NEW DRUGS

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Tixagevimab and cilgavimab

Approved indication: COVID-19 prophylaxis
Evusheld (AstraZeneca)
vials containing tixagevimab 100 mg/mL solution
vials containing cilgavimab 100 mg/mL solution

Immunisation remains the best protection against severe COVID-19, however some people may not have an adequate immune response to the current vaccines. They include those who are immunocompromised or taking immunosuppressant drugs. There is also a need for alternative prophylaxis for people who have had a severe adverse reaction to a COVID-19 vaccine. One approach is to give antibodies to people at risk. The combination of casirivimab and imdevimab has already been used in post-exposure prophylaxis while the combination of tixagevimab and cilgavimab has been approved for pre-exposure prophylaxis.

Tixagevimab and cilgavimab are monoclonal antibodies that bind to different regions of the spike protein of SARS-CoV-2. After intramuscular injection of the two drugs at separate sites, it takes approximately two weeks for the two antibodies to reach their maximum concentrations. However, a protective concentration may be reached six hours after gluteal injection. Both drugs are cleared like other antibodies. The elimination half-life of tixagevimab is 89 days and it is 84 days for cilgavimab. Following injection of the two antibodies, the duration of protection against infection is thought to be at least six months.

The efficacy and safety of tixagevimab and cilgavimab are being assessed in a phase III trial.[1] A preliminary efficacy analysis, a median of 83 days after injection, included 3441 adults given 150 mg tixagevimab and 150 mg cilgavimab, and 1731 given placebo. These participants had an average age of 53.5 years with most having conditions that placed them at a high risk of severe COVID-19. In the preliminary analysis, symptomatic infection with SARS-CoV-2 occurred in eight (0.2%) of the people given antibodies and 17 (1%) of those given placebo. None of the infections was severe in the antibody group. Analysis at a median follow-up of six months showed a relative risk reduction of 82.8% for developing symptomatic COVID-19 following injections of tixagevimab and cilgavimab.[1]

Adverse event rates were similar for the antibodies and placebo. Injection-site reactions occurred in 2.4% of the antibody group and 2.1% of the placebo group.[1] Although the incidence was low, a greater proportion of those given the antibodies had serious cardiovascular adverse events such as heart failure.

The last participant in the phase III trial was injected in March 2021.[1] Since then the pattern of the pandemic has changed with Omicron now being the most frequent variant of the virus. While tixagevimab and cilgavimab will have some activity against the Omicron variant, it may be reduced. The US Food and Drug Administration has therefore recommended using a higher dose than that studied in the trial.[2]

Although the combination is approved for immunocompromised patients, less than 4% of the trial participants were taking immunosuppressive therapy or had immunosuppressive disease.[1] It is not approved for children under 12 years old. There is also little information about using the combination during pregnancy or lactation. The Australian approval of the combination is provisional as there is a need for evidence of long-term efficacy and safety including any development of viral resistance.

T manufacturer provided the AusPAR and the product information

REFERENCES

1. Levin MJ, Ustianowski A, De Wit S, Launay O, Avila M, Templeton A, et al; PROVENT Study Group. Intramuscular AZD7442 (tixagevimab–cilgavimab) for prevention of Covid-19. N Engl J Med 2022;386:2188-200. https://doi.org/10.1056/NEJMoa2116620
2. Food and Drug Administration. FDA authorizes revisions to Evusheld dosing. 2022 Feb 2; updated 2022 Jun 29. www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-revisions-evusheld-dosing

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.