

# Interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under Emergency Use Listing

Interim guidance

8 January 2021



## Background

This interim guidance has been developed based on the advice issued by the Strategic Advisory Group of Experts on Immunization (SAGE) at its 5 January 2021 extraordinary meeting [1].

Declarations of interests were collected from all external contributors and assessed for any conflicts of interest. Summaries of the reported interests can be found on the [SAGE meeting website](#) and [SAGE Working Group website](#).

## Methods

SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing or updating recommendations [2]. Specifically for COVID-19 vaccines, a detailed description of the methodological processes can be found in the SAGE evidence framework for COVID-19 vaccines. This framework is intended to offer guidance for considering data emerging from clinical trials in support of issuing vaccine-specific evidence-based recommendations [3].

## General goal and strategy for the use of the mRNA vaccine BNT162b2 against COVID-19 (Pfizer–BioNTech)

The COVID-19 pandemic has caused significant morbidity and mortality throughout the world, as well as major social, educational and economic disruptions. There is an urgent global need for effective and safe vaccines. On 31 December 2020, WHO listed the COVID-19 mRNA vaccine BNT162b2 for emergency use, making the Pfizer–BioNTech vaccine the first to receive emergency validation from WHO since the outbreak began a year earlier. The WHO Emergency Use Listing Procedure (EUL) is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency.

BNT162b2, an mRNA vaccine against COVID-19 developed by BioNTech and Pfizer, has been shown to have an efficacy of approximately 95%, based on a median follow-up of two months. The data reviewed by WHO at this time support the conclusion that the known and potential benefits of BNT162b2 outweigh the known and potential risks. As sufficient vaccine supply will not be immediately available to immunize all who could benefit from it, countries are recommended to use the WHO Prioritization Roadmap [4] and the WHO Values Framework [5] as guidance for their prioritization of target groups. As long as vaccine supplies are very limited (stage I in the WHO Prioritization Roadmap), in settings with community transmission, the Roadmap recommends that priority be given initially to health workers at high risk and older people with and without comorbidities. Protecting high-risk health workers has a threefold purpose: (i) to protect the individual health workers; (ii) to protect critical essential services during the COVID-19 pandemic, and (iii) to prevent onward transmission to vulnerable people. Protecting older people will have the greatest public health impact in terms of reducing the number of deaths. As more vaccine becomes available, additional priority groups should be vaccinated as outlined in the WHO Prioritization Roadmap [4], taking into account national epidemiological data and other relevant considerations.

### Intended use

Persons aged 16 years and above.

## **Administration**

The recommended schedule is two doses (30 µg, 0.3 ml each) given intramuscularly into the deltoid muscle. An interval of 21–28 days between the doses is recommended. If the second dose is inadvertently administered less than 21 days after the first, the dose does not need to be repeated. If administration of the second dose is inadvertently delayed it should be given as soon as possible thereafter, according to the manufacturer's instructions. It is currently recommended that individuals receive no more than two doses in total.

## **Considerations for deferring the second dose**

WHO acknowledges that a number of countries face exceptional circumstances of vaccine supply constraints combined with a high disease burden. Some countries have therefore considered delaying the administration of the second dose to allow for a higher initial coverage. This is based on the observation that efficacy has been shown to start from day 12 after the first dose and reached about 89% between days 14 and 21, at the time when the second dose was given. No data on longer term efficacy for a single dose of the mRNA vaccine BNT162b2 currently exist, as the trial participants received 2 doses with an interval between doses in the trial ranging from 19 to 42 days. Of note, neutralizing antibody responses are modest after the first dose and increase substantially after the second dose.

Countries experiencing exceptional epidemiological circumstances may consider delaying for a short period the administration of the second dose as a pragmatic approach to maximizing the number of individuals benefiting from a first dose while vaccine supply continues to increase. WHO's recommendation at present is that the interval between doses may be extended up to 42 days (6 weeks), on the basis of currently available clinical trial data. Should additional data become available on longer intervals between doses, revision of this recommendation will be considered. Countries should ensure that any such programme adjustments to dose intervals do not affect the likelihood of receiving the second dose.

## **Booster doses**

There is currently no evidence on the need for a booster dose or booster doses of the vaccine after the current two-dose vaccine series is complete. The need for and timing of booster doses will be evaluated as further data accumulate.

## **Interchangeability with other vaccines**

No data are available on the interchangeability of this vaccine with other mRNA vaccines or other COVID-19 vaccine platforms. It is currently recommended that the same product should be used for both doses. If different COVID-19 vaccine products are inadvertently administered in the two doses, no additional doses of either vaccine are recommended at this time. Recommendations may be updated as further information becomes available on interchangeability.

## **Co-administration with other vaccines**

There should be a minimum interval of 14 days between administration of this vaccine and any other vaccine against other conditions, until data on co-administration with other vaccines become available.

## **Contraindications**

A history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine is a contraindication to vaccination. In particular, BNT162b2 should not be administered to individuals with a known history of severe allergic reaction to polyethylene glycol (PEG) or related molecules as PEG is a component of the vaccine.

## **Precautions**

Anaphylactic reactions after administration of BNT162b2 vaccine have been reported outside of clinical trials. A history of any immediate allergic reaction to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is considered as a precaution but not a contraindication to vaccination. For such persons, a risk assessment should be conducted to determine the type and severity of reaction and the reliability of the information. Such individuals may still receive vaccination, but they should be counselled about the risks of developing a severe allergic reaction and the risks should be weighed against the benefits of vaccination. Such persons should be observed for 30 minutes after vaccination in health care settings where anaphylaxis can be immediately treated.

In general, persons with an immediate allergic reaction to the first dose should not receive additional doses. For the purposes of this guidance, an immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms, such as anaphylaxis, urticaria, angioedema, respiratory distress (e.g. wheezing, stridor), that occur within hours of administration. However, subject to individual risk-benefit assessment, specialist services for immunization may allow BNT162b2 to be provided under close medical supervision if it is the only available option for persons at high risk of severe COVID-19.

As a small number of anaphylactic reactions have also been reported in vaccinees without a history of severe allergic reactions, WHO recommends that BNT162b2 vaccine should be administered only in settings where anaphylaxis can be treated. Until more data and insights are available with regard to severe allergic reactions to BNT162b2 vaccination, all vaccinees should be observed for at least 15 minutes after vaccination.

Food, contact, or seasonal allergies are not considered a precaution. The vial stoppers are not made with natural rubber latex, and there is no contraindication or precaution to vaccination for persons with a latex allergy. In addition, as BNT162b2 does not contain eggs or gelatin, there is no contraindication or precaution to vaccination for persons with allergies to these substances.

Anyone with an acute febrile illness (body temperature over 38.5 °C) should postpone vaccination until they are afebrile.

## Vaccination of specific populations

### Populations for which supportive data are available from phase 2/3 clinical trials

#### Older people

The risk of severe COVID-19 and death increases steeply with age. Data from the phase 3 trial indicate that the efficacy and safety of the vaccine are comparable across all age groups (above the age of 16). Vaccination is recommended for older persons.

#### Persons with comorbidities

Certain comorbidities have been identified as increasing the risk of severe COVID-19 disease and death. Phase 2/3 clinical trials have demonstrated that the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased risk for severe COVID-19. The comorbidities studied in phase 2/3 clinical trials include hypertension; diabetes; asthma; and pulmonary, liver and kidney disease; as well as chronic (stable and controlled) infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV). Vaccination is recommended for persons with comorbidities that have been identified as increasing the risk of severe COVID-19.

### Populations for which limited or no data exist from phase 2/3 clinical trials

#### Persons above 85 years of age

Persons above the age of 85 years and very frail older persons were not included in the clinical trials. However, the safety and immunogenicity data obtained in a large subset of older people with and without comorbidities suggest that the benefits of vaccination outweigh the potential risks. Vaccination is recommended for older persons without an upper age limit.

#### Children and adolescents below the age of 16 years

There are currently no efficacy or safety data for children or adolescents below the age of 16 years. Until such data are available, individuals below 16 years of age should not be vaccinated.

#### Pregnant women

Pregnant women are at higher risk of severe COVID-19 compared to women of child-bearing age who are not pregnant, and COVID-19 has been associated with an increased risk of preterm birth. The available data on BNT162b2 vaccination of pregnant women are insufficient to assess vaccine efficacy or vaccine-associated risks in pregnancy. However, it should be noted that the BNT162b2 vaccine is not a live virus vaccine, the mRNA does not enter the nucleus of the cell and is degraded quickly.

Developmental and reproductive toxicology (DART) studies in animals have not shown harmful effects in pregnancy. Further studies are planned in pregnant women in the coming months. As data from these studies become available, recommendations on vaccination will be updated accordingly. In the interim, WHO recommends not to use BNT162b2 in pregnancy, unless the benefit of vaccinating a pregnant woman outweighs the potential vaccine risks, such as in health workers at high risk of exposure and

pregnant women with comorbidities placing them in a high-risk group for severe COVID-19. Information and, if possible, counselling on the lack of safety and efficacy data for pregnant women should be provided. WHO does not recommend pregnancy testing prior to vaccination.

### **Lactating women**

Breastfeeding offers substantial health benefits to lactating women and their breastfed children. Vaccine efficacy is expected to be similar in lactating women as in other adults. However, there are no data on the safety of COVID-19 vaccines in lactating women or on the effects of mRNA vaccines on breastfed children. As the BNT162b2 vaccine is not a live virus vaccine and the mRNA does not enter the nucleus of the cell and is degraded quickly, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. On the basis of these considerations, a lactating woman who is part of a group recommended for vaccination, e.g. health workers, should be offered vaccination on an equivalent basis. WHO does not recommend discontinuing breastfeeding after vaccination.

### **Persons living with HIV**

Persons living with HIV may be at higher risk of severe COVID-19. Among the phase 2/3 clinical trial participants with well controlled HIV, there were no reported differences in safety signals. HIV-positive persons who are well controlled on highly active antiretroviral therapy and are part of a group recommended for vaccination can be vaccinated. Available data on administration of the vaccine are currently insufficient to allow assessment of vaccine efficacy or safety for persons living with HIV who are not well controlled on therapy. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim, given that the vaccine is not a live virus, persons living with HIV who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.

### **Immunocompromised persons**

Immunocompromised persons are at higher risk of severe COVID-19. Available data are currently insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons. It is possible that the immune response to the vaccine may be reduced, which may alter its effectiveness. In the interim, given that the vaccine is not a live virus, immunocompromised persons who are part of a group recommended for vaccination may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment.

### **Persons with autoimmune conditions**

No data are currently available on the safety and efficacy of BNT162b2 in persons with autoimmune conditions, although these persons were eligible for enrolment in the clinical trials. Persons with autoimmune conditions who have no contraindications to vaccination may be vaccinated.

### **Persons with a history of Bell's palsy**

Cases of Bell's palsy were reported following vaccination in participants in the Pfizer-BioNTech clinical trials. However, there is currently no conclusive evidence that these cases were causally related to vaccination. Post-authorization safety surveillance will be important to assess any possible causal association. In the absence of such evidence, persons with a history of Bell's palsy may receive BNT162b2 unless they have a contraindication to vaccination.

### **Persons who have previously had SARS-CoV-2 infection**

Vaccination may be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Available data from the phase 2/3 trials indicate that BNT162b2 is safe in people with evidence of prior SARS-CoV-2 infection. The added protection of vaccinating previously infected individuals is yet to be established. Despite the potential for reinfection, currently available data indicate that symptomatic reinfection within 6 months after an initial infection is rare. Thus, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may delay vaccination until near the end of this period. When more data on duration of immunity after natural infection become available, the length of this time period may be revised.

### **Persons with current acute COVID-19**

Vaccination of persons with acute symptomatic SARS-CoV-2 should be deferred until they have recovered from acute illness and the criteria for discontinuation of isolation have been met. There are no data to support a recommendation of a minimal interval between onset of symptoms and vaccination.

### **Persons who previously received passive antibody therapy for COVID-19**

Currently there are no data on the safety or efficacy of vaccination in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Hence, as a precautionary measure, vaccination should be deferred for at least 90 days to avoid interference of the antibody treatment with vaccine-induced immune responses.

## **Special settings**

Persons in settings such as refugee and detention camps, prisons, slums, and other settings with high population densities, where physical distancing is not implementable, should be prioritized for vaccination as outlined in the WHO Prioritization Roadmap [4], taking into account national epidemiological data, vaccine supply and other relevant considerations.

As noted in the WHO Prioritization Roadmap, national programmes should give special consideration to groups that are disproportionately affected by COVID-19 or that face health inequities as a result of social or structural inequities. Such groups should be identified, barriers to vaccination should be addressed, and programmes should be developed to enable equitable access to vaccines.

In the current period of very limited vaccine supply, preferential vaccination of international travelers would counter the principle of equity. Because of this and the lack of evidence on whether vaccination reduces the risk of transmission, WHO currently does not recommend COVID-19 vaccination of travelers (unless they are also part of a high-risk group or in epidemiological settings identified in the WHO Prioritization Roadmap [4]). With increasing vaccine supply, these recommendations will be revisited.

## **Other considerations**

### **SARS-CoV-2 tests**

Prior receipt of the vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection. However, it is important to note that currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein. The vaccine contains mRNA that encodes the spike protein; thus, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate for evidence of prior infection in an individual who has received the BNT162b2 vaccine, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. A positive nucleocapsid protein-based assay indicates prior infection. Antibody testing is not currently recommended to assess immunity to COVID-19 following BNT162b2 vaccination.

### **Role of vaccines among other preventive measures**

As there is not yet any evidence of an effect of the vaccine on transmission, non-pharmaceutical interventions must continue, including use of face masks, physical distancing, handwashing and other measures based on the epidemiology of SARS-CoV-2 in particular settings. Government advice on non-pharmaceutical interventions should continue to be followed by vaccinated individuals, as well as those who have not yet been vaccinated. This advice will be updated as information on the impact of vaccination on virus transmission and indirect protection in the community is assessed.

### **Community engagement, effective communication, and legitimacy**

Community engagement and effective communication (including risk communication) are essential to the success of COVID-19 vaccination programmes. Prioritization decisions should be made through transparent processes that are based on shared values, the best available scientific evidence, and appropriate representation and input by affected parties. Furthermore, communication about the mechanism of action of mRNA vaccines, and efficacy and safety data derived from clinical trials and post-marketing studies, needs to be strengthened. Strategies should include: (1) culturally acceptable and linguistically accessible communications regarding COVID-19 vaccination made freely available; (2) active community engagement and involvement of community opinion leaders

and trusted voices to improve awareness and understanding of such communications, and (3) inclusion of diverse and affected stakeholder opinions in decision-making. Such efforts are especially important in subpopulations who may be unfamiliar with or distrustful of health care systems and immunization.

### Vaccination logistics

The BNT162b2 vaccine currently requires ultra-cold-chain distribution and storage conditions that will be challenging in many country settings. When assessing the feasibility of deploying BNT162b2, immunization programmes should consider the cold-chain requirements, the current minimum number of doses per shipment, the need to administer a whole batch of vaccine within a short time frame after removal from cold storage, and the need to ensure bundling with an adequate independent supply of the correct diluent. Conditions must be met to avoid exposure of vials to sunlight and ultraviolet light

When scheduling vaccination for occupational groups, e.g. health workers, consideration should be given to the reactogenicity profile of BNT162b2 observed in clinical trials, leading to time off work in the 24-48 hours following vaccination.

Appropriate medical treatment to manage anaphylaxis must be immediately available. Hence, this vaccine should only be administered in settings with the necessary resources and trained health workers, and in settings that allow for at least 15 minutes of post-vaccination observation.

In considering the programme implications of implementing these recommendations, particular attention should be given to equity, including the feasibility, acceptability, and effectiveness of the programme in resource-constrained settings (for example, how to ensure ultra-cold chain storage and the need to be able to provide treatment for anaphylaxis).

### Recommendations on addressing current knowledge gaps through further research

In order to confirm the safety profile demonstrated in the clinical trials in the short term, active surveillance of large numbers of vaccinated individuals is necessary in the general population studied for a longer duration, as well as of specific at-risk subpopulations. It is essential for Pfizer–BioNTech and vaccination providers to report the following to adverse event reporting systems in countries: all vaccine administration errors, serious adverse events, cases of multisystem inflammatory syndrome (MIS) following vaccination, anaphylaxis and other serious allergic reactions, Bell’s palsy, and cases of COVID-19 following vaccination that result in hospitalization or death.

WHO recommends the following research and post-authorization monitoring activities:

- vaccine effectiveness over time;
- ongoing collection of safety data in vaccine recipients;
- surveillance for COVID-19 among vaccinated individuals, looking for vaccine-induced enhanced disease (possibly as vaccine-induced antibody levels decline);
- safety data from inadvertently vaccinated pregnant women during trials and post-authorization;
- safety data from pregnant women who receive vaccine because they are members of prioritized groups, e.g. health workers;
- prospective studies on the safety of BNT162b2 in pregnant women;
- impact on infants of vaccination of breastfeeding mothers;
- safety data on vaccination in immunocompromised persons, including persons living with HIV and persons with autoimmune disease;
- impact of delayed second dose as currently implemented by certain countries;
- clinical trials on the efficacy and safety of vaccination of children below the age of 16 years;
- immunogenicity and safety studies of co-administration with other vaccines, including influenza and pneumococcal vaccines, to adults and older persons;
- studies to determine how protection changes with time since vaccination and whether protection can be prolonged by booster doses;
- studies to demonstrate whether this vaccine reduces SARS-CoV-2 transmission and viral shedding;
- stability of vaccine under alternative cold-chain distribution and storage conditions;
- effectiveness of the proposed strategies for the prevention and management of anaphylactic reactions;
- interchangeability and “mix and match” studies within and across COVID-19 vaccine platforms;
- global surveillance of virus evolution and the impact of virus mutants on vaccine effectiveness to support possible update of vaccines if needed;
- head-to-head studies with other vaccines on extent and duration of immunity using standardized neutralization assays and mucosal immunity assays.

## References

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WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication.

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