COVID-19 VACCINE JANSSEN®

Ad26.COV2.S

DATA SHEET

1. PRODUCT NAME

COVID-19 Vaccine Janssen 5×10^{10} virus particles (VP) in 0.5 mL suspension for injection

COVID-19 vaccine (Ad26.COV2.S [recombinant])

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multi-dose vial which contains 5 doses of 0.5 mL.

One dose (0.5 mL) contains:
Adenovirus type 26 encoding the SARS-CoV-2 spike (S) glycoprotein* (Ad26.COV2-S), 5×10^{10} virus particles (VP) (equivalent to not less than 8.92 $\log_{10}$ infectious units (Inf.U)).

* Produced in the PER.C6® TetR Cell Line and by recombinant DNA technology.

The product contains genetically modified organisms (GMOs) under GMO regulations in other jurisdictions. Please note that under the New Zealand Hazardous Substances and New Organisms (HSNO) Act, this product is not considered a GMO.

Excipients with known effect
Each dose (0.5 mL) contains approximately 2 mg of ethanol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection (injection).

Colourless to slightly yellow, clear to very opalescent suspension (pH 6-6.4).

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

COVID-19 Vaccine Janssen has provisional consent (see section 5.1) for the indication below:

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 Dose and method of administration

Dose

Individuals 18 years of age and older

Primary vaccination

COVID-19 Vaccine Janssen is administered as a single dose of 0.5 mL by intramuscular injection only.

Booster dose

A booster dose (second dose) of 0.5 mL of COVID-19 Vaccine Janssen may be administered intramuscularly at least 2 months after the primary vaccination in individuals 18 years of age and older. Higher immune responses are observed with an interval up to 6 months between primary vaccination and the booster dose (see section 5.1).

A booster dose of the COVID-19 Vaccine Janssen (0.5 mL) may be administered to individuals 18 years of age and older as a heterologous booster dose following completion of primary vaccination with a mRNA COVID-19 Vaccine, an adenoviral vector-based COVID-19 vaccine or an inactivated whole-virion COVID-19 vaccine (see section 5.1). The dosing interval for the heterologous booster dose is the same as that authorised for a booster dose of the vaccine used for primary vaccination (see section 5.1).

Paediatric population

The safety and efficacy of COVID-19 Vaccine Janssen in children and adolescents (less than 18 years of age) have not yet been established. No data are available.

Elderly

No dose adjustment is required in elderly individuals ≥65 years of age. See also sections 4.8 and 5.1.

Method of administration

COVID-19 Vaccine Janssen is for intramuscular injection only, preferably in the deltoid muscle of the upper arm.

Do not inject the vaccine intravascularly, intravenously, subcutaneously or intradermally.

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

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

For instructions on handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- A history of confirmed thrombosis with thrombocytopenia syndrome (TTS) following vaccination with any COVID-19 vaccine (see section 4.4)
- A history of Capillary Leak Syndrome (CLS)

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

Events of anaphylaxis have been reported. 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.

Capillary leak syndrome

Very rare cases of capillary leak syndrome (CLS) have been reported in the first days after vaccination with COVID-19 Vaccine Janssen, in some cases with a fatal outcome. A history of CLS has been reported. CLS is a rare disorder characterised by acute episodes of oedema mainly affecting the limbs, hypotension, haemoconcentration and hypoalbuminaemia. Patients with an acute episode of CLS following vaccination require prompt recognition and treatment. Intensive supportive therapy is usually warranted. Individuals with a known history of CLS should not be vaccinated with this vaccine. See also section 4.3.

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. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

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

Coagulation disorders

- **Thrombosis with thrombocytopenia syndrome**

  A combination of thrombosis and thrombocytopenia, including thrombosis with thrombocytopenia syndrome (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with COVID-19 Vaccine Janssen. This includes severe cases of venous thrombosis at unusual sites such as cerebral venous sinus thrombosis (CVST), splanchnic vein thrombosis as well as arterial thrombosis concomitant with thrombocytopenia. Cases of TTS occurred mostly within the first three weeks following vaccination, in males and females 18 years of age and older and were reported more frequently in females under 50 years of age. Fatal outcome has been reported.

  TTS following administration of COVID-19 Vaccine Janssen has a clinical course that resembles autoimmune heparin-induced thrombocytopenia (HIT).

  Individuals who have experienced HIT should only receive COVID-19 Vaccine Janssen if the potential benefits outweigh the potential risks.

  Individuals who have experienced TTS following vaccination with any COVID-19 vaccine should not receive COVID-19 Vaccine Janssen (see section 4.3).

  In individuals with suspected TTS following administration of COVID-19 Vaccine Janssen, immediate medical care should be provided. The use of heparin may be harmful and alternative treatments may be needed. Thrombosis in combination with thrombocytopenia requires specialised clinical management. Healthcare professionals should consult applicable guidance and/or consult specialists (e.g., haematologists, specialists in coagulation) to promptly diagnose and treat this condition.

  Individuals diagnosed with thrombocytopenia within 3 weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.

- **Immune thrombocytopenia**

  Cases of immune thrombocytopenia (ITP) with very low platelet levels (<20,000 per µL) have been reported very rarely after vaccination with COVID-19 Vaccine Janssen, usually within the first four weeks after receiving COVID-19 Vaccine Janssen. If an individual has a history of ITP, the risks of developing low platelet levels should be considered before vaccination, and platelet monitoring is recommended after vaccination.

Healthcare professionals should be alert to the signs and symptoms of thromboembolism and/or thrombocytopenia. Those vaccinated should be instructed to seek immediate medical attention if they develop symptoms such as shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain following vaccination. Additionally, anyone with neurological symptoms including severe or persistent headaches, seizures, mental status changes or blurred vision after vaccination, or who experiences spontaneous bleeding, skin bruising (petechia) beyond the site of vaccination after a few days, should seek prompt medical attention.

Risk of bleeding with intramuscular administration

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.

Guillain-Barré syndrome

Guillain-Barré syndrome (GBS) has been reported very rarely following vaccination with COVID-19 Vaccine Janssen. Healthcare professionals should be alert of GBS signs and symptoms to ensure correct diagnosis, in order to initiate adequate supportive care and treatment and to rule out other causes.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COVID-19 Vaccine Janssen may be lower in immunosuppressed individuals.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.

Limitations of vaccine effectiveness

Protection starts around 14 days after vaccination. As with all vaccines, vaccination with COVID-19 Vaccine Janssen may not protect all vaccine recipients (see section 5.1).

Excipients

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 mL dose, that is to say essentially ‘sodium-free’.

Ethanol
This medicinal product contains 2 mg of alcohol (ethanol) per 0.5 mL dose. The small amount of alcohol in this medicinal product will not have any noticeable effects.

Paediatric population

The safety and efficacy of COVID-19 Vaccine Janssen in children and adolescents (less than 18 years of age) have not yet been established. No data are available.

4.5 Interactions with other medicines and other forms of interactions

No interaction studies have been performed. Concomitant administration of COVID-19 Vaccine Janssen with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Female reproductive toxicity and fertility were assessed in a combined embryo-foetal and pre- and postnatal development study in the rabbit. In this study a first vaccination of COVID-19 Vaccine Janssen was administered intramuscularly to female rabbits 7 days prior to mating, at a dose equivalent to 2-fold above the recommended human dose, followed by two vaccinations at the same dose during the gestation period (i.e., at gestational days 6 and 20). There were no vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development. The parental females as well as their foetuses and offspring exhibited SARS-CoV-2 S protein-specific antibody titers, indicating that maternal antibodies were transferred to the foetuses during gestation.

In addition, a conventional (repeat-dose) toxicity study in rabbits with COVID-19 Vaccine Janssen did not reveal any effects on male sex organs that would impair male fertility.

Pregnancy - Pregnancy Category B1

There is limited experience with the use of COVID-19 Vaccine Janssen in pregnant women. Animal studies with COVID-19 Vaccine Janssen do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or postnatal development (see Fertility).

Safety data with COVID-19 Vaccine Janssen when administered within 3 months before pregnancy as well as during pregnancy have shown no safety concerns in the mother or child in over 500 reported pregnancies, with over 100 reported pregnancy outcomes.

Administration of COVID-19 Vaccine Janssen in pregnancy should only be considered when the potential benefits outweigh any potential risks to the mother and foetus.

Breast feeding

No COVID-19 Vaccine Janssen data are available on vaccine excretion in milk. It is unknown whether COVID-19 Vaccine Janssen is excreted in human milk.

4.7 Effects of ability to drive and use machines

COVID-19 Vaccine Janssen 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

Clinical trial data

Summary of safety profile

Primary Vaccination (Primary Analysis)

The safety of COVID-19 Vaccine Janssen was evaluated in an ongoing phase 3 study (COV3001). A total of 21 895 adults aged 18 years and older received a single-dose primary vaccination of COVID-19 Vaccine Janssen. The median age of individuals was 52 years (range 18-100 years). The safety analysis was performed once the median follow-up duration of 2 months after vaccination was reached. Longer safety follow-up of >2 months is available for 11 948 adults who received COVID-19 Vaccine Janssen.

In study COV3001, the most common local adverse reactions reported was injection site pain (48.6%). The most common systemic adverse reactions were headache (38.9%), fatigue (38.2%),

myalgia (33.2%) and nausea (14.2%). Pyrexia (defined as body temperature ≥38.0°C) was observed in 9% of participants. Most adverse reactions occurred within 1-2 days following vaccination and were mild to moderate in severity and of short duration (1-2 days).

Reactogenicity was generally milder and reported less frequently in older adults (763 adults ≥65 years old).

The safety profile was generally consistent across participants with or without prior evidence of SARS-CoV-2 infection at baseline; a total of 2 151 adults seropositive at baseline received COVID-19 Vaccine Janssen (9.8%).

Booster Dose (Second Dose) following Primary Vaccination with COVID-19 Vaccine Janssen

Overall, in 5 clinical studies conducted in Belgium, Brazil, Colombia, France, Germany, Japan, Netherlands, Philippines, South Africa, Spain, United Kingdom and the United States, approximately 9000 individuals have received 2 doses of COVID-19 Vaccine Janssen, administered at least 2 months apart and approximately 2700 individuals had at least 2 months of safety follow-up after the booster dose. There were no new safety concerns identified and the data from these individual studies show the reactogenicity of a homologous booster dose of COVID-19 Vaccine Janssen is similar to that seen with the first dose of COVID-19 Vaccine Janssen.

A randomised, double-blind, placebo-controlled Phase 3 Study (COV3009) evaluated the safety of a booster dose (second dose) with COVID-19 Vaccine Janssen administered approximately 2 months after the primary vaccination. A total of 31300 individuals were enrolled in this study, of whom 15708 individuals were randomized to receive 2 doses of COVID-19 Vaccine Janssen. Only 8655 individuals received 2 doses of COVID-19 Vaccine Janssen and 7053 individuals received one dose of COVID-19 Vaccine Janssen during the double-blind phase. A reactogenicity subset of 6068 individuals was included in the analysis, of whom 3016 received one dose of COVID-19 Vaccine Janssen and 3052 received one dose of placebo. Of these, only 2984 individuals received a second dose and were included in the second dose analysis, of whom 1559 received COVID-19 Vaccine Janssen and 1425 received placebo. The median age of individuals was 53.0 years (range: 18-99 years). Demographic characteristics were similar among individuals who received the COVID-19 Vaccine Janssen and those who received placebo.

A randomised, double-blind, placebo-controlled Phase 2 study (COV2001) evaluated the frequency and severity of local and systemic adverse reactions within 7 days of administration of a booster dose with COVID-19 Vaccine Janssen administered approximately 2 months after the primary vaccination in healthy adults 18 through 55 years of age and adults 65 years and older in good or stable health. 137 individuals received both the primary vaccination and the booster dose at an interval of 2 months. The median age of individuals was 48 years, and 48 individuals (34%) were 65 years of age and older.

A randomised, double-blind, placebo-controlled Phase 1/2a study (COV1001) evaluated the safety of a booster dose with COVID-19 Vaccine Janssen in 190 individuals who received a primary dose of COVID-19 Vaccine Janssen and a booster dose at 2 months and 19 individuals who received a primary dose and a booster dose of COVID-19 Vaccine Janssen with a 6-month interval. Across the three Phase 1/2a studies additional supportive safety data of 2 doses of COVID-19 Vaccine Janssen administered at less than 6-month time intervals, are available from a larger set of individuals (N=548).

A randomised, double-blind Phase 2 study (COV2008) evaluated the safety of a booster dose with COVID-19 Vaccine Janssen in individuals 18 years of age and older. Cohort 1 of the study evaluated a homologous booster dose of COVID-19 Vaccine Janssen, administered at least 6 months after the primary vaccination (N=330). The median age of individuals was 57 years.

Booster Dose following Primary Vaccination with a mRNA COVID-19 Vaccine

Overall, in 3 clinical studies (including 2 independent studies) conducted in the United Kingdom and United States, approximately 500 individuals have received primary vaccination with 2 doses of an mRNA COVID-19 vaccine and received a single booster dose of COVID-19 Vaccine Janssen, at least 3 months after primary vaccination. There were no new safety concerns identified. However, a

trend towards an increase in frequency and severity of solicited local and systemic adverse events after the heterologous booster dose was observed when compared with the homologous booster dose of COVID-19 Vaccine Janssen.

Study COV2008 (see study design above) - Cohort 2, evaluated a heterologous booster dose of COVID-19 Vaccine Janssen, administered at least 6 months after completing primary vaccination with 2 doses of Pfizer-BioNTech COVID-19 Vaccine (N=326). The median age of individuals was 45 years. Adverse events were assessed through 28 days after the booster dose.

The safety of a heterologous booster dose of COVID-19 Vaccine Janssen was evaluated in the COV-BOOST study, an independent, multicentre, randomised Phase 2 investigator-initiated study (NCT73765130) conducted in the United Kingdom. Participants were adults aged 30 years or older that had received 2 doses of Pfizer–BioNTech COVID-19 Vaccine (N=106), followed by a booster dose of COVID-19 Vaccine Janssen, and were at least 84 days post second dose at the time of boost. Adverse events were assessed through 28 days after the booster dose.

The safety of a heterologous booster dose of COVID-19 Vaccine Janssen was assessed in an independent Phase 1/2 open-label clinical study (NCT04889209) conducted in the United States. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series, at least 12 weeks prior to enrolment and who reported no history of SARS-CoV-2 infection were randomised to receive a booster dose of COVID-19 Vaccine Janssen (N=100). Adverse events were assessed through 28 days after the booster dose.

Booster Dose following Primary Vaccination an Adenoviral Vector-based COVID-19 Vaccine

The safety of a heterologous booster dose of COVID-19 Vaccine Janssen was evaluated in the COV-BOOST study (see study design above) following primary vaccination with an adenoviral vector-based COVID-19 vaccine. Participants received 2 doses of Oxford-Astra Zeneca COVID-19 vaccine (N=108) followed by a booster dose of COVID-19 Vaccine Janssen, and were at least 70 days post second dose at the time of boost. Adverse events were assessed through 28 days after the booster dose. There were no new safety concerns identified.

Booster Dose following Primary Vaccination with an Inactivated Whole-virion COVID-19 Vaccine

The safety of a heterologous booster dose of COVID-19 Vaccine Janssen was evaluated in the RHH-001 study, an independent, randomised Phase 4 study (RBR-9nn3scw) conducted at 2 sites in Brazil following primary vaccination with an inactivated whole-virion COVID-19 vaccine. Participants were adults 18 years of age or older that had received 2 doses of CoronaVac (N=305) followed by a booster dose of COVID-19 Vaccine Janssen, and were 182 days (plus or minus 30 days) post second dose at the time of boost. Adverse events were assessed through 28 days after the booster dose. There were no new safety concerns identified.

Tabulated list of adverse reactions

Adverse drug reactions observed during study COV3001 are organised by MedDRA System Organ Class (SOC). Frequency categories are defined as follows:
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).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions reported following vaccination with COVID-19 Vaccine Janssen

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)	Not known (cannot be estimated from the available data)
Immune system disorders				Hypersensitivity[a]; urticaria	Anaphylaxis[b]
Nervous system disorders	Headache		Tremor		
Respiratory, thoracic and mediastinal disorders		Cough	Sneezing; oropharyngeal pain		
Gastrointestinal disorders	Nausea				
Skin and subcutaneous tissue disorders			Rash; hyperhidrosis		
Musculoskeletal and connective tissue disorders	Myalgia	Arthralgia	Muscular weakness; pain in extremity; back pain		
General disorders and administration site conditions	Fatigue; injection site pain	Pyrexia; injection site erythema; injection site swelling; chills	Asthenia; malaise		

[a] Hypersensitivity refers to allergic reactions of the skin and subcutaneous tissue.
[b] Cases received from an ongoing open-label study in South Africa.

Postmarketing Data

In addition to the adverse reactions listed above, the following adverse reactions have been reported during postmarketing experience. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Severe and very rare cases of thrombosis in combination with thrombocytopenia have been reported post-marketing. These included venous thrombosis such as cerebral venous sinus thrombosis, splanchnic vein thrombosis, as well as arterial thrombosis (see section 4.4)

In Table 2, the frequencies are provided according to the following convention:
Very common ≥ 1/10 (≥10%)
Common ≥ 1/100 and < 1/10 (≥1% and < 10%)
Uncommon ≥ 1/1000 and < 1/100 (≥ 0.1% and < 1%)
Rare ≥ 1/10000 and < 1/1000 (≥0.01 and < 0.1%)
Very rare < 1/10000, including isolated reports (< 0.01%).
Not known Cannot be estimated from the available data

Table 2: Postmarketing Experience

System Organ Class	Frequency Category Estimated from Spontaneous Reporting Rates	System Organ Class Adverse Reaction
Blood and lymphatic system disorders	Very rare	Lymphadenopathy
Nervous system disorders	Very rare	Paresthesia
	Very rare	Hypoesthesia
	Very rare	Guillain-Barré syndrome
	Uncommon	Dizziness
Anxiety-related reactions	Not known	Syncope
Ear and labyrinth disorders	Very rare	Tinnitus
Gastrointestinal disorders	Very rare	Diarrhea
	Very rare	Vomiting
Vascular disorders	Not known	Capillary leak syndrome

Reporting suspected adverse effects

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 https://nzphvc.otago.ac.nz/reporting/ and include batch or lot number if available.

4.9 Overdose

No case of overdose has been reported. In phase 1/2 studies where a higher dose (up to 2-fold) was administered COVID-19 Vaccine Janssen remained well-tolerated, however vaccinated individuals reported an increase in reactogenicity (increased vaccination site pain, fatigue, headache, myalgia, nausea and pyrexia).

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

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: J07BX03

Mechanism of action

COVID-19 Vaccine Janssen is a monovalent vaccine composed of a recombinant, replication-incompetent human adenovirus type 26 vector that encodes a SARS-CoV-2 full-length spike (S) glycoprotein in a stabilised conformation. Following administration, the S glycoprotein of SARS-CoV-2 is transiently expressed, stimulating both neutralising and other functional S-specific antibodies, as well as cellular immune responses directed against the S antigen, which may contribute to protection against COVID-19.

Clinical efficacy and safety

Efficacy from a Single-dose Primary Vaccination

Primary analysis

A primary analysis (cut-off date 22 January 2021) of a multicentre, randomised, double-blind, placebo-controlled phase 3 study (COV3001) was conducted in the United States, South Africa and Latin American countries to assess the efficacy, safety, and immunogenicity of a single-dose primary vaccination of COVID-19 Vaccine Janssen for the prevention of COVID-19 in adults aged 18 years and older. The study excluded individuals with abnormal function of the immune system resulting from a clinical condition, individuals who are under immunosuppressive therapies within 6 months, as well as pregnant women. Participants with stable HIV infection under treatment were not excluded. Licensed vaccines, excluding live vaccines, could be administered more than 14 days before or more than 14 days after the vaccination in the study. Licensed live attenuated vaccines could be administered more than 28 days before or more than 28 days after the vaccination in the study.

A total of 44 325 individuals were randomised in parallel in a 1:1 ratio to receive an intramuscular injection of COVID-19 Vaccine Janssen or placebo. A total of 21 895 adults received COVID-19 Vaccine Janssen and 21 888 adults received placebo. Participants were followed for a median of 58 days (range: 1-124 days) after vaccination.

The primary efficacy analysis population of 39 321 individuals included 38 059 SARS-CoV-2 seronegative individuals at baseline and 1 262 individuals with an unknown serostatus.

Demographic and baseline characteristics were similar among individuals who received the COVID-19 Vaccine Janssen and those who received placebo. In the primary efficacy analysis population, among the individuals who received COVID-19 Vaccine Janssen, the median age was 52.0 years (range: 18 to 100 years); 79.7% (N=15 646) of individuals were 18 to 64 years old [with 20.3% (N=3 984) aged 65 or older and 3.8% (N=755) aged 75 or older]; 44.3% of individuals were female; 46.8% were from Northern America (United States), 40.6% were from Latin America and 12.6% were from Southern Africa (South Africa). A total of 7 830 (39.9%) individuals had at least one pre-existing comorbidity associated with increased risk of progression to severe COVID-19 at baseline (comorbidities included: obesity defined as BMI ≥30 kg/m^2 (27.5%), hypertension (10.3%), type 2 diabetes (7.2%), stable/well-controlled HIV infection (2.5%), serious heart conditions (2.4%) and asthma (1.3%)). Other comorbidities were present in ≤1% of the individuals.

COVID-19 cases were confirmed by a central laboratory based on a positive SARS-CoV-2 viral RNA result using a polymerase chain reaction (PCR)-based test. Vaccine efficacy overall and by key age groups are presented in Table 3.

Table 3: Analysis of vaccine efficacy against COVID-19[b] in SARS-CoV-2 seronegative adults - primary efficacy analysis population

Subgroup	COVID-19 Vaccine Janssen N=19 630		Placebo N=19 691		% Vaccine Efficacy[c] (95% CI)
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
14 days post-vaccination					
All subjects[a]	116	3 116.57	348	3 096.12	66.9 (59.03; 73.40)
18 to 64 years of age	107	2 530.27	297	2 511.23	64.2 (55.26; 71.61)
65 years and older	9	586.31	51	584.89	82.4 (63.90; 92.38)
75 years and older	0	107.37	8	99.15	100 (45.90; 100.00)
28 days post-vaccination					
All subjects[a]	66	3 102.00	193	3 070.65	66.1 (55.01; 74.80)[d]
18 to 64 years of age	60	2 518.73	170	2 490.11	65.1 (52.91; 74.45)
65 years and older	6	583.27	23	580.54	74.0 (34.40; 91.35)
75 years and older	0	106.42	3	98.06	--

[a] Co-primary endpoint as defined in the protocol.
[b] Symptomatic COVID-19 requiring positive RT-PCR result and at least 1 respiratory sign or symptom or 2 other systemic signs or symptoms, as defined in the protocol.
[c] Confidence intervals for 'All Subjects' were adjusted to implement type I error control for multiple testing. Confidence intervals for age groups are presented unadjusted.

Vaccine efficacy against severe COVID-19 is presented in Table 4 below.

Table 4: Analyses of vaccine efficacy against severe COVID-19[a] in SARS-CoV-2 seronegative adults - primary efficacy analysis population

Subgroup	COVID-19 Vaccine Janssen N=19 630		Placebo N=19 691		% Vaccine Efficacy (95% CI)[b]
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
14 days post-vaccination					
Severe	14	3 125.05	60	3 122.03	76.7 (54.56; 89.09)
28 days post-vaccination					
Severe	5	3 106.15	34	3 082.58	85.4 (54.15; 96.90)

[a] Final determination of severe COVID-19 cases was made by an independent adjudication committee, who also assigned disease severity according to the definition per FDA guidance.
[b] Confidence intervals were adjusted to implement type I error control for multiple testing.

Of the 14 vs. 60 severe cases with onset at least 14 days after vaccination in the COVID-19 Vaccine Janssen group vs. placebo group, 2 vs. 6 were hospitalised. Three individuals died (all in the placebo group). The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO_2) criterion for severe disease (≤93% on room air).

Prior to unblinding, supplementary analyses, considered post-hoc, of positive cases using PCR-based tests regardless of confirmation by the central laboratory generally support the results of the primary analysis.

Beyond 14 days after vaccination, 2 vs. 8 cases of molecularly confirmed COVID-19 were hospitalised, respectively in the COVID-19 Vaccine Janssen vs. placebo group. One case in the placebo group required Intensive Care Unit (ICU) admission and mechanical ventilation. The finding was supported by post-hoc analysis of all COVID-19 related hospitalisations implementing a broader search based on all available information from any source (2 vs. 29 cases in the extended data set).

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates for male and female participants, as well as for participants with and without medical comorbidities associated with high risk of severe COVID-19.

Exploratory subgroup analyses of vaccine efficacy against COVID-19 and severe COVID-19 for Brazil, South Africa, and the United States were conducted (see Table 5). For the subgroup analyses, all COVID-19 cases accrued up to the primary efficacy analysis data cut-off date, including cases confirmed by the central laboratory and cases with documented positive SARS-CoV-2 PCR from a local laboratory which are still awaiting confirmation by the central laboratory, were included.

Table 5: Summary of vaccine efficacy against COVID-19 and severe COVID-19 for countries with >100 reported cases

		Severity	
	Onset	**COVID-19 point estimate (95% CI)**	**Severe COVID-19 point estimate (95% CI)**
US	at least **14 days** after vaccination	74.4% (65.00; 81.57)	78.0% (33.13; 94.58)
	at least **28 days** after vaccination	72.0% (58.19;81.71)	85.9% (-9.38; 99.69)
Brazil	at least **14 days** after vaccination	66.2% (51.01; 77.14)	81.9% (17.01; 98.05)
	at least **28 days** after vaccination	68.1% (48.81; 80.74)	87.6% (7.84; 99.72)
South Africa	at least **14 days** after vaccination	52.0% (30.26; 67.44)	73.1% (40.03; 89.36)
	at least **28 days** after vaccination	64.0% (41.19; 78.66)	81.7% (46.18; 95.42)

Samples from 71.7% of central laboratory confirmed primary analysis cases had been sequenced [United States (73.5%), South Africa (66.9%) and Brazil (69.3%)]. Of the sequenced samples there is an imbalance in the completeness of the dataset between COVID-19 Vaccine Janssen and placebo. In the United States, 96.4% of strains were identified as the Wuhan-H1 variant D614G; in South Africa, 94.5% of strains were identified as the 20H/501Y.V2 variant (B.1.351 lineage); in Brazil, 69.4% of strains were identified to be a variant of the P.2 lineage and 30.6% of strains were identified as the Wuhan-H1 variant D614G.

Final Analyses

The final efficacy analyses at the end of the double-blind phase were performed (cut-off date 09 July 2021) with additional confirmed COVID-19 cases accrued during blinded, placebo-controlled follow-up, with a median follow-up of 4 months after a single dose of COVID-19 Vaccine Janssen in the efficacy analysis population.

Vaccine efficacy estimates against moderate to severe/critical COVID-19 at least 14 days after vaccination was 56.3% (95% CI: 51.30; 60.84) and 52.9% (95% CI: 47.06; 58.08) at least 28 days after vaccination.

Vaccine efficacy estimates against severe/critical COVID-19 at least 14 days after vaccination was 73.3% (95% CI: 63.94; 80.49) and 74.6% (95% CI: 64.70; 82.06) at least 28 days after vaccination. Efficacy against moderate to severe/critical COVID-19, 14 and 28 days after vaccination was 43.8% (95% CI: 34.43; 51.86) and 44.4% (95% CI: 34.61; 52.76), respectively for pooled variant strains/mutations (excluding the reference strain and other minor variants). Efficacy against moderate to severe/critical COVID-19, 14 and 28 days post-dose one from the final analysis was 71.5% (95% CI: 57.31; 81.39) and 58.2% (95% CI: 34.96; 73.72), respectively for the reference strain.

Efficacy against severe/critical COVID-19, 14 and 28 days after vaccination was 70.0% (95% CI: 54.72; 80.61) and 71.8% (95% CI: 56.31; 82.34), respectively for pooled variant strains/mutations (excluding the reference strain and other minor variants). Efficacy against severe/critical COVID-19, 14 and 28 days after vaccination was 89.7% (CI: 57.33; 98.84) and 93.1% (CI: 54.39; 99.84), respectively for the reference strain.

Efficacy of a Booster Dose (Second Dose) following Primary Vaccination with COVID-19 Vaccine Janssen

A global, randomised, placebo-controlled study COV3009 was conducted to demonstrate efficacy of 2 doses of COVID-19 Vaccine Janssen administered with a 56-day interval. A total of 31300 individuals were randomised in the double-blind phase of the study. A total of 15708 individuals received COVID-19 Vaccine Janssen and 15592 individuals received placebo. In total, 14492 (46.3%) individuals were included in the per-protocol efficacy population (7484 individuals received COVID-19 Vaccine Janssen and 7008 individuals received placebo). The study was conducted in multiple regions (North and Latin America, Africa, Europe and Asia) at a time when new lineages of the virus were emerging.

Vaccine efficacy against moderate to severe/critical COVID-19 and severe/critical COVID-19 is presented in Table 6 below:

Table 6: Analysis of vaccine efficacy against moderate to severe/critical and severe/critical COVID-19a – 14 days post-booster dose (second dose)

Endpoint	COVID-19 Vaccine Janssen N=7484[b]		Placebo N=7008[b]		% Vaccine Efficacy (95% CI)[a]
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
Moderate to severe/critical COVID-19	14	1729.99	52	1594.98	75.2 (54.55; 87.30)
Severe/critical COVID-19	0	1730.72	8	1598.87	100 (32.62; 100.00)

[a] Confidence intervals were adjusted to implement type I error control for multiple testing.
[b] Per-protocol efficacy population.

Approximately 68% of centrally confirmed strains have been sequenced as of this analysis (July 2021). Preliminary analysis results of variants with sufficient cases available for meaningful interpretations (Alpha [B.1.1.7)] and Mu [B.1.621]) show that, after the first dose of COVID-19 Vaccine Janssen, efficacy 14 days post-dose for these 2 variants was 75.9% [95% CI: 57.91; 87.02] and 43.9% [95% CI: -12.96; 73.16], respectively which is similar as observed in COV3001. The COVID-19 Vaccine Janssen booster dose increased efficacy for Alpha to 94.2% [95% CI: 62.91; 99.86] and for Mu to 63.1% [95% CI: -27.86; 91.56]. There were no reference strain cases in either the vaccine or placebo group in the follow-up 14 days after the booster dose (≥71 days).

Vaccine efficacy against moderate to severe/critical COVID-19 from 14 days after the booster dose administered at 2 months was 68.8% (95% CI: 9.78; 91.14) in Europe; 65.2% (95% CI: 6.40; 88.85)

in Colombia, 60.0% (95% CI: -144.53; 96.19) in South Africa and 93.7% (95% CI: 58.45; 99.85) in the United States.

Efficacy against moderate to severe/critical COVID-19 14 days post-dose 1 and 14 days after the booster dose (≥71 days) was 66.6% (95% CI: 52.20; 77.07) and 81.6% (95% CI: 57.87; 93.09), respectively for pooled variant strains/mutations (excluding the reference strain and other minor variants). Efficacy against moderate to severe/critical COVID-19 14 days post-dose 1 was 67.9% (95% CI: 57.95; 75.79).

Immunogenicity

Immunogenicity data are based on the following studies:

- Study COV1001 is a randomised, double-blind, placebo-controlled, Phase 1/2a study, conducted in healthy adults ≥18 to ≤55 years of age (Cohort 1 and Cohort 2) and adults ≥65 years of age (Cohort 3).
- Study COV1002 is a randomised, double-blind, placebo-controlled Phase 1 study, conducted in healthy adults ≥20 to ≤55 years of age and ≥65 years.
- Study COV2001 is a randomised, double-blind, placebo-controlled Phase 2a study, conducted in healthy adults ≥18 to ≤55 years of age and adults ≥65 years of age.
- Study COV3001 is a randomised, double-blind, placebo-controlled Phase 3 study, conducted in healthy adults 18 years of age and older.

Across the Phase 1 and 2 studies (COV1001, COV1002, COV2001), COVID-19 Vaccine Janssen elicited a SARS-CoV-2 neutralising antibody response (measured by wild type virus neutralisation assay). In individuals ≥18 to ≤55 years of age, neutralising antibody responder rates were at least 83% and 88% at 14 days and 28 days post-vaccination, respectively and in individuals ≥65 years of age the responder rates were at least 71% and 93% at 14 days and 28 days post-vaccination, respectively.

In the Phase 1/2a study (COV1001), neutralising antibody responder rates increased to at least 96% 56 days post-vaccination and reached 100% 70 days post-vaccination, and were maintained up to at least 84 days post-vaccination in individuals ≥18 to ≤55 years of age. In individuals ≥65 years of age, neutralising antibody responses were maintained from 28 days post-vaccination up to at least 86 days post-vaccination.

Similarly, in the Phase 1/2a study (COV1001), COVID-19 Vaccine Janssen elicited a SARS-CoV-2 spike-binding antibody response (measured by S-ELISA) in at least 99% of individuals ≥18 to ≤55 years of age, 28 days post-vaccination and in at least 73% and 95% of individuals ≥65 years of age, 14 days and 28 days post-vaccination, respectively. Responder rates reached 100%, 56 days post-vaccination and were maintained in individuals ≥18 to ≤55 years of age up to at least 84 days post-vaccination. In individuals ≥65 years of age, binding antibody responses were maintained from 28 days post-vaccination up to at least 86 days post-vaccination.

In the Phase 3 study (COV3001), COVID-19 Vaccine Janssen induced similar SARS-CoV-2 spike-binding antibody responses 28 days post-vaccination in a subset of individuals over 18 years of age from different countries and regions. These responses were consistent with data from the Phase 1/2a Study (COV1001).

In the Phase 1/2a study (COV1001), COVID-19 Vaccine Janssen elicited CD4 and CD8 T cell responses in individuals ≥18 to ≤55 years of age and individuals ≥65 years of age, 14 days post-vaccination and up to 28 days. All measurable CD4 T cell responses were skewed towards a Th1 phenotype.

For both age groups, in each study, later timepoints are being evaluated.

Immunogenicity of a Booster Dose (Second Dose) following Primary Vaccination with COVID-19 Vaccine Janssen

Study COV1001 evaluated the immunogenicity of a single primary vaccination with COVID-19 Vaccine Janssen which induced durable antibody responses, with a slight decline in antibody levels and seropositivity up to 9 months after vaccination.

Study COV1001 further assessed the immunogenicity of a single-dose of COVID-19 Vaccine Janssen, followed by a booster dose at 6 months, which elicited a rapid antibody response:

- There was a 4.2-fold increase in binding antibodies at 7 days post-boost, and a 5.4-fold increase at 28 days post-boost compared to pre-boost.
- There was a 9-fold increase in binding antibodies at 7 days post-boost, and a 12-fold increase at 28 days post-boost compared to 28 days post-primary vaccination.
- There was a 3.2-fold increase in neutralising antibodies at 7 days post-boost, and a 5.6-fold increase at 28 days post-boost compared to pre boost.
- There was a 6.7-fold increase in neutralising antibodies at 7 days post-boost, and a 13.5-fold increase at 28 days post-boost compared to 28 days post-primary vaccination.

A randomised, double-blind Phase 2 study conducted in the United States (COV2008) evaluated the immunogenicity of a booster dose with COVID-19 Vaccine Janssen in individuals 18 years of age and older. Cohort 1 of the study evaluated a homologous booster dose of COVID-19 Vaccine Janssen, administered at least 6 months after the primary vaccination (N=330).

In this study, the effectiveness of a booster dose of COVID-19 Vaccine Janssen was inferred from an assessment of the neutralising antibody titers (IC50) against the SARS-CoV-2 reference strain and the Delta (B.1.617.2) and Omicron (B.1.1.529) variants using pseudovirion expressing S protein neutralisation assays. Immunogenicity analyses included an assessment of IC50 geometric mean titer (GMT) differences following the booster dose compared to the IC50 following the primary vaccination and differences in responder or seropositivity rates.

In Cohort 1, the homologous booster regimen of COVID-19 Vaccine Janssen met the pre-planned statistical criterion (i.e. non-inferiority (NI) of post-booster to post-primary response) for both GMT and differences in response rates for the homologous booster vaccination. These analyses are summarised in Tables 7 and 8. The NI of neutralising antibodies following booster immunisation link the booster response to the clinical efficacy demonstrated after the initial priming immunisation.

Table 7: SARS-CoV-2 Neutralising Antibody Titers, Study COV2008 Cohort 1; Homologous Booster Given At Least 6 Months After Primary Vaccination*

SARS-CoV-2 Neutralising Antibody Assay (psVNA)	28 Days Post Primary Vaccination	Pre-Booster	14 Days Post-Booster	GMFI (95% CI) 14 Days Post-Booster vs Pre-Booster[a]	GMFI (95% CI) 14 Days Post-Booster vs 28 Days Post Primary Vaccination	Met Non-inferiority Objective[b] (Y/N)
Reference Strain						
N[c]	312	313	298	298	297	
GMT[d] (95% CI)	98 (85; 113)	119 (102; 140)	1130 (989; 1291)	6.8 (5.9; 7.8)	8.1 (7.0; 9.4)	Y
Delta Variant						
N[c]	311	313	298	298	296	
GMT[d] (95% CI)	< LLOQ (< LLOQ; < LLOQ)	65 (< LLOQ; 74)	471 (411; 539)	4.8 (4.2; 5.4)	5.6 (4.9; 6.4)	Y
Omicron Variant						
N[c]	45	45	45	45	45	
GMT[d] (95% CI)	< LLOQ (< LLOQ;< LLOQ)	< LLOQ (< LLOQ;< LLOQ)	82 (< LLOQ; 110)	1.7 (1.4; 2.1)	1.7 (1.4; 2.1)	Y[e]

Abbreviations: CI = confidence interval, GMT = geometric mean titer, GMFI = geometric mean fold increase, LLOQ = lower limit of quantification, ULOQ = upper limit of quantification, NI = Non-Inferiority, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, psVNA = pseudotyped virus/pseudovirion neutralization assay, IC50 = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

* Analysis conducted on the Non-inferiority set. This includes all participants in the per-protocol immunogenicity analysis set who are SARS-CoV-2 seronegative at baseline, as of 15 December 2021.

[a] GMFIs and 2-sided 95% CIs were calculated by exponentiating the mean difference in the logarithms of the assay and the corresponding CIs (based on the Student t distribution). The psVNA (IC50) LLOQ values for the reference strain, the Delta and the Omicron variants are 75, 65 and 66, respectively. Assay results below the LLOQ were set to LLOQ. Assay results above ULOQ were set to ULOQ. Participants with assay results at both time points within specified window were included.

[b] Non-inferiority is declared if the lower bound of the 2-sided 95% CI for the difference in seroresponder percentages is > −10 percentage points, and the lower bound of the 2-sided 95% CI for the GMFI is > 0.67 with a GMFI point estimate > 0.80, when comparing neutralizing antibody responses 14 days after booster dose and those at 28 days after primary vaccination.

[c] N = Number of participants (18 years of age and older) with non-missing data at the corresponding timepoint.

[d] GMTs and 2-sided 95% CIs were calculated by exponentiating the mean in the logarithms of the assay and the corresponding CIs (based on the Student t distribution). The psVNA (IC50) LLOQ values for the reference strain, the Delta and the Omicron variants are 75, 65 and 66, respectively. Assay results below the LLOQ were set to 0.5 × LLOQ. Assay results above ULOQ were set to ULOQ.

[e] This assessment is conducted descriptively as it was not part of the formal non-inferiority hypothesis testing strategy. Based on the computed statistics with their confidence intervals, it is observed that the data are consistent with all non-inferiority criteria: the lower bound of the 2-sided 95% CI for the difference in seroresponder percentages is > −10 percentage points, and the lower bound of the 2-sided 95% CI for the GMFI is > 0.67 with a GMFI point estimate > 0.80. The time points for this comparison are the 14 days post-booster time point and the 28 days post primary vaccination time point.

Table 8: SARS-CoV-2 Neutralising Antibody Responder Rates, Study COV2008 Cohort 1; Homologous Booster Given At Least 6 Months After Primary Vaccination*

SARS-CoV-2 Neutralising Antibody Assay (psVNA)	28 Days Post Primary Vaccination	Pre-Booster	14 Days Post-Booster	Responder Rate Difference 14 Days Post-Booster vs 28 Days Post Primary Vaccination (95% CI)	Met Non-inferiority Objective[a] (Y/N)
Reference Strain					
N[b]	312	312	298	297	
Responder rates: n[c] (%) (95% CI)[d]	48 (15.4%) (11.6%; 19.9%)	74 (23.7%) (19.1%; 28.8%)	189 (63.4%) (57.7%; 68.9%)	47.8 (41; 54.6)	Y
Seropositivity rate n[e] /N[f] (%) (95% CI)[g]	147/312 (47.1%) (41.5%; 52.8%)	154/313 (49.2%) (43.5%; 54.9%)	288/298 (96.6%) (93.9%; 98.4%)		
Delta Variant					
N[b]	308	309	298	293	
Responder rates: n[c] (%) (95% CI)[d]	27 (8.8%) (5.9%; 12.5%)	41 (13.3%) (9.7%; 17.6%)	169 (56.7%) (50.9%; 62.4%)	47.1 (40.7; 53.6)	Y
Seropositivity rate n[e] /N[f] (%) (95% CI)[g]	64/311 (20.6%) (16.2%; 25.5%)	101/313 (32.3%) (27.1%; 37.8%)	274/298 (91.9%) (88.3%; 94.8%)		
Omicron Variant					
N[b]	45	45	45	45	
Responder rates: n[c] (%) (95% CI)[d]	0	0	6 (13.3%) (5.1%; 26.8%)	12.8 (2.4; 23.2)	Y[h]
Seropositivity rate n[e] /N[f] (%) (95% CI)[g]	0	1/45 (2.2%) (0.1%; 11.8%)	24/45 (53.3%) (37.9%; 68.3%)		

Abbreviations: CI = confidence interval, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, psVNA = pseudotyped virus/pseudovirion neutralization assay, IC50 = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

* Analysis conducted on the Non-inferiority set. This includes all participants in the per-protocol immunogenicity analysis set who are SARS-CoV-2 seronegative at baseline, as of 15 December 2021.

[a] Non-inferiority is declared if the lower bound of the 2-sided 95% CI for the difference in seroresponder percentages is > −10 percentage points, and the lower bound of the 2-sided 95% CI for the GMFI is > 0.67 with a GMFI point estimate > 0.80, when comparing neutralizing antibody responses 14 days after booster dose and those at 28 days after primary vaccination.

[b] N = Number of participants (18 years of age and older) with non-missing data at the corresponding timepoint.

[c] n = Number of responders. For pre-booster time points (Day 29), a participant is considered a responder if the post-vaccination titer is at least 4-fold higher than the pre-dose 1 titer, or at least 4-fold higher than LLOQ when the pre-dose 1 titer is below LLOQ. For post-booster time points, a participant is considered a responder if the post-booster titer is at least 4-fold higher than the pre-booster titer, or at least 4-fold higher than LLOQ when the pre-booster titer is below LLOQ.

[d] Exact Clopper-Pearson 95% confidence intervals are shown for Responders. The assay status is: validated.

[e] n = Number of participants with a positive sample. Positive sample refers to a quantifiable response.

[f] N = Number of participants with data at that time point.

[g] Exact Clopper-Pearson 95% confidence intervals are shown for % Seropositivity. The assay status is: validated.

[h] This assessment is conducted descriptively as it was not part of the formal non-inferiority hypothesis testing strategy. Based on the computed statistics with their confidence intervals, it is observed that the data are consistent with all non-inferiority criteria: the lower bound of the 2-sided 95% CI for the difference in seroresponder percentages is > −10 percentage points, and the lower bound of the 2-sided 95% CI for the GMFI is > 0.67 with a GMFI point estimate > 0.80. The time points for this comparison are the 14 Days post-booster time point and the 28 days post primary vaccination time point.

Immunogenicity of a Booster Dose following Primary Vaccination with a mRNA COVID-19 Vaccine

Study COV2008 (see study design above) – Cohort 2, evaluated the immunogenicity of a heterologous booster dose of COVID-19 Vaccine Janssen, administered at least 6 months after completing primary vaccination with 2 doses of Pfizer BioNTech COVID-19 Vaccine (N=326).

In Cohort 2, baseline neutralising antibody titers for individuals in the external sample set used as a comparison for responses after primary vaccination with 2 doses of Pfizer BioNTech COVID 19 Vaccine, are not available. Therefore, seropositivity rates rather than responder rates are used for the non-inferiority assessments. The heterologous booster regimen of COVID-19 Vaccine Janssen met the pre-planned statistical criterion (i.e. NI) for both GMT and differences in seropositivity rates for the heterologous booster vaccination. These analyses are summarised in Tables 9 and 10. The NI of neutralising antibody following booster immunisation link the booster response to the clinical efficacy demonstrated after the initial priming immunisation.

Table 9: SARS-CoV-2 Neutralizing Antibody Titers, Study COV2008 Cohort 2; Heterologous Booster Given At Least 6 Months After Primary Vaccination*

SARS-CoV-2 Neutralising Antibody Assay (psVNA)	Day 14 to 60 Post Primary Regimen with Pfizer BioNTech COVID-19 Vaccine[a]	Pre-Booster	14 Days Post-Booster	GMFI (95% CI) 14 Days Post Booster vs Pre-Booster[b]	GMR (97.5% CI) 14 Days Post Booster vs 14 to 60 Days Post Primary Regimen with Pfizer BioNTech COVID-19 Vaccine[c]	Met Non-inferiority Objective[d] (Y/N)
Reference Strain						
N[e]	309	310	299	297	608	
GMT[f] (95% CI)	1281 (1086; 1510)	167 (147; 191)	4439 (4027; 4893)	21.9 (19.7; 24.5)	3.3 (2.7; 4.0)[c]	Y
Delta Variant						
N[e]	309	310	299	297	608	
GMT[f] (95% CI)	502 (422; 598)	76 (68; 86)	2318 (2049; 2623)	20.7 (18.3; 23.4)	4.1 (3.3; 5.2)[c]	Y
Omicron Variant						
N[e]	Not available	45	45	45	Not available	
GMT[f] (95% CI)		< LLOQ (< LLOQ;< LLOQ)	526 (357; 776)	8.2 (5.7; 11.9)		Not assessed[g]

Abbreviations: CI = confidence interval, GMT = geometric mean titer, GMFI = geometric mean fold increase, GMR = geometric mean ratio, LLOQ = lower limit of quantification, ULOQ = upper limit of quantification, NI = Non-Inferiority, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, psVNA = pseudotyped virus/pseudovirion neutralization assay, IC50 = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

* Analysis conducted on the Non-inferiority set. This includes all participants in the per-protocol immunogenicity analysis set who are SARS-CoV-2 seronegative at baseline, as of 15 December 2021.

[a] Neutralizing antibody levels post primary regimen with Pfizer BioNTech COVID-19 vaccine were measured in an external sample set and includes individuals who received 2 doses of the Pfizer BioNTech COVID-19 vaccine as a primary vaccination and for whom blood samples are available between Day 14 and Day 60 post primary vaccination.

[b] GMFIs and 2-sided 95% CIs were calculated by exponentiating the mean difference in the logarithms of the assay and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to LLOQ. Assay results above ULOQ were set to ULOQ. Participants with assay results at both time points within specified window were included.

[c] GMRs and 2-sided 97.5% CIs were calculated by exponentiating difference of the means in the logarithms of the assay and the corresponding CIs (based on the Student t distribution, independent samples). Assay results below the LLOQ were set to LLOQ. Assay results above ULOQ were set to ULOQ.

[d] Non-inferiority is declared if the lower bound of the 2-sided 97.5% CI for the difference in sample positivity percentages is > −10 percentage points, and the lower bound of the 2-sided 97.5% CI for the GMR is > 0.67 with a GMR point estimate > 0.80, when comparing neutralizing antibody responses 14 days after booster dose and those at Day 14 to 60 after primary regimen with Pfizer BioNTech COVID-19 vaccine.

[e] Number of participants (18 years of age and older) with non-missing data at the corresponding timepoint.

[f] GMTs and 2-sided 95% CIs were calculated by exponentiating the mean in the logarithms of the assay and the corresponding CIs (based on the Student t distribution). The psVNA (IC50) LLOQ values for the reference strain, the Delta and the Omicron variants are 75, 65 and 66, respectively. Assay results below the LLOQ were set to 0.5 × LLOQ. Assay results above ULOQ were set to ULOQ.

[g] This assessment was not performed due to the unavailability of data at Day 14 to Day 60 post primary regimen with Pfizer BioNTech COVID 19 Vaccine.

Table 10: SARS-CoV-2 Neutralising Antibody Seropositivity Rates, Study COV2008 Cohort 2; Heterologous Booster Given At Least 6 Months After Primary Vaccination*

SARS-CoV-2 Neutralising Antibody Assay (psVNA)	Day 14 to 60 Post Primary Regimen with Pfizer BioNTech COVID-19 Vaccine	Pre-Booster	14 Days Post-Booster	Seropositivity % Difference 14 Days Post Booster vs 14 to 60 Days Post Primary Vaccination with Pfizer BioNTech COVID-19 Vaccine (97.5% CI)	Met Non-inferiority Objective[a] (Y/N)
Reference Strain					
N[b]	309	310	299	608	
Seropositivity rate[c] n[d] (%) (95% CI)[e]	284 (91.9%) (88.3%; 94.7%)	225 (72.6%) (67.3%; 77.5%)	299 (100.0%) (98.8%; 100.0%)	8.1 (3.0; 13.2)	Y
Delta Variant					
N[b]	309	310	299	608	
Seropositivity rate[c] n[d] (%) (95% CI)[e]	259 (83.8%) (79.2%; 87.7%)	140 (45.2%) (39.5%; 50.9%)	298 (99.7%) (98.2%; 100.0%)	15.8 (9.8; 21.9)	Y
Omicron Variant					
N[b]	Not available	45	45	Not available	
Seropositivity rate[c] n[d] (%) (95% CI)[e]		0	43 (95.6%) (84.9%; 99.5%)		Not assessed[f]

Abbreviations: CI = confidence interval, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, psVNA = pseudotyped virus/pseudovirion neutralization assay, IC50 = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

* Analysis conducted on the Non-inferiority set. This includes all participants in the per-protocol immunogenicity analysis set who are SARS-CoV-2 seronegative at baseline, as of 15 December 2021.

[a] Non-inferiority is declared if the lower bound of the 2-sided 97.5% CI for the difference in seroresponder percentages is > −10 percentage points, and the lower bound of the 2-sided 97.5% CI for the GMFI is > 0.67 with a GMFI point estimate > 0.80, when comparing neutralizing antibody responses 14 days after booster dose and those at Day 14 to 60 after primary regimen with Pfizer BioNTech COVID-19 vaccine.

[b] N = Number of participants (18 years of age and older) with non-missing data at the corresponding timepoint.

[c] Baseline neutralizing antibody titers for individuals in the Pfizer external sample set used as a comparison for responses after primary vaccination with 2 doses of Pfizer BioNTech COVID-19 Vaccine, are not available. Therefore, seropositivity rates rather than responder rates are used for the NI assessments.

[d] n = Number of participants with a positive sample. Positive sample refers to a quantifiable response.

[e] Exact Clopper-Pearson 95% confidence intervals are shown for % Seropositivity. The assay status is: validated.

[f] This assessment was not performed due to the unavailability of data at Day 14 to Day 60 post primary regimen with Pfizer BioNTech COVID 19 Vaccine.

COV-BOOST study is an independent, multicentre randomised Phase 2 investigator-initiated study (NCT73765130) conducted in the United Kingdom, to evaluate a booster vaccination against COVID-19. Participants were adults aged 30 years or older. A Cohort of participants received 2 doses of Pfizer–BioNTech (N=89) (first dose in December 2020, January 2021 or February 2021), followed by a booster dose of COVID-19 Vaccine Janssen, and were at least 84 days post second dose by the time of boost. Binding antibody titers and neutralising antibody titers, as measured by a pseudovirus and/or wild type virus neutralisation assay, were assessed up to Day 84 after the booster dose. COVID-19 Vaccine Janssen boosted binding (N=90), pseudovirus neutralising (N=90) and wild type neutralising antibody responses (N=21) against the reference strain. Furthermore, COVID-19 Vaccine Janssen boosted pseudovirus neutralising antibody responses against the Delta (B.1.617.2) variant assessed up to Day 28 (N=89).

In an independent Phase 1/2 open-label clinical study conducted in the United States, a booster dose of COVID-19 Vaccine Janssen was administered in two cohorts to adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series or a Pfizer-BioNTech COVID-19 Vaccine 2-dose series at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection. Binding antibodies and neutralising antibody titers, as measured by a pseudovirus

neutralisation assay, were assessed up to Day 28 after the booster dose. COVID-19 Vaccine Janssen boosted binding and pseudovirus neutralising antibody responses against the reference strain and the Delta (B.1.617.2) variant in individuals primed with Moderna COVID 19 Vaccine 2 dose series (N=49) or Pfizer-BioNTech COVID-19 Vaccine 2 dose series (N=50). Furthermore, in a sub-cohort COVID-19 Vaccine Janssen boosted pseudovirus neutralising antibody responses against the Omicron (B.1.1.529) variant in individuals primed with Pfizer-BioNTech COVID-19 Vaccine 2 dose series (N=20).

Booster Dose following Primary Vaccination with an Adenoviral Vector-based COVID-19 Vaccine

COV-BOOST study (see study design above) also evaluated a booster vaccination against COVID 19, in participants who had received 2 doses of Oxford–Astra Zeneca (N=101) (first dose in December 2020, January 2021 or February 2021), followed by a booster dose of COVID-19 Vaccine Janssen, and were at least 70 days post second dose by the time of boost. Binding antibody titers and neutralising antibody titers, as measured by a pseudovirus and/or wild type virus neutralisation assay, were assessed up to Day 84 after the booster dose. COVID-19 Vaccine Janssen boosted binding (N=94) pseudovirus neutralising (N=94) and wild type neutralising antibody responses (N=21) against the reference strain. Furthermore, COVID-19 Vaccine Janssen boosted pseudovirus neutralising antibody responses against the Delta (B.1.617.2) variant assessed up to Day 28 (N=101).

Booster Dose following Primary Vaccination with an Inactivated Whole-virion COVID-19 Vaccine

RHH-001 study is an independent, randomised Phase 4 study (RBR-9nn3scw) conducted at 2 sites in Brazil, to evaluate a booster vaccination against COVID-19 in adults 18 years of age or older. The primary analysis population included participants who had received 2 doses of CoronaVac (N=295) followed by a booster dose of COVID-19 Vaccine Janssen, and were 182 days (plus or minus 30 days) post second dose at the time of boost. Binding antibody titers and neutralising antibody titers, as measured by a pseudovirus and/or wild type virus neutralisation assay, were assessed on Day 28 after the booster dose. COVID-19 Vaccine Janssen boosted binding (N=294) and pseudovirus neutralising antibody responses (N=47) against the reference strain. In a subset of participants (N=20), wild type virus neutralising antibodies were also boosted against the Delta (B.1.617.2) and Omicron (B.1.1.529) variants.

Elderly population

COVID-19 Vaccine Janssen was assessed in individuals 18 years of age and older. The efficacy of COVID-19 Vaccine Janssen was consistent between elderly (≥65 years) and younger individuals (18-64 years).

This medicine has been given a provisional consent under Section 23 of the Act. This means that further evidence on this medicine is awaited or that there are specific conditions of use. Refer to the consent notice published in the New Zealand Gazette for the specific conditions.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

Genotoxicity and Carcinogenicity

COVID-19 Vaccine Janssen has not been evaluated for its genotoxic or carcinogenic potential. The components of the vaccine are not expected to have genotoxic or carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxypropylbetadex
Citric acid monohydrate
Ethanol absolute
Hydrochloric acid
Polysorbate-80
Sodium chloride
Sodium hydroxide
Sodium citrate dihydrate
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

6.3 Shelf life

Please also see sections 6.4 and 6.6 for special precautions for storage and detailed instructions for storage and handling.

Unopened vial

2 years when stored at -25°C to -15°C.

Once removed from the freezer, the unopened vaccine may be stored refrigerated at 2°C to 8°C, protected from light, for a single period of up to 11 months, not exceeding the printed expiry date (EXP).

Once thawed, the vaccine should not be re-frozen.

For special precautions for storage, see section 6.4.

Opened vial (after first puncture of the vial)

Chemical and physical in-use stability, including during transportation, of the vaccine has been demonstrated for 6 hours at 2°C to 25°C. From a microbiological point of view, the product should preferably be used immediately after first puncture of the vial; however, the product can be stored between 2°C-8°C for a maximum of 6 hours or remain at room temperature (maximally 25°C) up to 3 hours after first puncture of the vial. Beyond these times, in-use storage is the responsibility of the user.

6.4 Special precautions for storage

Please also see section 6.6 for detailed instructions for storage and handling.

Storage Prior to Use

Store and transport frozen at -25°C to -15°C. The expiry date for storage at -25°C to -15°C is printed on the vial and outer carton after “EXP”.

When stored frozen at -25°C to -15°C, the vaccine can be thawed either at 2°C to 8°C or at room temperature:

- at 2°C to 8°C: a carton of 10 vials will take approximately 12 hours to thaw, and a single vial will take approximately 2 hours to thaw.
- at room temperature (maximally 25°C): a carton of 10 vials will take approximately 2 hours to thaw, and a single vial will take approximately 1 hour to thaw.

The vaccine can also be stored in a refrigerator or transported at 2°C to 8°C for a single period of up to 11 months, not exceeding the original expiry date (EXP). Upon moving the product to 2°C to 8°C storage, the updated expiry date must be written on the outer carton and the vaccine should be used or discarded by the updated expiry date. The original expiry date should be made unreadable. The vaccine can also be transported at 2°C to 8°C as long as the appropriate storage conditions (temperature, time) are applied.

Once thawed, the vaccine cannot be re-frozen.

Keep the vials in the original carton in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

A 2.5 mL suspension in a multi-dose vial (Type I glass) with a rubber stopper (chlorobutyl with fluoropolymer coated surface), aluminium crimp and blue plastic cap. Each vial contains 5 doses of 0.5 mL.

Pack size of 10 multi-dose vials.

6.6 Special precautions for disposal and other handling

Handling instructions and administration

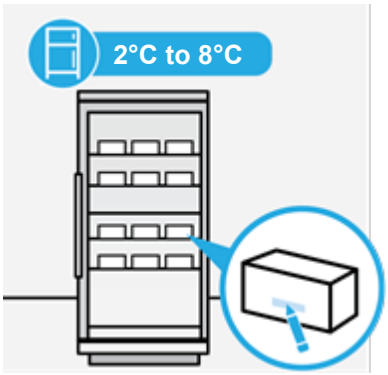
This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

- The vaccine comes ready to use once thawed.
- The vaccine may be supplied frozen at -25°C to -15°C or thawed at 2°C to 8°C.
- Do not re-freeze vaccine once thawed.
- Keep the vials in the original carton in order to protect from light and to record the expiry for the different storage conditions, if applicable.

1. Storage upon receipt of vaccine

IF YOU RECEIVE YOUR VACCINE FROZEN AT -25°C to -15°C you may:

OR



Store in a freezer

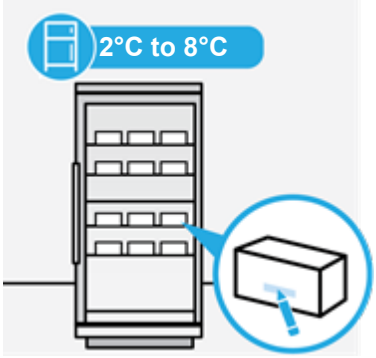
- The vaccine can be stored and transported frozen at **-25°C to -15°C**.
- The expiry date for storage is printed on the vial and outer carton after "EXP" (see section 6.4).

Store in a refrigerator

- The vaccine can also be stored and transported at **2°C to 8°C** for a single period of **up to 11 months**, not exceeding the original expiry date (EXP).
- Upon moving the product **to a refrigerator at 2°C to 8°C**, the updated

expiry date must be written on the outer carton and the vaccine should be used or discarded by the updated expiry date. **The original expiry date should be made unreadable** (see section 6.4).

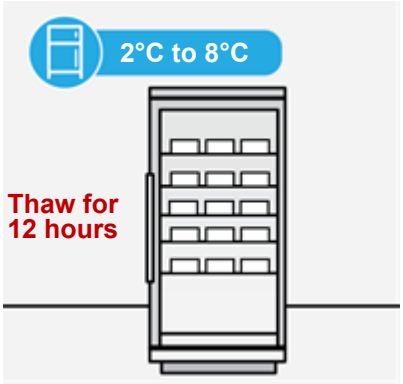
IF YOU RECEIVE YOUR VACCINE THAWED AT 2°C to 8°C you should store in a refrigerator:



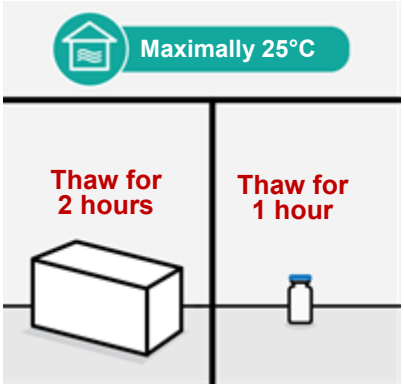
Do not re-freeze if the product is received already thawed at 2°C to 8°C.

Note: If the vaccine is received refrigerated at 2°C to 8°C, check that the expiry date has been updated by the local supplier upon receipt. If you cannot find the new EXP date, contact the local supplier to confirm the refrigerated EXP date. Write the **new expiry date** on the outer carton before the vaccine is stored in the refrigerator. **The original expiry date should be made unreadable** (see section 6.4).

2. If stored frozen, thaw vial(s) either in a refrigerator or at room temperature before administration



OR



Thaw in refrigerator

- When stored frozen at -25°C to -15°C, a carton of 10 vials will take approximately 12 hours to thaw or individual vials will take approximately 2 hours to thaw **at 2°C to 8°C**.
- If the vaccine is not used immediately, refer to the instructions in section Store in a refrigerator.
- The vial must be kept in the original carton in order to protect from light and to record the expiry for the different storage conditions, if applicable.

Thaw at room temperature

- When stored frozen at **-25°C to -15°C**, a carton of 10 vials or individual vials should be thawed at room temperature maximally **25°C**.
- A carton of 10 vials will take approximately **2 hours** to thaw.
- Individual vials will take approximately **1 hour** to thaw.
- The vaccine is stable for a total of **12 hours at 9°C to 25°C**. This is not a recommended storage or shipping condition but may guide decisions for

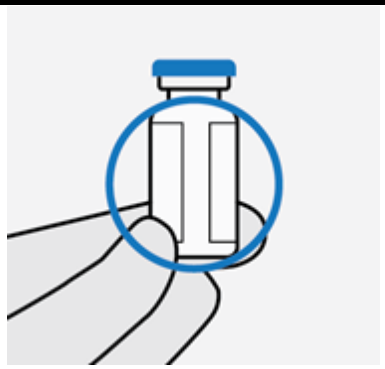
Do not re-freeze once thawed.

use in case of temporary temperature excursions.

- If the vaccine is not used immediately, refer to the instructions in section Store in a refrigerator.

Do not re-freeze once thawed.

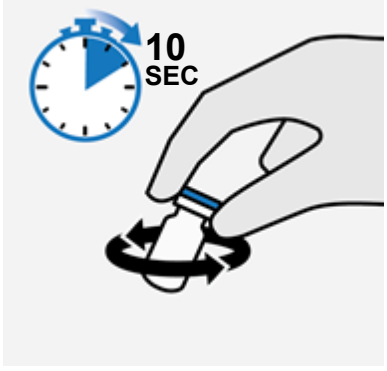
3. Inspect vial and vaccine



- COVID-19 Vaccine Janssen is a colourless to slightly yellow, clear to very opalescent suspension (pH 6-6.4).
- The vaccine should be inspected visually for particulate matter and discoloration prior to administration.
- The vial should be inspected visually for cracks or any abnormalities, such as evidence of tampering prior to administration.

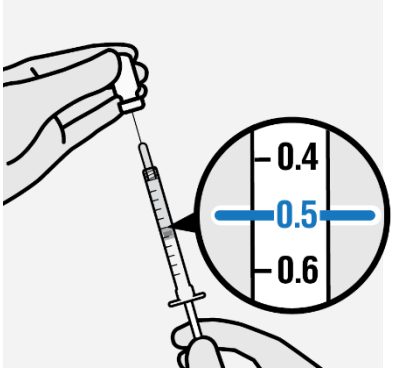
If any of these should exist, do not administer the vaccine.

4. Prepare and administer vaccine



Swirl the vial gently

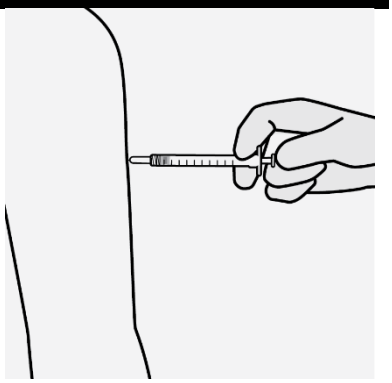
- Before administering a dose of vaccine, swirl the vial gently **in an upright position for 10 seconds**.
- **Do not** shake.



Withdraw 0.5 mL

- Use a sterile needle and sterile syringe to extract a single dose of **0.5 mL** from the multidose vial (see section 4.2).

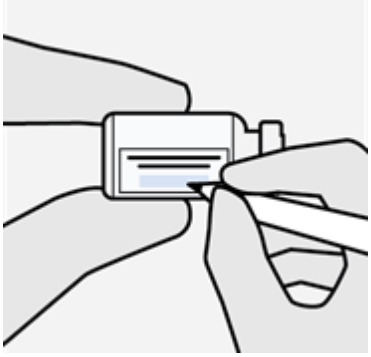
A maximum of 5 doses can be withdrawn from the multi-dose vial. Discard any remaining vaccine in the vial after 5 doses have been extracted.



Inject 0.5 mL

- Administer by **intramuscular injection only** into the deltoid muscle of the upper arm (see section 4.2).

5. Storage after first puncture



Record date and time the vial should be discarded

- After first puncture of the vial record the date and time the vial should be discarded on each vial label.

⚠ Preferably, use immediately after first puncture.

- After the first puncture of the vial, the vaccine can be held at **2°C to 8°C** for **up to 6 hours**.
- Discard if vaccine is not used within this time.

OR

- After the first puncture of the vial, the vaccine can be held at **room temperature (maximally 25°C)** for a single period of **up to 3 hours**. (see section 6.3).
- Discard if vaccine is not used within this time.

6. Disposal

Any unused vaccine or waste material should be disposed of in compliance with local guidance for pharmaceutical waste. Potential spills should be disinfected with agents with viricidal activity against adenovirus.

7. MEDICINE SCHEDULE

Prescription

8. SPONSOR

Janssen-Cilag (New Zealand) Ltd
Auckland, NEW ZEALAND
Telephone: 0800 800 806
FAX: (09) 588 1398
Email: medinfo@janau.jnj.com

9. DATE OF FIRST APPROVAL

7 July 2021

10. DATE OF REVISION OF THE TEXT

9 March 2023

Summary table of changes

Section	Summary of changes
4.2	Updated booster dose recommendations
4.8	Updated safety information for booster dose
5.1	Updated immunogenicity information for booster dose