Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Comirnaty Original/Omicron BA.1 (15/15 micrograms)/dose dispersion for injection

COVID-19 mRNA Vaccine (nucleoside modified)

Tozinameran/riltozinameran

PLGB 53632/0010

BioNTech Manufacturing GmbH

LAY SUMMARY

Comirnaty Original/Omicron BA.1 (15/15 micrograms)/dose dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified) Tozinameran/riltozinameran

This is a summary of the Public Assessment Report (PAR) for Comirnaty Original/Omicron BA.1 (15/15 micrograms)/dose dispersion for injection. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Comirnaty Original/Omicron BA.1 Vaccine in this lay summary for ease of reading.

For practical information about using Comirnaty Original/Omicron BA.1 Vaccine, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Comirnaty Original/Omicron BA.1 Vaccine and what is it used for?

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 01 September 2022 (EMEA/H/C/005735/II/0140), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

Comirnaty Original/Omicron BA.1 Vaccine is a vaccine used for preventing COVID-19 caused by SARS-CoV-2. It is given to adults and adolescents from 12 years of age and older.

Comirnaty Original/Omicron BA.1 Vaccine is only for individuals who have previously received at least a primary vaccination course against COVID-19.

The application is a line extension of the existing product, Comirnaty 30 micrograms/dose concentrate for dispersion for injection (PLGB 53632/0002).

How does Comirnaty Original/Omicron BA.1 Vaccine work?

The vaccine causes the immune system (the body’s natural defences) to produce antibodies and blood cells that work against the virus, so giving protection against COVID-19.

How is Comirnaty Original/Omicron BA.1 Vaccine used?

The pharmaceutical form of this medicine is a dispersion for injection and the route of administration is intramuscular (into the muscle).

Comirnaty Original/Omicron BA.1 Vaccine is given as an injection of 0.3 mL into a muscle of the upper arm.

Comirnaty Original/Omicron BA.1 Vaccine may be given at least 3 months after the most recent dose of a COVID-19 vaccine.

Comirnaty Original/Omicron BA.1 Vaccine is only indicated for individuals who have previously received at least a primary vaccination course against COVID-19. Individuals should check with their healthcare provider regarding eligibility for and timing of the booster dose.

For details on the primary vaccination course in individuals 12 years of age and older, individuals should see the Package Leaflet for Comirnaty 30 micrograms/dose dispersion for injection or Comirnaty 30 micrograms/dose concentrate for dispersion for injection.

For further information on how Comirnaty Original/Omicron BA.1 Vaccine is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The individual should ask the administering healthcare practitioner if they have any questions concerning the vaccine.

What benefits of Comirnaty Original/Omicron BA.1 Vaccine have been shown in studies?
The company submitted clinical study data which supported the use of Comirnaty Original/BA.1 Vaccine as a booster dose, as the immune responses against the Omicron BA.1 COVID-19 variant were superior compared to the original Comirnaty vaccine. The immune responses to the original reference strain of virus were also non-inferior.

What are the possible side effects of Comirnaty Original/Omicron BA.1 Vaccine?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Comirnaty Original/Omicron BA.1 Vaccine (which may affect more than 1 in 10 people) are injection site: pain, swelling; tiredness; headache; muscle pain; chills; joint pain; diarrhoea; fever. Some of these side effects were slightly more frequent in adolescents 12 to 15 years than in adults.

Why was Comirnaty Original/Omicron BA.1 Vaccine approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine/these medicines can be approved for use.

Comirnaty Original/Omicron BA.1 Vaccine has been authorised with a conditional marketing authorisation (CMA). CMAs are intended for medicinal products that address an unmet medical need, such as a lack of alternative therapy for a serious and life-threatening disease. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon.

What measures are being taken to ensure the safe and effective use of Comirnaty Original/Omicron BA.1 Vaccine?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Comirnaty Original/Omicron BA.1 Vaccine. The RMP details the important risks of Comirnaty Original/Omicron BA.1 Vaccine, how these risks can be minimised, any uncertainties about Comirnaty Original/Omicron BA.1 Vaccine (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Comirnaty Original/Omicron BA.1 Vaccine:

Important identified risks	Myocarditis and Pericarditis
Important potential risks	Vaccine-associated enhanced disease (VAED) including Vaccine-associated enhanced respiratory disease (VAERD)
Missing information	Use in pregnancy and while breast feeding
	Use in immunocompromised patients
	Use in frail patients with co-morbidities (e.g., chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders)
	Use in patients with autoimmune or inflammatory disorders
	Interaction with other vaccines
	Long term safety data

An additional risk minimisation measure to address myocarditis and pericarditis is a Direct Healthcare Professional Communication (DHPC) to ensure that healthcare providers (HCPs) are aware of the potential for myocarditis and pericarditis associated with COVID-19 mRNA vaccine use.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Comirnaty Original/Omicron BA.1 Vaccine are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Comirnaty Original/Omicron BA.1 Vaccine
A marketing authorisation was granted in Great Britain on 02 September 2022.
The full PAR for Comirnaty Original/Omicron BA.1 Vaccine follows this summary.

This summary was last updated in October 2022.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Comirnaty Original/Omicron BA.1 (15/15 micrograms)/dose dispersion for injection (PLGB 53632/0010) could be approved.

The product is approved for the following indications:
For active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 12 years of age and older who have previously received at least a primary vaccination course against COVID-19. The use of this vaccine should be in accordance with official recommendations.

The active substances in this product are tozinameran and riltozinameran.

Tozinameran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Original).

Riltozinameran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2 (Omicron BA.1).

The nucleoside-modified messenger RNA in Comirnaty is formulated in lipid nanoparticles, which enable delivery of the non replicating RNA into host cells to direct transient expression of the SARS CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 01 September 2022 (EMEA/H/C/005735/II/0140), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended). The application is a line extension of the existing product, Comirnaty 30 micrograms/dose concentrate for dispersion for injection (PLGB 53632/0002).

Comirnaty Original/Omicron BA.1 Vaccine has been authorised as a conditional marketing authorisation (CMA). CMAs are granted in the interest of public health and are intended for medicinal products that fulfil an unmet medical need and the benefit of immediate availability outweighs the risk posed from less comprehensive data than normally required. Unmet medical needs include, for example, treatment or diagnosis of serious and life-threatening diseases where no satisfactory treatment methods are available. CMAs may be

granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon. Adequate evidence of safety and efficacy to enable the MHRA to conclude that the benefits are greater than the risks is required, and has been provided for Comirnaty Original/Omicron BA.1 Vaccine. The CMA for Comirnaty Original/Omicron BA.1 Vaccine, including the provision of any new information, will be reviewed every year and this report will be updated as necessary.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) MHRA-100392-PIP01-21-M0. The applicant has made a post-marketing commitment to submit a PIP modification.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Advice was sought from the Commission of Human Medicines (CHM) on 02 September 2022.

A marketing authorisation was granted on 02 September 2022.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.
The grant of a marketing authorisation is recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.
The grant of a marketing authorisation is recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.
The grant of a marketing authorisation is recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional pharmacovigilance and risk minimisation measures have been proposed:

Important Identified Risk: Myocarditis and Pericarditis

Evidence for linking the risk to the medicine	Events of Myocarditis and Pericarditis have been reported.
Risk factors and risk groups	Post-authorization reports have been reported more frequently in adolescent and young adult male patients following the second dose of vaccine; however, reports have been received for adult males and females of broader age range and following the first vaccination also.
Risk minimisation measures	Routine risk minimisation measures SmPC sections 4.4. and 4.8. Additional risk minimisation measures: DHCP letter and communication plan
Additional pharmacovigilance activities	• C4591009 • C4591011 • C4591012 • C4591021 (former ACCESS/VAC4EU) • C4591038 (former C4591021 sub-study) • C4591036 (former Pediatric Heart Network study) See Section II.C this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Vaccine-Associated Enhanced Disease (VAED) including Vaccine-Associated Enhanced Respiratory Disease (VAERD)

Evidence for linking the risk to the medicine	VAED is considered a potential risk because it has not been seen in human studies with this or other COVID-19 vaccines being studied. It has not been seen in vaccine studies in animal models of the SARS-CoV-2 virus either. However, in selected vaccine studies in animal models as well as in some laboratory studies in animal cells infected with 2 other related coronaviruses (SARS-CoV-1 and MERS-CoV), abnormalities in immune responses or cellular responses indicative of VAED were observed. Because of this, VAED is considered a potential risk. In the past there have been other examples of particularly respiratory viruses where VAED has been observed. For example, some children who received an inactivated respiratory syncytial virus vaccine (a different type of virus), had worse signs of disease when they were subsequently infected with respiratory syncytial virus. VAED is thought to occur by several mechanisms where the immune response is not fully protective and actually either causes the body to have an inflammatory reaction due to the type of immune response with specific types of T-cells, or the body does not produce enough strong antibodies to prevent SARS-CoV-2 infection of cells or produces weak antibodies that actually bind to the virus and help it to enter cells more easily, leading to worse signs of disease.
Risk factors and risk groups	It is thought that the potential risk of VAED may be increased in individuals producing a weak antibody response or in individuals with decreasing immunity over time.

Risk minimisation measures	Routine risk minimisation measures None. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	• C4591001 • C4591007 • C4591009[a] • C4591011[a] • C4591012[a] • C4591021 (former ACCESS/VAC4EU)[a] See Section II.C of this summary for an overview of the post-authorisation development plan.

a. Addresses AESI-based safety events of interest including vaccine associated enhanced disease

Missing Information: Use in Pregnancy and while Breast Feeding

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6; PL section 2. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• C4591009[a] • C4591010[a] • C4591011[a] • C4591015 • C4591021 (former ACCESS/VAC4EU)[a] • C4591022[a] See Section II.C of this summary for an overview of the post-authorisation development plan.

a. Please note that studies C4591009, C4591010, C4591011, C4591021 (former ACCESS/VAC4EU) and C4591022 address only "Use in pregnancy" and not "Breast feeding".

Missing Information: Use in Immunocompromised Patients

Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 5.1. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• BNT162-01 cohort 13 • C4591010[a] • C4591011 • C4591012 • C4591021 (former ACCESS/VAC4EU) • C4591024 (former Safety and Immunogenicity in high-risk adults) See Section II.C of this summary for an overview of the post-authorisation development plan.

a. Addresses AESI-based safety events of interest

Missing Information: Use in Frail Patients with Co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronicneurological disease, cardiovascular disorders)

Risk minimisation measures	Routine risk minimisation measures: SmPC section 5.1. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• C4591001 subset • C4591011 • C4591012 • C4591021 (former ACCESS/VAC4EU) • C4591024 (former Safety and immunogenicity in high-risk adults) See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Use in Patients with Autoimmune or Inflammatory Disorders

Risk minimisation measures	Routine risk minimisation measures: None. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• C4591011 • C4591012 • C4591021 (former ACCESS/VAC4EU) • C4591024 (former Safety and immunogenicity in high-risk adults) See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Interaction with other Vaccines

Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.5. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• C4591030 (Co-administration study with seasonal influenza vaccine) See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Long Term Safety Data

Risk minimisation measures	Routine risk minimisation measures: None. Additional risk minimisation measures: No risk minimisation measures.
Additional pharmacovigilance activities	• C4591001 • C4591007 • C4591010 • C4591011 • C4591012 • C4591021 (former ACCESS/VAC4EU) • C4591038 (former C4591021 substudy) • C4591036 (former PHN) See Section II.C of this summary for an overview of the post-authorisation development plan.

This is acceptable.

VII. USER CONSULTATION

A suitable patient Information Leaflet (PIL) text has been evaluated.

The PIL for Comirnaty 30 micrograms/dose concentrate for dispersion for injection (PLGB 53632/0002) has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

A readability test has not been requested by the EMA for the current application. Consequently, no user test/bridging report has been provided by the applicant in the EC Decision Reliance Procedure submission. The proposed changes to the PIL with this application are not expected to affect readability and this is acceptable.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

Comirnaty Original/Omicron BA.1 Vaccine has been authorised with a conditional marketing authorisation (CMA). The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

Description	Due date
1. In order to confirm the efficacy and safety of Comirnaty, the MAH should submit the final Clinical Study Report for the randomized, placebo controlled, observer-blind study C4591001.	31/12/2023

Comirnaty Original/Omicron BA.1 Vaccine has been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

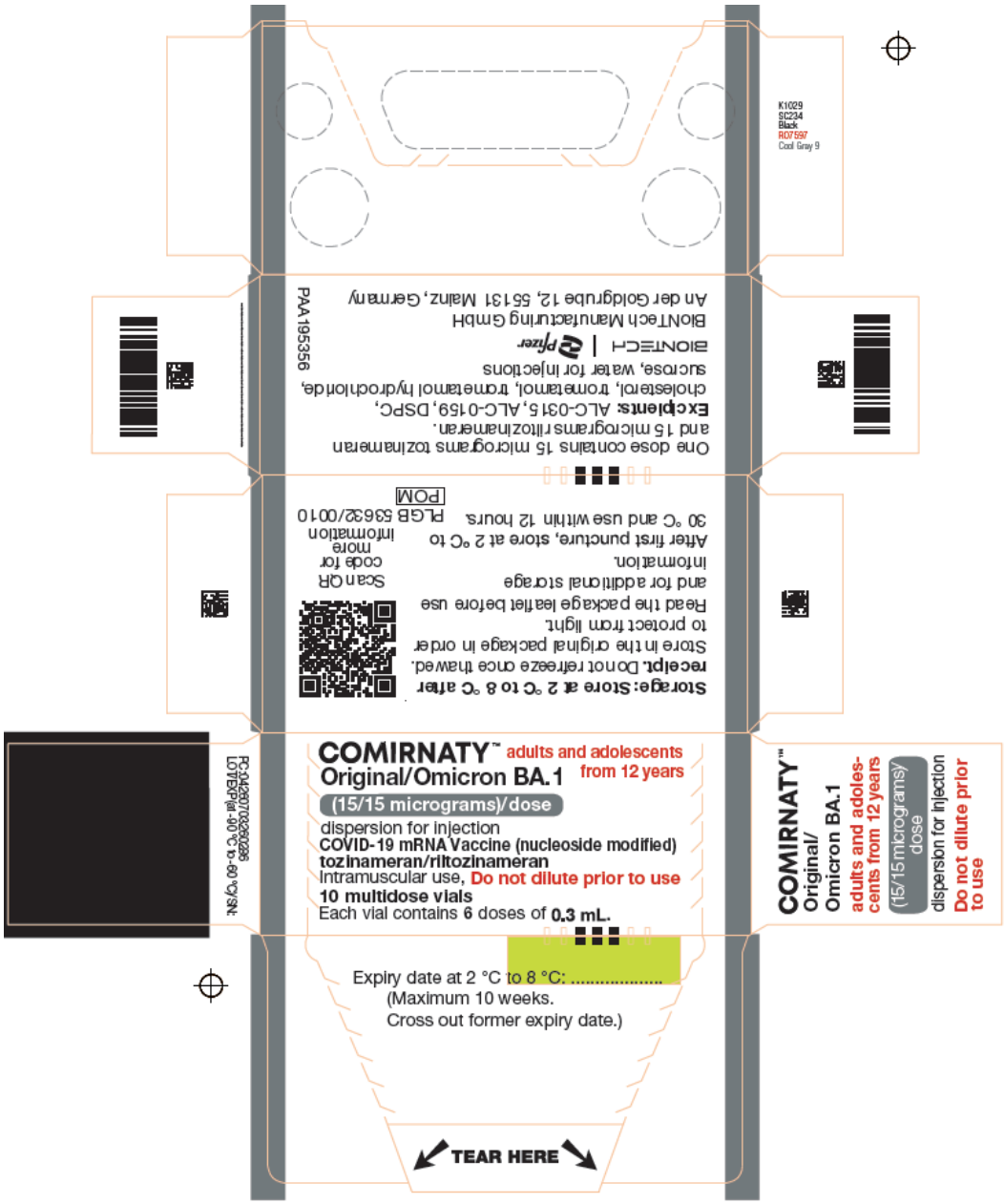
Description	Due date
1. The MAH should submit the 3 and 6 month post dose 4 immunogenicity and safety results in participants aged > 55 years from Study C4591031 Substudy E.	31/01/2023
2. The MAH should submit the cellular immunogenicity results from study C4591031 Substudy E.	31/03/2023
3. The MAH should submit the 1, 3 and 6 month post dose 4 immunogenicity and safety results in participants aged 18 to 55 years from Study C4591031 Substudy E. Due date 31 March 2023 (1 month data due by 31 October 2022)	31/03/2023
4. The MAH should submit a standalone summary safety report for the Original/Omicron BA.1 bivalent product, with the data lock point falling 3 months after the date of approval in Great Britain.	16/12/2022
5. Within one month of approval, the MAH must submit the following concerning Post- Authorisation Vaccine Effectiveness: a. Confirmation that ongoing UK-based effectiveness study WI255886 will be promptly amended to include the collection of effectiveness data for the bivalent vaccine b. An analysis of the feasibility and power of study WI255886 to generate robust results for the bivalent vaccine c. Milestones for the provision of results for the bivalent vaccine d. A full updated study protocol to reflect the investigation of the bivalent product	02/10/2022
6. Where there is a business need to manufacture Omicron (BA.1) circular plasmid	31/12/2024

DNA and linear DNA template at Pfizer Zagreb, the batch analysis data obtained from the first commercial batch from Pfizer Zagreb shall be provided.	
7. Comparative accelerated stability data between the prototype and bivalent vaccine drug product should be presented to ensure comparable stability profiles are seen for the vaccines.	31/03/2023

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.




COMIRNATY™ injection
Original/Omicron BA.1
COVID-19 mRNA Vaccine
6 doses 15/15 mcg
Do not dilute
IM
Discard time:
LOT/EXP:
PAA195357

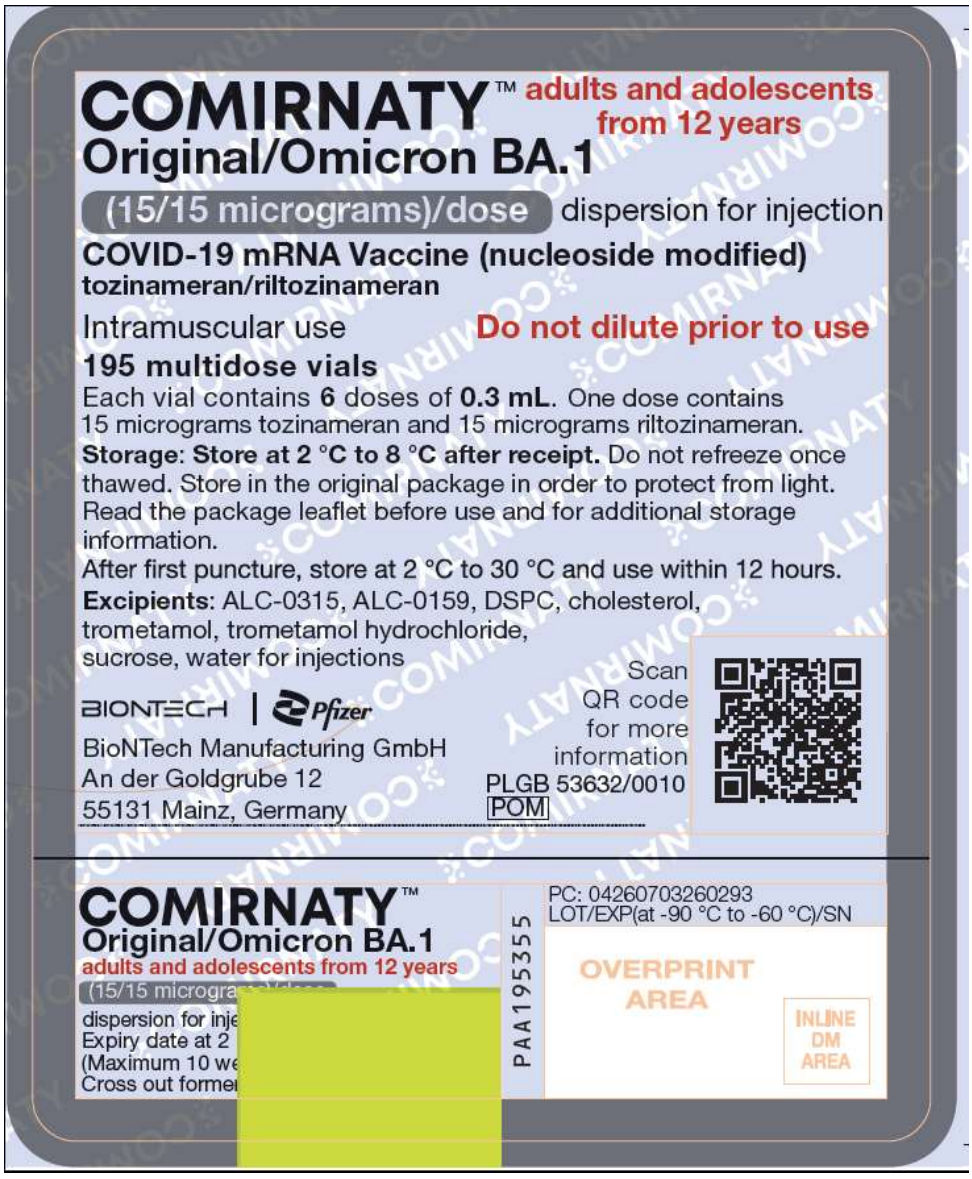

COMIRNATY™ adults and adolescents from 12 years
Original/Omicron BA.1
(15/15 micrograms)/dose dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran/riltozinameran
Intramuscular use
Do not dilute prior to use
195 multidose vials
Each vial contains 6 doses of 0.3 mL. One dose contains 15 micrograms tozinameran and 15 micrograms riltozinameran.
Storage: Store at 2 °C to 8 °C after receipt. Do not refreeze once thawed. Store in the original package in order to protect from light. Read the package leaflet before use and for additional storage information.
After first puncture, store at 2 °C to 30 °C and use within 12 hours.
Excipients: ALC-0315, ALC-0159, DSPC, cholesterol, trometamol, trometamol hydrochloride, sucrose, water for injections
BIONTECH | Pfizer
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany
Scan QR code for more information
PLGB 53632/0010
POM
COMIRNATY™
Original/Omicron BA.1
adults and adolescents from 12 years
PAA195355
PC: 04260703260293
LOT/EXP(at -90 °C to -60 °C)/SN
OVERPRINT AREA
INLINE DM AREA

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**