and Food Sanitation Council:

- 1) An emergency situation requires an unapproved medical product to be used to prevent damage to the public health caused by the spread of diseases, and such emergency situation cannot be managed appropriately by any means other than the use of the unapproved product;
- 2) Such product is legally available in a country with a regulatory system for medical products that is equivalent to Japan

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Source

1. Alina Baum, Benjamin O Fulton, Elzbieta Wloga, et al. Science 2020 Aug 21;369(6506):1014-1018.
2. FACT SHEET FOR HEALTH CARE PROVIDERS EMERGENCY USE AUTHORIZATION (EUA) OF REGEN-COVTM (casirivimab and imdevimab)
3. Richard Copin, Alina Baum, Elzbieta Wloga, et al. Cell. 2021 Jul 22;184(15):3949-3961.

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