NEW DRUGS

## Tozinameran+riltozinameran

**Comirnaty original/Omicron BA.1 (Pfizer) multidose vials containing doses of 15+15 micrograms/0.3 mL suspension for injection**

## Tozinameran+famtozinameran

**Comirnaty original/Omicron BA.4-5 (Pfizer) multidose vials containing doses of 15+15 micrograms/0.3 mL suspension for injection**

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**Approved indication: prevention of COVID-19**

Tozinameran (Comirnaty [Pfizer]), originally known as BNT162b2, was the first messenger RNA (mRNA) vaccine to be approved in Australia for the prevention of COVID-19. This vaccine was based on the ancestral strain of SARS-CoV-2 and provided broad protection against the previously dominant SARS-CoV-2 variants. Most infections in Australia are currently caused by subvariants of the Omicron variant.

To address this viral evolution, manufacturers have developed bivalent vaccines. These combine the original vaccine with another mRNA vaccine aimed at Omicron subvariants. Tozinameran has been combined with riltozinameran, which encodes for the spike protein of the Omicron BA.1 subvariant, and with famtozinameran, which encodes for the spike protein of the Omicron BA.4-5 subvariants.

These bivalent vaccines are provisionally approved for use as booster doses. Tozinameran+riltozinameran can be given to adults at least 5 months after a primary vaccination course. Tozinameran+famtozinameran can be used in people 12 years and older, at least 3 months after a primary vaccination course or a previous booster.

Both vaccines are packaged in multidose vials with 6 doses in each vial. As the volume of each dose is only 0.3 mL, it is important to use a low dead-volume syringe when preparing the intramuscular injection. Unlike the original formulation of tozinameran, no dilution is required. Dosage adjustment in patients with liver or kidney impairment is not addressed in the product information for these vaccines.

At present, most of the efficacy data for the bivalent boosters come from short-term studies of their immunogenicity. One of these ongoing studies has reported results for people older than 55 years who had received 3 previous doses of tozinameran. Within this cohort there were 306 people who were randomised to receive a booster dose of tozinameran (30 micrograms) and 306 who were randomised to receive a booster dose of tozinameran+riltozinameran (15+15 micrograms). One month after the booster dose, concentrations of neutralising antibodies against the ancestral strain of SARS-CoV-2 and the Omicron BA.1 subvariant had increased in both groups. The bivalent vaccine's neutralising activity was statistically superior to tozinameran alone against BA.1, and noninferior against the ancestral strain.[1]

A similar ongoing study in people older than 55 years compared a fourth dose (booster) of tozinameran (30 micrograms) with tozinameran+famtozinameran (15+15 micrograms). After one month, neutralising antibodies had increased with both vaccines, but the increases tended to be larger with the bivalent vaccine, particularly for antibodies against BA.4-5.[2] Neutralisation of newer Omicron BQ.1.1 and XBB.1 subvariants was also higher than with the original vaccine. The bivalent vaccine was noninferior for ancestral strain neutralisation. Similar trends were seen in the 12–17- and 18–55-year age groups.[3]

At present, the adverse effects of the bivalent vaccines resemble those of tozinameran alone. Common adverse effects include injection-site reactions, headache, fatigue and fever. The risk of myocarditis and pericarditis with the bivalent vaccines is currently unclear. Long-term safety data are not available for either bivalent vaccine.

Tozinameran+riltozinameran will provide some protection against BA.4-5 as well as BA.1,[1] while tozinameran+famtozinameran will provide some protection against BA.1 as well as BA.4-5.[2] However, the differences in neutralisation may not be large enough to be relevant in practice.[4] The question is how will these laboratory observations translate to clinical effectiveness?

An observational study assessed protection against symptomatic infection in patients who did and did not receive a single BA.4-5 bivalent booster dose following 2 or more monovalent doses. For people who received a monovalent dose 8 or more months previously, relative vaccine effectiveness of the bivalent booster was 48% for those aged 50–64 years and 43% for those aged 65 years and older.[5]

An observational study of BA.4-5 bivalent boosters reported that they offered greater effectiveness against hospitalisation or death than monovalent boosters (61.8% versus 24.9%).[6]

In the USA, monovalent boosters are no longer recommended, and the Australian Technical Advisory Group on Immunisation has expressed a preference for use of mRNA bivalent vaccines as boosters for those age groups in whom they are approved.[7]

At present, the duration of protection following a booster of tozinameran+riltozinameran or tozinameran+famtozinameran is unknown.

TT manufacturer provided additional useful information. 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.

## REFERENCES

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