31 January 2022

Ronapreve solution for injection or infusion 120 mg/mL; reduced neutralisation activity of the antibody combination against the full-length S protein of the Omicron variant of COVID-19.

Dear Healthcare Professional,

Roche Products (New Zealand) Limited would like to inform you of the following in relation to the use of Ronapreve (casirivimab and imdevimab 120 mg/ml solution for injection or infusion) for the treatment and prevention of COVID-19. The label on the product supplied in New Zealand is 'Casirivimab 120 mg/mL and Imdevimab 120 mg/mL Concentrates for Solution for Infusion'.

Summary

- **Following initial analysis of neutralisation activity against selected mutations of the Omicron variant, Ronapreve has demonstrated significantly diminished potency against this Variant of Concern (VoC).**
- **Ronapreve has been shown to retain its activity against all other currently circulating Variants of Concern, including the Delta variant.**
- **Decisions regarding the use of Ronapreve for treatment or prophylaxis should take into consideration what is known about the characteristics of the circulating SARS-CoV-2 viruses including regional or geographical differences and available information on Ronapreve susceptibility patterns.**
- **When molecular testing or sequencing data is available, it should be considered when selecting antiviral therapy to rule out SARs-CoV-2 variants that are shown to have reduced susceptibility to Ronapreve.**
- **Accordingly, the Ministry of Health may provide further clinical guidance in the future as more information becomes available. Any changes to the eligibility criteria will be updated by Pharmac, if necessary.**

This letter contains information on the reduced neutralisation potency against the omicron variant:

Regeneron and Roche in partnership together monitor and test the activity of Ronapreve against variants under surveillance i.e. Variants of Concern (VOC) and Variants of Interest (VOI) etc. Initial data from in vitro studies, which tested pseudotyped virus-like particles (VLPs), created to express the full-length S protein of the SARS-CoV-2 Omicron variant demonstrated reduced neutralisation potency against this variant the details of which are presented in Table 1 below. It should be noted that Ronapreve has been shown to retain neutralisation activity against other currently circulating VOC/VOI.

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Table 1: Pseudotyped Virus-Like Particle Neutralisation Data for Full Sequence or Key SARS-CoV-2 S-Protein Variant Substitutions from Variants Under Surveillance with Casirivimab and Imdevimab Alone or Together

Lineage with Spike Protein Substitutions	Key Substitutions Tested	Reduced Susceptibility to Casirivimab and Imdevimab Together	Reduced Susceptibility to Casirivimab Alone	Reduced Susceptibility to Imdevimab Alone
B.1.1.7 (Alpha)	Full S protein	no change	no change	no change
B.1.351 (Beta)	Full S protein	no change	45-fold	no change
P.1 (Gamma)	Full S protein	no change	418-fold	no change
B.1.427/B.1.429 (Epsilon)	L452R	no change	no change	no change
B.1.526 (Iota)	E484K	no change	25-fold	no change
B.1.617.1/B.1.617.3 (Kappa)	L452R+E484Q	no change	7-fold	no change
B.1.617.2 (Delta)	L452R+T478K	no change	no change	no change
B.1.621 (Mu)	R346K+E484K+N501Y	no change	23-fold	no change
B.1.1.529/BA.1 (Omicron)	**Full S protein**	**>1013-fold**	**>1732-fold**	**>754-fold**

It is important for healthcare professionals to use Ronapreve in accordance with their current official recommendations. Decisions regarding the use of Ronapreve for treatment or prophylaxis should take into consideration what is known about the characteristics of the circulating SARS-CoV-2 viruses including regional or geographical differences and available information on Ronapreve susceptibility patterns (see table 1 above). Roche will be submitting an application shortly to update the NZ Data Sheet to include information on the Omicron variant.

When molecular testing or sequencing data is available, it should be considered when selecting antiviral therapy to rule out SARs-CoV-2 variants that are shown to have reduced susceptibility to Ronapreve.

Accordingly, the Ministry of Health may provide further clinical guidance in the future as more information becomes available.

Before prescribing, please review the full Data Sheet available on Medsafe's website www.medsafe.govt.nz/Medicines/infoSearch.asp

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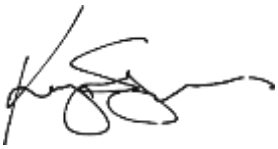
Further Information

If you have any questions or require additional information regarding the use of Ronapreve (casirivimab and imdevimab) please contact Roche Medical Information by telephone on 0800 276 243 or auckland.medinfonz@roche.com

Roche product vigilance

Roche will continue to monitor the safety of Ronapreve (casirivimab and imdevimab) through established reporting mechanisms and notify regulatory authorities as per current regulations. You can assist us in monitoring the safety of Ronapreve by reporting adverse events via email to nz.drugsafety@roche.com and product complaints to nz.quality@roche.com. Alternatively, this information may be reported to the Centre for Adverse Reactions Monitoring (CARM) in Dunedin by telephone on (03) 479 7247, by fax on (03) 479 7150, online at www.nzphvc.otago.ac.nz/reporting or by email to nzphvc@otago.ac.nz.

Yours sincerely,
Roche Products (New Zealand) Limited



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