



# Drug Information Bulletin

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## Editorial

**Warm Greetings on the eve of World Health Day!**

It is my proud privilege to write the editorial of the first issue of the 15<sup>th</sup> year of the Drug Information Bulletin (DIB). This bulletin started its journey fourteen years back on April 2007 under the Drug Information Centre (DIC), IPA Bengal Branch. Initially it started as a weekly bulletin and continued for eight years; thereafter this bulletin is being published on fortnightly basis. Initially it was sent to the members of IPA Bengal Branch, but on request it expanded its horizon including IPA members of the entire country and now is available globally to anyone interested to receiving it. During the last seven years it has been a joint publication of Drug Information Centre (DIC), IPA Bengal & Regulatory Affairs Division of IPA. It has earned several accolades to its credit from some international agencies like -Health Information for All, UK and Commonwealth Pharmacists Association (CPA).

The most satisfying fact is that a good number of electronic bulletins have been published during last couple of years by the individuals/institution who were the readers of this bulletin. It has also been reported that a number of Group of Hospitals both in India and abroad are forwarding this bulletin amongst their doctors, pharmacists and nurses. Some of the pharmacy & medical colleges are keeping the printed copy of this bulletin in their library for archiving. Our reader base is growing day by day on request from health personnel and even lay persons from India and abroad. We expect your inputs to serve you better. **Stay safe and healthy!**

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## **NEW Drug: BNT162b2 vaccine for prevention of COVID-19**

Approved indication: prevention of COVID-19  
Comirnaty (Pfizer)  
Multidose vials containing 0.45 mL suspension for dilution

In March 2020, the World Health Organization declared that the COVID-19 outbreak was a pandemic. Since then, there have been over 111 million confirmed cases worldwide and over 2.4 million deaths resulting from SARS-CoV-2 viral infection (WHO COVID-19 dashboard).<sup>1</sup> In response, hundreds of vaccines are being rapidly developed in an effort to prevent further disease.<sup>2</sup>

The BNT162b2 COVID-19 vaccine was the first to be given provisional approval in Australia and is indicated for those aged 16 years and over. It is made up of single-stranded messenger RNA (mRNA) which encodes the viral spike protein of the SARS-CoV-2 virus. The RNA is encapsulated in lipid nanoparticles which allows uptake by antigen-presenting cells (e.g. dendritic cells). Once inside, the mRNA is translated into the spike protein by host-cell machinery and presented on the cell surface. These antigen-presenting cells then show the spike protein to other immune cells including B cells which produce anti-spike protein antibodies.

The approval of this vaccine is based on short-term efficacy and safety data from an ongoing global trial. In the phase I part of the study, basic safety data including reactogenicity and immunogenicity of the vaccine were established.<sup>3</sup> Two 30 microgram doses given intramuscularly 21 days apart were found to elicit high titres of neutralising antibodies to the SARS-CoV-2 virus and robust cell-mediated responses involving CD8 and CD4 T cells.<sup>4</sup> This dosing regimen was progressed into the phase II/III part of the trial,<sup>5</sup> which randomised 43,548 participants (aged 16–91 years) 1:1 to receive the vaccine or a matching placebo.

The primary outcome of the phase II/III study was efficacy against COVID-19 disease onset at least seven days after the second dose in participants who were naïve to the SARS-CoV-2 virus. During the surveillance period, there were eight cases of

COVID-19 among those who received the vaccine and 162 cases among those who received placebo. This equates to a vaccine efficacy of 95% (confidence interval (CI) 90.3–97.6%). A subgroup analysis found that protective efficacy was similar regardless of age, sex, ethnicity, obesity and co-existing hypertension.<sup>5</sup>

There were also less COVID-19 cases with the vaccine compared to placebo after the first dose but before the second dose (39 vs 82 cases) indicating that one dose of the vaccine confers some protective efficacy (52%, CI 29.5–68.4%). Severe COVID-19 occurred in one person who received the vaccine after the first dose and nine people who received placebo.<sup>5</sup>

In a safety cohort of 21,744 people who received at least one vaccine dose, the most common adverse events were injection-site pain (>80% of patients), fatigue (>60%), headache (>50%), myalgia and chills (>30%), arthralgia (>20%) and fever and injection-site swelling (>10%). Most reactions were mild to moderate in severity and often occurred at a higher frequency after the second vaccine dose. In general, older participants reported fewer and less severe adverse events. There were four cases of Bell's palsy with the vaccine versus none with the placebo. In the phase II/III part of the study, there were two deaths in the vaccine group (from arteriosclerosis and cardiac arrest) and four in the placebo group (deemed not related to study intervention).

Anaphylaxis has been reported with this vaccine following its rollout in the UK and USA. Two cases in the UK were in people who had a history of severe allergic reactions. Close observation for at least 15 minutes after vaccine administration is recommended and the second dose should not be given to someone who had an anaphylactic reaction with the first dose. Vaccination is appropriate in those with minor infections or low-grade fevers but should be postponed in those with acute severe febrile illness.

There have so far been no interaction studies with the vaccine. It is unclear whether it can be given at the same time as other vaccines.

There are limited data on use of the vaccine during pregnancy and lactation. Studies in animals did not indicate any harmful effects.

Given the low level of community transmission in Australia, routine use of COVID-19 vaccines during pregnancy is not currently recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists.<sup>6</sup> However, its guidance states that vaccination may be considered in some groups with a high risk of complications from COVID-19. Pregnant healthcare workers in an at-risk work environment should be allocated to lower-risk duties, work from home or take leave of absence. If this is not possible, they should be offered vaccination. The Australian Department of Health has published a guide to help women making decisions about vaccination during pregnancy and breastfeeding.

The vaccine is supplied in frozen multidose vials. Once thawed, the vaccine should be diluted with 1.8 mL of normal saline. This allows for administration of six 0.3 mL doses using low dead-volume syringes and needles. Opened vials should be discarded after six hours. Training modules for vaccination providers have been developed by the Department of Health in partnership with the Australian College of Nursing to ensure COVID-19 vaccines are administered safely.

The vaccine should be given by intramuscular injection into the deltoid muscle of the upper arm. The patient's name and the batch number of the vaccine must be recorded in the Australian Immunisation Register. Enhanced monitoring of adverse events following COVID-19 vaccination is in place at national and state and territory levels.<sup>2</sup> This vaccine appears to be well tolerated and very effective at preventing COVID-19. Duration of protection is not currently known, and clinical trials are ongoing. Although the Australian Government's COVID-19 vaccination plan is for vaccines to be universally available, free and voluntary, they will initially be rolled out to priority groups including quarantine and border workers, frontline health workers, and staff and residents in aged care. Other vulnerable groups and high-risk workers will be targeted in later phases before the vaccine is rolled out to everyone.

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Ref. Australian Prescriber

## Covid-19 vaccination: India leads globally with average of more than 34 lakh doses given per day

With an average of 34,30,502 anti-coronavirus doses being given per day, India has topped globally in terms of the number of jabs administered daily, the Union Health Ministry said on Thursday. Cumulatively, 9,01,98,673 vaccine doses have been given so far through 13,77,304 sessions, according to a provisional report till 7 am.

These include 89,68,151 healthcare workers (HCWs) and 97,67,538 frontline workers (FLWs) who have taken the first dose and 54,18,084 HCWs and 44,11,609 FLWs who have taken the second dose. Besides, 3,63,32,851 and 11,39,291 beneficiaries above 60 years have been administered the first and second dose respectively.

According to the ministry's data, 2,36,94,487 and 4,66,662 beneficiaries aged 45 to 60 years have been given the first and second dose respectively.

"In terms of the number of daily doses administered globally, India stands at the top with an average of 34,30,502 doses administered per day," the ministry said. Eight states -- Maharashtra, Rajasthan, Gujarat, Uttar Pradesh, West Bengal, Karnataka, Madhya Pradesh and Kerala -- account for 60 per cent of the total doses given so far in the country.

"In its collective and collaborative fight against the global pandemic, India has crossed a landmark milestone under the world's largest vaccination drive, which was launched on January 16 this year," the ministry said.

"The cumulative number of Covid-19 vaccine doses administered in the country has crossed 9 crore," it said. Nearly 30 lakh vaccination doses were given in a span of 24 hours.

As on day-82 of the vaccination drive (April 7, 2021), 29,79,292 vaccine doses were given. Out of which, 26,90,031 beneficiaries were vaccinated across 38,760 sessions for the first dose and 2,89,261 beneficiaries received the second dose of vaccine.

Source: Economic Times

### **Carbimazole: Risk of congenital malformations**

The Health Products Regulatory Authority (HPRA) has announced that the product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for carbimazole has been updated to reflect the risk of congenital malformations. Carbimazole is a pro-drug that undergoes rapid metabolism into the active metabolite, thiamazole. The Pharmacovigilance Risk Assessment Committee (PRAC) completed a review of the known risk of congenital malformations associated with carbimazole exposure during pregnancy. Data from epidemiological studies and case reports

strengthens the evidence that carbimazole/thiamazole exposure during pregnancy is associated with an increased risk of congenital malformations, especially when administered in the first trimester of pregnancy and at high doses. Women of childbearing potential should use effective contraception during treatment with carbimazole. Carbimazole must only be used during pregnancy after a strict individual benefit/risk assessment and only at the lowest effective dose without additional administration of thyroid hormones.

Reference: Drug Safety Newsletter, HPRA, May 2020 ([www.hpra.ie](http://www.hpra.ie)) (See also WHO Pharmaceuticals Newsletter No.2, 2019: Increased risk of congenital malformations in UK)

### **Fluoxetine, levothyroxine Potential interaction affecting TSH level**

Medsafe is highlighting a safety concern and encouraging reporting of cases of potential interaction between fluoxetine (Arrow®, Fluox® etc.) and levothyroxine (Eltroxin®, Synthroid® etc.) leading to reduced serum levels of levothyroxine and increased thyroid-stimulating hormone (TSH) levels. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) indicated for depression, bulimia, obsessivecompulsive disorder and premenstrual dysphoric disorder. Levothyroxine is a synthetic form of the natural hormone thyroxine (T4) indicated for the treatment of hypothyroidism. This investigation was triggered by a report received by the Centre for Adverse Reactions Monitoring (CARM). There are also some published case reports describing reduced thyroid function during treatment with other SSRIs such as escitalopram, paroxetine and sertraline. The mechanism for this potential interaction and whether this is a class effect of SSRIs are not clear. The monitoring will continue until November 2020.

Reference: Safety Communication, Medsafe, 21 May 2020 ([www.medsafe.govt.nz/](http://www.medsafe.govt.nz/))

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