COMIRNATY ▼ (COVID-19 mRNA Vaccine)

Storage and Handling of VIALS Outside of Recommendations in the Product Labeling DURING and AFTER DILUTION

Refer to the Comirnaty (COVID-19 mRNA Vaccine) Summary of Product Characteristics for information regarding the Vaccine. Pfizer does not suggest or recommend the use of Comirnaty (COVID-19 mRNA Vaccine) in any manner other than as described.

▼ Relevant to member states of the EU and the European Economic Area (including Norway, Liechtenstein and Iceland): This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Comirnaty has been authorised under a "conditional approval" scheme. The European Medicines Agency will review new information on this medicinal product at least every year and the Summary of Product Characteristics will be updated as necessary.

TEMPERATURE EXCURSIONS

Pfizer has conducted stability studies to support **temporary inadvertent temperature excursions**.[1] Note that the data provided below are based on physical stability testing only; product stored outside the recommended temperature range was not tested or evaluated for clinical immunogenicity or efficacy.

This information is not intended to recommend storage of Comirnaty (COVID-19 mRNA Vaccine) at temperatures other than those recommended in the Prescribing Information. Pfizer does not suggest or recommend the use of Comirnaty (COVID-19 mRNA Vaccine) that has been stored or handled outside of the recommendations described in the Prescribing Information.

Healthcare Professionals (HCPs) should consider these data, including the limitations, in determining whether Comirnaty (COVID-19 mRNA Vaccine) exposed to temperatures outside of the recommended storage and handling conditions remains suitable for patient use. It is the responsibility of the vaccination provider to evaluate these data in the context of the actual temperature excursion and the duration of excursion that occurred. Pfizer is unable to make any treatment recommendations for individual patients.

Note that the stability information can be updated; therefore, we recommend that you contact Pfizer Medical Information following future temperature excursions from the recommended storage conditions to ensure you have the most up to date information on this topic.

TOPICS COVERED IN THIS DOCUMENT

1. WHAT ARE THE RECOMMENDED STORAGE AND HANDLING REQUIREMENTS FOR Comirnaty (COVID-19 mRNA Vaccine) DURING AND AFTER DILUTION?

Summary of Product Characteristics

Section 6.3 Shelf life[2]

Diluted medicinal product

Chemical and physical in-use stability has been demonstrated for 6 hours at 2ºC to 30ºC after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Section 6.4 Special precautions for storage[2]

When you are ready to thaw or use the vaccine

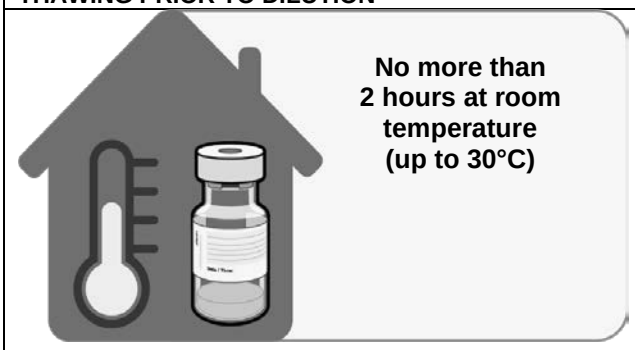
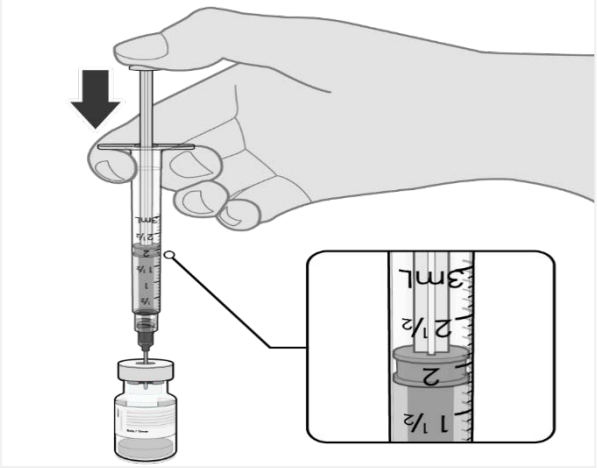
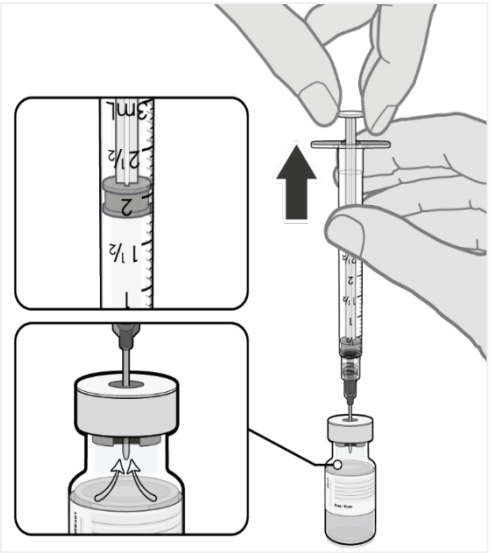
- Open-lid vial trays, or vial trays containing less than 195 vials removed from frozen storage (< -60°C) may be at room temperature (< 25°C) for up to 3 minutes to remove vials or for transfer between ultra-low-temperature environments.
- Once a vial is removed from the vial tray, it should be thawed for use.
- After vial trays are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.

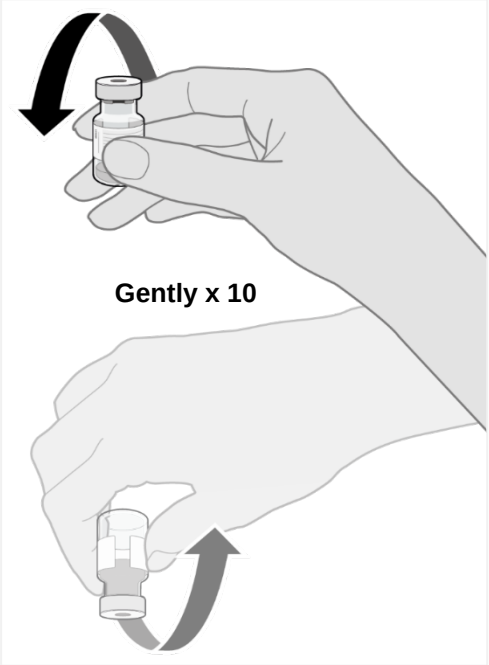
For storage conditions after thawing and dilution of the medicinal product, see section 6.3.

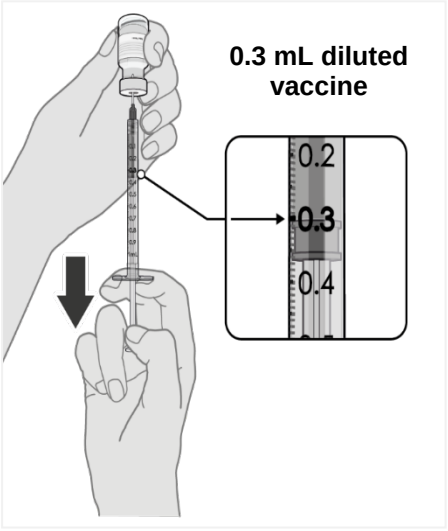
Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

THAWING PRIOR TO DILUTION	
	• The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use. • Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. Do not shake. • Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.
DILUTION	
 **1.8 mL of 0.9% sodium chloride injection**	• The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.
 **Pull back plunger to 1.8 mL to remove air from vial**	• Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

	• Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as an off-white dispersion with no particulates visible. Discard the diluted vaccine if particulates or discolouration are present.
 **Record appropriate date and time.** **Use within 6 hours after dilution**	• The diluted vials should be marked with the appropriate date and time. • Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.

PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	• After dilution, the vial contains 2.25 mL from which 6 doses of 0.3 mL can be extracted. • Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab. • Withdraw 0.3 mL of Comirnaty. Low dead-volume syringes and/or needles should be used in order to extract 6 doses from a single vial. The low dead-volume syringe and needle combination should have a dead volume of no more than 35 microlitres. If standard syringes and needles are used, there may not be sufficient volume to extract a sixth dose from a single vial. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Discard any unused vaccine within 6 hours after dilution.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

2. WHAT DATA IS AVAILABLE FOR VIALS OR DOSING SYRINGES CONTAINING DILUTED VACCINE STORED BETWEEN 2 TO 30°C FOR >6 HOURS FROM THE POINT OF DILUTION?

Summary of Product Characteristics

Section 6.3 Shelf life[2]

Diluted medicinal product

Chemical and physical in-use stability has been demonstrated for 6 hours at 2ºC to 30ºC after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Section 6.6 Special precautions for disposal and other handling[2]

- The diluted vials should be marked with the appropriate date and time.
- Discard any unused vaccine within 6 hours after dilution.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Vials

The in-use period for the diluted vial is 6 hours between 2°C and 30°C. Some countries have limited the label conditions to between 2°C and 25°C due to concerns around the potential for microbiological growth at warmer temperatures. Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all its measured quality attributes when diluted vaccine is stored

in the **vial** at 2°C to 30°C for up to a cumulative period of 18 hours, in addition to the routine/labelled in-use period. Microbiological risk must be considered.[1]

For easier reference, the results of the stability studies are also provided in table format:

Temperature Conditions	**Vials:** **2°C to 30°C**
CUMULATIVE EXCURSION TIME for Diluted Vaccine at Point-Of-Use (time beyond routine allowance)	18 hours physical and chemical stability. Microbiological risk must be considered.
Point-Of-Use ROUTINE/LABELLED Handling Allowances for Diluted Vaccine	6 hours, including up to 6 hours of transport.

Pfizer has not studied storage of diluted vaccine **in vials** that have been stored between 2°C to 32°C for >24 hours, at temperatures <2°C or at temperatures >32°C.

Syringes

Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all its measured quality attributes when diluted vaccine is stored in **syringes** for 6 hours at 2°C to 30°C. Microbiological risk must be considered. Degradation of RNA in the vaccine has been observed when stored for longer than 6 hours in syringes. Pre-drawing can increase risk of medication errors. [1]

For easier reference, the results of the stability studies are also provided in table format:

Temperature Conditions	**Syringes:** **2°C to 30°C**
CUMULATIVE EXCURSION TIME for Diluted Vaccine at Point-Of-Use (time beyond routine allowance)	None
Point-Of-Use ROUTINE/LABELLED Handling Allowances for Diluted Vaccine	6 hours. 6 hours of physicochemical data to support transport. Microbiological risk must be considered.

Microbiological risk was assessed through a microbiological challenge study. No logarithmic growth of spiked microorganisms was seen until 12 hours at 25° C. A 2x safety factor is applied resulting in the 6 hours in use period. Microbiological growth has greater potential to occur after 6 hours.[1]

3. IS THE PERIOD OF TIME IT TAKES TO THAW THE VACCINE AT ROOM TEMPERATURE OR IN THE REFRIGERATOR INCLUDED IN THE TIME ALLOWED AFTER DILUTION (I.E. WHEN DOES THE TIMEFRAME START)?

Summary of Product Characteristics

Section 6.3 Shelf life[2]

Once removed from the freezer, the unopened vaccine can be stored for up to 5 days at 2°C to 8°C, and up to 2 hours at temperatures up to 30°C, prior to use.

Once thawed, the vaccine should not be re-frozen.

Diluted medicinal product

Chemical and physical in-use stability has been demonstrated for 6 hours at 2ºC to 30ºC after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Section 6.6 Special precautions for disposal and other handling[2]

The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2°C to 8°C to thaw; a 195 vial pack may take 3 hours to thaw.

Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30°C for immediate use.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Vials thawed at room temperature must be diluted within 2 hours. The allowable 2 hours at room temperature timeframe prior to dilution starts when the vials are removed from the refrigerator or freezer. The allowable time in the refrigerator (5 days or 120 hours), starts when the vaccine is removed from storage under ultra-low temperatures. From the point of dilution, the vaccine may be stored at 2°C to 30ºC for up to 6 hours.[1]

4. WHAT DATA IS AVAILABLE FOR THE PREPARATION OF THE DILUTED VIALS OUTSIDE OF THE RECOMMENDED METHOD IN THE PRESCRIBING INFORMATION? (i.e. gently inverted <10 times or >10 times, shaken too vigorously, etc.)

Summary of Product Characteristics

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

According to the Product Labeling, Comirnaty (COVID-19 mRNA Vaccine) should be gently inverted 10 times before and after dilution. Do not shake**.**[2]

The Summary of Product Characteristics does not include any data on the use of Comirnaty (COVID-19 mRNA Vaccine) when prepared in any manner other than as recommended.[2]

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Vials should be mixed before and after dilution by gentle inversion. No studies have been done to evaluate shaking of vials during preparation, but the results of the transportation study support the conclusion that the vaccine can be exposed to some shaking stress. Without additional data, vaccine vials which are aggressively shaken should be discarded. Studies have been conducted demonstrating that the solution is fully mixed after at least 2 inversions prior to dilution, and 2 inversions after dilution. Vials that have not been gently inverted 2 times should be remixed by gently inverting to ensure they are fully mixed. Vials gently inverted for more than 10 times are safe to use.[1]

5. CAN A DILUENT OTHER THAN 0.9% SODIUM CHLORIDE INJECTION, USP (such as sterile water for injection, D5W, etc.) BE USED TO DILUTE THE VACCINE?

Summary of Product Characteristics

Section 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Vials of Comirnaty (COVID-19 mRNA Vaccine) must be diluted with 1.8 mL of 0.9% (9 mg/mL) sodium chloride injection prior to administration. Pfizer has not investigated the use of any other solution to dilute the vaccine. [1]

6. IS THERE ANY DATA FOR USE OF A DILUTION VOLUME OTHER THAN 1.8 ML?

Summary of Product Characteristics

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Alternate dilution volumes may impact the dose. A 1.5 mL dilution would result in a 34.6 mcg dose per injection, and there will not be enough volume in the vial to withdraw the fifth dose. A 2 mL dilution would result in a 28 mcg dose per injection. Dilutions between 1.5 and 2 mL are not expected to impact efficacy. [1]

7. IS THERE ANY DATA FOR ADDING THE DILUENT TO THE VIAL BEFORE THE VACCINE IS FULLY THAWED?

Summary of Product Characteristics

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

- The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use.
- Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. Do not shake.
- Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.
- The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

Pfizer BioNTech COVID-19 Vaccine must be thawed before use. It is recommended to thaw in the refrigerator (2°C to 8°C). It will take about 3 hours for an entire 195 count tray to thaw in the refrigerator. A smaller number of vials, or those spaced apart, will thaw more quickly. Vials needed for immediate use can be thawed at room temperature. They will typically thaw in less than 10 minutes, but it is recommended to wait approximately 30 minutes to ensure complete thawing. Vials thawed at room temperature may be returned to the refrigerator for storage if necessary, but total time at room temperature must be tracked to ensure the vial stays within the 2 hours at room temperature limit. It is also recommended to allow vials to come to room temperature (not cold to touch) prior to dilution to ensure thawing is complete. No impact to vaccine stability is anticipated if diluent is added to a vial with a small amount of undetected unthawed product remaining. No data is available if diluent is added directly into a vial of frozen vaccine.[1]

8. WHY IS A 21 GAUGE OR NARROWER NEEDLE RECOMMENDED TO BE USED WHEN ADDING THE DILUENT? CAN I USE A LARGER GAUGE NEEDLE?

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

A 21 gauge or narrower needle must be used to add the diluent. Use of a larger needle does not harm the vaccine but may result in leaking from the stopper when doses are withdrawn. Stoppers meet USP<381>, ISO 8871-5, and Ph Eur 3.2.9 requirements for functional testing of the stopper (penetrability, fragmentation, and self-sealing capacity) when punctured up to 10 times with a 21 gauge needle and with an 18 gauge needle, however use of an 18 gauge needle in dose preparation studies led to leaking during dose withdrawal.[1]

9. WHAT DOES THE SPRAY CONTAIN THAT CAN RESULT IF I FORGET TO WITHDRAW AIR PRIOR TO REMOVING THE DILUENT NEEDLE FROM THE VIAL? DOES IT IMPACT THE DOSE?

Summary of Product Characteristics

Section 6.6 Special precautions for disposal and other handling[2]

Handling instructions

Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

For further information regarding this vaccine, please refer to the Comirnaty Summary of Product Characteristics.[2]

Internal Data

The instructions for use instruct the preparer to equalize the pressure in the vial after adding the diluent by withdrawing 1.8 mL of air prior to removing the diluent needle from the vial. Failure to equalize the pressure results in a small spray of 0.9% sodium chloride when the needle is pulled out of the stopper. This spray consists only of diluent, not vaccine, and has no safety impact to the preparer or impact to the dose.[1]

10. IS THERE DATA FOR THE STERILITY/STABILITY AND TIMEFRAME FOLLOWING REMOVAL OF THE FLIP-OFF CAP WITH AN INTACT ALUMINUM OVERSEAL (UNPUNCTURED)?

Removal of the flip-off cap with no impact on the underlying aluminum overseal (i.e. aluminum overseal remains intact, unpunctured) does not compromise the sterility/stability of the vaccine.[1]

11. ARE THERE OFFICIAL RECOMMENDATIONS ON THE COVID-19 VACCINATION PROGRAMME?

The use of Comirnaty vaccine should be in accordance with official recommendations.[2] Please refer to your local country recommendations, if available.

Please note that Pfizer is independent of these recommendations.

REFERENCES

1. COVID-19 mRNA Vaccine BNT162b2. Data on file (28). Pfizer.
2. Comirnaty (COVID-19 mRNA Vaccine). Summary of Product Characteristics (centralized license), applicable to all countries in the EU and NO [V: Date of revision of text 01/2021; LC].