Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection

COVID-19 mRNA Vaccine (nucleoside modified)

Tozinameran / famtozinameran

PLGB 53632/0012

BioNTech Manufacturing GmbH

LAY SUMMARY

Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified)
Tozinameran / famtozinameran

This is a summary of the Public Assessment Report (PAR) for Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified). 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.4-5 in this lay summary for ease of reading.

For practical information about using Comirnaty Original/Omicron BA.4-5, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Comirnaty Original/Omicron BA.4-5 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 12 September 2022 (EMEA/H/C/005735/II/0143), 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.4-5 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.4-5 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 dispersion for injection (PLGB 53632/0002).

How does Comirnaty Original/Omicron BA.4-5 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. As Comirnaty Original/Omicron BA.4-5 does not contain the virus to produce immunity, it cannot give you COVID-19.

How is Comirnaty Original/Omicron BA.4-5 used?
The pharmaceutical form of this medicine is a dispersion for injection and the route of administration is injection into a muscle most often a muscle called the deltoid (intramuscular injection).

Comirnaty Original/Omicron BA.4-5 is given as an injection of 0.3 mL into a muscle of the upper arm.

Comirnaty Original/Omicron BA.4-5 may be given at least 3 months after the most recent dose of a COVID-19 vaccine.

Comirnaty Original/Omicron BA.4-5 is only indicated for individuals who have previously received at least a primary vaccination course against COVID-19.

The vaccine recipient should check with your 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.4-5 is used, refer to the PIL and Summary of Product Characteristics (SmPC/SmPCs) 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 their medicine.

What benefits of Comirnaty Original/Omicron BA.4-5 have been shown in studies?
Apart from containing mRNA matching different, but closely related, Omicron subvariants, Comirnaty Original/BA.1 and Comirnaty Original/Omicron BA.4-5 have the same composition. Therefore, based on clinical studies showing that Comirnaty Original/Omicron BA.1 triggers an immune response to the original strain and Omicron BA.1, Comirnaty Original/Omicron BA.4-5 is expected to generate an immune response against both the original strain and the subvariants BA.4 and BA.5.

In particular, Comirnaty Original/Omicron BA.4-5 is expected to be more effective than Comirnaty at triggering an immune response against the BA.4 and BA.5 subvariants. These data are further supported by non-clinical laboratory data on the ability of Comirnaty Original/Omicron BA.4-5 to trigger an adequate immune response.

At the time of the MHRA approval short-term safety data were also available with the Comirnaty Original/Omicron BA.4-5 vaccine. This showed that the side effects observed were the same as those seen for the original Pfizer/BioNTech booster dose and were typically mild and self-resolving.

Further reassurances on the safety of this vaccine were obtainable from the post-marketing data available from over 12 million individuals that have received a booster dose of this vaccine in the US; these data have not revealed any new safety concerns.

What are the possible side effects of Comirnaty Original/Omicron BA.4-5?
For the full list of all side effects reported with this medicine/these medicines, 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.4-5 (which may affect more than 1 in 10 people) are injection site: pain, swelling; tiredness; headache; muscle pain; chills; joint pain; diarrhoea; fever.

Why was Comirnaty Original/Omicron BA.4-5 approved?
MHRA decided that the benefits are greater than the risks and recommended that these medicines can be approved for use.

What measures are being taken to ensure the safe and effective use of Comirnaty Original/Omicron BA.4-5?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Comirnaty Original/Omicron BA.4-5. The RMP details the important risks of Comirnaty Original/Omicron BA.4-5, how these risks can be minimised, any uncertainties about Comirnaty Original/Omicron BA.4-5 (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.4-5.

Important Identified Risks	Anaphylaxis
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

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.4-5 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.4-5
A marketing authorisation was granted in Great Britain on 9 November 2022.

The full PAR for Comirnaty Original/Omicron BA.4-5 follows this summary.
This summary was last updated in December 2022.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare product Regulatory Agency (MHRA) considered that the application for Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified) (PLGB 53632/0012) could be approved.

The product is approved for the following indications:

Comirnaty Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection is indicated 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 (see sections 4.2 and 5.1).

The use of this vaccine should be in accordance with official recommendations.

Tozinameran / famtozinameran is the nucleoside-modified messenger RNA in Comirnaty, which 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 12 September 2022 (EMEA/H/C/005735/II/0143), 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).

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-M01. 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.

A marketing authorisation was granted on 9 November 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 measures have been proposed:

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.

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

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".

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

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.

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.

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.

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 full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

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.

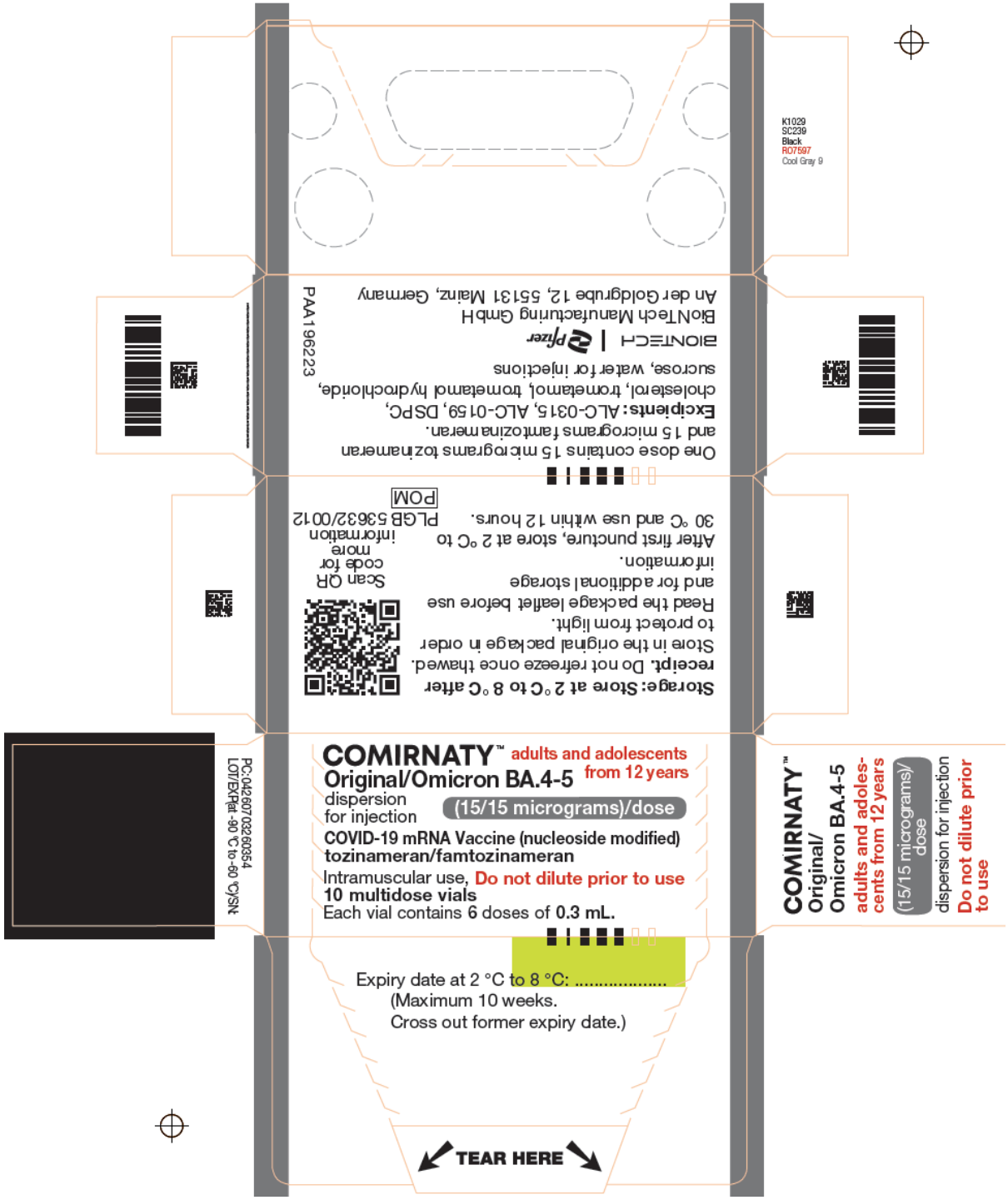
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

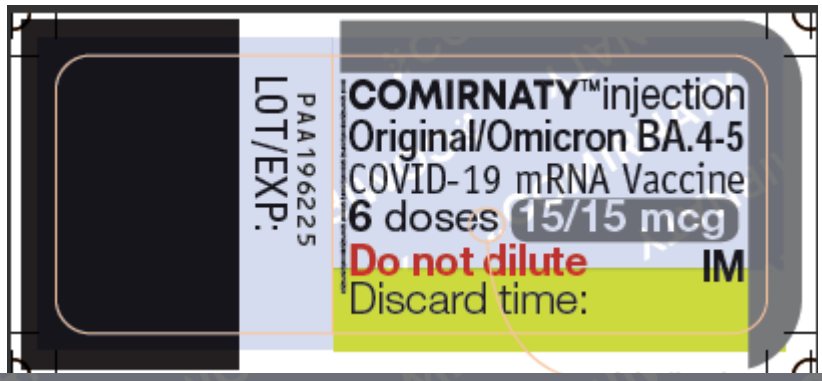
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

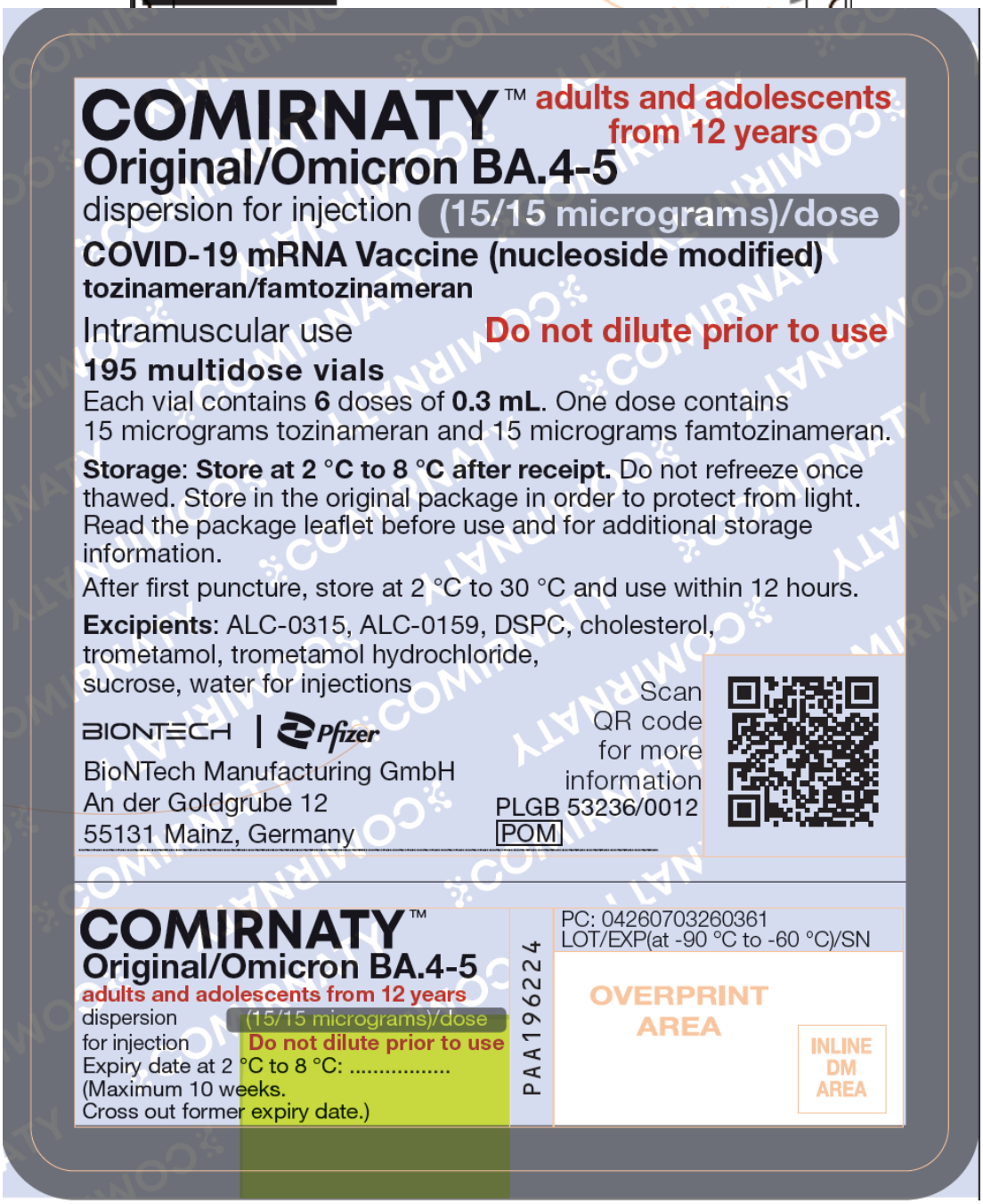
The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product is available on the MHRA website.

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




LOT/EXP:
PAA196225
COMIRNATY™injection
Original/Omicron BA.4-5
COVID-19 mRNA Vaccine
6 doses 15/15 mcg
Do not dilute
IM
Discard time:


COMIRNATY™ adults and adolescents from 12 years
Original/Omicron BA.4-5
dispersion for injection (15/15 micrograms)/dose
COVID-19 mRNA Vaccine (nucleoside modified)
tozinameran/famtozinameran
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 famtozinameran.
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 53236/0012
POM
COMIRNATY™
Original/Omicron BA.4-5
adults and adolescents from 12 years
dispersion for injection
(15/15 micrograms)/dose
Do not dilute prior to use
Expiry date at 2 °C to 8 °C: .....
(Maximum 10 weeks.
Cross out former expiry date.)
PAA196224
PC: 04260703260361
LOT/EXP(at -90 °C to -60 °C)/SN
OVERPRINT AREA
INLINE DM AREA

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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

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