

Langen, 13 January 2022

INFORMATION FOR HEALTHCARE PROFESSIONALS

CASIRIVIMAB/IMDEVIMAB (RONAPREVE) 120 MG/ML SOLUTION FOR INJECTION/INFUSION

Considerably reduced neutralisation of the Omicron variant full-length spike protein from the casirivimab/imdevimab antibody combination

The German Federal Ministry of Health (BMG) and the Paul-Ehrlich-Institut (PEI) have provided the following information related to the use of casirivimab and imdevimab (Ronapreve) 120 mg/ml injection/infusion solution.

Summary

- The first in vitro neutralisation assays of the monoclonal antibodies casirivimab/imdevimab (authorised since 12 November 2021 under the product name Ronapreve), which are available as a therapeutic option in Germany, show significantly reduced neutralisation activity against the Omicron variant of SARS-CoV-2 and indicate reduced efficacy.
- The medicine maintains its neutralisation activity, and thus likely its efficacy, against all other virus variants of concern that are circulating at present (the Delta variant is still of particular concern).
- All known information on the properties of the circulating SARS-CoV-2 viruses should be taken into account when deciding whether to use the antibody combination for treatment or prophylaxis. This information includes regional or geographical variations and available information about the efficacy of casirivimab/imdevimab (Table 1).
- If data confirming the virus variant is available, that data should be considered when selecting an antiviral therapy in order to exclude therapeutic use of Ronapreve for SARS-CoV-2 variants that have been shown to be less sensitive to neutralisation from Ronapreve.



This document contains information on the reduced neutralising activity of casirivimab/imdevimab (Ronapreve) against the Omicron variant.

The companies Regeneron and Roche are jointly monitoring and testing the activity of the casirivimab/imdevimab antibodies against SARS-CoV-2 variants that are under special surveillance, such as variants of concern (VOC) and variants of interest (VOI). Initial data from in vitro assays, in which neutralisation activity was tested against pseudotyped virus-like particles (VLPs) that contained the entire (full-length) spike protein of the Omicron variant of SARS-CoV-2, shows a lower neutralising effect (potency) of Ronapreve against the Omicron variant (see Table 1). It should be noted that the combination of casirivimab/imdevimab has been shown to retain in vitro neutralising activity against other currently circulating variants of concern and variants of interest.

Table 1: In vitro neutralising activity of casirivimab and imdevimab, alone or in combination, against virus particles pseudotyped with full-length spike proteins of SARS-CoV-2 and the specified variants

| Spike protein origin | Most significant amino acid substitutions compared to the Wuhan strain | Reduction of the neutralisation activity (compared with casirivimab/imdevimab combination) | Reduction in neutralisation activity (compared with casirivimab) | Reduction in neutralisation activity (compared with imdevimab) |
|---------------------------------|--|--|--|--|
| B.1.1.7 (Alpha) | - | no change | no change | no change |
| B.1.351 (Beta) | - | no change | 45-fold | no change |
| P.1 (Gamma) | - | 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 times | no change |
| B.1.1.529/BA.1 (Omicron) | - | > 1013-fold | > 1732-fold | > 754-fold |

It is important that healthcare professionals use the therapy option available in Germany that is in accordance with the currently valid official recommendations.

- Association of the Scientific Medical Societies in Germany (AWMF), including S3-classification guidelines for inpatient therapy:
www.awmf.org/leitlinien/detail/ll/113-001LG.html (German only)
- Therapy instructions from the Permanent Working Group of Competence and Treatment Centres for High Consequence Infectious Diseases (STAKOB):
www.rki.de/covid-19-therapie (German only)
- COVRIIN Expert Group: www.rki.de/covriin (German only)

Decisions about the use of casirivimab/imdevimab (Ronapreve) for therapy or prophylaxis should take the known characteristics of circulating SARS-CoV-2 variants into account, including regional or geographic differences and available information about Ronapreve's efficacy against the variants (see Table 1).

If data on molecular tests or sequencing is available, it should be considered when selecting an antiviral therapy in order to exclude Ronapreve use in the presence of SARS-CoV-2 variants that have been shown to be less sensitive to neutralisation from Ronapreve.

Accordingly, the BMG advises taking the following measures with regard to the use of Ronapreve:

- Consider the current regional epidemiological situation.
- The antibody combination of casirivimab/imdevimab should continue to be used frequently according to the indications in regions where the Delta variant is still circulating.
- Consider individual exposure and individual risk of infection with a variant against which the antibody combination of casirivimab/imdevimab is not effective (e.g., infection after exposure in a virus variant area or after contact with an index case with known infection by the Omicron variant).
- Mutation analyses (sequencing), which exclude the presence of the Delta variant and suggest the presence of the Omicron variant, can be carried out and used as a basis of decision if analysis results are available promptly. However, the diagnosis should not delay the therapeutic decision.

- In the case of unusually long virus persistence and seronegativity, sequencing should be complete prior to the administration of microsomal antibodies and, if necessary, the case should be discussed with an infectious disease centre (e.g. via the advisory network of STAKOB and the German Society of Infectious Diseases, DGI).

Call for adverse event reports

Reports of suspected adverse events after use are of great importance. They allow for continuous monitoring of the medicine's benefit-risk ratio. Healthcare professionals are encouraged to report any suspected adverse events to:

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Federal Institute for Vaccines and Biomedicines
Paul-Ehrlich-Str. 51-59
63225 Langen
Email: Cov2mab@pei.de
Fax: +49 6103 77 1234
Website: www.pei.de

Contacts

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