Medicines & Healthcare products Regulatory Agency

MHRA

Vaccine BNT162b2 – CONDITIONS OF AUTHORISATION UNDER REGULATION 174

2 December 2020, amended on 30 December 2020, 28 January 2021 and 30 March 2021

This authorisation under Regulation 174 of the Human Medicine Regulations 2012 (as amended) is subject to a number of conditions attached under regulation 174A(1) to all the entities involved in the manufacture and supply of this product across the medicines supply chain.

General

- This temporary Authorisation under Regulation 174 permits the supply of identified COVID-19 mRNA Vaccine BNT162b2 batches, based on the safety, quality and efficacy data submitted by Pfizer/BioNTech to MHRA in the period from 1 October to 2 December 2020;
- This authorisation is not a marketing authorisation;
- This authorisation applies to supply within the United Kingdom of Great Britain and Northern Ireland.
- As provided in Regulation 174A(2) of the Human Medicine Regulations the sale or supply of this vaccine will not be deemed authorised if the supply is for the purpose of any use other than the recommended or required use, or if a condition in this authorisation is breached;
- The entity responsible for physically supplying the product in the United Kingdom is Pfizer Limited (incorporated in England and Wales under registered number 526209). Pfizer Limited and BioNTech Manufacturing GmbH (An der Goldgrube 12, 55131 Mainz, Germany) will be jointly and separately responsible for placing the product on the market in the United Kingdom for the purposes of The Human Medicines Regulations including Reg 345(3) (hereinafter “Pfizer/BioNTech”);
- Pfizer/BioNTech are jointly and separately responsible, with the manufacturers of the product, for the conditions relating to the manufacture of the product and to product release to the market under the terms of this authorisation;
- Pfizer/BioNTech is not only responsible for compliance with the conditions expressly applied to it in this authorisation but also, where the conditions apply legislation or guidance that confers responsibilities on marketing authorisation holders, for compliance with any responsibility however worded that applies to a marketing authorisation holder in the applied legislation or guidance;
- Pfizer/BioNTech must promptly provide to MHRA any further data that is generated by them, or which otherwise come into their possession, which is relevant to the risk / benefit profile of the product;

- Pfizer/BioNTech must respond in a timely manner to any requests for further supplementary data relating to product;
- Any deviations from any of these conditions can only be made with the prior agreement of the MHRA;
- MHRA may review and adjust these conditions for temporary supply in response to any developments which it considers material, including any subsequent market authorisations that might be issued by other medicines regulators;
- This authorisation will be valid until expressly withdrawn by MHRA or upon issue of a full market authorisation by the MHRA.

Quality

- The supply of batch EJ0553 is authorised providing that:
    - Pfizer/BioNTech ensure that Good Laboratory Practice studies are performed to standards in UK national regulations, relevant guidelines and the OECD Principles of Good Laboratory Practice.
    - Pfizer/BioNTech ensure that clinical trials are performed to national regulations and relevant guidelines including ICH GCP E6R2
    - Pfizer/BioNtech submit to MHRA GCP inspections to assess the compliance any of the clinical trials and applicable data attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327
    - Pfizer/BioNtech ensure that all drug substance and drug product manufacture outside the UK is in accordance with EU GMP and the Human Medicines Regulations 2012 (as amended) in facilities with current EU GMP certificates or other acceptable and suitable authorisation to MHRA.
    - QP certification is provided for the final dosage form and applying the approach and standards in EU GMP Annex 16.
    - Any importation or manufacturing facilities located within the UK must be authorised by the MHRA to handle Regulation 174 products. All drug substance and drug product manufacture must be in accordance with EU GMP and the Human Medicines Regulations 2012 (as amended) in facilities with current EU GMP certificates or other acceptable and suitable authorisation to MHRA.
    - Compliance with GMP requirements is documented in the QP check sheets and Pfizer/BioNTech provide these to the MHRA for each batch along with the QP certificates of conformance. QP certification must take into NIBSC certification process, as this in itself does not imply release to market.
    - QP certification declares: (i) compliance with all stages of EU GMP (where non-compliant, a gap analysis must be performed, and captured on the QP checksheet), and (ii) that the batch has been manufactured as per the dossier supplied (currently Emergency Use Authorisation).

  - A certificate of conformance with GMP and the conditions of this authorization must be generated by the releasing QP and supplied to the onward supply chain.

- Further batches are authorised for supply, subject to batch specific approval by MHRA and providing that the full product lifecycle is in compliance with the conditions specified above in relation to batch EJ0553;
- Pfizer/BioNTech must provide relevant additional characterization data regarding drug product manufacturing process and product quality reasonably requested by MHRA, and will provide relevant additional characterization data regarding drug product manufacturing process and product quality, whether or not requested by MHRA, as soon as they become available.
- Any changes to or deviation from the manufacture of the product must be notified to MHRA for approval on allocation of the batch to UK use.

Product information and Instructions for Use (PIL and SmPC equivalent)

- Pfizer/BioNTech must liaise with the Agency to provide suitable instructions for usage of the product.
- The instructions for usage that will be agreed with Pfizer/BioNTech are to be considered as conditions of this authorisation.
- This authorisation does not preclude an authorised prescriber administering this vaccine to a patient for whom it is not recommended in accordance with the instructions of use, in circumstances where that authorised prescriber is directly responsible for that patient and the administration of the vaccine is to fulfil the special needs of that patient where, in the professional judgement of that authorised prescriber, the welfare of the patient is likely to be in jeopardy unless the vaccine is administered.

Clinical and Pharmacovigilance

- Pfizer/BioNTech must operate a comprehensive pharmacovigilance system for this product in accordance with UK legislation for licensed products, as if they were market authorisation holders

- Pfizer/BioNtech must submit to MHRA inspections to assess compliance with any and all pharmacovigilance obligations attached to the authorisation by virtue of regulation 174A. The powers of inspection will be the same as those outlined in regulations 325, 326 and 327.

- Pfizer/BiotNTech must ensure compliance with the BTN162b2 RMP, including the additional pharmacovigilance elements laid out in sections 6b-g of the MHRA core RMP for COVID-19 vaccines.

- Pfizer/BioNTech must:

- Submit protocols for the studies stated in the BTN162b2 RMP pharmacovigilance plan
- Provide the interim analysis and final clinical study reports for study BNT162-01 once available, including data on healthy subjects
- Ensure that any participants in study c4591001 that choose to be unblinded and then have a Covid-19 vaccination if they are on placebo arm, should have an end of study visit including immunogenicity assessment (including anti-N antibodies) and also NAAT. This is to ensure that they have a complete status before they become unevaluable for the control arm.

Deployment

Pfizer/BioNTech has assured the MHRA that, in light of the UK and Crown Dependency deployment model:

- The product as supplied in ultra-low temperature conditions (ULT) has a stability of six months at a temperature of -70 +/- 10 degrees Centigrade.

- Distribution as part of the deployment can be controlled at either ULT (-70 +/- 10 degrees Centigrade) within four transitions below -15 degrees Centigrade, or in 2-8 degrees Centigrade within 120 hours of leaving ULT.

- Further packing down of lots to aid deployment can occur at 2-8 degrees Centigrade within the 120 hours shelf life of leaving ULT.

- Transit of the undiluted product at 2-8 degree Centigrade can occur either in two journeys each up to 6 hours or, where there are real deployment needs, for a maximum of 12 hours in one sitting. These times are to be taken within the 120-hour shelf life.

- The undiluted product can be held at room temperature below 25 degrees Centigrade for up to two hours prior to dilution.

- The product can be diluted at room temperature less than 25 degrees Centigrade using sterile unpreserved 0.9 percent sodium chloride and in line with the healthcare professional information supplied by the company

- The diluted product can be used within 6 hours of dilution and then must be discarded. Diluted product cannot be transported.

It is a condition of the authorisation to supply the product that the above assurances are accurate and that the product can be supplied and held safely in accordance with the above assurances throughout the supply chain.

Transfers of frozen vials stored at ultra-low temperature (below -60 degrees Centigrade)

- Unopened closed-lid vial trays containing 195 vials removed from ultra-low temperature frozen storage (below -60 degrees Centigrade) may be at temperatures up to 25 degrees Centigrade for up to 5 minutes after which they may be returned to below -60 degrees Centigrade

- Open-lid vial trays, or vial trays containing less than 195 vials, removed from ultra-low temperature frozen storage (below -60 degrees Centigrade) may be at temperatures up to 25 degrees Centigrade for up to 3 minutes after which they may be resealed and returned to below -60 degrees Centigrade (with remaining number of vials recorded).
- After vial trays are returned to frozen storage following temperature exposure up to 25 degrees Centigrade, they must remain in frozen storage for at least 2 hours before they can be removed again.
- Once an individual vial has been removed from the vial tray, it should be thawed for use.

Handling of temperature excursions

The additional stability information below is not intended to replace or override the recommended storage conditions set out in the Information for Health Care Professionals leaflet. Based on additional stability data submitted to the MHRA, the following information can be used to inform decision making in the event of a temporary excursion from those recommended storage conditions.

When considering the implications of temperature excursions whilst stored in the freezer:

Data have been provided which support temperature excursion of -60 degrees Centigrade to -15 degrees Centigrade for up to 2 weeks. Following a single temperature excursion within these conditions, the vials may be returned one time to the recommended storage condition of -80 degrees Centigrade to -60 degrees Centigrade. Transfers of frozen vials that have been exposed to this excursion should be treated in the same way as vials stored at below -60 degrees Centigrade (see above).

When considering the implications of temperature excursions once removed from the freezer:

Vaccine in unopened vials has been found to be stable for up to 24 hours at temperatures from -3 degrees Centigrade to 2 degrees Centigrade. Data also indicates that a total storage time of 4 hours, at temperatures from 8 degrees Centigrade to 30 degrees Centigrade, does not adversely affect the stability of the vaccine. The total of 4 hours includes the 2 hours at up to 25 degrees Centigrade allowed in the Information for Health Care Professionals leaflet.

Supply chain and distribution

The deployment model developed for the distribution and administration of the product by the NHS in each of the four countries of the United Kingdom and Crown Dependencies should comply with the above conditions in order to ensure the safety, quality and efficacy of the product is not compromised. Where appropriate, the above assurances must be reflected in the conditions imposed on NHS contractors by NHS commissioners.

In the United Kingdom, the vaccines will be delivered to designated NHS bodies or NHS contractors that have capacity to hold the vaccines at ultra-low temperatures (expected to

be, but not necessarily, Movianto (in Scotland, England and Northern Ireland) and the Welsh Blood Service).

Thereafter, the NHS arrangements for the onward and (if different) final distribution of the products, and their final deployment, are still being developed, but the bodies responsible under NHS arrangements in each of the four countries for any aspect of the distribution or final deployment of the vaccine must comply, as conditions of this authorisation, with the conditions that are applicable to that aspect of the distribution or final deployment in this authorisation.

The bodies responsible for the transit of the product to the designated NHS bodies or NHS contractors in the UK from the manufacturer must also comply, as conditions of this authorisation, with the conditions of the authorisation that are applicable to them.

In addition:

- All wholesalers and manufacturing license holders distributing or holding this product must be authorised to handle Regulation 174 products
- All activities are to be conducted in accordance with good distribution practice (GDP).
- A manufacturing licence holder can pack down the authorised product without being named on the Company submission.
- Pack down prior to distribution must occur in accordance with good manufacturing practice (GMP) and requires QP certification that it has occurred in accordance with GMP and the specification provided by the contract giver.
- Manufacturers and authorised persons performing the pack down activities must be authorised to handle regulation 174 products and immunological products.
- WDA(H) holders and NHS acute trusts and Boards in Wales, Scotland and Northern Ireland are authorised to apply the change in storage condition label to the product, to indicate the timing of the removal from ultra-low temperature without a manufacturing licence.
- All distribution must be controlled at either ULT within four transitions, or in 2-8 degrees Centigrade within 120 hours from leaving ULT
- The WDA(H) receiving the boxes must be authorised for Regulation 174 products and ULT cold chain.
- Pack down under section 10 of the Medicines Act 1968 or regulation 3 of the Human Medicines Regulations 2012 for supply by the same legal entity must take place in a manner and environment that ensure, and must be subject to NHS governance arrangements and standard operating procedures that ensure, that the safety, quality and efficacy of the product is not compromised. Any guidance in respect of the packing down of the product under section 10 or regulation 3 published by the licensing authority on GOV.UK must be appropriately adhered to.

- Final preparation of the product for administration must take place in a manner and environment ensure, and must be subject to NHS governance arrangements and standard operating procedures that ensure, the safety, quality or efficacy of the product is not compromised. Any guidance in respect of the final preparation of the product published by the licensing authority on GOV.UK must be appropriately adhered to