ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼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. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Kostaive powder for dispersion for injection
COVID-19 sa-mRNA Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial and must be reconstituted before use.

One vial contains 16 doses of 0.5 mL after reconstitution with 10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection; see sections 4.2 and 6.6.

One dose (0.5 mL) contains 5 micrograms of zapomeran, a COVID-19 self-amplifying messenger RNA (sa-mRNA) (encapsulated in lipid nanoparticles).

Zapomeran is a single-stranded, 5'-capped sa-mRNA replicon, produced using a cell-free *in vitro* transcription from the corresponding DNA templates encoding a replicase and the spike glycoprotein of the ancestral strain of SARS-CoV-2 with D614G mutation.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for dispersion for injection

White to off-white lyophilised cake or powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kostaive is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older.

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

4.2 Posology and method of administration

Posology

A single dose of 0.5 mL.

For individuals who have previously been vaccinated with a COVID-19 vaccine, Kostaive should be administered at least 5 months after the most recent dose.

Severely immunocompromised adults

Additional doses may be administered to individuals who are severely immunocompromised in accordance with official recommendations (see section 4.4).

Paediatric population

The safety and efficacy of Kostaive in children and adolescents less than 18 years of age have not been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥ 60 years of age.

Method of administration

Kostaive must be administered intramuscularly after reconstitution (see section 6.6).

Preferred site for the intramuscular injection is the deltoid muscle of the upper arm.

Use of a needle length appropriate for intramuscular injection is recommended.

The vaccine should not be injected intravascularly, subcutaneously, or intradermally.

The vaccine should not be mixed with any other vaccines or medicinal products in the same syringe.

For precautions to be taken before and after administering the vaccine, see section 4.4.

For instructions on reconstitution of the vaccine before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Cases of hypersensitivity, including anaphylaxis, have been reported with Kostaive (see section 4.8). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. No further dose of the vaccine should be given to those who have experienced anaphylaxis after a prior dose of Kostaive.

Myocarditis and pericarditis

An increased risk of myocarditis and pericarditis has been observed following vaccination with some other COVID-19 vaccines. These conditions can develop within a few days and primarily occur within 14 days. They have been observed more often in younger males.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccine recipients (including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions, may occur in association with vaccination as a psychogenic response to the needle injection. Procedures should be in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy and safety of the vaccine have not been assessed in immunocompromised individuals, including those with a known diagnosis of the human immunodeficiency virus (HIV) or those receiving immunosuppressant therapy (see section 5.1). The efficacy of Kostaive may be lower in immunocompromised individuals.

Limitations of vaccine effectiveness

As with any vaccine, vaccination with Kostaive may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their vaccination.

Excipients with known effect

Potassium
This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially "potassium-free".

Sodium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration of Kostaive with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of Kostaive in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Administration of Kostaive in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

No effects on the breast-fed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to Kostaive is negligible. Kostaive can be used during breast-feeding.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

Kostaive has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

Primary vaccination series

The most frequent adverse reactions (≥ 10%) after dose 1 or dose 2 are pain at the injection site (49.1%), tenderness at the injection site (49.0%), fatigue (42.3%), headache (35.4%), myalgia (30.1%), chills (28.5%), arthralgia (27.2%), dizziness (20.1%), and pyrexia (10.8%). The majority of adverse reactions were mild in intensity and resolved within a few days of vaccination. One case of anaphylaxis was reported as related to Kostaive (see section 4.4).

Booster dose

The overall safety profile for participants who received a booster dose of Kostaive was similar to that seen after 2 doses (primary vaccination series).

Tabulated list of adverse reactions

The safety profile presented below is based on data from 2 clinical studies:

- Study ARCT-154-01, conducted to evaluate the safety, immunogenicity, and efficacy of a 2-dose regimen of Kostaive, involving participants 18 years of age and older who received at least one dose of Kostaive (N=8 807).
- Study ARCT-154-J01, conducted to evaluate the safety and immunogenicity for booster immunisation. In this study, a single dose of Kostaive was administered to participants aged 18 years or older (N=420) who had previously received 3 doses of authorised COVID-19 mRNA vaccines at least 3 months prior to enrollment.

Adverse reactions observed during clinical studies are listed according to the following frequency categories:
Very common (≥ 1/10)
Common (≥ 1/100 to < 1/10)
Uncommon (≥ 1/1 000 to < 1/100)
Rare (≥ 1/10 000 to < 1/1 000)
Very rare (< 1/10 000)
Not known (cannot be estimated from the available data)

Table 1 Adverse reactions

MedDRA System Organ Class	Adverse reactions	Frequency
Immune system disorders	Hypersensitivity (e.g., rash, urticaria, allergic dermatitis, type IV hypersensitivity) Anaphylaxis	Uncommon Very rare
Nervous system disorders	Headache Dizziness	Very common Very common
Gastrointestinal disorders	Diarrhoea Nausea Vomiting	Common Common Common
Musculoskeletal and connective tissue disorders	Arthralgia Myalgia	Very common Very common
General disorders and administration site conditions	Injection site pain Injection site tenderness Fatigue/malaise Chills Pyrexia Injection site swelling Injection site induration Injection site erythema Injection site pruritus	Very common Very common Very common Very common Very common Common Common Common Common

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of an overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, COVID-19 vaccines, RNA-based vaccine, ATC code: J07BN01

Mechanism of action

Kostaive is composed of a self-amplifying mRNA encoding the spike protein of SARS-CoV-2, encapsulated in lipid nanoparticles. The self-amplifying mRNA is designed to produce extra copies of mRNA within the host cells after intramuscular injection, to achieve enhanced expression of the spike protein antigen. This gives rise to neutralising antibody and cellular immune responses to the spike antigen, which contributes to protection against COVID-19. The mRNA self-amplification process is transient and does not generate infectious particles.

Clinical efficacy

Study ARCT-154-01 was a randomised, controlled, observer-blind, multicentre clinical study conducted in participants 18 years of age and older in Vietnam at a time when the dominant variant was delta.

The efficacy was evaluated in the mITT analysis set, including 15 458 participants, 7 762 in Kostaive (zapomeran) group and 7 696 in placebo group.

Randomisation was stratified by age (< 60 or ≥ 60 years of age) and, for participants < 60 years of age, by risk of severe COVID-19 (those with asthma, cancer, cerebrovascular disease, chronic kidney/liver/lung disease, cystic fibrosis, diabetes mellitus Type 1 or 2, cardiovascular conditions, mental health conditions, smoking, pulmonary fibrosis, Down syndrome, obesity, sickle cell disease, or substance abuse disorder). All participants ≥ 60 years of age were deemed to be at high risk for severe COVID-19. Among participants who received Kostaive, 5.5% (n=485) had significant underlying medical conditions, including cardiovascular diseases, diabetes, obesity, liver disorders, chronic obstructive pulmonary disease (COPD), and asthma. The study excluded participants who were immunocompromised, including those with a known diagnosis of the human immunodeficiency virus (HIV) or taking immunosuppressive medication, and those who had a previous clinical or microbiological diagnosis of COVID-19.

Participants with pre-existing acute or chronic medical conditions, including participants with known infection with hepatitis C virus (HCV) or hepatitis B virus (HBV) disease, were eligible for inclusion. Demographic and baseline characteristics were similar between groups for individuals in the 2 age cohorts and by risk groups. Among the total participants who received Kostaive, 49% were male and 51% were female, 99.6% were Asian, and 0.4% were described as "other" for race, respectively. At the time of vaccination, the mean age of the population was 46.4 years (age range 18-89 years).

The overall primary efficacy endpoint was vaccine efficacy (VE), defined as the first occurrence of virologically confirmed, protocol-defined COVID-19 with onset between day 36 (7 days after dose 2) and day 92, inclusive.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after dose 2, vaccine efficacy against confirmed COVID-19 occurring at least 7 days after dose 2 was 56.7% (95% confidence interval: 48.8% to 63.4%). The number of COVID-19 cases was 200 and 440 in the Kostaive and placebo groups, respectively. At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for in total 1 146 person-years for Kostaive and in total 1 120 person-years in the placebo group.

The information relating to the evaluation of overall vaccine efficacy is presented in Table 2.

Table 2 Vaccine efficacy against virologically confirmed, protocol-defined COVID-19 between day 36 and day 92 – modified intent-to-treat (mITT) population

Subgroup	Kostaive	Placebo	VE % (95% CI)[a]
All participants			
N	7 762	7 696	56.7 (48.8 – 63.4)
Number of confirmed COVID-19 cases, n (%)	200 (2.6)	440 (5.7)	
Surveillance time[b] (person-years)	1 146.2	1 120.2	
Healthy ≥ 18 to < 60 years			
N	3 882	3 896	49.8 (37.8 – 59.5)
Number of confirmed COVID-19 cases, n (%)	126 (3.2)	246 (6.3)	
Surveillance time[b] (person-years)	572.1	566.1	
At risk ≥ 18 to < 60 years			
N	2 519	2 471	

Number of confirmed COVID-19 cases, n (%)	46 (1.8)	138 (5.6)	69.7 (57.6 – 78.3)
Surveillance time[b] (person-years)	372.9	359.5	
≥ 60 years			
N	1 361	1 329	53.5 (26.8 – 70.5)
Number of confirmed COVID-19 cases, n (%)	28 (2.1)	56 (4.2)	
Surveillance time[b] (person-years)	201.2	194.5	

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; N, number of participants at risk; n, number of participants with case reported; RR, relative risk; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VE, vaccine efficacy.
mITT, modified intent-to-treat (includes all participants who received all protocol-required doses of study vaccine (Kostaive or placebo) up to the evaluation timepoint, and who have no evidence of SARS-CoV-2 infection on day 1 or up to 7 days after the 2nd vaccination in the study).
'At-risk' was defined as individuals that are considered to have higher risk of developing severe COVID-19.
a VE is calculated by 1-HR from cox regression adjusting for risk group and region of study site, or 1-RR when number of confirmed cases is 0 in the Kostaive group.
b The surveillance time refers to the total person-time at risk in years for the given endpoint.

Efficacy against severe COVID-19

The efficacy of Kostaive for the prevention of virologically confirmed severe COVID-19, including death, was evaluated (Table 3). Severe COVID-19 comprised any of the following: respiratory rate ≥ 30 per minute, heart rate ≥ 125 per minute, oxygen saturation level (SpO2) ≤ 93% on room air at sea level or arterial oxygen partial pressure (PO2)/fractional inspired oxygen (FiO2) < 300 mm Hg, respiratory failure (defined as needing high flow oxygen, noninvasive ventilation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO)), shock (defined as systolic blood pressure < 90 mm Hg, diastolic blood pressure < 60 mm Hg, or requirement for vasopressors), significant acute renal, hepatic, or neurologic dysfunction, admission to an intensive care unit, death. The endpoint was the first occurrence of confirmed, protocol-defined severe COVID-19 with onset between days 36 and 92, inclusive.

Table 3 Vaccine efficacy against virologically confirmed, protocol-defined severe COVID-19 between day 36 and day 92 – modified intent-to-treat (mITT) population

Subgroup	Kostaive	Placebo	VE % (95% CI)[a]
All participants			
N	7 762	7 696	95.3 (80.5-98.9)
Number of confirmed COVID-19 cases, n (%)	2 (0.0)	41 (0.5)	
Surveillance time[b] (person-years)	1 162.9	1 154.7	
Healthy ≥ 18 to < 60 years			
N	3 882	3 896	100.0 (NE)
Number of confirmed COVID-19 cases, n (%)	0 (0.0)	15 (0.4)	
Surveillance time[b] (person-years)	582.7	585.8	
At risk ≥ 18 to < 60 years			
N	2 519	2 471	89.5 (16.8-98.7)
Number of confirmed COVID-19 cases, n (%)	1 (0.0)	9 (0.4)	
Surveillance time[b] (person-years)	376.9	370.9	
≥ 60 years			
N	1 361	1 329	94.4 (58.2-99.3)
Number of confirmed COVID-19 cases, n (%)	1 (0.1)	17 (1.3)	
Surveillance time[b] (person-years)	203.4	197.9	

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; N, number of participants at risk; n, number of participants with case reported; NE, not estimable; RR, relative risk; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VE, vaccine efficacy.
mITT, modified intent-to-treat (includes all participants who received all protocol required doses of study vaccine (Kostaive or placebo) up to the evaluation timepoint, and who have no evidence of SARS-CoV-2 infection on day 1 or up to 7 days after the 2nd vaccination in the study)
a VE is calculated by 1-HR from cox regression adjusting for risk group and region of study site, or 1-RR when number of confirmed cases is 0 in the Kostaive group.
b The surveillance time refers to the total person-time at risk in years for the given endpoint.

Immunogenicity in participants 18 years of age and older after booster dose

The evaluation of immunogenicity administered as a booster dose is based on the results of Study ARCT-154-J01, conducted in Japan, which compared the immune response that followed a booster dose of Kostaive (zapomeran) with that of the comparator (tozinameran, BNT162b2) in adult individuals who previously received the primary vaccination series and 1 booster dose with authorised COVID-19 mRNA vaccines. In this study, immunogenicity was assessed using a virus neutralisation assay against ancestral SARS-CoV-2 strain and Omicron BA.4/5 variant.

The primary objective of Study ARCT-154-J01 was to demonstrate the noninferiority of Kostaive compared to the comparator vaccine in terms of ratio of geometric mean antibody titres (GMTs) and difference in seroresponse rates (SRR) against ancestral SARS-CoV-2 strain on day 29 after vaccination. In case the noninferiority is demonstrated for ancestral strain, similar testing was to be performed for Omicron BA.4/5 variant. When the second noninferiority is demonstrated, the superiority of Kostaive versus the comparator for Omicron BA.4/5 variant was tested. Additional testing of GMTs up to 6 months was conducted to assess the duration of the antibody response.

A total of 828 participants were enrolled in the study and randomised (1:1) to Kostaive and comparator vaccine group. At the time of vaccination, the mean age was 48 years (age range 18-77 years). Of 828 participants, who were randomised and received the study vaccine, 759 participants were included in Per Protocol Set 1 (PPS-1), the analysis set for the primary immunogenicity endpoint.

The results of Study ARCT-154-J01 are presented in Table 4. One month after vaccination, Kostaive demonstrated noninferiority versus the comparator vaccine against ancestral SARS-CoV-2 strain and superiority against Omicron BA.4/5 variant. Longer term immunogenicity data showed that neutralising antibodies persisted, with approximately 2-fold higher GMTs detected for Kostaive compared to the comparator vaccine at 3 and 6 months after vaccination, for both strains.

Table 4 Summary of immune response against SARS-CoV-2 ancestral strain and Omicron BA.4/5 variant up to 6 months following administration of booster dose

Strain	Time Point Endpoint	GMT / SRR (95% CI)				GMT ratio / SRR difference (95% CI)
		N[a]	Kostaive	N[a]	Comparator*	
Ancestral strain (Wuhan-Hu-1)	Pre-vaccination GMT	385	813 (716, 924)	374	866 (755, 993)	0.94 (0.78, 1.13)
	1 month GMT	385	5 641 (4 321, 7 363)	374	3 934 (2 993, 5 169)	1.43[b] (1.26, 1.63)
	1 month SRR	385	65.2 (60.2, 69.9)	374	51.6 (46.4, 56.8)	13.6[b] (6.8, 20.5)
	3 months GMT	369	5 928 (5 414, 6 491)	356	2 899 (2 648, 3 175)	2.04[c] (1.80, 2.32)
	6 months GMT	332	4 119 (3 723, 4 557)	313	1 861 (1 667, 2 078)	2.21[c] (1.91, 2.57)

Omicron BA.4/5	Pre-vaccination GMT	385	275 (227, 335)	374	292 (236, 360)	0.94 (0.71, 1.26)
	1 month GMT	385	2 551 (1 687, 3 859)	374	1 958 (1 281, 2 993)	1.30[d] (1.07, 1.58)
	1 month SRR	385	69.9 (65.0, 74.4)	374	58.0 (52.8, 63.1)	11.6[d] (4.9, 18.3)
	3 months GMT	369	1 892 (1 646, 2 175)	356	888 (764, 1 031)	2.13[c] (1.74, 2.61)
	6 months GMT	332	1 119 (960, 1 305)	313	495 (413, 595)	2.26[c] (1.78, 2.86)

Abbreviations: CI, confidence interval; GMT, geometric mean titre; SARS-CoV-2, severe acute respiratory syndrome coronavirus; SRR, seroresponse rate.
Log-transformed neutralising antibody titre value for day 29 (1 month) was analysed using Analysis of Covariance (ANCOVA) model. Gender and period from last (3rd) vaccination (< 5 months, ≥ 5 months) were used as factors as prespecified in the protocol. GMTs at baseline, 3 and 6 months are unadjusted.
If a measured antibody titre is below the lower limit of quantitation, the value was imputed as 1/2 of the quantitation limit.
Seroresponse is defined as at least 4-fold increase of post-booster neutralising antibody titres from the baseline titre or from half of the lower limit of quantitation if undetectable at baseline.
a N = number of participants with valid assay results for the specific assay at the given sampling time point.
b Pre-specified criteria were met for noninferiority: the lower limit (LL) of 95% confidence interval (CI) for ratio of GMTs (Kostaive/comparator) exceeds 0.67, and the LL of 95% CI for the difference in SRRs (Kostaive minus comparator) exceeds -10%. Superiority test for ancestral strain was not pre-specified. Analysis was conducted in the PPS-1.
c Analysis was conducted in the PPS-1-ic, a modified version from PPS-1 in which participants with a positive nucleocapsid antibody test were excluded from all subsequent immunogenicity analyses.
d Pre-specified criteria were met for both noninferiority and superiority. Superiority criteria: the LL of 95% CI for GMT ratio exceeds 1.0, and the LL of 95% CI for SRR difference exceeds 0%. Analysis was conducted in the PPS-1.
* Comparator: tozinameran (BNT162b2)

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Kostaive in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat-dose toxicity and reproductive and developmental toxicity.

General toxicity

A general toxicity study was conducted with Kostaive in rabbits (intramuscularly receiving a total of 3 doses, each exceeding the human dose, once every 2 weeks).

Transient increases in mean body temperature (increases of up to ~1.7 °C), changes in laboratory tests (erythroid changes consistent with decreased erythropoiesis secondary to inflammation, minimally or mildly decreased platelet counts, minimally increased neutrophil and/or monocyte counts, mildly or moderately increased fibrinogen, and minimally increased globulin and/or minimally decreased serum albumin and increases in serum cytokines), as well as inflammatory findings in the spleen, lymph nodes (increased lymphocyte cellularity), consistent with an inflammatory response were observed.

Genotoxicity/carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine (lipids and mRNA) are not expected to have genotoxic potential.

Reproductive toxicity

Reproductive and developmental toxicity was investigated in rabbits in a combined fertility, embryo-foetal, and postnatal development study where female rabbits were intramuscularly vaccinated prior to mating, and during gestation (receiving 5 doses of vaccine each exceeding the human dose spanning between premating day 28 and gestational day 28). SARS-CoV-2 neutralising antibody responses were present in maternal animals from prior to mating to the end of the study on gestational day 28 as well as in foetus and offspring, indicating placental transfer of the maternal antibodies.

There were no vaccine-related effects noted on female fertility, development of the embryo and foetus or postnatal growth and development. No Kostaive data for excretion into milk are available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Di(pentadecan-8-yl)-4,4'-((((3-(dimethylamino)propyl)thio)carbonyl)azanediyl)dibutyrate (ATX-126)
Cholesterol
1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
Sucrose
Potassium sorbate
Sodium chloride
Trometamol
Poloxamer 188 (contains the antioxidant butylated hydroxytoluene)

6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

6.3 Shelf life

Unopened vial

2 years at -15 °C to -25 °C.
Vials can be stored at room temperature (up to 25 °C) for up to 4 hours before reconstitution.

Reconstituted medicinal product

After preparation, the reconstituted vaccine vial must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration and must be administered within 6 hours of initial puncture of the vial stopper.

Once thawed or reconstituted, the vaccine should not be refrozen.

Chemical and physical in-use stability has been demonstrated for 6 hours at 2 °C to 25 °C and includes transportation during this time. From a microbiological point of view, once the vial stopper has been punctured for reconstitution of the vaccine, the product may be stored for a maximum of 6 hours under refrigerated conditions or at room temperature (2 °C to 25 °C). Other in-use storage times and conditions are the responsibility of the user.

The reconstituted vaccine should be disposed of after 6 hours.

6.4 Special precautions for storage

Store in a freezer at -15 °C to -25 °C. Store in the original carton in order to protect from light.

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

6.5 Nature and contents of container

Powder contained in a vial (type I glass) with a stopper (bromobutyl rubber) and a plastic flip-off cap with seal (aluminum crimp).

Each multidose vial contains 16 doses of 0.5 mL; see section 6.6.

Pack size: 20 multidose vials.

6.6 Special precautions for disposal and other handling

Handling instructions

The vaccine should be prepared by a healthcare professional using aseptic techniques to ensure the sterility of the prepared dispersion.

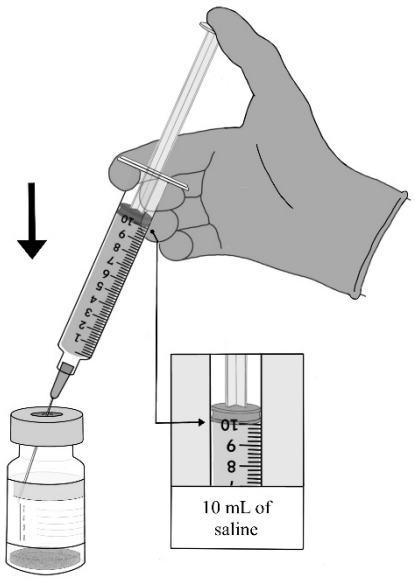
ONLY use 10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection or equivalent for reconstitution.

Upon reconstitution, the vaccine is a white to off-white opalescent suspension (pH: 7.5-8.5); osmolality: 300-400 mOsm/kg.

After reconstitution, each vial contains 16 doses of 0.5 mL.

Extract 0.5 mL of vaccine into individual use syringes.

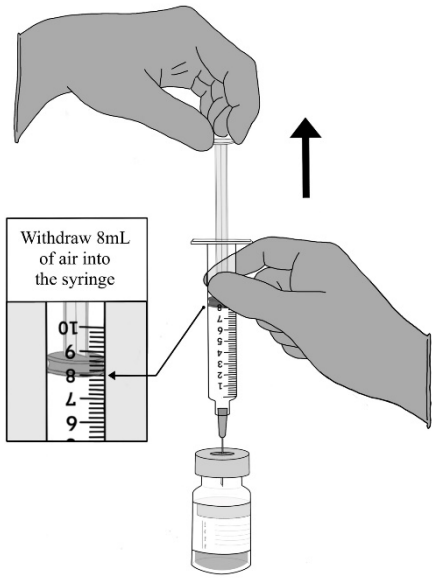
- Each dose must contain 0.5 mL of reconstituted dispersion for injection.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL, do not administer the remainder. Instead, discard the vial and any remaining volume.
- Excess vaccine from multiple vials should not be pooled.
- After preparation, the filled syringes must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration (including transportation during this time) and must be administered within 6 hours of initial puncture of the vial stopper.
- The reconstituted vaccine should be disposed of after 6 hours.

Preparation of individual doses of Kostaive powder for dispersion for injection	
STEP A. Visual inspection and temperature equilibration of vials 1. Bring the vial to room temperature for at least one hour. Vials can be stored at room temperature (up to 25 °C) for up to 4 hours before reconstitution. 2. Visually inspect for discolouration and gross defects/damages to container closure (e.g., breaks, glass shards, loose caps, missing stoppers, etc.). • Vial should contain white/off-white solid. DO NOT USE if there is damage to the container or other defects. DO NOT USE if unpunctured vial is at room temperature longer than 4 hours.	
STEP B. Addition of saline to vaccine 1. Reconstitution should be done immediately following complete temperature equilibration. 2. Obtain sodium chloride 9 mg/mL (0.9%) solution for injection (saline). Using a new sterile 10-mL syringe and 23G needle, withdraw 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. 3. Remove the vial flip-off cap. 4. Use an alcohol wipe on the vial stopper. To ensure that 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection is added, the syringe should not be removed from the vial during steps 5-8. 5. Puncture the stopper with the saline syringe needle. • Record the date and time of initial stopper puncture and the time at which the vaccine should be discarded. (Note that vaccine must be administered within 6 hours of this stopper puncture.) 6. Slowly add half (5 mL) of the 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection into the vial along the sidewall. 7. Equalise the vial pressure by withdrawing approximately 3 mL of air from the vial into the saline syringe while keeping the needle above the liquid. 8. For the second and third additions of sodium chloride 9 mg/mL (0.9%) solution for injection, add 2 to 3 mL, directing the solution flow onto the inside wall of the product vial. • Follow each addition with a withdrawal of air from the vial using the saline syringe to equalise the vial pressure. Repeat the steps as needed to complete the addition of all 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. Do not add more than 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection.	

Preparation of individual doses of Kostaive powder for dispersion for injection

STEP C. Equalise vial pressure

1. After the addition of sodium chloride 9 mg/mL (0.9%) solution for injection is complete, equalise the pressure before removing the needle from the vial by withdrawing air to the 8-mL line of the empty saline syringe.
2. Take care to adjust the position of the needle to be above the solution (to avoid inadvertent withdrawal of the reconstituted vaccine).
3. Remove the empty saline syringe and needle from the vial and discard.



STEP D. Mix and visually inspect the reconstituted vaccine

1. Gently invert the vial repeatedly for at least 1 minute until the solid is completely reconstituted.
    - Do not shake or vortex.
    - Avoid foaming and frothing.
2. Visually inspect the vaccine vial for particulates and discolouration. The liquid should be a white to off-white opalescent suspension.
    - DO NOT USE if particulates or discolouration are observed.
3. The reconstituted vaccine vial or filled syringes must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration and must be used within 6 hours of initial stopper puncture.

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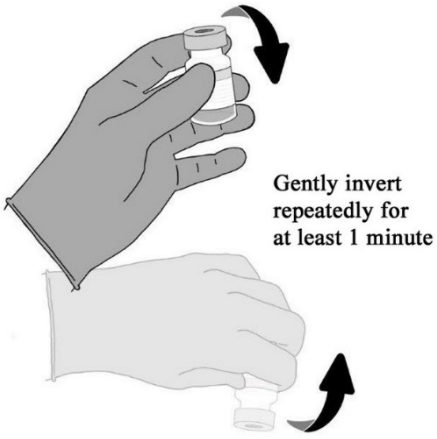
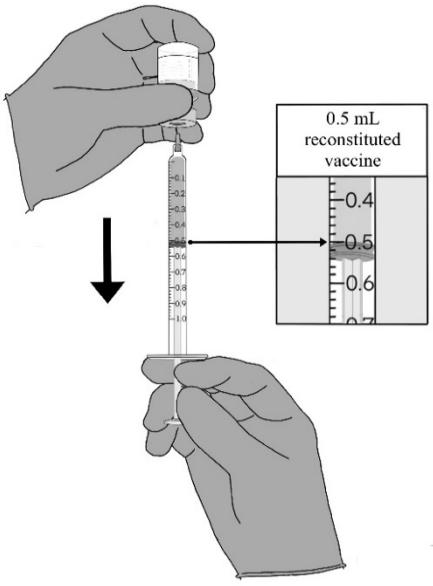


STEP E. Preparation of syringe

1. Ensuring that there are no air bubbles, withdraw 0.5 mL of the vaccine using a sterile 1 mL syringe.
2. Record the date and time of initial stopper puncture.
    - Each filled syringe will be used for one dose.
    - Store filled syringes under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration.
    - Each syringe should be used as soon as possible but must be used within 6 hours of the initial stopper puncture of the vial.



Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Arcturus Therapeutics Europe B.V.
Claude Debussylaan 10
1082 MD Amsterdam
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1873/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Catalent Pharma Solutions, LLC
726 Heartland Trail
Madison, WI 53717 USA

Name and address of the manufacturer(s) responsible for batch release

MIAS Pharma Limited
Suite 1 First Floor
Stafford House
Strand Road
Portmarnock
Co. Dublin
D13 WC83
Ireland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;

- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Kostaive powder for dispersion for injection
COVID-19 sa-mRNA Vaccine
zapomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, each vial contains 16 doses of 0.5 mL.
One dose (0.5 mL) contains 5 micrograms of zapomeran.

3. LIST OF EXCIPIENTS

Excipients: Lipid ATX-126, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), sucrose, potassium sorbate, sodium chloride, trometamol, poloxamer 188.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for dispersion for injection
20 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store unopened vial in a freezer at -15 °C to -25 °C in the original carton in order to protect from light.

After reconstitution, store the vaccine at 2 °C to 25 °C and **use within 6 hours**.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Arcturus Therapeutics Europe B.V.
Claude Debussylaan 10
1082 MD Amsterdam
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1873/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTIDOSE VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Kostaive powder for dispersion for injection
COVID-19 sa-mRNA Vaccine
zapomeran

IM

2. METHOD OF ADMINISTRATION

Intramuscular injection

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

After reconstitution, 16 doses of 0.5 mL

6. OTHER

Discard date/time:

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Kostaive powder for dispersion for injection
COVID-19 sa-mRNA Vaccine
zapomeran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kostaive is and what it is used for

Kostaive is a vaccine that helps protect adults aged 18 years and older against COVID-19 caused by SARS-CoV-2.

Kostaive works by preparing the body to defend itself against COVID-19. It contains a molecule called sa-mRNA which has instructions for making copies of the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

When a person is given the vaccine, some of their cells will read the sa-mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise the protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it.

If, later on, the person comes into contact with SARS-CoV-2, their immune system will recognise it and be ready to defend the body against it.

As Kostaive does not contain the virus to produce immunity, it cannot give you COVID-19.

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

2. What you need to know before you are given Kostaive

The vaccine must not be given

- if you are allergic to the active substance or any of the other ingredients of this vaccine (listed in section 6).

Warnings and precautions

Talk to your doctor, pharmacist, or nurse before you are given the vaccine if:
- you have ever had a severe allergic reaction or breathing problems after any other vaccine injection or after you were given Kostaive in the past.
- you are feeling nervous about the vaccination process or have ever fainted following any needle injection.
- you have a high fever or severe infection, however, you may be able to have your vaccination if you have a mild fever or upper airway infection like a cold.
- you have a bleeding problem, you bruise easily, or you use a medicine to prevent blood clots.
- you have a weakened immune system, because of a disease such as HIV infection or a medicine such as corticosteroid that affects your immune system.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist, or nurse before you are given Kostaive.

An increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) exists after vaccination with other COVID-19 vaccines. These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

Children and adolescents
Kostaive is not recommended for children aged below 18 years. Currently there is not enough information available on the use of Kostaive in children and adolescents younger than 18 years of age.

Other medicines and Kostaive
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines, or have recently been given any other vaccine.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, or think you may be pregnant, tell your doctor or pharmacist before you are given this vaccine.

There are limited data with the use of this vaccine in pregnant women.

Kostaive can be given during breastfeeding.

Driving and using machines
Some of the side effects of Kostaive listed in section 4 (Possible side effects) may temporarily reduce your ability to drive and use machines. Wait until any effects of the vaccine have worn off before you drive or use machines.

Kostaive contains potassium and sodium
This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially "potassium-free". This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How Kostaive is given

Kostaive is given as a single injection of 0.5 mL into a muscle of your upper arm.

If you were previously vaccinated with a COVID-19 vaccine, you should receive a dose of Kostaive at least 5 months after the most recent dose.

If you have any further questions on the use of Kostaive, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very rare side effects: may affect up to 1 in 10 000 people
- anaphylaxis (sudden, severe allergic reaction with symptoms including breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness)

Seek **urgent** medical assistance if you experience any of the symptoms of anaphylaxis.

Talk to your doctor or nurse if you develop any other side effects. These can include:

Very common side effects: may affect more than 1 in 10 people
- pain where the injection was given
- tenderness where the injection was given
- feeling tired (fatigue)
- chills
- fever
- joint pain (arthralgia)
- muscle pain (myalgia)
- headache
- feeling dizzy.

Common side effects: may affect up to 1 in 10 people
- diarrhoea
- feeling sick (nausea)
- vomiting
- hardening of the skin where the injection was given
- swelling where the injection was given
- redness where the injection was given
- itchy skin where the injection was given.

Uncommon side effects: may affect up to 1 in 100 people
- allergic reactions (hives and/or rash).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this vaccine.

5. How to store Kostaive

Keep this medicine out of the sight and reach of children.

The following information about storage, expiry, use, and handling is intended for healthcare professionals.

Do not use this medicine after the expiry date, which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store unopened vials in a freezer at -15 °C to -25 °C. Store in the original carton in order to protect from light. Vials can be stored at room temperature (up to 25 °C) for up to 4 hours before reconstitution.

After preparation, the reconstituted vaccine vial or filled syringes must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration (including during transportation) and must be administered within 6 hours of initial puncture of the product stopper.

Temperature-equilibrated vials can be handled in room light conditions.

Once thawed or reconstituted, the vaccine should not be refrozen.

6. Contents of the pack and other information

What Kostaive contains

- The active substance is a self-amplifying messenger RNA (sa-mRNA) called zapomeran.
- This is a multidose vial that, after reconstitution, contains 16 doses of 0.5 mL each.
- One dose (0.5 mL) contains 5 micrograms of zapomeran (encapsulated in lipid nanoparticles).
- The other ingredients are: di(pentadecan-8-yl)-4,4' ((((3(dimethylamino)propyl)thio)carbonyl)azanediyl)dibutyrate (ATX-126), cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG), sucrose, potassium sorbate, sodium chloride, trometamol and poloxamer 188 (contains the antioxidant butylated hydroxytoluene). See section 2 “Kostaive contains potassium and sodium”.

What Kostaive looks like and the contents of the pack

Kostaive is a white to off-white lyophilised powder/cake supplied in a glass vial with a rubber stopper and aluminum seal.

Upon reconstitution, the vaccine is a white to off-white opalescent suspension (pH: 7.5-8.5). Each vial contains 16 doses of 0.5 mL.

Pack size: 20 multidose vials

Marketing Authorisation Holder and Manufacturer
Arcturus Therapeutics Europe B.V.
Claude Debussylaan 10
1082 MD, Amsterdam
The Netherlands

Manufacturer:
MIAS Pharma Limited
Suite 1 First Floor
Stafford House
Strand Road
Portmarnock
Co. Dublin
D13 WC83
Ireland

This leaflet was last revised in .

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

<--->

The following information is intended for healthcare professionals only:

A single dose of 0.5 mL.

For individuals who have previously been vaccinated with a COVID-19 vaccine, Kostaive should be administered at least 5 months after the most recent dose.

Traceability
In order to improve the traceability of biological medicinal products, the name and the lot number of the administered product should be clearly recorded.

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

- ONLY use 10 mL of sterile sodium chloride 9 mg/mL (0.9%) solution for injection for reconstitution.

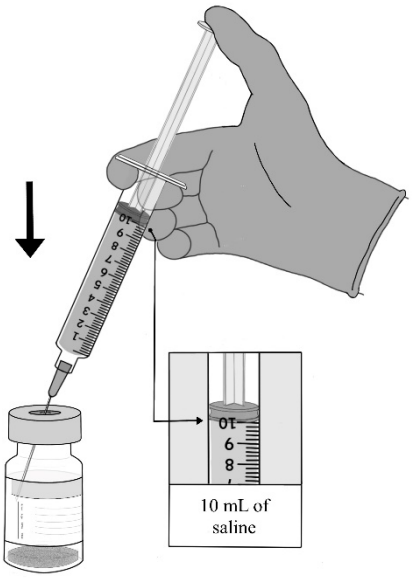
After reconstitution, each vial contains 16 doses of 0.5 mL.

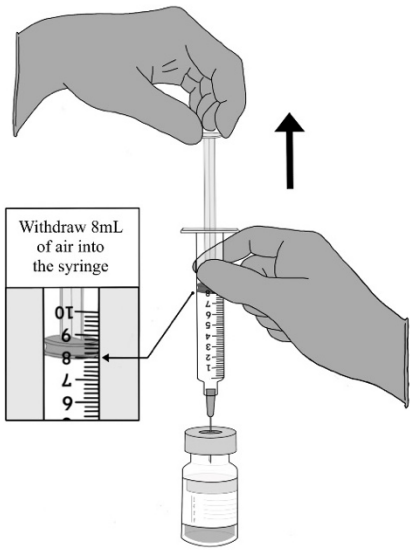
Extract 0.5 mL of vaccine into individual use syringes.

- Each dose must contain 0.5 mL of reconstituted Kostaive.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL, do not administer the remainder. Instead, discard the vial and any remaining volume.
- Do not pool excess vaccine from multiple vials.
- After preparation, the filled syringes must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration (including transportation during this time) and must be administered within 6 hours of initial puncture of the vial stopper.
- The reconstituted vaccine should be disposed of after 6 hours.

<table>
<tr><th colspan="2">Preparation of individual doses of Kostaive powder for dispersion for injection</th></tr>
<tr><td>STEP A. Visual inspection and temperature equilibration of vials
1. Bring the vial to room temperature for at least one hour. Vials can be stored at room temperature (up to 25 °C) for up to 4 hours before reconstitution.
2. Visually inspect for discolouration and gross defects/damages to container closure (e.g., breaks, glass shards, loose caps, missing stoppers, etc.).
• Vial should contain white/off-white solid.

DO NOT USE if there is damage to the container or other defects.
DO NOT USE if unpunctured vial is at room temperature longer than 4 hours.</td><td></td></tr>
<tr><td>STEP B. Addition of saline to vaccine
1. Reconstitution should be done immediately following complete temperature equilibration.
2. Obtain sodium chloride 9 mg/mL (0.9%) solution for injection (saline). Using a new sterile 10-mL syringe and 23G needle, withdraw 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection.
3. Remove the vial flip-off cap.
4. Use an alcohol wipe on the vial stopper.

To ensure that 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection is added, the syringe should not be removed from the vial during steps 5-8.
5. Puncture the stopper with the saline syringe needle.
• Record the date and time of initial stopper puncture and the time at which the vaccine should be discarded. (Note that vaccine must be administered within 6 hours of this stopper puncture.)
6. Slowly add half (5 mL) of the 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection into the vial along the sidewall.
7. Equalise the vial pressure by withdrawing approximately 3 mL of air from the vial into the saline syringe while keeping the needle above the liquid.
8. For the second and third additions of sodium chloride 9 mg/mL (0.9%) solution for injection, add 2 to 3 mL, directing the solution flow onto the inside wall of the product vial.
• Follow each addition with a withdrawal of air from the vial using the saline syringe to equalise the vial pressure. Repeat the steps as needed to complete the addition of all 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. Do not add more than 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection.</td><td> 
</td></tr>
</table>

<table>
<tr><th colspan="2">Preparation of individual doses of Kostaive powder for dispersion for injection</th></tr>
<tr><td>STEP C. Equalise vial pressure
1. After the addition of sodium chloride 9 mg/mL (0.9%) solution for injection is complete, equalise the pressure before removing the needle from the vial by withdrawing air to the 8-mL line of the empty saline syringe.
2. Take care to adjust the position of the needle to be above the solution (to avoid inadvertent withdrawal of the reconstituted vaccine).
3. Remove the empty saline syringe and needle from the vial and discard.</td><td> 
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1. Gently invert the vial repeatedly for at least 1 minute until the solid is completely reconstituted.
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• Avoid foaming and frothing.
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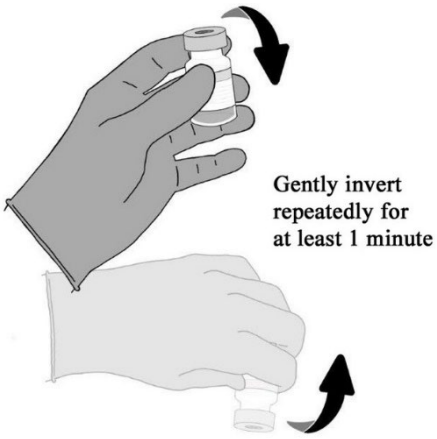
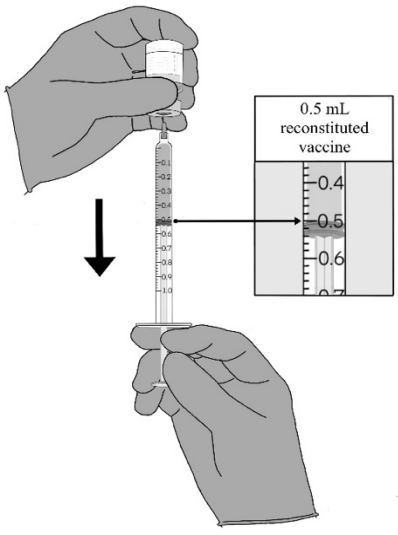
• DO NOT USE if particulates or discolouration are observed.
3. The reconstituted vaccine vial or filled syringes must be stored under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration and must be used within 6 hours of initial stopper puncture.</td><td> 
</td></tr>
<tr><td>STEP E. Preparation of syringe
1. Ensuring that there are no air bubbles, withdraw 0.5 mL of the vaccine using a sterile 1 mL syringe.
2. Ensure that there are no air bubbles.
3. Record the date and time of initial stopper puncture.
• Each filled syringe will be used for one dose.
• Store filled syringes under refrigerated conditions or at room temperature (2 °C to 25 °C) prior to administration.
• Each syringe should be used as soon as possible but must be used within 6 hours of the initial stopper puncture.</td><td> 
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Disposal

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