

### 3.2.P.1. DESCRIPTION AND COMPOSITION OF THE DRUG PRODUCT – [OMICRON (XBB.1.5) VARIANT]

The BNT162b2 Omicron (XBB.1.5) Variant drug product (herein referred to as Variant), is supplied as a preservative-free, sterile dispersion of RNA-containing lipid nanoparticles (LNPs) in aqueous cryoprotectant buffer for intramuscular administration.

There are 7 presentations for the Variant drug product providing doses of either 30, 10 or 3 µg of RNA per dose in multi-dose vial (MDV) and single-dose vial (SDV) presentations. Each presentation is formulated in 10 mM Tris buffer, 300 mM sucrose, pH 7.4. The presentations differ in RNA concentration, fill volume, and requirement for dilution prior to administration and are summarized in Table 3.2.P.1-1

**Table 3.2.P.1-1. Drug Product Presentations**

Drug Product Presentation <sup>a</sup>	Drug Product RNA Concentration (mg/mL)	Fill volume (mL)	Dilution with 0.9% sodium chloride (mL)	Injection Volume (mL)	Doses per vial
30 µg MDV	0.1	2.25	N/A	0.3	6
30 µg SDV	0.1	0.48	N/A	0.3	1
10 µg MDV	0.033	2.25	N/A	0.3	6
10 µg SDV	0.033	0.48	N/A	0.3	1
10 µg MDV (dilution required)	0.1	1.3	1.3	0.2	10
3 µg MDV (dilution required)	0.1	0.4	2.2	0.2	10
3 µg MDV (dilution required)	0.033	0.48	1.1	0.3	3

a. Dilution with 0.9% sodium chloride is only required for presentations described as “dilution required”  
Abbreviations: MDV= multi-dose vial, SDV= single dose vial; N/A = not applicable

The drug product is supplied in a 2 mL glass vial sealed with a bromobutyl elastomeric stopper and an aluminum seal with a flip-off plastic cap.

The composition of the drug product, including quality standard, function, concentration and amount per dose for each presentation is provided in [Table 3.2.P.1-2](#), [Table 3.2.P.1-3](#), [Table 3.2.P.1-4](#), [Table 3.2.P.1-5](#) and [Table 3.2.P.1-6](#).

**Table 3.2.P.1-2. Composition of Drug Product, 30 µg RNA dose in 0.3 mL Injection Volume, Multi-dose Vial (6 Doses) and Single-dose Vial**

Name of Ingredients	Reference to Standard	Function	Concentration (mg/mL)	Amount per 2.25 mL vial <sup>a</sup> (MDV = 6 doses)	Amount per 0.48 mL vial <sup>a</sup> (SDV = 1 dose)	Amount per 30 µg dose
BNT162b2 (XBB.1.5) drug substance	In-house specification	Active ingredient	0.1	225 µg	48 µg	30 µg
ALC-0315	In-house specification	Functional lipid	1.43	3.22 mg	0.69 mg	0.43 mg
ALC-0159	In-house specification	Functional lipid	0.18	0.41 mg	0.09 mg	0.05 mg
DSPC	In-house specification	Structural lipid	0.31	0.70 mg	0.15 mg	0.09 mg
Cholesterol	Ph. Eur.	Structural lipid	0.62	1.40 mg	0.30 mg	0.19 mg
Sucrose	USP-NF, Ph. Eur.	Cryoprotectant	103	231.8 mg	49.44 mg	31 mg
Tromethamine (Tris base) <sup>b</sup>	USP-NF, Ph. Eur.	Buffer component	0.20	0.45 mg	0.10 mg	0.06 mg
Tris (hydroxymethyl) aminomethane hydrochloride (Tris HCl) <sup>c</sup>	In-house specification	Buffer component	1.32	2.97 mg	0.63 mg	0.4 mg
Water for Injection	USP-NF, Ph. Eur.	Solvent/vehicle	q.s.	q.s.	q.s.	q.s.
<b>Processing Aids/Residues<sup>d</sup></b>						
Ethanol	Ph. Eur.	Processing aid	N/A			
Citric acid monohydrate	Ph. Eur.	Processing aid				
Sodium citrate	Ph. Eur.	Processing aid				
Sodium hydroxide	Ph. Eur.	Processing aid				
HEPES	In-house specification	Drug substance buffer component				
EDTA	Ph. Eur., USP-NF	Drug substance buffer component				

**Table 3.2.P.1-2. Composition of Drug Product, 30 µg RNA dose in 0.3 mL Injection Volume, Multi-dose Vial (6 Doses) and Single-dose Vial**

Name of Ingredients	Reference to Standard	Function	Concentration (mg/mL)	Amount per 2.25 mL vial <sup>a</sup> (MDV = 6 doses)	Amount per 0.48 mL vial <sup>a</sup> (SDV = 1 dose)	Amount per 30 µg dose
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- a. Values are rounded to maintain the same level of precision as the label claim, with trailing decimals not shown, where applicable.
- b. Also known as Trometamol
- c. Also known as Tromethamine HCl and Trometamol HCl
- d. The processing aids and drug substance formulation buffer components are residues that are essentially removed through the manufacturing process and are not considered ingredients (excipients).

## Abbreviations:

ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine

q.s. = quantum satis (as much as may suffice)

HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid

EDTA = edetate disodium dihydrate

MDV = multi-dose vial

SDV = single-dose vial

N/A = Not applicable

**Table 3.2.P.1-3. Composition of Drug Product, 10 µg total RNA dose in a 0.3 mL injection volume, Multi-dose Vial (6 doses) and Single-dose Vial**

Name of Ingredient	Reference to Standard	Function	Concentration (mg/mL) <sup>a</sup>	Amount per 2.25 mL Vial (MDV = 6 doses) <sup>a</sup>	Amount per 0.48 mL Vial (SDV = 1 dose) <sup>a</sup>	Amount per Dose
BNT162b2 (XBB.1.5) drug substance	In-house specification	Active ingredient	0.033	74 µg	16 µg	10 µg
ALC-0315	In-house specification	Functional lipid	0.472	1.06 mg	0.227 mg	0.14 mg
ALC-0159	In-house specification	Functional lipid	0.059	0.13 mg	0.028 mg	0.02 mg
DSPC	In-house specification	Structural lipid	0.1	0.23 mg	0.048 mg	0.03 mg
Cholesterol	Ph. Eur.	Structural lipid	0.21	0.47 mg	0.1 mg	0.06 mg
Sucrose	USP-NF, Ph. Eur.	Cryoprotectant	103	231.8 mg	49.44 mg	31 mg
Tromethamine (Tris base) <sup>b</sup>	USP-NF, Ph. Eur.	Buffer component	0.20	0.45 mg	0.10 mg	0.06 mg
Tris (hydroxymethyl) aminomethane hydrochloride (Tris HCl) <sup>c</sup>	In-house specification	Buffer component	1.32	2.97 mg	0.63 mg	0.4 mg
Water for Injection	USP-NF, Ph. Eur.	Solvent/vehicle	q.s.	q.s.	q.s.	q.s.
Processing Aids/Residues <sup>d</sup>						
Ethanol	Ph. Eur.	Processing aid	N/A			
Citric acid monohydrate	Ph. Eur.	Processing aid				
Sodium citrate	Ph. Eur.	Processing aid				
Sodium hydroxide	Ph. Eur.	Processing aid				
HEPES	In-house specification	Drug substance buffer component				
EDTA	Ph. Eur., USP-NF	Drug substance buffer component				

a. Values are rounded to maintain the same level of precision as the label claim, with trailing decimals not shown, where applicable.

b. Also known as Trometamol

c. Also known as Tromethamine HCl and Trometamol HCl

d. The processing aids and drug substance formulation buffer components are residues that are essentially removed through the manufacturing process and are not considered ingredients (excipients).

Abbreviations: ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate); ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide; DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine; q.s. = quantum satis (as much as may suffice); HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; EDTA = edetate disodium dihydrate; MDV= multi-dose vial; SDV= single-dose vial; N/A= Not applicable

**Table 3.2.P.1-4. Composition of Drug Product, 10 µg RNA dose in 0.2 mL Injection Volume, 10 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>a,b</sup>	Amount per dose
BNT162b2 (XBB.1.5) drug substance	In-house specification	Active ingredient	0.10	130 µg	10 µg
ALC-0315	In-house specification	Functional lipid	1.43	1.86 mg	0.14 mg
ALC-0159	In-house specification	Functional lipid	0.18	0.23 mg	0.02 mg
DSPC	In-house specification	Structural lipid	0.31	0.40 mg	0.03 mg
Cholesterol	Ph. Eur.	Structural lipid	0.62	0.81 mg	0.06 mg
Sucrose	USP-NF, Ph. Eur.	Cryoprotectant	103	133.9 mg	10.3 mg
Tromethamine (Tris base) <sup>c</sup>	USP-NF, Ph. Eur.	Buffer component	0.20	0.26 mg	0.02 mg
Tris (hydroxymethyl) aminomethane hydrochloride (Tris HCl) <sup>d</sup>	In-house specification	Buffer component	1.32	1.71 mg	0.13 mg
Water for Injection	USP-NF, Ph. Eur.	Solvent/vehicle	q.s.	q.s.	q.s.
<b>Processing Aids/Residues<sup>e</sup></b>					
Ethanol	Ph. Eur.	Processing aid	N/A		
Citric acid monohydrate	Ph. Eur.	Processing aid			
Sodium citrate	Ph. Eur.	Processing aid			
Sodium hydroxide	Ph. Eur.	Processing aid			
HEPES	In-house specification	Drug substance buffer component			
EDTA	Ph. Eur., USP-NF	Drug substance buffer component			

**Table 3.2.P.1-4. Composition of Drug Product, 10 µg RNA dose in 0.2 mL Injection Volume, 10 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>a,b</sup>	Amount per dose
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- a. Vials filled at 1.3 mL drug product and diluted to 2.6 mL with 0.9% sodium chloride (NaCl) prior to administration. NaCl at 11.7 mg/vial and 0.9 mg/dose after dilution.
- b. Values are rounded to maintain the same level of precision as the label claim, with trailing decimals not shown, where applicable.
- c. Also known as Trometamol
- d. Also known as Tromethamine HCl and Trometamol HCl
- e. The processing aids and drug substance formulation buffer components are residues that are essentially removed through the manufacturing process and are not considered ingredients (excipients).

Abbreviations:

ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine

HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; EDTA = edetate disodium dihydrate;

q.s. = quantum satis (as much as may suffice)

N/A= Not applicable

**Table 3.2.P.1-5. Composition of Drug Product, 3 µg RNA dose in 0.2 mL Injection Volume, 10 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>a b</sup>	Amount per dose
BNT162b2 (XBB.1.5) drug substance	In-house specification	Active ingredient	0.1	40 µg	3 µg
ALC-0315	In-house specification	Functional lipid	1.43	0.57 mg	0.04 mg
ALC-0159	In-house specification	Functional lipid	0.18	0.07 mg	0.006 mg
DSPC	In-house specification	Structural lipid	0.31	0.12 mg	0.01 mg
Cholesterol	Ph. Eur.	Structural lipid	0.62	0.25 mg	0.02 mg
Sucrose	USP-NF, Ph. Eur.	Cryoprotectant	103	41.2 mg	3.2 mg
Tromethamine (Tris base) <sup>c</sup>	USP-NF, Ph. Eur.	Buffer component	0.20	0.08 mg	0.006 mg
Tris (hydroxymethyl) aminomethane hydrochloride (Tris HCl) <sup>d</sup>	In-house specification	Buffer component	1.32	0.53 mg	0.04 mg
Water for Injection	USP-NF, Ph. Eur.	Solvent/vehicle	q.s.	q.s.	q.s.
<b>Processing Aids/Residues<sup>e</sup></b>					
Ethanol	Ph. Eur.	Processing aid	N/A		
Citric acid monohydrate	Ph. Eur.	Processing aid			
Sodium citrate	Ph. Eur.	Processing aid			
Sodium hydroxide	Ph. Eur.	Processing aid			
HEPES	In-house specification	Drug substance buffer component			
EDTA	Ph. Eur., USP-NF	Drug substance buffer component			

**Table 3.2.P.1-5. Composition of Drug Product, 3 µg RNA dose in 0.2 mL Injection Volume, 10 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>a b</sup>	Amount per dose
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- a. Vials filled at 0.4 mL drug product and diluted to 2.6 mL with 0.9% sodium chloride (NaCl) prior to administration. NaCl at 19.8 mg/vial and 1.52 mg/dose after dilution.
- b. Values are rounded to maintain the same level of precision as the label claim, with trailing decimals not shown, where applicable.
- c. Also known as Trometamol
- d. Also known as Tromethamine HCl and Trometamol HCl
- e. The processing aids and drug substance formulation buffer components are residues that are essentially removed through the manufacturing process and are not considered ingredients (excipients).

## Abbreviations:

ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine

HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; EDTA = edetate disodium dihydrate;

q.s. = quantum satis (as much as may suffice)

N/A= Not applicable



**Table 3.2.P.1-6. Composition of Drug Product, 3 µg RNA dose in 0.3 mL Injection Volume, 3 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>ab</sup>	Amount per dose
BNT162b2 (XBB.1.5) drug substance	In-house specification	Active ingredient	0.033	16 µg	3 µg
ALC-0315	In-house specification	Functional lipid	0.472	0.227 mg	0.04 mg
ALC-0159	In-house specification	Functional lipid	0.059	0.028 mg	0.005 mg
DSPC	In-house specification	Structural lipid	0.1	0.048 mg	0.01 mg
Cholesterol	Ph. Eur.	Structural lipid	0.21	0.1 mg	0.02 mg
Sucrose	USP-NF, Ph. Eur.	Cryoprotectant	103	49.44 mg	9.4 mg
Tromethamine (Tris base) <sup>c</sup>	USP-NF, Ph. Eur.	Buffer component	0.20	0.10 mg	0.02 mg
Tris (hydroxymethyl) aminomethane hydrochloride (Tris HCl) <sup>d</sup>	In-house specification	Buffer component	1.32	0.63 mg	0.12 mg
Water for Injection	USP-NF, Ph. Eur.	Solvent/vehicle	q.s.	q.s.	q.s.
<b>Processing Aids/Residues<sup>e</sup></b>					
Ethanol	Ph. Eur.	Processing aid	N/A		
Citric acid monohydrate	Ph. Eur.	Processing aid			
Sodium citrate	Ph. Eur.	Processing aid			
Sodium hydroxide	Ph. Eur.	Processing aid			
HEPES	In-house specification	Drug substance buffer component			
EDTA	Ph. Eur., USP-NF	Drug substance buffer component			

**Table 3.2.P.1-6. Composition of Drug Product, 3 µg RNA dose in 0.3 mL Injection Volume, 3 Dose Multi-dose Vials, Dilution Required:**

Name of Ingredients	Reference to Standard	Function	Concentration Prior to Dilution (mg/mL)	Amount per vial after dilution <sup>ab</sup>	Amount per dose
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- a. Vials filled at 0.48 mL drug product and diluted to 1.58 mL with 0.9% sodium chloride (NaCl) prior to administration. NaCl at 9.9 mg/vial and 1.88 mg/dose after dilution.
- b. Values are rounded to maintain the same level of precision as the label claim, with trailing decimals not shown, where applicable.
- c. Also known as Trometamol
- d. Also known as Tromethamine HCl and Trometamol HCl
- e. The processing aids and drug substance formulation buffer components are residues that are essentially removed through the manufacturing process and are not considered ingredients (excipients).

## Abbreviations:

ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

DSPC = 1,2-distearoyl-sn-glycero-3-phosphocholine

HEPES = 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; EDTA = edetate disodium dihydrate;

q.s. = quantum satis (as much as may suffice)

N/A= Not applicable