

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

Interim guidance

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Updated 15 June 2021

Updated 19 November 2021



Background

This interim guidance has been developed on the basis of the advice issued by the Strategic Advisory Group of Experts (SAGE) on Immunization at its extraordinary meeting on 5 January 2021 (1) and updated during its extraordinary meeting on 27 May 2021 (2) and was further updated on 19 November 2021.

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](#).

The guidance is based on the evidence summarized in the background document on mRNA vaccine BNT162b2 (Pfizer-BioNTech) against COVID-19 (3) and the background paper on COVID-19 disease and vaccines (4).

[Annexes](#) (5) which include GRADE and evidence-to-recommendations (ETR) tables have also been updated to reflect the updated recommendations.

All referenced documents are available on the SAGE COVID-19 webpage: <https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials>.

These interim recommendations refer to the mRNA vaccine BNT162b2, manufactured by Pfizer and BioNTech. The International nonproprietary name (INN) is Tozinameran. The vaccine is also known as Pfizer-BioNTech COVID-19 Vaccine or Comirnaty. In the subsequent text the vaccine will be referred to as BNT162b2.

On 31 December 2020, BNT162b2 was granted WHO's Emergency Use Listing (EUL).

Methods

SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing or updating recommendations (6). 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 (7).

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 to develop effective and safe vaccines and to make them available at scale and equitably across all countries.

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 (8) and the WHO Values Framework (9) 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. As more vaccine becomes available, additional priority groups should be vaccinated as outlined in the WHO Prioritization Roadmap (8), taking into account national epidemiological data and other relevant considerations. Also, as a matter of global equity, as long as many parts of the world are facing extreme vaccine shortages, WHO recommends that countries that have achieved high vaccine coverage in the high-risk populations prioritize global sharing of COVID-19 vaccines through the COVAX facility before proceeding to vaccination of children and adolescents who are at low risk for severe disease. The same rationale applies to boosters, and WHO is developing a Roadmap for prioritization of booster vaccination.

Vaccine performance

BNT162b2 is an mRNA vaccine against COVID-19. A two-dose regimen of BNT162b2 given 21 days apart conferred 91% protection (95% CI 89–93%) 7 days post dose 2 against symptomatic SARS-CoV2- infection in persons aged 16 and above, based on a median follow-up of six months(10) . Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups, defined by age, sex, race, body mass index and comorbidities.

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 BNT162b2 currently exist from Phase 3 trials, as the trial participants received 2 doses with an interval between doses in the trial ranging from 19 to 42 days. Neutralizing antibody responses were shown to be modest after the first dose and increase substantially after the second dose, and the second dose increased the efficacy against symptomatic disease to 95%. Post second dose studies showed that immunogenicity in terms of neutralizing antibodies is increased with a longer inter-dose interval to 12 weeks (11) highlighting that extended inter-dose intervals will result in a good immune response, even in older adults.

Multiple studies have shown that post-introduction effectiveness of two doses is consistent with findings from the Phase 3 trials in the general population (12).

Several observational studies have suggested waning of protection against infection and mild disease in the setting of the Delta variant surge among individuals who previously received a 2-dose series. Waning has been less pronounced against severe disease. (13, 14) Re-enrolling unblinded participants from the phase 1 and phase 3 trials, a booster dose of BNT162b2 was administered approximately 6 months after completing the two-dose regimen. Immunogenicity studies showed that a third dose induces a strong and broad immune response that is expected to confer extended protection against COVID-19, including against variants of concern. Overall, the safety profile associated with a third dose of BNT162b2 at 30 µg administered approximately 6 months after completing the two-dose regimen is highly similar to the safety profile of the initial regimen itself, with no new safety concerns identified in the booster population and no increased reactogenicity or unusual AEs or other safety findings.

A recent trial in adolescents 12-15 years of age showed a vaccine efficacy against symptomatic SARS-CoV-2 infection of 100% (95% CI 75–100%) from at least 7 days after dose 2(15). Only limited safety data are available for this age group given the small sample size of the trial. A Phase 3 trial was completed in children aged 5-11 and showed similar immunogenicity and reactogenicity as to young adults. Safety data in these age groups are limited to Phase 3 trial data and data from early roll-out.

Intended use

Persons aged 12 years and above (refer to the WHO Prioritization Roadmap (16)).

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.

Considerations for deferring the second dose in settings with limited vaccine supply

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 with one dose, and have chosen an inter-dose interval of 12 to 16 weeks. Based on post-introduction vaccine effectiveness

studies from these countries, data on persistence of post dose 1 effectiveness are available and suggest ongoing high protection against severe disease and death(17). Other post-introduction studies have shown similar one-dose effectiveness against infection with the Alpha variant but lower effectiveness against Delta variant infection.

Countries should take into account the following factors when considering deferring of the second dose. During an initial period of limited vaccine supply, prioritizing distribution of first doses of vaccine to as many highly vulnerable individuals as possible will avert more deaths than covering fewer such people with two doses - so long as the effectiveness of a single dose against COVID-19 mortality is at least half that of two doses and does not wane below this level before receipt of the second dose. The optimal interval before offering second doses depends not only on vaccine effectiveness and waning but also on population vaccine coverage, supply projections, pre-existing naturally acquired immunity and country-specific vaccine prioritization plans (18-21). Furthermore, for settings with substantial circulation of variants of concern which have been shown to have reduced single doses effectiveness, the importance of providing the most vulnerable groups with 2 doses must be considered.

In conclusion, for countries that have not yet achieved high vaccine coverage rates in the high-priority groups who are experiencing a high incidence of COVID-19 cases combined with vaccine supply constraints, WHO recommends that such countries should focus on achieving a high first dose coverage in the high priority groups by extending the inter-dose interval up to 12 weeks.

Additional doses to the primary series

Additional doses of a vaccine may be needed as part of an extended primary vaccination series for target populations where the immune response following the standard primary series is likely to be insufficient. Emerging evidence suggests that immunocompromised individuals mount a lower immune response after a standard primary series compared to those without immunocompromising conditions. Therefore, for immunocompromised persons who have received a standard 2-dose primary series of BNT162b2, WHO recommends an additional dose, see under “Immunocompromised persons”.

The benefit of an additional dose has largely been assessed with respect to immunogenicity and using the same vaccine product as for the first two doses (homologous doses) (22). Advice as to whether the additional dose should be a homologous or heterologous vaccine will be updated once more data are available.

In situations of interrupted supply of the vaccine used for the primary series, or for countries with access to COVID-19 vaccines from another vaccine platform that has received WHO emergency use listing, a heterologous third dose can be considered for those requiring an additional dose in the primary vaccination series.

Booster doses

Booster doses are administered to a vaccinated population that has completed a *primary vaccination series* when, with time, the immunity and clinical protection has fallen below a rate deemed sufficient in that population. The objective of a booster dose is to restore vaccine effectiveness from that deemed no longer sufficient.

The need and optimal timing for a booster dose (homologous, heterologous, or variant-adapted) in non-immunocompromised individuals is currently being assessed.

Interchangeability with other vaccines

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 homologous or heterologous vaccine are recommended at this time.

Studies are ongoing with regards to the interchangeability of this vaccine with other COVID-19 vaccine platforms in the primary series or as a booster dose. Available evidence to date indicates that individuals receiving a first dose of ChAdOx1-S [recombinant] vaccine followed by an mRNA vaccine generate similar neutralizing antibody levels and T cell-mediated immune responses when compared to those receiving two doses of mRNA vaccines, and these responses are superior to those of individuals receiving two doses of ChAdOx1-S [recombinant] vaccine (23, 24). The order of the vaccines administered affected immune response levels, with a first dose mRNA vaccine followed by ChAdOx1-S [recombinant] vaccine being less immunogenic compared to first dose ChAdOx1-S [recombinant] vaccine followed by an mRNA vaccine.

In situations of interrupted supply of vaccine used for the for the first dose, a heterologous second dose can be considered. Recommendations will be updated as further information becomes available on interchangeability between vaccine products and platforms.

Co-administration with inactivated influenza vaccines

Evidence on co-administration of BNT162b2 vaccine with inactivated influenza vaccine suggests that neither adverse events and reactogenicity nor immunogenicity are increased as a result of co-administration. The BNT162b2 vaccine can be co-administered with inactivated influenza vaccines(25). Different arms for injection should be used when both vaccines are delivered during the same visit. Continued pharmacovigilance monitoring is recommended.

Co-administration with vaccines other than inactivated influenza vaccines

No co-administration data are available for other live or inactivated vaccines. There should be a minimum interval of 14 days between administration of this vaccine and all other vaccines except influenza vaccine. This recommendation will be updated as data on co-administration with other vaccines, including live vaccines, become available.

Contraindications

A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. If anaphylaxis occurs after the first dose, a second dose of the vaccine should not be administered.

Precautions

A history of anaphylaxis to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is not a contraindication to vaccination. For such persons, a risk assessment should be conducted by a health professional. It remains uncertain if there is an increased risk of anaphylaxis, but counselling should be given about the potential risk of anaphylaxis 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 non-anaphylactic allergic reaction to the first dose (such as urticaria, angioedema or respiratory symptoms without any other symptoms (cough, wheezing, stridor), that occur within 4 hours of administration) should not receive additional doses, unless recommended after review by a health professional with specialist expertise. However, subject to individual risk–benefit assessment, BNT162b2 could be provided under close medical supervision if it is the only available vaccine 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 anaphylaxis, WHO recommends that BNT162b2 should be administered only in settings where anaphylaxis can be treated. Until more data are available with regard to anaphylaxis after BNT162b2 vaccination, all vaccinees should be observed for at least 15 minutes after vaccination.

Food, insect venom and contact allergies and allergic rhinitis, eczema and asthma are not considered a contraindication to vaccination. 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 gelatine, there is no contraindication or precaution to vaccination for persons with allergies to any food substances.

A very rare signal of myocarditis/pericarditis has been reported with BNT162b2 vaccine. Current evidence suggests a likely causal association between myocarditis and BNT162b2. Further information on the risk remains to be assessed.

In October 2021, the Global Advisory Committee on Vaccine Safety (GACVS) COVID-19 subcommittee concluded that the benefits of mRNA COVID-19 vaccines have clear benefits in all age groups in reducing hospitalizations and deaths due to COVID-19. Countries should consider the individual and population benefits of immunisation relevant to their epidemiological and social context when developing their COVID-19 immunisation policies and programs(26).

Vaccinated individuals should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as new onset and persisting chest pain, shortness of breath, or palpitations following vaccination. It is important to rule out other potential causes of myocarditis and pericarditis, including COVID-19 infection and other viral aetiologies.

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 and post introduction vaccine effectiveness studies.

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). Persons above the age of 85 years and very frail older persons were not included in the clinical trials. 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. Post introduction vaccine effectiveness studies have shown high effectiveness and good safety profiles in this age group, including very old persons. Vaccination is recommended for older persons without an upper age limit.

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 in alignment with the WHO Prioritization Roadmap.

Children and adolescents below the age of 16 years

For children and adolescents COVID-19 is rarely severe. Evidence suggests that adolescents, particularly older adolescents, are as likely to transmit SARS-CoV-2 as adults. WHO recommends that countries should consider using BNT162b2 in children aged 12 to 15 only when high vaccine coverage with 2 doses has been achieved in the high priority groups as identified in the WHO Prioritization Roadmap.

Children 12-15 years of age with comorbidities that put them at significantly higher risk of serious COVID-19 disease, alongside other high-risk groups, may be offered vaccination.

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

Pregnant women

Pregnant women with COVID-19 are at higher risk of developing severe disease, with increased risk of intensive care unit admission and invasive ventilation, compared to non-pregnant women of reproductive age. COVID-19 in pregnancy is also associated with an increased risk of preterm birth, and of neonates requiring neonatal intensive care(23, 24). It may also be associated with an increased risk of maternal mortality (27-29). Pregnant women who are older (age 35 years and above), or have high body mass index, or have an existing comorbidity such as diabetes or hypertension, are at particular risk of severe outcomes from COVID-19.

Developmental and reproductive toxicology (DART) studies of BNT162b2 have not shown harmful effects in pregnant animals and their offspring. Clinical trial data on safety and immunogenicity in pregnancy are limited. However, a growing body of post-introduction vaccine pharmacovigilance data has not identified any acute safety problems, with obstetric outcomes including spontaneous abortion and neonatal outcomes similar to reported background rates(30-32)Based on previous experience with other vaccine use during pregnancy, the effectiveness of BNT162b2 in pregnant women is expected to be comparable to that observed for non-pregnant women in similar age groups. Data from small studies have demonstrated that COVID-19 mRNA vaccines are immunogenic in pregnant women and that vaccine-elicited antibodies are transported to infant cord blood and breast milk, suggesting possible neonatal as well as maternal protection (33, 34).

Given the adverse consequences of COVID-19 during pregnancy and the increasing data supporting a favorable safety profile of BNT162b2 in pregnancy, WHO recommends the use of BNT162b2 in pregnant individuals.

Pregnant individuals should be informed that they can receive the vaccine and provided with information about the increased risks of COVID-19 in pregnancy, the likely benefits of vaccination, and the current limitations of safety data. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy or terminating pregnancy because of vaccination

Breastfeeding women

Breastfeeding offers substantial health benefits to breastfeeding women and their breastfed children. Vaccine effectiveness is expected to be similar in breastfeeding women as in other adults. Data are not available on the potential benefits or risks of the vaccine to breastfed children. However, as BNT162b2 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, WHO recommends the use of BNT162b2 in breastfeeding women as in other adults. WHO does not recommend discontinuing breastfeeding because of vaccination.

Moderately and severely immunocompromised persons, including persons living with HIV with CD4 cell count of <200 cells/μl

Moderately and severely immunocompromised persons (ICPs) are at higher risk of severe COVID-19, regardless of age, although increasing age remains an important co-factor. For purposes of this interim recommendation, moderately and severely immunocompromised persons include those with active cancer, transplant recipients, immunodeficiency, and active treatment with immunosuppressives. It also includes people living with HIV with a current CD4 cell count of <200 cells/μl, evidence of an opportunistic infection, not on HIV treatment, and/or with a detectable viral load (i.e., advanced HIV disease).^a For more details, see (22).

Available data for WHO EUL COVID-19 vaccine products suggest that vaccine effectiveness and immunogenicity are lower in ICPs compared to persons without immunocompromising conditions (22). The emerging evidence suggests that an additional dose included in an extended primary series enhances immune responses in some ICPs(35). Reactogenicity data of an additional (third) dose given to ICPs, where reported, have generally been similar to those observed for the standard primary series of the vaccine being administered. Given the significant risk of severe COVID-19 for ICPs, if infected, WHO considers that the benefits of an additional (third) dose in an extended primary series outweigh the risks based on available data, though additional safety monitoring is required.

WHO recommends an extended primary series including an additional (third) dose (30 μg) for ICPs.

Available evidence(22) suggests that an additional (third) dose should be given 1-3 months after the second dose in the standard primary series in order to increase protection as quickly as possible in ICPs. If more than 3 months have elapsed since the second dose in the primary series, the additional (third) dose should be given at the earliest opportunity. The most appropriate timing for the additional dose may vary depending on the epidemiological setting and the extent and timing of immune suppressive therapy, and should be discussed with the treating physician.

Information and, where possible, counselling about the limitations around the data on administration of an additional dose to ICPs should be provided to inform individual benefit–risk assessment.

Given that protection may remain inadequate in a portion of immunocompromised persons even after the administration of an additional dose, WHO further recommends that close contacts (in particular caregivers) of such individuals should be vaccinated if eligible (according to the product-specific vaccines that have received EUL). Additional public health and social measures at household level to protect immunocompromised persons are also warranted depending on the local epidemic circumstances.

^a **Active cancer:** Active immunosuppressive treatment for solid tumor or hematologic malignancy (including leukemia, lymphoma, and myeloma), or within 12 months of ending such treatment. **Transplant recipients:** Receipt of solid organ transplant and taking immunosuppressive therapy; receipt of stem cell transplant (within 2 years of transplantation, or taking immunosuppressive therapy). **Immunodeficiency:** Severe primary immunodeficiency; chronic dialysis. **HIV** with a current CD4 count of <200 cells/μl and/or lacking viral suppression. **Immunosuppressives:** Active treatment causing significant immunosuppression (including high-dose corticosteroids), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents, tumor-necrosis factor (TNF) blockers, and other drugs that are significantly immunosuppressive or have received in the previous 6 months immunosuppressive chemotherapy or radiotherapy

Persons living with HIV who are stable on Antiretroviral Therapy

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.

Persons who have previously had SARS-CoV-2 infection

Vaccination should 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. Data from the pooled analyses indicate that the vaccine is safe in people with evidence of prior SARS-CoV-2 infection. Within 6 months after an initial natural infection, available data show that symptomatic reinfection is uncommon. The optimal time interval between a natural infection and vaccination is not yet known. Given limited vaccine supply, persons with PCR-confirmed SARS-CoV-2 infection in the preceding 6 months may therefore choose to delay vaccination until near the end of this 6-month period. However, emerging data indicate that symptomatic reinfection may occur in settings where variants of concern are circulating. In these settings earlier immunization after infection is advisable, e.g. within 90 days following natural infection. 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

Persons with acute PCR-confirmed COVID-19, including occurrence in-between doses, should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met. The optimal minimum interval between a natural infection and vaccination is not yet known.

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.

Other considerations

SARS-CoV-2 variants

SARS-CoV-2 viruses undergo evolution. Variants of concern may have higher transmissibility, disease severity, risk of reinfection, or a change in antigenic composition resulting in lower vaccine effectiveness. Data show some reduction in neutralization activity of BNT162b2 against the Beta variant, as well as against Gamma and Delta, and less marked reduction against Alpha(36). These findings highlight the urgent need for a coordinated approach for surveillance and evaluation of variants and their potential impact

on vaccine effectiveness. WHO will continue to monitor the situation; as new data become available, recommendations will be updated accordingly.

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 BNT162b2, 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 sufficient evidence of the extent of vaccine impact 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 and vaccine coverage rates. 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 has been better assessed.

Countries' strategies related to COVID-19 control should be designed to facilitate children's participation in education and other aspects of social life (37).

Community engagement and effective communication

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

BNT162b2 currently requires ultra-cold-chain distribution and storage conditions that will be challenging in many country settings. The storage period of the unopened thawed vial at 2–8 °C (i.e. in a normal fridge after taking out of deep-freeze conditions) is one month (31 days).

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

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

- Safety surveillance and monitoring:
 - serious adverse events including myocarditis (38), thromboembolic events, thrombosis with thrombocytopenia syndrome (TTS), anaphylaxis and other serious allergic reactions, Bell's palsy, and transverse myelitis
 - cases of multisystem inflammatory syndrome following vaccination, cases of COVID-19 following vaccination that result in hospitalization or death;
 - rates of myocarditis after booster doses
 - rates of myocarditis by age and sex
 - background rates of AESIs (including myocarditis, thromboembolic events and TTS), maternal and neonatal outcomes, and mortality in groups prioritized for vaccination.
- Vaccine effectiveness:
 - vaccine effectiveness in relation to time interval between the first and second dose;
 - vaccine effectiveness in relation to new virus variants;
 - vaccine effectiveness over time and whether protection can be prolonged by booster doses;
 - vaccine effectiveness and safety of booster doses with homologous and heterologous vaccines;
 - studies to investigate whether this vaccine reduces SARS-CoV-2 transmission and viral shedding;
 - assessment and reporting of breakthrough infections and virus sequence information;
 - head-to-head studies with other vaccines on extent and duration of immunity using standardized neutralization, T-cell and mucosal immunity assays;
 - vaccine effectiveness against post-COVID-19 conditions
 - indirect protection against unvaccinated populations
 - impact on enabling in person-schooling for children and adolescents
- Subpopulations:
 - prospective studies on the safety in pregnant and lactating women;
 - safety data on vaccination in immunocompromised persons, including persons living with HIV and persons with autoimmune disease.
- Vaccination logistics
 - immunogenicity and safety studies of co-administration with other vaccines, including influenza and pneumococcal vaccines, to adults and older persons;
 - safety, immunogenicity, and impact of a delayed second dose, as currently implemented by certain countries;
 - interchangeability and “mix and match” studies within and across COVID-19 vaccine platforms;
 - stability of vaccine under alternative cold-chain distribution and storage conditions.
- Virus variants
 - global surveillance of virus evolution and the impact of virus variants on vaccine effectiveness to support update of vaccines;
 - Modelling to determine the trade-offs for the use of vaccines with reduced effectiveness against emergent variants;
 - Booster studies with updated vaccine formulations.

Table of updates

Update 19 November 2021

Section	Rationale for update
Additional dose	Reflects recent authorization of a third dose to immunocompromised individuals with certain underlying conditions.
Interchangeability between vaccine products and platforms	Mix-and-match studies remain limited, but recent evolving evidence led to an update in this section.
Pregnant and breastfeeding women	Text was updated to reflect more recent evidence on vaccination of pregnant women. Given the increasing evidence on safety and effectiveness of this vaccine in pregnant women, WHO now recommends the use of BNT162b2 vaccine in pregnant women.
Immunocompromised persons	Updated regarding the need for a third dose in certain immunocompromised populations.
SARS-CoV-2 variants	This section has been updated to reflect the latest data with regards to the circulation of variants of concern and evidence on the impact on immunogenicity and effectiveness of the vaccine

Update 15 June 2021

Section	Rationale for update
Considerations for deferring the second dose in settings with limited vaccine supply	Post-introduction vaccine effectiveness studies in countries that have implemented an inter-dose interval longer than per emergency use authorization (up to 12 weeks) have shown a high public health impact. This observation combined with additional immunological data support that countries facing a high incidence of COVID-19 combined with severe vaccine supply constraints could consider delaying the second dose up to 12 weeks in order to achieve a higher first dose coverage in high priority populations.
Interchangeability between vaccine products and platforms	Mix-and-match studies remain limited, but recent evolving evidence led to an update in this section.
Paediatric age indication	A Phase 3 trial in children aged 12-15 years showed high efficacy and good safety in this age group, leading to an extension of the previous age indication from 16 years onwards down to age 12 onwards.
Children and adolescents below the age of 16 years	<p>The following statement was added: For children and adolescents COVID-19 is rarely severe. Evidence suggests that adolescents, particularly older adolescents, are as likely to transmit SARS-CoV-2 as adults. WHO recommends that countries should consider using BNT162b2 in children aged 12 to 15 only when high vaccine coverage with 2 doses has been achieved in the high priority groups as identified in the WHO Prioritization Roadmap.</p> <p>Children 12-15 years of age with comorbidities that put them at significantly higher risk of serious COVID-19 disease, alongside other high-risk groups, may be offered vaccination.</p>

	There are currently no efficacy or safety data for children below the age of 12 years. Until such data are available, individuals below 12 years of age should not be routinely vaccinated.
Pregnant and lactating women	Text was updated as reassuring data on safety and immunogenicity in pregnancy has become available since the first Issue of this Recommendation.
Role of vaccines among other preventive measures	The following statement was added: “Countries’ strategies related to COVID-19 control should be designed to facilitate children’s participation in education and other aspects of social life.”.
SARS-CoV-2 variants	This section has been added to reflect the latest data with regards to the circulation of variants of concern and evidence on the impact on effectiveness of the vaccine.
Vaccination logistics	Based on additional storage studies, the storage period of the unopened thawed vial at 2–8 °C (i.e. in a normal fridge after taking out of deep-freeze conditions) has been extended from five days to one month (31 days).

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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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