NEW ZEALAND DATA SHEET

1. PRODUCT NAME

JYNNEOS suspension for subcutaneous injection 5 x 10^8 to 3.95 x 10^8 infectious units

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

JYNNEOS is a live vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus. MVA-BN is grown in primary Chicken Embryo Fibroblast (CEF) cells suspended in a serum-free medium containing no material of direct animal origin, harvested from the CEF cells, purified and concentrated by several Tangential Flow Filtration (TFF) steps including benzonase digestion.

Each 0.5 mL dose is formulated to contain 0.5 x 10^8 to 3.95 x 10^8 infectious units of MVA-BN live virus in 10 mM Tris (tromethamine), 140 mM sodium chloride at pH 7.7.

Each 0.5 mL dose may contain residual traces of host-cell DNA (≤ 20 mcg), chicken protein (≤ 500 mcg), benzonase (≤ 0.0025 mcg), gentamicin (≤ 0.400 mcg) and ciprofloxacin (≤ 0.005 mcg) (see section 4.3).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for subcutaneous injection

When thawed, JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Non replicating) is a milky, light yellow to pale white coloured suspension for subcutaneous injection.

JYNNEOS is a sterile vaccine formulated without preservatives.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

JYNNEOS is indicated for prevention of mpox disease in adults 18 years of age and older:

- At risk of occupational exposure to mpox
- At risk of mpox infection during a local mpox outbreak
- At risk of mpox infection because they
    - Gay, bisexual, men who have sex with men, transgender or nonbinary people who in the past 6 months have had one of the following
        - A new diagnosis of a sexually transmitted disease
        - More than one sex partner
        - Sex at a commercial venue
        - Sex in association with a large public event in an area where mpox transmission is occurring
    - Sexual partners of the people with the above risks
    - People who anticipate experiencing any of the above.

4.2 Dose and method of administration

For subcutaneous injection only.
Appropriate medical treatment must be available to manage possible anaphylactic reactions following administration of JYNNEOS.

Dose

Administer two doses (0.5 mL each) of JYNNEOS at least 4 weeks apart.

There is no information on the need for a booster dose.

Paediatric population
The safety and efficacy of JYNNEOS in children below 18 years have not been established.
No data are available.

Method of administration

Allow the vaccine to thaw and reach room temperature before use.

Swirl the vial gently before use for at least 30 seconds.
Withdraw a dose of 0.5 mL into a sterile syringe for injection.

Administer JYNNEOS by subcutaneous injection, preferably into the upper arm.

For instructions on handling of the medicine 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 or trace residues (chicken protein, benzonase, gentamicin and ciprofloxacin).

JYNNEOS is contraindicated in subjects with known hypersensitivity to eggs or to any other component of the vaccine.

4.4 Special warnings and precautions for use

Severe Allergic Reactions

Persons who experienced a severe allergic reaction following a previous dose of JYNNEOS or following exposure to any component of JYNNEOS may be at increased risk for severe allergic reactions after JYNNEOS. The risk for a severe allergic reaction should be weighed against the risk for disease due to monkeypox.

Concurrent illness
Immunisation should be postponed in individuals suffering from an acute severe febrile illness or acute infection. The presence of a minor infection and/or low grade fever does not need to result in deferral of vaccination.

Anxiety-related reactions

Anxiety-related reactions including vasovagal reactions (syncope), hyperventilation or stress-related reactions have been reported following vaccination with JYNNEOS. Procedures should be in place to avoid injury from fainting.

Altered Immunocompetence

Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response to JYNNEOS.

Limitations of Vaccine Effectiveness

The protective efficacy of JYNNEOS against mpox has not been studies in humans see section 5.1. Vaccination with JYNNEOS may not protect all recipients.

Individuals with atopic dermatitis
Individuals with atopic dermatitis developed more local and general symptoms after vaccination see section 4.8.

Immunocompromised individuals
In HIV infected individuals with CD4 counts ≥ 100 cells/microlitre and ≤ 750 cells per microlitre lower immune response have been observed. There are no data on the immune response in other immunosuppressed individuals

4.5 Interaction with other medicines and other forms of interaction

No interaction studies with other vaccines or medicinal products have been performed. Therefore, concomitant administration of JYNNEOS with other vaccines should be avoided.
The concomitant administration of the vaccine with any immunoglobulin including Vaccinia Immune Globulin (VIG) has not been studied and should be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited data (less than 300 pregnancy outcomes) from use of JYNNEOS in pregnant people. Available human data on JYNNEOS administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

The effect of JYNNEOS on embryo-fetal and post-natal development was evaluated in four developmental toxicity studies conducted in female rats and rabbits. In two studies, rats were administered a single human dose of JYNNEOS (0.5 mL) once prior to mating and on one or two occasions during gestation. In the third study, rats were administered a single human dose of JYNNEOS (0.5 mL) on two occasions during gestation. In the fourth study, rabbits were administered a single human dose of JYNNEOS (0.5 mL) once prior to mating and on two occasions during gestation. These animal studies revealed no evidence of harm to the fetus.

As a precautionary measure it is preferable to avoid the use of JYNNEOS in pregnancy. Administration in pregnancy should only be considered when the potential benefits to the mother outweigh the potential risks to the mother and fetus.

Breast-feeding

Risk Summary
It is not known whether JYNNEOS is excreted in human milk. Data are not available to assess the effects of JYNNEOS in the breastfed infant or on milk production/excretion.

Administration of JYNNEOS during breast-feeding should only be considered when the potential benefits outweigh any potential risks to the mother and baby.

Fertility
Animal studies did not reveal any evidence of impaired female or male fertility.

4.7 Effects on ability to drive and use machines

There is no information on the effect of JYNNEOS on the ability to drive or use machines. However, some of the undesirable effects mentioned in sections 4.4 and 4.8 may affect the ability to drive or use machines (e.g. dizziness).

4.8 Undesirable effects

Summary of the safety profile

The overall clinical trial program included 22 studies and a total of 7,859 individuals 18 through 80 years of age who received at least 1 dose of JYNNEOS (7,093 smallpox vaccine-naïve and 766 smallpox vaccine-experienced individuals). For the purpose of pooling safety data, a later study with freeze-dried formulation of JYNNEOS (>1,100 subjects) was added for completeness.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice. There is the possibility that broad use of JYNNEOS could reveal adverse reactions not observed in clinical trials.

Table 1:
Adverse Reactions Reported in Completed Clinical Trials[a] with MVA-BN (N = 8992[b] subjects)

MedDRA System Organ Class	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)	Unknown *
Infections and infestations	-	-	Nasopharyngitis, Upper respiratory tract infection	Sinusitis, Influenza, Conjunctivitis, Gastroenteritis	
Blood and lymphatic system disorders	-	-	Lymphadenopathy		

MedDRA System Organ Class	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)	Unknown *
Metabolism and nutrition disorders	-	Appetite disorder	-		
Psychiatric disorders	-	-	Sleep disorder		
Nervous system disorders	Headache	-	Dizziness, Paresthesia	Migraine, Peripheral sensory neuropathy, Somnolence	Acute peripheral facial paralysis (Bell's palsy)
Ear and labyrinth disorders	-	-		Vertigo, Ear pain	
Cardiac disorders	-	-	-	Tachycardia	
Respiratory, thoracic and mediastinal disorders	-	-	Pharyngolaryngeal pain, Rhinitis, Cough	Oropharyngeal pain	
Gastrointestinal disorders	Nausea	-	Diarrhea, Vomiting, Dry mouth	Abdominal Pain	
Skin and subcutaneous tissue disorders	-	-	Rash, Pruritus, Dermatitis, Urticaria	Skin discolouration, Hyperhidrosis, Ecchymosis, Night sweats, Subcutaneous nodule, Angioedema	
Musculoskeletal and connective tissue disorders	Myalgia	Pain in extremity, Arthralgia	Musculoskeletal stiffness, Neck pain	Back pain, Muscle spasms, Musculoskeletal pain, Muscular weakness	

MedDRA System Organ Class	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)	Unknown *
General disorders and administration site conditions	Injection site pain, Injection site erythema, Injection site swelling, Injection site induration, Injection site pruritus, Fatigue	Rigor/Chills, Injection site nodule, Injection site discolouration, Injection site haematoma, Injection site warmth, Axillary pain	Underarm swelling, Malaise, Injection site haemorrhage, Injection site irritation, Flushing, Chest pain, Injection site bruising, Injection site vesicles,	Injection site exfoliation, Injection site inflammation, Injection site paraesthesia, Injection site reaction Injection, site rash, Oedema, peripheral Asthenia, Injection site anesthesia, Injection site dryness, Injection site movement impairment, Influenza like illness	
Investigations	-	Body temperature increased, Pyrexia	Troponin I increased, Hepatic enzyme increased, White blood cell count decreased, Mean platelet volume decreased	White blood cell count increased	
Injury, poisoning and procedural complications	-	-	-	Contusion	

Note: The frequency groups for adverse drug reactions, and the naming conventions for these groups, are based on the WHO guidance for reporting adverse events following immunization (AEFI).

[a] POX-MVA-001, -002, -004, -005, -006, -007, -008, -009, -010, -011, -013, -023, -024, -027, -028, -029, -030, -031, -036, -037, -03X, HIV-NEF-004 and HIV-POL-002

[b] 8 subjects exposed but not included in analysis. 7 subjects in POX-MVA-009 received Dryvax either on the same day or within 7 days after MVA-BN administration and were therefore not included to avoid a potential bias in the adverse event reporting. 1 subject in POX-MVA-029 was not vaccinated according to the randomization, therefore removed from analysis set.

*cannot be estimate from the available data

Serious Adverse Events

The integrated analyses of serious adverse events (SAEs) pooled safety data across 22 studies, which included a total of 7,093 smallpox vaccine-naïve subjects and 766 smallpox vaccine-experienced subjects who received at least 1 dose of JYNNEOS and 1,206 smallpox vaccine-naïve subjects who received placebo only. SAEs were monitored from the day of the first study vaccination through at least 6 months after the last study vaccination.

Among the smallpox vaccine-naïve subjects, SAEs were reported for 1.5% of JYNNEOS recipients and 1.1% of placebo recipients. Among the smallpox vaccine-experienced subjects enrolled in studies without a placebo comparator, SAEs were reported for 2.3% of JYNNEOS recipients. Across all studies, a causal relationship to JYNNEOS could not be excluded for 4 SAEs, all non-fatal, which included Crohn's disease, sarcoidosis, extraocular muscle paresis and throat tightness.

Cardiac Adverse Events of Special Interest

Evaluation of cardiac adverse events of special interest (AESIs) included any cardiac signs or symptoms, ECG changes determined to be clinically significant, or troponin-I elevated above 2 times the upper limit of normal. In the 22 studies, subjects were monitored for cardiac-related signs or symptoms through at least 6 months after the last vaccination.

The numbers of JYNNEOS and placebo recipients, respectively, with troponin-I data were: baseline level (6,376 and 1,203); level two weeks after first dose (6,279 and 1,166); level two weeks after second dose (1,683 and 193); unscheduled visit, including for clinical evaluation of suspected cardiac adverse events (500 and 60).

Cardiac AESIs were reported to occur in 1.3% (95/7,093) of JYNNEOS recipients and 0.2% (3/1,206) of placebo recipients who were smallpox vaccine-naïve. Cardiac AESIs were reported to occur in 2.1% (16/766) of JYNNEOS recipients who were smallpox vaccine-experienced. The higher proportion of JYNNEOS recipients who experienced cardiac AESIs was driven by 28 cases of asymptomatic post-vaccination elevation of troponin-I in two studies: Study 5, which enrolled 482 HIV-infected subjects and 97 healthy subjects, and Study 6, which enrolled 350 subjects with atopic dermatitis and 282 healthy subjects. An additional 127 cases of asymptomatic post-vaccination elevation of troponin-I above the upper limit of normal but not above 2 times the upper limit of normal were documented in JYNNEOS recipients throughout the clinical development program, 124 of which occurred in Study 5 and Study 6. Proportions of subjects with troponin-I elevations were similar between healthy and HIV-infected subjects in Study 5 and between healthy and atopic dermatitis subjects in Study 6. A different troponin assay was used in these two studies

compared to the other studies, and these two studies had no placebo controls. The clinical significance of these asymptomatic post-vaccination elevations of troponin-I is unknown.

Among the cardiac AESIs reported, 6 cases (0.08%) were considered to be causally related to JYNNEOS vaccination and included tachycardia, electrocardiogram T wave inversion, electrocardiogram abnormal, electrocardiogram ST segment elevation, electrocardiogram T wave abnormal, and palpitations.

None of the cardiac AESIs considered causally related to study vaccination were considered serious.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

No case of overdose has been reported.

In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, other viral vaccines, ATC code: J07BX

Mechanism of Action

JYNNEOS is an attenuated, live, non-replicating smallpox and monkeypox vaccine that elicits humoral and cellular immune responses to orthopoxviruses. Vaccinia neutralizing antibody responses in humans were evaluated to establish the effectiveness of JYNNEOS for prevention of smallpox and monkeypox.

Clinical efficacy and safety

Clinical studies
Vaccine Effectiveness
Vaccine effectiveness against smallpox was inferred by comparing the immunogenicity of JYNNEOS to a licensed smallpox vaccine (ACAM2000) based on a Plaque Reduction Neutralization Test (PRNT) using the Western Reserve strain of vaccinia virus and was supported by efficacy data from animal challenge studies. *[see Nonclinical Toxicology (13.2)]*

Vaccine effectiveness against monkeypox was inferred from the immunogenicity of JYNNEOS in a clinical study and from efficacy data from animal challenge studies.
[see Nonclinical Toxicology (13.2)]

Immunogenicity

Study 7 [7] (N=433) was a randomized, open-label study conducted at US military facilities in South Korea to compare the immunogenicity of JYNNEOS to ACAM2000 in healthy smallpox vaccine-naïve adults 18 through 42 years of age. Subjects were randomized to receive either two doses of JYNNEOS (N=220) administered 28 days apart or one dose of ACAM2000 (N=213). In the total study population, the mean age was 24 years and 23 years in subjects receiving JYNNEOS and ACAM2000, respectively; 82.3% and 86.4% of the subjects were men; 57.3% and 63.8% were white/Caucasian, 21.8% and 18.8% black/African American, 6.4% and 5.6% Asian, 3.6% and 2.8% American Indian/Alaska Native, 2.3% and 1.4% Native Hawaiian/Other Pacific, 8.6% and 7.5% other racial groups, and 24.5% and 18.8% of Hispanic/Latino ethnicity (JYNNEOS and ACAM2000, respectively).

The primary immunogenicity endpoint was geometric mean titer (GMT) of vaccinia neutralizing antibodies assessed by PRNT at "peak visits" defined as two weeks after the second dose of JYNNEOS and four weeks after the single dose of ACAM2000. Analyses of antibody responses were performed in the per-protocol immunogenicity (PPI) population, consisting of individuals who received all vaccinations and completed all visits up until the peak visit without major protocol violations pertaining to immunogenicity assessments. Table 2 presents the pre-vaccination and "peak visit" PRNT GMTs from Study 7.

Table 2: Comparison of Vaccinia-Neutralizing Antibody Responses Following Vaccination with JYNNEOS or ACAM2000 in Healthy Smallpox Vaccine-Naïve Adults 18 through 42 Years of Age, Study 7[x], Per Protocol Set for Immunogenicity[y]

Time Point	JYNNEOS[a] (N=185) GMT[b] [95% CI]	ACAM2000[a] (N=186) GMT[b] [95% CI]
Pre-Vaccination	10.1 [9.9, 10.2]	10.0 [10.0, 10.0]
Post-Vaccination "Peak Visit"[y]	152.8[c] [133.3, 175.0]	84.4[c] [73.4, 97.0]

[x] NCT01913353

[y] Per Protocol Set for Immunogenicity included subjects who received all vaccinations, completed all visits up until the specified "peak visits" (two weeks after the second dose of JYNNEOS or 4 weeks after the single dose of ACAM2000) without major protocol violations pertaining to immunogenicity assessments.

[a] JYNNEOS was administered as a series of two doses given 28 days apart, and ACAM2000 was administered as a single dose.

[b] GMT of vaccinia-neutralizing antibody titers assessed by plaque reduction neutralization test (PRNT) using the Western Reserve vaccinia strain. Values below the assay lower limit of quantitation (LLOQ) of 20 were imputed to a titer of 10; the proportions of subjects with pre-vaccination titers less than the assay lower limit of detection were 98.9% among subjects randomized to JYNNEOS and 97.8% among subjects randomized to ACAM2000, respectively.

[c] Non-inferiority of the "peak visit" PRNT GMT for JYNNEOS compared to ACAM2000 was demonstrated as the lower bound of the 1-sided 97.5% CI for the GMT ratio (JYNNEOS/ACAM2000) was > 0.5.

N: Number of subjects in the specified treatment group; GMT: Geometric Mean Titer; 95% CI: 95% confidence interval, lower limit and upper limit.

PRNT GMTs were also evaluated at pre-specified time points post-vaccination and prior to the "peak visits". The PRNT GMTs at two and four weeks after the first dose of JYNNEOS (prior to the second dose), were 23.4 (95% CI: 20.5, 26.7) and 23.5 (95% CI: 20.6, 26.9), respectively. The PRNT GMT at two weeks after the single dose of ACAM2000 was 23.7 (95% CI: 20.9, 26.8).

Paediatric population

The safety and efficacy of JYNNEOS in children below 18 years have not been established.

Elderly

Clinical studies of JYNNEOS did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Carcinogenesis, Mutagenesis, Impairment of Fertility

JYNNEOS has not been evaluated for carcinogenic or mutagenic potential, or for impairment of male fertility in animals. Developmental toxicity studies conducted in rats and rabbits vaccinated with JYNNEOS revealed no evidence of impaired female fertility (see section 4.6 Fertility, pregnancy and lactation).

Animal Toxicology and/or Pharmacology

The efficacy of JYNNEOS to protect cynomolgus macaques (*Macaca fascicularis*) against a monkeypox virus (MPXV) challenge was evaluated in several studies. Animals were administered Tris-Buffered Saline (placebo) or JYNNEOS (1×10^8 $TCID_{50}$) sub-cutaneously on day 0 and day 28. On day 63, animals were challenged with MPXV delivered by aerosol (3×10^5 pfu), intravenous (5×10^7 pfu) or intratracheal (5×10^6 pfu) route. Across all studies, 80-100% of JYNNEOS-vaccinated animals survived compared to 0-40% of control animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol
Sodium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years at -20°C +/-5°C
5 years at -50°C +/-10°C
9 years at -80°C +/-10°C

If the vaccine has been stored prior at -20°C, once thawed, it may be kept at +2°C to +8°C for 4 weeks.
If the vaccine has been stored prior at -50°C, once thawed, it may be kept at +2°C to +8°C for up to 24 weeks.

Do not re-freeze a vial once it has been thawed.

6.4 Special precautions for storage

Store in a freezer at -20°C +/-5°C or -50°C +/-10°C or -80°C +/-10°C. Expiry date depends on storage temperature.

For storage conditions after thawing of the medicine, see section 6.3.
Store in the original package to protect from light.
Do not re-freeze a vial once it has been thawed.

6.5 Nature and contents of container

Each dose 0.5 ml of suspension is supplied in a vial (Type I glass) with stopper (bromobutyl rubber). The vial stoppers are not made with natural rubber latex.

Pack sizes of 2, 5, or 15 single-dose vials.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Allow the vaccine to thaw and reach room temperature before use. Swirl the vial gently before use for at least 30 seconds.

When thawed, JYNNEOS is a milky, light yellow to pale white coloured suspension.
The suspension should be visually inspected for particulate matter and discoloration before use. In the event of any damage to the vial, foreign particulate matter and/or variation of physical aspect being observed, discard the vaccine.
A dose of 0.5 ml is withdrawn into a syringe for injection.
Each vial is for single use.

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

No data are available for keeping the product in the syringe before use. Store the drug product at 2-8°C in the original glass vial until right before use; do not draw up the product into the syringe until right before use

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Phone - +64 9 918 5100
Email: HNZvaccines@prnzl.co.nz
Website: www.hcl.co.nz

9. DATE OF FIRST APPROVAL

11 September 2024
Date of publication in the New Zealand Gazette of consent to distribute the medicine: 11 September 2024

10. DATE OF REVISION OF THE TEXT

11 September 2024