PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

JCOVDEN™

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

Suspension for intramuscular injection

Multidose Vial, 5×10^{10} virus particles/0.5 mL

(contains 5 doses of 0.5 mL)

Active Immunizing Agent

J07BX03

Janssen Inc.
19 Green Belt Drive
Toronto, ON
M3C 1L9
www.janssen.com/canada

Date of Initial Authorization:
November 23, 2021

Date of Revision:
February 16, 2023

Submission Control Number: 267263

All trademarks used under license

© 2023 Janssen Inc.

RECENT MAJOR LABEL CHANGES

2 CONTRAINDICATIONS	03/2022
3 SERIOUS WARNINGS AND PRECAUTIONS	04/2021
4 DOSAGE AND ADMINISTRATION	01/2023
7 WARNING AND PRECAUTIONS	01/2023

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

JCOVDEN™ (COVID-19 Vaccine (Ad26.COV2-S [recombinant])) is indicated for active immunization for the prevention of coronavirus disease-2019 (COVID-19) caused by SARS-CoV-2 virus in individuals 18 years of age and older.

1.1 Pediatrics

The safety and efficacy of JCOVDEN in individuals younger 18 years of age have not yet been established.

1.2 Geriatrics

Clinical studies of JCOVDEN include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see **8 ADVERSE REACTIONS,** and **14 CLINICAL TRIALS**).

2 CONTRAINDICATIONS

JCOVDEN is contraindicated in individuals who are hypersensitive to the active ingredient, any other adenovirus-based vaccines, or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. (see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).**

JCOVDEN is contraindicated in individuals with a history of thrombosis with thrombocytopenia following vaccination with JCOVDEN or any other adenovirus-vectored COVID-19 vaccine (see 7 Warnings and Precautions).

JCOVDEN is contraindicated in individuals with a history of Capillary Leak Syndrome (CLS).

3 SERIOUS WARNINGS AND PRECAUTIONS

A combination of thrombosis and thrombocytopenia, in some cases accompanied by bleeding, has been observed very rarely following vaccination with JCOVDEN (see **7 WARNINGS AND PRECAUTIONS, Hematologic).**

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

JCOVDEN is a suspension for intramuscular injection that should be administered by a trained healthcare worker.

4.2 Recommended Dose and Dosage Adjustment

Vaccination Schedule for Individuals 18 Years of Age and Older

Primary vaccination

JCOVDEN should be administered intramuscularly as a single dose of 0.5 mL in individuals 18 years of age and older. There are no data available on the use of JCOVDEN to complete a primary vaccination series initiated with another COVID-19 Vaccine.

Booster dose

A booster dose of 0.5 mL of JCOVDEN may be administered intramuscularly at least 2 months after the primary vaccination in individuals 18 years of age and older.

A booster dose of JCOVDEN (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 an mRNA COVID-19 Vaccine. The dosing interval of 3- 6 months for the heterologous booster following the primary vaccination with an mRNA COVID-19 Vaccine was studied in the clinical trials.

4.3 Reconstitution

JCOVDEN must not be reconstituted, mixed with other medicinal products, or diluted.

4.4 Administration

JCOVDEN is a colorless to slightly yellow, clear to very opalescent suspension. 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.

Before administering a dose of vaccine, carefully mix the contents of the multi-dose vial by swirling gently in an upright position for 10 seconds. Do not shake. Use a sterile needle and sterile syringe to extract a single dose of 0.5 mL from the multi-dose vial and administer by intramuscular injection only. The preferred site is the deltoid muscle of the upper arm. A needle length of ≥1 inch should be used as needles <1 inch may be of insufficient length to penetrate muscle tissue in some adults. Do not administer this vaccine intravenously or subcutaneously.

Changing needles between extracting vaccine from a vial and injecting it into an individual is not necessary unless the needle has been damaged or contaminated. Discard any remaining vaccine in the multi-dose vial after 5 doses have been extracted. After the first puncturing of the vial, the vial/filled syringe can be held at 2°C to 8°C for up to 6 hours or at room temperature (maximally 25°C) for up to 3 hours. Discard if vaccine is not used within this time.

5 OVERDOSAGE

No case of overdose has been reported. In Phase 1/2 studies, where a higher dose (up to 2-fold) was administered, JCOVDEN remained well-tolerated however vaccinated individuals reported an increase in reactogenicity.

In the event of a suspected overdose, monitoring of vital functions and symptomatic treatment are recommended.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

Table 1 Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Suspension, (5×10^{10} virus particles/0.5 mL), adenovirus type 26 (Ad26) vectored COVID-19 vaccine encoding the SARS-CoV-2 Spike (S) protein (original strain) in a stabilized confirmation Multi-dose vial (total fill volume 3.1 mL, containing 5 doses of 0.5 mL)	• 2-hydroxypropyl-β-cyclodextrin (HBCD) • Citric acid monohydrate • Ethanol • Hydrochloric acid • Polysorbate-80 • Sodium chloride • Sodium hydroxide • Trisodium citrate dihydrate • Water for injection

JCOVDEN is a colourless to slightly yellow, clear to very opalescent sterile suspension for intramuscular injection. JCOVDEN contains an Adenovirus type 26 (Ad26) vectored COVID-19 vaccine (replication-incompetent, recombinant), encoding the SARS-CoV-2 Spike (S) protein (original strain) in a stabilized conformation and the non-medicinal ingredients listed in **Table 1.** The product contains no preservatives.

The Adenovirus type 26 (Ad26) vectored COVID-19 vaccine is produced in the PER.C6® TetR Cell Line and by recombinant DNA technology.

JCOVDEN is supplied as a suspension in a multi-dose Type I glass vial with a latex-free rubber stopper (chlorobutyl), aluminum seal and flip-off blue plastic cap. Vials are packaged in a carton containing a total of ten (10) JCOVDEN multi-dose vials per carton.

7 WARNINGS AND PRECAUTIONS

General

The clinical data available for JCOVDEN are derived from the COV3001 Phase 3 study and from Phase 1 and Phase 2 studies. Serious and unexpected adverse events may occur that have not been previously reported with the JCOVDEN use.

As with any vaccine, vaccination with JCOVDEN may not protect all vaccinated individuals.

JCOVDEN is not intended to prevent diseases caused by coronaviruses other than SARS-CoV-2. JCOVDEN is not intended to treat COVID-19.

Hypersensitivity and Anaphylaxis

Anaphylaxis has been reported. As with all vaccines, training for immunizers, and appropriate medical treatment and supervision after immunization should always be readily available in case of rare anaphylactic reactions following administration of this vaccine. Vaccine recipients should be kept under observation for at least 15 minutes after immunization; 30 minutes is a preferred interval when there is a specific concern about a possible vaccine reaction.

Acute illness

Consideration should be given to postponing immunization in persons with severe febrile illness or severe acute infection. Persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved.

Hematologic

Coagulation disorders

Thrombosis and thrombocytopenia

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 JCOVDEN during post-authorization use. This includes severe cases at unusual sites such as cerebral venous sinus thrombosis (CVST) and splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. The majority of cases occurred within three weeks following vaccination.

Cases of TTS following administration of JCOVDEN have been reported in individuals, in a wide age range of individuals 18 years and older, with the highest reporting rate (approximately 1 case per 100,000 doses administered) in females ages 30-49 years; overall, approximately 15% of TTS cases have been fatal. The clinical course of these events shares features with autoimmune heparin-induced thrombocytopenia (HIT). Currently available evidence supports a causal relationship between TTS and JCOVDEN.

Individuals who have experienced thrombosis with thrombocytopenia syndrome following vaccination with adenovirus-vectored COVID-19 vaccine should not receive JCOVDEN (see **2 CONTRAINDICATIONS**).

Immune thrombocytopenia

Cases of immune thrombocytopenia with very low platelet levels (<20,000 per uL) have been reported very rarely after vaccination with JCOVDEN, usually within the first four weeks after receiving JCOVDEN. This included cases with bleeding and cases with fatal outcome. Some of these cases occurred in individuals with a history of immune thrombocytopenia (ITP). 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 thrombosis, 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 or swelling, or progressive abdominal pain following vaccination. Additionally, anyone with neurological symptoms after vaccination including sudden onset of severe headaches, persistent or worsening headaches, blurred vision, confusion or seizure, or who experiences spontaneous bleeding, unusual skin bruising or petechiae beyond the site of vaccination after a few days, should seek prompt medical attention.

Since medical management of a post-vaccine thrombosis, thromboembolism, and/or thrombocytopenia may be different than medical management of other thromboses, if patients present with thrombosis, thromboembolism, and/or thrombocytopenia, healthcare professionals should consult with current guidance and hematologic specialists to diagnose and treat this post-vaccine event.

Individuals diagnosed with thrombocytopenia following vaccination with JCOVDEN should be actively investigated for signs of thrombosis, and similarly individuals who present with thrombosis following vaccination should be evaluated for thrombocytopenia.

Venous thromboembolism

Venous thromboembolism (VTE) has been observed rarely following vaccination with JCOVDEN. In individuals with a pre-existing increased risk for thromboembolism, the possible increased risk of VTE with vaccine use should be considered. Healthcare professionals should be alert to the signs and symptoms of VTE.

Risk of bleeding with intramuscular administration

As with other intramuscular injections, JCOVDEN should be given with caution in individuals with bleeding disorders, such as haemophilia, or individuals currently on anticoagulant therapy, to avoid the risk of haematoma following the injection, and when the potential benefit clearly outweighs the risk of administration.

Capillary Leak Syndrome

Cases of capillary leak syndrome (CLS) have been reported very rarely in the first days following vaccination with JCOVDEN during post-authorization use. Some of the reported cases had a history of CLS. Some cases had a fatal outcome. CLS is a very rare disease characterized by acute episodes of limb edema, hypotension, hemoconcentration and hypoalbuminemia. Patients with an acute episode of CLS following vaccination require prompt medical attention and treatment. Intensive supportive therapy is usually warranted. Individuals with a known history of CLS should not be vaccinated with this vaccine.

Immune

Adults with stable/well-controlled HIV infection or adults receiving chronic low-dose (less than 20 mg of prednisone or equivalent) immunosuppressive therapy were included in JCOVDEN Phase 3 clinical studies.

Immunocompromised individuals including those receiving substantial immunosuppressant therapy may have a diminished immune response to JCOVDEN.

Neurologic

Neurologic events

Very rare events of demyelinating disorders, such as Guillain-Barré syndrome (GBS) and transverse myelitis (TM) have been reported following vaccination with JCOVDEN during post-authorization use. Healthcare professionals should be alert to GBS and TM signs and symptoms to ensure correct diagnosis, in order to initiate adequate supportive care and treatment and to rule out other causes.

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

Reproductive Health

No data are available on fertility in humans following the use of JCOVDEN.

7.1 Special Populations

7.1.1 Pregnant Women

There is limited experience with the use of JCOVDEN in pregnant women. Animal studies with JCOVDEN did not indicate harmful effects with respect to reproductive toxicity (see **16 NON-CLINICAL TOXICOLOGY**).

Administration of JCOVDEN in pregnancy should only be considered when the potential benefits outweigh any potential risks to the mother and fetus.

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to JCOVDEN during pregnancy. Women who are vaccinated with JCOVDEN during pregnancy are encouraged to enroll in the registry by visiting https://c-viper.pregistry.com

7.1.2 Breast-feeding

It is not known whether the components of JCOVDEN or antibodies induced by JCOVDEN are excreted in human milk. Human data are not available to assess the impact of JCOVDEN on milk production or its effects on the breastfed child.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of JCOVDEN in children under 18 years of age have not yet been established.

7.1.4 Geriatrics

Clinical studies of JCOVDEN include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (see **8 ADVERSE REACTIONS**, and **14 CLINICAL TRIALS**).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile presented below is based on the primary pooled analysis of data generated from the double-blind phase of 5 randomized, double blind, placebo-controlled studies (COV1001, COV1002, COV2001, COV3001 and COV3009) conducted in North America, South America. Europe, Japan and South Africa. At the time of the primary pooled analysis, a total of 76,347 participants ≥18 years of age had been randomized and received, at least a single-dose primary vaccination of JCOVDEN (n=38,538) or placebo (n=37,809). Overall, the percentages of participants were balanced between the JCOVDEN and placebo groups. In the group who received JCOVDEN, 13,259 (34.4%) participants were ≥60 years of age. At the time of the primary pooled analysis, the median follow-up time for individuals who received JCOVDEN was approximately 4 months (111 days) after primary vaccination. Longer safety follow-up of ≥ 6 months is available for 6,136 adults who received JCOVDEN.

Solicited Adverse Events (AEs) to day 7 post-vaccination and Unsolicited AEs to day 28 post-vaccination were measured in the Safety Subset, which consisted of a subset of 14,064 participants from the US, Brazil and South Africa. In this Safety Subset, 7,310 participants received JCOVDEN and 6,754 received the placebo.

In the primary pooled analysis, the most common solicited local adverse reaction (AR) reported was injection site pain (54.3%). The most common solicited systemic ARs reported were: fatigue (44.0%), headache (43.0%), myalgia (38.1%), and nausea (16.9%). Pyrexia (defined as body temperature ≥ 38.0°C) was observed in 7.2% of participants (see **Tables 2 and 3**). Solicited ARs were generally more common in younger than in older age groups. Most adverse reactions were mild to moderate in severity. Across the studies, most adverse reactions occurred within 2 days following vaccination and were of short duration (2 to 3 days).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another vaccine. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Primary Vaccination

Solicited adverse reactions

Solicited ARs were collected from Day 1 to Day 7 and reported by participants in the Safety Subset via e-diary. Shown below are the frequencies of solicited local ARs (**Table 2**) and

systemic ARs (**Table 3**) reported in adults by age group (≥18 to 59 years of age and ≥60 years of age) in the in the primary pooled analysis. There were no Grade 4 ARs.

Table 2: Solicited Local Adverse Reactions Reported in the 7 Days Following Vaccination, Safety Subset - Primary Pooled Analysis

Adverse Reactions	Aged 18-59 Years		Aged ≥60 Years	
	JCOVDEN N=4450[a] n (%)	Placebo N=4058[a] n (%)	JCOVDEN N=2860[a] n (%)	Placebo N=2696[a] n (%)
Injection Site Pain				
Any	2878 (64.7%)	780 (19.2%)	1092 (38.2%)	401 (14.9%)
Grade 3[b]	16 (0.4%)	2 (<0.1%)	3 (0.1%)	6 (0.2%)
Injection Site Erythema				
Any (≥25 mm)	401 (9.0%)	187 (4.6%)	122 (4.3%)	89 (3.3%)
Grade 3[c]	7 (0.2%)	4 (0.1%)	2 (0.1%)	2 (0.1%)
Injection Site Swelling				
Any (≥25 mm)	298 (6.7%)	68 (1.7%)	82 (2.9%)	36 (1.3%)
Grade 3[c]	5 (0.1%)	2 (<0.1%)	3 (0.1%)	0

Note: Subjects are counted only once within a period for any given event, regardless of the number of times they actually experienced the event in that period. Primary pooled analysis includes data from the double-blind placebo-controlled phase of studies COV1001, COV1002, COV2001, COV3001 and COV3009.

[a] N=Analysis set: Safety Subset

[b] Grade 3 injection site pain: Defined as incapacitating symptoms; inability to do work, school, or usual activities; use of narcotic pain reliever.

[c] Grade 3 injection site swelling and erythema: Defined as >100 mm.

Table 3: Solicited Systemic Adverse Reactions and Use of Antipyretic or Pain Medication Reported in the 7 Days Following Vaccination, Safety Subset - Primary Pooled Analysis

Adverse Reactions	Aged 18-59 Years		Aged ≥60 Years	
	JCOVDEN N=4450[a] n (%)	Placebo N=4058[a] n (%)	JCOVDEN N=2860[a] n (%)	Placebo N=2696[a] n (%)
Fatigue				
Any	2298 (51.6%)	1062 (26.2%)	920 (32.2%)	581 (21.6%)
Grade 3[b]	74 (1.7%)	10 (0.2%)	13 (0.5%)	8 (0.3%)
Headache				
Any	2241 (50.4%)	1107 (27.3%)	905 (31.6%)	592 (22.0%)
Grade 3[c]	69 (1.6%)	9 (0.2%)	12 (0.4%)	6 (0.2%)
Myalgia				
Any	2045 (46.0%)	623 (15.4%)	737 (25.8%)	361 (13.4%)
Grade 3[b]	72 (1.6%)	5 (0.1%)	8 (0.3%)	9 (0.3%)
Grade 4[d]	1 (<0.1%)	0	0	0
Nausea				
Any	871 (19.6%)	408 (10.1%)	367 (12.8%)	285 (10.6%)
Grade 3[b]	22 (0.5%)	6 (0.1%)	6 (0.2%)	9 (0.3%)
Fever[e]				
Any	454 (10.2%)	18 (0.4%)	70 (2.4%)	8 (0.3%)
Grade 3	33 (0.7%)	0	2 (0.1%)	0
Use of antipyretic or pain medication	1217 (27.3%)	278 (6.9%)	296 (10.3%)	121 (4.5%)

Note: Subjects are counted only once within a period for any given event, regardless of the number of times they actually experienced the event in that period. Primary pooled analysis includes data from the double-blind placebo-controlled phase of studies COV1001, COV1002, COV2001, COV3001 and COV3009.

[a] N=Analysis set: Safety Subset

[b] Grade 3 fatigue, myalgia, nausea: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

[c] Grade 3 headache: Defined as incapacitating symptoms; requires bed rest and/or results in loss of work, school, or cancellation of social activities; use of narcotic pain reliever.

[d] Grade 4 myalgia: Defined as hospitalization; inability to perform basic self-care functions.

[e] Fever of any grade: Defined as body temperature ≥38°C/100.4°F. Grade 3 fever: Defined as 39.0°C - 40.0°C (102.1°F - 104.0°F).

Unsolicited Adverse Events (AEs)

Individuals within the safety subset of the primary pooled analysis (N=14,064) were monitored for unsolicited adverse events (AEs) for 28 days following vaccination with JCOVDEN. The proportion of individuals who reported one or more unsolicited AEs was 17.8% in the JCOVDEN group and 13.7% in the placebo group.

Most of these AEs were of Grade 1 or Grade 2 severity, with 1.0% after vaccination with JCOVDEN versus 0.7% with placebo reporting an unsolicited AE of Grade 3 severity. The most common unsolicited AEs occurring within 28 days after vaccination were predominantly reactogenicity events, some of which overlapped with the solicited AEs. Chills were reported in 1.6% of vaccine recipients and 0.5% of placebo recipients.

Serious Adverse Events

In the primary pooled analysis, with a median follow-up of approximately 4 months after primary vaccination, SAEs were reported by 0.9% (n=355) of individuals who received JCOVDEN and 1.3% (n=501) of individuals who received placebo. When COVID-19-related SAEs were excluded, 0.9% (n=337) of participants in the JCOVDEN group and 1.0% (n=375) participants in the placebo group reported an SAE.

Twenty-two SAEs were considered likely related to JCOVDEN. Most related SAEs were reported within the 28-day period after first vaccination. The most frequently reported related SAEs were Bell's palsy and pericarditis. Other SAEs include, complex regional pain syndrome, cerebrovascular accident, facial paresis, Guillain-Barré syndrome, and ischaemic stroke.

Of the 22 related SAEs reported for JCOVDEN, 19 were reported as resolved or resolving and 3 were reported as not resolved at time of data-cut off (18 November 2021) of the individual studies included in the pooled analyses.

No deaths were considered related to JCOVDEN.

Other Adverse Events of Interest

Imbalances in adverse events between the vaccine and placebo group were noted for hypersensitivity, thromboembolic events, tinnitus, vertigo and seizures. The assessment of causality was confounded by the presence of underlying medical conditions that may have predisposed individuals to these events.

Hypersensitivity adverse events were reported in 0.4% of vaccine recipients and 0.3% of placebo recipients. Hypersensitivity events in the vaccine group included rash and urticaria, which are likely related to vaccination. Additional hypersensitivity events considered related to vaccination included 2 cases of facial swelling and the SAE of Type IV hypersensitivity. In addition, severe allergic reactions, including one case of anaphylaxis in an ongoing open-label study in South Africa (COV3012), have been reported following JCOVDEN administered in clinical studies.

Thromboembolic AEs occurred in 15 vaccine recipients and in 10 placebo recipients. Thromboembolic events where the vaccine could not be excluded as a contributing factor include: a case of transverse sinus thrombosis; 2 cases of deep vein thrombosis; one case of pulmonary embolism; and one case of hemiparesis.

Episodes of tinnitus were more common in the JCOVDEN group than in the placebo group (6 cases vs 0 cases), with 3 cases occurring within 3 days of vaccination. Vertigo was also more common in the vaccine group than in the placebo group (13 cases vs 7 cases), with 5 participants in the vaccine group of the Safety Subset experiencing vertigo in the first 28 days. Seizures occurred in 4 vaccine recipients and in one placebo recipient.

The following uncommon adverse events have also been noted: Malaise, Asthenia, Muscular Weakness, Pain in Extremities.

For these adverse events, a causal relationship with JCOVDEN cannot be determined.

No imbalances in adverse events were noted for Guillain-Barré syndrome or facial palsy (Bell's palsy).

Booster Dose

Homologous Booster Dose

Booster Dose following Primary Vaccination with JCOVDEN

The safety of a booster dose with JCOVDEN administered approximately 2 months after the primary vaccination was evaluated in an ongoing randomized, double-blind, placebo-controlled Phase 3 Study (COV3009). In the FAS (full analysis set), from the 15708 adults aged 18 years and older who received 1 dose of JCOVDEN, a total of 8646 individuals received a second dose during the double-blind phase. In the reactogenicity subset, from the 3016 individuals who received 1 dose of JCOVDEN, 1559 individuals received a second dose during the double-blind phase. The median age of individuals was 53.0 years (range: 18-99 years). At the data-cut off (25 June 2021), the median follow-up duration after the booster dose with JCOVDEN was 38 days. At the data cut- off date (23 August 2021), the median follow-up duration after the homologous booster dose with JCOVDEN was 166 days.

A randomized, double-blind Phase 2 study (COV2008) also evaluated the safety of a booster dose with JCOVDEN in individuals 18 years of age and older. Cohort 1 of the study evaluated a homologous booster dose of JCOVDEN, administered at least 6 months after the primary vaccination (N=330). The median age of individuals was 57 years. At the data cut- off date (15 December 2021), the median follow-up duration after the homologous booster dose with JCOVDEN was 104 days.

Overall, the solicited adverse reaction profile for the homologous booster dose was similar to that after the first dose. There were no new safety concerns identified.

Heterologous Booster Dose

Booster Dose following Primary Vaccination with an 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 JCOVDEN, at least 3 months after primary vaccination.

- Cohort 2 of study COV2008 (see study design above), evaluated a heterologous booster dose of JCOVDEN, 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. At the data cut- off date (15 December 2021), the median follow-up duration after the heterologous booster dose with JCOVDEN was 78 days

- The safety of a heterologous booster dose of JCOVDEN was evaluated in the COV-BOOST study, an independent, multicenter, randomized 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 JCOVDEN. There were at least 84 days between the post second dose and the time of the booster dose. Adverse events were assessed through 28 days after the booster dose.

- The safety of a heterologous booster dose of JCOVDEN was assessed in an independent Phase 1/2 open-label clinical trial study (NCT04889209) conducted in the United States. In this study, adults who had completed primary vaccination series of 2 doses with a Moderna (N=49) or Pfizer-BioNTech COVID-19 vaccine (N=50) at least 12 weeks prior to enrolment and who reported no history of SARS-CoV-2 infection, were randomized to receive a booster dose of JCOVDEN. Adverse events were assessed through 28 days after the booster dose.

There were no new safety concerns identified in any of the studies. 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 JCOVDEN.

8.3 Post Market Adverse Reactions

In addition to the adverse reactions listed above, the following adverse reactions have been reported during post-marketing 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.

Blood and lymphatic system disorders: Lymphadenopathy, Thrombocytopenia

Cardiac disorders: Myocarditis, Pericarditis

Ear, nose, and throat disorders: Tinnitus

Gastrointestinal disorders: Diarrhea, Vomiting

Nervous system disorders: Paresthesia, Hypoesthesia, Guillain-Barré syndrome, Dizziness, Transverse Myelitis, Facial Paralysis (including Bell's Palsy)

Vascular disorders:

- Small-vessel vasculitis with cutaneous manifestations.

- 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 JCOVDEN. This includes severe cases at unusual sites such as cerebral venous sinus thrombosis and splanchnic vein thrombosis, as well as arterial thrombosis, concomitant with thrombocytopenia. (See **7 WARNINGS AND PRECAUTIONS**).
- In addition, cases of capillary leak syndrome (CLS) have been observed very rarely following vaccination with JCOVDEN. (See **7 WARNINGS AND PRECAUTIONS**).
- Rare cases of venous thrombosis and thromboembolism have been observed (See **7 WARNINGS AND PRECAUTIONS**).

9 DRUG INTERACTIONS

No interaction studies have been performed.
Do not mix JCOVDEN with any other vaccine in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

JCOVDEN is a monovalent vaccine composed of a recombinant, replication-incompetent human adenovirus type 26 vector that encodes a SARS-CoV-2 Spike (S) protein (original strain) in a stabilized conformation. Following administration, the S glycoprotein of SARS-CoV-2 is transiently expressed stimulating both neutralizing and other functional S antibodies, and cellular immune responses directed against the S antigen, which may contribute to protection against COVID-19.

11 STORAGE, STABILITY AND DISPOSAL

Storage prior to use

The vaccine can be stored and/or transported frozen at -25°C to -15°C. The expiry date for storage at -25°C to -15°C is printed on the vial and carton after “EXP”. The vaccine can also be transported at 2°C to 8°C as long as the appropriate storage conditions (temperature, time) are applied.

When stored frozen at -25°C to -15°C, a carton of 10 vials or an individual vial should be thawed overnight at 2°C to 8°C. At room temperature (maximally 25°C), a carton of 10 vials will take approximately 4 hours to thaw, and an individual vial will take approximately 1 hour to thaw. **DO NOT REFREEZE ONCE THAWED.**

The vaccine can also be stored in a refrigerator at 2°C to 8°C for a single period of up to 11 months, not exceeding the original expiry date (EXP).

The vial must be kept in the original package in order to protect from light and to track the expiry for the different storage conditions, if applicable.

JCOVDEN is stable for a total of 12 hours at 9°C to 25°C. It is not a recommended storage or shipping condition but may guide decisions for use in case of temporary temperature excursions.

Method of determining the expiry date:

- The expiry date for storage at -25°C to -15°C is printed on the vial and carton after "EXP".
- The expiry date at 2°C to 8°C after thaw is for a single period of up to 11 months, not exceeding the original expiry date (EXP) on the labels.
- Upon moving the product to a refrigerator at 2°C to 8°C, the updated expiry date must be written on the carton and the vaccine should be used or discarded by the updated expiry date. The original expiry date should be made unreadable.
- 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 carton before the vaccine is stored in the refrigerator. The original expiry date should be made unreadable.

Storage After First Puncture of the Vaccine Vial

After the first dose has been withdrawn, the vial/filled syringe can be held at 2°C to 8°C for up to 6 hours or at room temperature (maximally 25°C) for up to 3 hours, after the first puncturing of the vial. The discard date and time should be recorded on each vial. Discard if vaccine is not used within this time.

12 SPECIAL HANDLING INSTRUCTIONS

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

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Ad26.COV2-S [recombinant]

Product Characteristics:

JCOVDEN is a colourless to slightly yellow, clear to very opalescent sterile suspension for intramuscular injection. JCOVDEN contains an Adenovirus type 26 (Ad26) vectored COVID-19 vaccine (replication-incompetent, recombinant), encoding the SARS-CoV-2 Spike (S) protein (original strain) in a stabilized conformation. The Adenovirus type 26 (Ad26) vectored COVID-19 vaccine is produced in the PER.C6® TetR Cell Line and by recombinant DNA technology. JCOVDEN contains genetically modified organisms (GMOs). JCOVDEN does not contain a preservative.

JCOVDEN is supplied as a suspension in a multi-dose Type I glass vial with a latex-free rubber stopper (chlorobutyl), aluminum seal and blue plastic cap. Each vial contains 5 doses of 5 x 10^{10}

viral particles/dose. Vials are packaged in a carton containing a total of ten (10) JCOVDEN multi-dose vials per carton.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

JCOVDEN used in clinical trials contains Ad26 vectored COVID-19 vaccine encoding the SARS-CoV-2 Spike (S) protein from the original strain.

Efficacy from a Single-dose Primary Vaccination

An ongoing multicenter, randomized, double-blind, placebo-controlled Phase 3 study (COV3001) is being conducted in the United States, South Africa, Brazil, Chile, Argentina, Colombia, Peru, and Mexico to assess the efficacy, safety, and immunogenicity of a single-dose primary vaccination of JCOVDEN for the prevention of COVID-19 in adults aged 18 years and older. Randomization was stratified by age (18-59 years, 60 years and older) and presence or absence of comorbidities associated with an increased risk of progression to severe COVID-19. The study allowed for the inclusion of individuals with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy during the 3 months preceding vaccination, as well as individuals with stable human immunodeficiency virus (HIV) infection. Participants who had previously received a coronavirus vaccine, pregnant women and participants with abnormal function of the immune system were ineligible. Participants were also excluded if they had known or suspected allergy or a history of anaphylaxis or serious adverse reactions to vaccines or their excipients.

A total of 44,325 participants were randomized in parallel in a 1:1 ratio to receive an IM injection of JCOVDEN (at a dose level of 5×10^{10} VP) or saline placebo. According to protocol, participants are to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The primary efficacy endpoint was defined as a symptomatic moderate to severe/critical COVID-19 case, confirmed by positive SARS COV-2 viral RNA results using a Polymerase Chain Reaction (PCR)-based test in a central laboratory.

Moderate COVID-19 was defined based on the following criteria:

- the participant must have experienced any one of the following new or worsening signs or symptoms: respiratory rate ≥20 breaths/minute, abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level, clinical or radiologic evidence of pneumonia, radiologic evidence of deep vein thrombosis (DVT), shortness of breath or difficulty breathing
- OR any two of the following new or worsening signs or symptoms: fever (≥38.0°C or ≥100.4°F), heart rate ≥90 beats/minute, shaking chills or rigors, sore throat, cough, malaise, headache, muscle pain (myalgia), gastrointestinal symptoms, new or changing olfactory or taste disorders, red or bruised appearing feet or toes.

Severe/critical COVID-19 was defined based on the following criteria:

- the participant must have experienced any one of the following at any time during the course of observation: clinical signs at rest indicative of severe systemic illness [respiratory rate ≥30 breaths/minute, heart rate ≥125 beats/minute, oxygen saturation (SpO2) ≤93% on room air at sea level, or partial pressure of oxygen/fraction of inspired oxygen (PaO2/FiO2) <300 mmHg), respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation- ECMO-), evidence of shock (defined as systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg, or requiring vasopressors], significant acute renal, hepatic, or neurologic dysfunction, admission to intensive care unit (ICU), death.

Final determination of severe/critical COVID-19 cases were made by an independent adjudication committee.

The population for the analysis of the primary efficacy endpoint included participants who did not have evidence of prior infection with SARS-CoV-2 through 14 days after the first dose (co-primary efficacy endpoint), as well participants who did not have evidence of prior infection with SARS-CoV-2 through 28 days after the first dose (co-primary efficacy endpoint).

The primary efficacy analysis population of 39,321 individuals (19,630 in the JCOVDEN group and the 19,691 in the placebo group) included 38,059 SARS-CoV-2 seronegative individuals at baseline, and 1,262 individuals with an unknown serostatus. Table 4 presents the demographic characteristics in the studied population.

Table 4: Summary of Demographics and Baseline Characteristics - Primary Efficacy Analysis Population

	JCOVDEN (N=19,630) n (%)	Placebo (N=19,691) n (%)
Sex		
Male	10,924 (55.6)	10,910 (55.4)
Female	8,702 (44.3)	8,777 (44.6)
Age (years)		
Mean (SD)	51.1 (15.04)	51.2 (14.97)
Median	52.0	53.0
Min, max	(18; 100)	(18; 94)
Age group		
≥18 to 59 years of age	12,830 (65.4)	12,881 (65.4)
≥60 years of age of age	6,800 (34.6)	6,810 (34.6)
≥65 years of age of age	3,984 (20.3)	4,018 (20.4)
≥75 years of age of age	755 (3.8)	693 (3.5)
Race[a]		
White	12,200 (62.1)	12,216 (62.0)
Black or African American	3,374 (17.2)	3,390 (17.2)
Asian	720 (3.7)	663 (3.4)
American Indian/Alaska Native[b]	1,643 (8.4)	1,628 (8.3)
Native Hawaiian or other Pacific Islander	54 (0.3)	45 (0.2)
Multiple	1,036 (5.3)	1,087 (5.5)
Unknown	262 (1.3)	272 (1.4)
Not reported	341 (1.7)	390 (2.0)
Ethnicity		
Hispanic or Latino	8,793 (44.8)	8,936 (45.4)
Not Hispanic or Latino	10,344 (52.7)	10,259 (52.1)
Unknown	173 (0.9)	162 (0.8)
Not reported	319 (1.6)	333 (1.7)
Region		
Northern America (United States)	9,185 (46.8)	9,171 (46.6)
Latin America	7,967 (40.6)	8,014 (40.7)
Southern Africa (South Africa)	2,478 (12.6)	2,506 (12.7)
Comorbidities[c]		
Yes	7,830 (39.9)	7,867 (40.0)
No	11,800 (60.1)	11,824 (60.0)

[a] Some individuals could be classified in more than one category.

[b] Including 175 individuals in the United States, which represents 1% of the population recruited in the United States

[c] Number of individuals who have 1 or more comorbidities at baseline that increase the risk of progression to severe/critical COVID-19: 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%), asthma (1.3%) and in ≤1% of individuals: cancer, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, cystic fibrosis, immunocompromised state (weakened immune system) from blood or organ transplant, liver disease, neurologic conditions, pulmonary fibrosis, sickle cell disease, thalassemia and type 1 diabetes, regardless of age.

14.2 Study Results

Primary Analysis

At the time of the final primary efficacy analysis (cut-off date of 22 January 2021), participants had been followed for symptomatic COVID 19 disease for a median of 8 weeks post-vaccination, corresponding to 3,143.7 person years for the JCOVDEN and 3,146.7 person years in the placebo group.

Vaccine efficacy for the co-primary endpoints against moderate to severe/critical COVID-19 in individuals who were seronegative or who had an unknown serostatus at baseline was 66.9% (95% CI: 59.0; 73.4) at least 14 days after vaccination and 66.1% (95% CI: 55.0; 74.8) at least 28 days after vaccination. Vaccine efficacy results against moderate to severe/critical COVID-19 are presented in Table 5.

Table 5 Analyses of Vaccine Efficacy Against Confirmed Moderate to Severe/Critical COVID-19 – With Onset at Least 14 Days and at Least 28 Days Post-Vaccination – Primary Efficacy Analysis Population

Subgroup	JCOVDEN N=19,630		Placebo N=19,691		% Vaccine Efficacy (95% CI)
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
14 days post-vaccination					
All subjects[a]	116	3116.57	348	3096.12	66.9 (59.03; 73.40) [b]
≥18-59 years old	95	2106.8	260	2095.0	63.7 (53.9; 71.6) [c]
≥60 years and older	21	1009.8	88	1001.2	76.3 (61.6; 86.0)[c]
28 days post-vaccination					
All subjects[a]	66	3102.00	193	3070.65	66.1 (55.01; 74.80)[b]
≥18-59 years old	52	2097.6	152	2077.0	66.1 (53.3; 75.8)[c]
≥60 years and older	14	1004.4	41	993.6	66.2 (36.7; 83.0)[c]

[a] Co-primary endpoint.
[b] The adjusted CI implements type I error control for multiple testing and is presented upon meeting the prespecified testing conditions
[c] CI not adjusted for multiplicity

With onset at least 14 days (28 days) after vaccination, there were 4 (2) cases of mild COVID-19, 309 (220) cases of moderate COVID-19 and 74 (39) cases of severe/critical of COVID-19.

The findings of vaccine efficacy against severe/critical COVID-19 at least 14 days after vaccination and at least 28 days after vaccination are shown in Table 6.

Table 6: Analyses of Vaccine Efficacy: Secondary Endpoints of Confirmed Severe/Critical COVID-19 – in Adults 18 Years of Age and Older With Onset at Least 14 Days and at Least 28 Days Post-Vaccination – Primary Efficacy Analysis Population

Subgroup	JCOVDEN N=19,630		Placebo N=19,691		% Vaccine Efficacy (95% CI)
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
14 days post-vaccination					
Severe/critical	14	3125.05	60	3122.03	76.7 (54.56; 89.09)[a]
28 days post-vaccination					
Severe/critical	5	3106.15	34	3082.58	85.4 (54.15; 96.90)[a]

[a] The adjusted CI implements type I error control for multiple testing and is presented upon meeting the prespecified testing conditions.

There were 2 COVID-19 related hospitalizations in the vaccine group and 29 in the placebo group among all COVID-19 cases with onset at least 14 days post vaccination, including cases diagnosed by a positive PCR from a local laboratory and still awaiting confirmation at the central laboratory. There were no COVID-19 related hospitalizations in the vaccine group and 16 in the placebo group, among all COVID-19 cases with onset at least 28 days post vaccination, including cases diagnosed by a positive PCR from a local laboratory and still awaiting confirmation at the central laboratory.

There were no COVID-19-related deaths reported in JCOVDEN recipients, compared to 5 COVID-19-related deaths reported in placebo recipients, who were SARS-CoV-2 PCR negative at baseline.

Strain sequencing was conducted on available samples with sufficient viral load from centrally confirmed COVID-19 cases (one sequence per case). 71.7% of central laboratory confirmed primary analysis cases have been sequenced [United States (73.5%), South Africa (66.9%) and Brazil (69.3%)]. 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. As of February 12, 2021, SARS-CoV-2 variants from the B1.1.7 or P.1 lineages were not found in any of the sequenced samples. Exploratory subgroup analyses of vaccine efficacy against moderate to severe/critical COVID-19 and severe/critical COVID-19 for Brazil, South Africa, and the United States were conducted. For these subgroup analyses, all COVID-19 cases (PCR-positive cases confirmed and pending confirmation by the central laboratory) accrued up to the primary efficacy analysis data cut-off date of 22 January 2021 were included. The concordance rate observed up to the data cut-off date between the PCR results from the local laboratory and the central laboratory was 90.3%. The results are shown in Table 7.

Table 7: Summary of Vaccine Efficacy against Moderate to Severe/Critical and Severe/Critical COVID-19 for Countries With >100 Reported Moderate to Severe/Critical Cases

		Severity	
	Onset	**Moderate to Severe/Critical Point estimate (95% CI)[a]**	**Severe/Critical Point estimate (95% CI)[a]**
US	at least **14 days** after vaccination	74.4% (65.0; 81.6)	78.0% (33.1; 94.6)
	at least **28 days** after vaccination	72.0% (58.2;81.7)	85.9% (-9.4; 99.7)
Brazil	at least **14 days** after vaccination	66.2% (51.0; 77.1)	81.9% (17.0; 98.1)
	at least **28 days** after vaccination	68.1% (48.8; 80.7)	87.6% (7.8; 99.7)
South Africa	at least **14 days** after vaccination	52.0% (30.3; 67.4)	73.1% (40.0; 89.4)
	at least **28 days** after vaccination	64.0% (41.2; 78.7)	81.7% (46.2; 95.4)

[a] CI's are not adjusted for multiplicity

Updated Analyses

The updated 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 JCOVDEN 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 of a Booster Dose following Primary Vaccination with JCOVDEN

A global, randomized, placebo-controlled study COV3009 was conducted to demonstrate efficacy of 2 doses of JCOVDEN administered with a 56-day interval. A total of 31300 individuals were randomized in the double-blind phase of the study. A total of 15708 individuals received JCOVDEN and 15592 individuals received placebo. In total, 14492 (46.3%) individuals were included in the per-protocol efficacy population (7484 individuals received JCOVDEN 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 8 below:

Table 8: Analysis of Vaccine Efficacy Against Moderate To Severe/Critical And Severe/Critical COVID19 – 14 Days Post-Booster Dose

Endpoint	JCOVDEN 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	1730.0	52	1595.0	75.2 (54.6; 87.3)
Severe/critical COVID-19	0	1730.7	8	1598.9	100 (32.6; 100.0)

[a] Confidence intervals were adjusted to implement type I error control for multiple testing.

[b] Per-protocol efficacy population.

Immunogenicity of a Booster Dose following Primary Vaccination with JCOVDEN

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

In this study, the effectiveness of a booster dose of JCOVDEN was inferred from an assessment of the neutralizing antibody titers (IC_{50}) against the SARS-CoV-2 reference strain and the Delta (B.1.617.2) and Omicron (B.1.1.529) variants using a pseudovirion expressing the S protein in a neutralizing antibody assay. Immunogenicity analyses included an assessment of IC_{50} geometric mean titer (GMT) differences 14 days following the booster dose compared to the IC_{50} 28 days following the primary vaccination and differences in responder or seropositivity rates.

In Cohort 1, the homologous booster regimen of JCOVDEN 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 summarized in Table 9. The NI of neutralizing antibodies following booster immunization link the booster response to the clinical efficacy demonstrated after the initial priming immunization.

Table 9: SARS-CoV-2 Neutralising Antibody Titres and 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	14 Days Post-Booster	GMFI (95% CI) 14 Days Post-Booster vs 28 Days Post Primary Vaccination[a]	Responder Rate Difference 14 Days Post-Booster vs 28 Days Post Primary Vaccination (95% CI)	Met Non-inferiority Objective[b] (Y/N)
Reference Strain					
N[c]	312	298	297		
GMT[d] (95% CI)	98 (85; 113)	1130 (989; 1291)	8.1 (7.0; 9.4)		Y
N[c]	312	298	n/a	297	
Responder rates: n[e] (%) (95% CI)[f]	48 (15.4%) (11.6%; 19.9%)	189 (63.4%) (57.7%; 68.9%)	n/a	47.8 (41; 54.6)	Y
Delta Variant					
N[c]	311	298	296		
GMT[d] (95% CI)	< LLOQ (< LLOQ; < LLOQ)	471 (411; 539)	5.6 (4.9; 6.4)		Y
N[c]	308	298	n/a	293	
Responder rates: n[e] (%) (95% CI)[f]	27 (8.8%) (5.9%; 12.5%)	169 (56.7%) (50.9%; 62.4%)	n/a	47.1 (40.7; 53.6)	Y

Abbreviations: CI = confidence interval, GMT = geometric mean titre, 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 neutralisation assay, IC_{50} = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

* Analysis conducted with 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 logarithms and the corresponding CIs were based on the Student t distribution. The psVNA's (IC_{50}) LLOQ values for the reference strain and Delta variant were 75 and 65, 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 was demonstrated if the lower bound of the 2-sided 95% CI for the GMFI was > 0.67 with a GMFI point estimate > 0.80, when comparing neutralising 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 and the corresponding CIs (based on the Student t distribution). The psVNA's LLOQ values (IC_{50}) for the reference strain and Delta variant were 75 and 65, respectively. Assay results below the LLOQ were set to 0.5 × LLOQ. Assay results above ULOQ were set to ULOQ.

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

[f] Exact Clopper-Pearson 95% confidence intervals are shown for Responders.

A descriptive analysis of neutralizing antibody titers against the Omicron BA.1 variant of SARS-CoV-2 was performed using a validated pseudovirion neutralization assay. The GMT at 14 days after the booster dose of JCOVDEN among 45 randomly selected study participants without evidence of prior SARS-CoV-2 infection (82 [95% CI: <LLOQ [=66]; 110]) was increased compared to the GMT before the booster dose (<LLOQ [95% CI: <LLOQ, <LLOQ]).

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

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

In Cohort 2, baseline neutralizing 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 JCOVDEN 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 summarized in Table 10.

Table 10: SARS-CoV-2 Neutralising Antibody Titres and Seropostivity 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 Comirnaty[a]	14 Days Post-Booster	GMR (97.5% CI) 14 Days Post Booster vs 14 to 60 Days Post Primary Regimen with Comirnaty[b]	Seropositivity % Difference 14 Days Post Booster vs 14 to 60 Days Post Primary Vaccination with Comirnaty (97.5% CI)	Met Non-inferiority Objective[c] (Y/N)
Reference Strain					
N[d]	309	299	608		
GMT[e] (95% CI)	1281 (1086; 1510)	4439 (4027; 4893)	3.3 (2.7; 4.0)[b]	n/a	Y
N[d]	309	299		608	
Seropositivity rate[f] n[g] (%) (95% CI)[i]	284 (91.9%) (88.3%; 94.7%)	299 (100.0%) (98.8%; 100.0%)	n/a	8.1 (3.0; 13.2)	Y
Delta Variant					
N[d]	309	299	608		
GMT[e] (95% CI)	502 (422; 598)	2318 (2049; 2623)	4.1 (3.3; 5.2)[b]		Y
N[d]	309	299		608	
Seropositivity rate[f] n[g] (%) (95% CI)[h]	259 (83.8%) (79.2%; 87.7%)	298 (99.7%) (98.2%; 100.0%)	n/a	15.8 (9.8; 21.9)	Y

Abbreviations: CI = confidence interval, GMT = geometric mean titre, 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 neutralisation assay, IC_{50} = serum concentration conferring 50% inhibition, (Y/N) = yes/no.

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

a Neutralising antibody levels post primary regimen with Comirnaty were measured in an external sample set and includes individuals who received 2 doses of the Comirnaty as a primary vaccination and for whom blood samples are available between Day 14 and Day 60 post primary vaccination.

b GMRs and 2-sided 97.5% CIs were calculated by exponentiating difference of the means in logarithms and the corresponding CIs were 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.

c Non-inferiority was demonstrated if the lower bound of the 2-sided 97.5% CI for the GMR was > 0.67 with a GMR point estimate > 0.80, when comparing neutralising antibody responses 14 days after booster dose and those at Day 14 to 60 after primary regimen with Comirnaty.

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

e GMTs and 2-sided 95% CIs were calculated by exponentiating the mean in logarithms and the corresponding CIs were based on the Student t distribution. The psVNA's LLOQ value (IC_{50}) for the reference strain and Delta variant were 75 and 65, respectively. Assay results below the LLOQ were set to 0.5 × LLOQ. Assay results above ULOQ were set to ULOQ.

f Seropositivity rates rather than responder rates are used for the NI assessments.

g n = Number of participants with a positive sample. Positive sample refers to a quantifiable response (≥LLOQ).

h Exact Clopper-Pearson 95% confidence intervals are shown for % Seropositivity.

A descriptive analysis of neutralizing antibody titers against the Omicron strain of SARS-CoV-2 was performed using a validated pseudovirion neutralization assay. The GMT at 14 days after the booster dose of JCOVDEN among 45 randomly selected study participants without evidence of prior SARS-CoV-2 infection (526 [95% CI: (357; 776)]) was increased compared to the GMT before the booster dose (<LLOQ [=66] [95% CI: <LLOQ; <LLOQ]).

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: In a repeat-dose toxicity study, New Zealand White rabbits were administered JCOVDEN by intramuscular injection at a dose of $1x10^{11}$ vp/dose (in 1 mL), every two weeks for a total of 3 doses. Vaccine administration resulted in inflammation at the site of injection, as well as increased germinal centre cellularity in draining lymph nodes and spleen (correlating with enlargement of draining lymph nodes and increased spleen weights), transient increase in body temperature, increased white blood cell counts, and clinical chemistry changes indicative of an acute phase response. Full or partial recovery from all findings was observed following a 3-week recovery period. These changes are consistent with an expected immunostimulatory response following intramuscular administration of a vaccine and are not deemed adverse.

Carcinogenicity: JCOVDEN has not been evaluated for its carcinogenic potential. The components of the vaccine are not expected to have carcinogenic potential.

Genotoxicity: JCOVDEN has not been evaluated for its genotoxic potential. The components of the vaccine are not expected to have genotoxic potential.

Reproductive and Developmental Toxicology: Female reproductive toxicity, fertility, and developmental toxicity were assessed in a combined embryo-fetal and pre- and postnatal development study in the rabbit. In this study a first vaccination of JCOVDEN was administered intramuscularly to female rabbits 7 days prior to mating at a dose ($1x10^{11}$ vp/dose in 1 mL) equivalent to 2-fold above the recommended human dose on an absolute basis, followed by two vaccinations at the same dose during the gestation period (i.e. on gestation days 6 and 20, respectively). There was no adverse effect of JCOVDEN on reproductive performance, fertility, ovarian and uterine examinations, or parturition; however, one female died on gestation day 23 from unknown causes. In addition, there was no adverse effect of vaccination on fetal body weights, external, visceral and skeletal evaluations, or on postnatal development of the offspring.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

JCOVDEN™

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

Read this carefully before you start taking **JCOVDEN**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **JCOVDEN**.

What is JCOVDEN used for?

JCOVDEN is a vaccine used to prevent COVID-19 disease caused by the SARS-CoV-2 virus. JCOVDEN can be given to protect people aged 18 years and older.

How does JCOVDEN work?

JCOVDEN uses a recombinant human adenovirus type 26 vector (Ad26.COV2-S) that cannot replicate (replication-incompetent), to stimulate the body's natural defenses (immune system). The body will then produce its own protection (antibodies) against the virus.

The vaccine is given as a single dose, by injection with a needle, usually in the upper arm.

You cannot get COVID-19 from this vaccine.

As with any vaccine, JCOVDEN may not fully protect all those who receive it. Even after you have had the vaccine, continue to follow the recommendations of local public health officials to prevent spread of COVID-19.

What are the ingredients in JCOVDEN?

Medicinal ingredients: 5×10^{10} virus particles of Ad26.COV2-S per dose of vaccine, encoding the SARS-CoV-2 Spike (S) protein.

JCOVDEN is produced by recombinant DNA technology.

Non-medicinal ingredients:

- 2-hydroxypropyl-β-cyclodextrin
- Citric acid monohydrate
- Ethanol
- Hydrochloric acid
- Polysorbate-80
- Sodium chloride
- Sodium hydroxide
- Trisodium citrate dihydrate
- Water for injection

JCOVDEN comes in the following dosage forms:

Colourless to slightly yellow, clear to very opalescent suspension provided in a multiple dose vial of 5 doses of 0.5 mL.

Do not use JCOVDEN if:

- you have previously had a severe allergic reaction to any of the active substance(s) or any of the other ingredients of JCOVDEN
- you have ever had a severe allergic reaction after a dose of any other 'adenovirus-based vaccine'
- you have ever had a diagnosis of capillary leak syndrome, a very rare, serious condition where fluid (plasma) leaks out of the small blood vessels into the body tissues. (see ***What are the possible side effects from using JCOVDEN***).
- you currently have symptoms that could be due to COVID-19. Talk to your healthcare professional about your symptoms and getting a COVID-19 test. Your healthcare professional will advise you when you are able to receive the vaccine.
- you have had a blood clot occurring at the same time as having low levels of blood platelets (thrombosis with thrombocytopenia syndrome, TTS) after receiving JCOVDEN or any other adenovirus-vectored COVID-19 vaccine (see **What are the possible side effects from using JCOVDEN**).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take JCOVDEN. Talk about any health conditions or problems you may have, including if you:

- Have ever had a severe allergic reaction after any type of vaccine
- Have had a history of venous sinus thrombosis in the brain with low platelets (thrombocytopenia), a history of TTS, a history of heparin-induced thrombocytopenia (HIT), or a history of very low platelets (immune thrombocytopenia)
- Have been told you are at risk of blood clots
- Have previously experienced episodes of capillary leak syndrome.
- Have a weakened immune system due to a medical condition or are on a medicine that affects your immune system
- Are pregnant, think you may be pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have a bleeding problem, bruise easily or use a blood thinning medication
- Have a high fever or severe infection
- Have any serious illness
- Have ever fainted following any needle injection

Do not drive or use machines if you are feeling unwell after vaccination.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given JCOVDEN.
Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There is no information on the use of JCOVDEN with other vaccines. Tell your healthcare professional if you have recently taken or might take any other vaccine.

How JCOVDEN is given:

- Your doctor, pharmacist, or nurse will inject the vaccine into a muscle (intramuscular injection) - usually in your upper arm.
- During and after each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least 15 minutes to monitor for signs of an allergic reaction.

Usual dose:

A single dose (0.5 mL) primary vaccination of JCOVDEN should be administered in individuals 18 years of age and older.

A booster dose of JCOVDEN may be given at least 2 months after the primary vaccination in individuals 18 years of age and older.

JCOVDEN may be administered as a single booster dose to eligible individuals who have completed primary vaccination with an mRNA COVID-19 vaccine.

Overdose:

If you think you, or a person you are caring for, have received too much JCOVDEN, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using JCOVDEN?

Like all vaccines, JCOVDEN can cause side effects. In clinical studies with the vaccine, most of the side effects, happened within 2 days of getting the injection, were mild to moderate in intensity, and resolved within 1-2 days.

If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

The following side effects may happen with this vaccine:

Very common (may affect more than 1 in 10 people):

- headache
- nausea
- muscle aches
- pain at injection site
- feeling very tired (fatigue)

Common (may affect up to 1 in 10 people):

- fever
- redness at injection site
- swelling at injection site
- chills
- joint pain

Uncommon (may affect up to 1 in 100 people):

- rash
- muscle weakness
- arm or leg pain
- feeling weak
- feeling generally unwell
- dizziness

Rare (may affect up to 1 in 1000 people):

- allergic reaction, including hives

  Should you develop any serious symptoms or symptoms that could be an allergic reaction, seek medical attention immediately. Symptoms of an allergic reaction include:

  - hives (bumps on the skin that are often very itchy)
  - swelling of the face, tongue or throat
  - difficulty breathing

Very rare (may affect up to 1 in 10000 people):

- persistent ringing in the ears (tinnitus)
- diarrhea
- unusual feeling in the skin, such as a persistent tingling feeling (paresthesia)
- swollen lymph nodes (lymphadenopathy)
- vomiting
- decreased feeling or sensitivity, especially in the skin (hypoesthesia)
- serious nerve inflammation, which may cause paralysis and difficulty breathing (Guillain-Barré syndrome, Transverse Myelitis)
- unexplained bleeding

- **Small-vessel vasculitis with cutaneous manifestation:** inflammation of small blood vessels with skin rash or small red or purple, flat, round spots under the skin's surface or bruising.

- **Thrombosis with thrombocytopenia syndrome (TTS):** A combination of blood clots and low level of platelets, in some cases together with bleeding, has been observed very rarely in unusual locations (e.g., brain, liver) following vaccination with JCOVDEN and some cases have resulted in death. This has been reported in men and women 18 years of age and older, but more frequently in women below 50 years of age. ~~Seek immediateJCOVDEN.~~ Seek medical attention if any of the following symptoms occur within the first month following vaccination:

  - new severe headaches, worsening or persistent headaches; blurred vision, confusion or seizures
  - shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain
  - unexplained skin bruising or pinpoint round spots under the skin beyond the site of vaccination

- Unusual or excessive bleeding

- **Venous thromboembolism (VTE):** Blood clots in veins have been observed rarely following vaccination with JCOVDEN. In individuals with a pre-existing increased risk for thromboembolism, the possible increased risk of VTE with vaccine use should be considered.
- **Capillary leak syndrome (CLS):** Very rare cases of CLS have been reported following vaccination with JCOVDEN. Some affected patients had a previous diagnosis of CLS. CLS is a serious, potentially fatal condition causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint (low blood pressure). Seek medical attention right away if you develop these symptoms in the days following vaccination.
- **Guillain-Barré syndrome (GBS):** GBS is a neurological disorder where inflammation of peripheral nerves causes rapid muscle weakness and can sometimes lead to paralysis. This has been reported very rarely after vaccination with JCOVDEN. Seek immediate medical attention if you develop weakness and paralysis in the extremities that can progress to the chest and face.
- **Facial Paralysis (including Bell's Palsy):** Drooping eyelid and/or sagging muscles usually on one side of the face ('facial palsy' or 'Bell's palsy') have been observed rarely following vaccination with JCOVDEN. This is usually temporary.
- **Transverse Myelitis (TM)**: TM is a neurological disorder where the inflammation of the spinal cord causes weakness in the arms or legs, sensory symptoms (such as tingling, numbness, pain or loss of pain sensation) or problems with bladder or bowel function. This has been reported very rarely after vaccination with JCOVDEN. Seek immediate medical attention if you develop weakness, sensory symptoms or problems with bladder or bowel function.
- **Immune thrombocytopenia:** Very low levels of blood platelets (immune thrombocytopenia), that can be associated with bleeding, have been reported very rarely, usually within the first four weeks following vaccination with JCOVDEN.

These may not be all the possible side effects of JCOVDEN. If you experience any side effects not listed here, tell your healthcare professional.

Tell your doctor, pharmacist or nurse if you have any side effects that bother you, interfere with your daily activities, or do not go away.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Janssen Inc. cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) and send it to your local Health Unit.

Storage:

Your doctor, pharmacist or nurse is responsible for storing this vaccine and disposing of any unused product correctly.

Keep JCOVDEN out of reach and sight of children.

If you want more information about JCOVDEN:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (www.janssen.com/canada), or by calling Janssen Inc. at: 1-800-567-3331.

This leaflet was prepared by Janssen Inc.
Toronto, Ontario M3C 1L9

Last revised: February 16, 2023

© 2023 JANSSEN Inc.

All trademarks used under license.