

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

COVID-19 Vaccine Janssen suspension for injection
COVID-19 vaccine (Ad26.COVS-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 glycoprotein* (Ad26.COVS-S), not less than 8.92 log₁₀ infectious units (Inf.U).

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

The product contains genetically modified organisms (GMOs).

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

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

4.2 Posology and method of administration

Posology

Individuals 18 years of age and older

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

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.

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.

Individuals who have previously experienced episodes of capillary leak syndrome (CLS) (see also section 4.4).

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.

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, 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. Fatal outcome has been reported. These cases occurred within the first three weeks following vaccination, and mostly in individuals under 60 years of age.

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 diagnose and treat this condition.

Individuals who have experienced thrombosis with thrombocytopenia syndrome following vaccination with any COVID-19 vaccine should not receive COVID-19 Vaccine Janssen (See also section 4.3).

Individuals with a history of heparin-induced thrombocytopenia and thrombosis (HITT or HIT type 2) should only receive the COVID-19 Vaccine Janssen if the potential benefits outweigh the potential risks.

- **Venous thromboembolism:** Venous thromboembolism (VTE) has been observed rarely following vaccination with COVID-19 Vaccine Janssen (see section 4.8). This should be considered for individuals at increased risk for VTE.
- **Immune thrombocytopenia:** Cases of immune thrombocytopenia with very low platelet levels (<20000 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. 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 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.

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.

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.

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.

Guillain-Barré syndrome and transverse myelitis

Guillain-Barré syndrome (GBS) and transverse myelitis (TM) have been reported very rarely following vaccination with COVID-19 Vaccine Janssen. 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.

Risk of very rare events after a booster dose

The risk of very rare events (such as coagulation disorders including thrombosis with thrombocytopenia syndrome, CLS and GBS) after a booster dose of COVID-19 Vaccine Janssen has not yet been characterised.

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.

4.5 Interaction with other medicinal products and other forms of interaction

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

Pregnancy

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 section 5.3).

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

It is unknown whether COVID-19 Vaccine Janssen is excreted in human milk.

Fertility

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

4.7 Effects on ability to drive and use machines

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

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 21895 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 11948 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 \geq 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 \geq 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 2151 adults seropositive at baseline received COVID-19 Vaccine Janssen (9.8%).

Booster dose (second dose) following primary vaccination with COVID-19 Vaccine Janssen

The safety of a booster dose (second dose) with COVID-19 Vaccine Janssen administered approximately 2 months after the primary vaccination was evaluated in an ongoing randomised, 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 COVID-19 Vaccine Janssen, 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 COVID-19 Vaccine Janssen, 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 COVID-19 Vaccine Janssen was 38 days. The solicited adverse reaction profile for the booster dose was similar to that after the first dose. There were no new safety signals identified.

Booster dose following primary vaccination with an approved mRNA COVID-19 vaccine

The safety of a booster dose with COVID-19 Vaccine Janssen administered at least 12 weeks after the primary vaccination with an approved mRNA COVID-19 vaccine regimen was assessed after 2 doses of Spikevax (49 individuals) or Comirnaty (51 individuals), or 1 dose of COVID-19 Vaccine Janssen (50 individuals). The median age of individuals was 55.0 years (range: 20-77 years). At the data-cut off (24 September 2021), 98.7% of the subjects had completed the Day 29 visit after booster vaccination (none has reached Day 91). Following the COVID-19 Vaccine Janssen heterologous booster, the solicited adverse reaction profile was similar to that following a COVID-19 Vaccine Janssen primary vaccination or homologous booster dose.

Tabulated list of adverse reactions

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

Very common ($\geq 1/10$);

Common ($\geq 1/100$ to $< 1/10$);

Uncommon ($\geq 1/1000$ to $< 1/100$);

Rare ($\geq 1/10000$ to $< 1/1000$);

Very rare ($< 1/10000$);

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 (≥ 1/1000 to < 1/100)	Rare (≥ 1/10000 to < 1/1000)	Very Rare (< 1/10000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders				Lymph-adenopathy		Immune thrombocytopenia
Immune system disorders				Hypersensitivity ^a ; urticaria		Anaphylaxis ^b
Nervous system disorders	Headache		Tremor; dizziness; paraesthesia	Hypoaesthesia	Guillain-Barré syndrome	Transverse myelitis
Ear and labyrinth disorders				Tinnitus		
Vascular disorders				Venous thromboembolism	Thrombosis in combination with thrombocytopenia	Capillary leak syndrome
Respiratory, thoracic and mediastinal disorders		Cough	Sneezing; oropharyngeal pain			
Gastrointestinal disorders	Nausea		Diarrhoea	Vomiting		
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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. If you are concerned about an adverse event, it should be reported on a Yellow Card.

Reporting forms and information can be found at <https://coronavirus-yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store and include the vaccine brand and batch/Lot number if available. Alternatively, adverse events of concern in association with COVID-19 Vaccine Janssen can be reported to Janssen on +442076602872/0080056540088 Or visit the URL: www.covid19vaccinejanssen.com

Please do not report the same adverse event(s) to both systems as all reports will be shared between Janssen and MHRA (in an anonymised form) and dual reporting will create unnecessary duplicates.

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.

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

An ongoing, multicentre, randomised, double-blind, placebo-controlled phase 3 study (COV3001) is being conducted in the United States, South Africa and Latin American countries to assess the efficacy, safety, and immunogenicity of a single-dose 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=15646) of individuals were 18 to 64 years old [with 20.3% (N=3984) 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 7830 (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 \geq 30 kg/m² (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 \leq 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 2.

Table 2: 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 (95% CI) ^c
	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)
18 to 64 years of age	107	2530.27	297	2511.23	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	3102.00	193	3070.65	66.1 (55.01; 74.80)
18 to 64 years of age	60	2518.73	170	2490.11	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 3 below.

Table 3: 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	3125.05	60	3122.03	76.7 (54.56; 89.09)
28 days post-vaccination					
Severe	5	3106.15	34	3082.58	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 (SpO₂) criterion for severe disease ($\leq 93\%$ 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 4). 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 4: Summary of vaccine efficacy against COVID-19 and severe COVID-19 for countries with > 100 reported cases

	Onset	Severity	
		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.

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 (\geq 65 years) and younger individuals (18-64 years).

Paediatric population

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

Conditional approval

This medicinal product has been authorised under a so-called ‘conditional approval’ scheme. This means that further evidence on this medicinal product is awaited. New information on this medicinal product will be reviewed at least every year and this SmPC will be updated as necessary.

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.

Reproductive toxicity and fertility

Female reproductive toxicity and fertility were assessed in a combined embryo-foetal and pre- and post-natal 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. No COVID-19 Vaccine Janssen data are available on vaccine excretion in milk.

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.

6.1 List of excipients

10 vial pack

2-hydroxypropyl- β -cyclodextrin (HBCD)

Citric acid monohydrate

Ethanol

Hydrochloric acid

Polysorbate-80

Sodium chloride

Sodium hydroxide

Trisodium 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

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 4.5 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 to 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

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 13 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 4 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 4.5 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 crossed out. 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.

Unopened COVID-19 Vaccine Janssen 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 during the 4.5 month storage at 2°C to 8°C .

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.

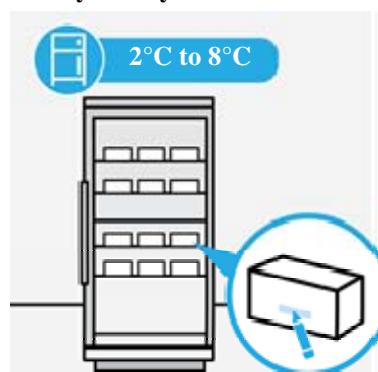
- The vaccine comes ready to use once thawed.
- The vaccine may be supplied frozen at -25°C to -15°C or thawed at 2°C to 8°C .
- Do not re-freeze vaccine once thawed.
- Keep the vials in the original carton in order to protect from light and to record the expiry for the different storage conditions,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

a. 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 4.5 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 crossed out** (see section 6.4).

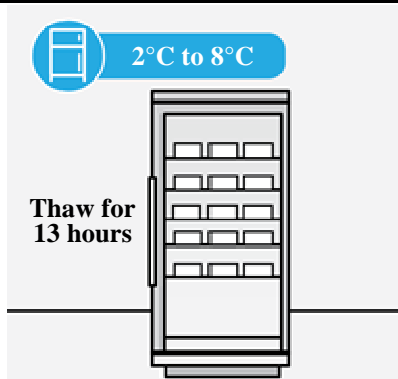
IF YOU RECEIVE YOUR VACCINE THAWED AT 2°C to 8°C you should store in a refrigerator:



⚠ 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 crossed out** (see section 6.4).

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

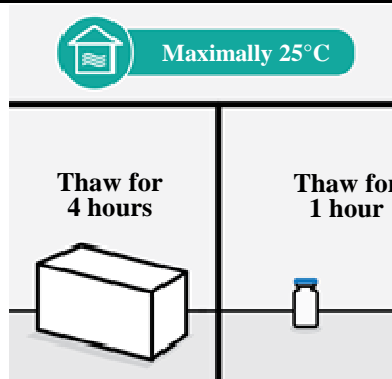


Thaw in refrigerator

- When stored frozen at -25°C to -15°C, a carton of 10 vials will take approximately 13 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.

⚠ Do not re-freeze once thawed.

OR



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 **4 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**. It is not a recommended storage or shipping condition but may guide decisions for use in case of temporary temperature excursions.
- If the vaccine is not used immediately, refer to the instructions

in section Store in a refrigerator.

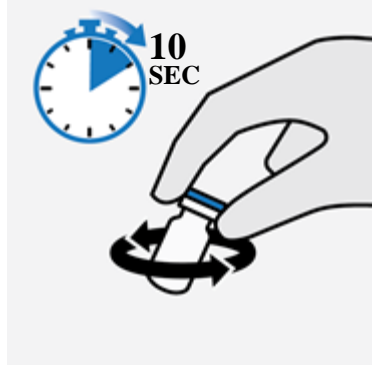
⚠ Do not re-freeze once thawed.

c. Inspect vial and vaccine

- COVID-19 Vaccine Janssen is a colorless 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.

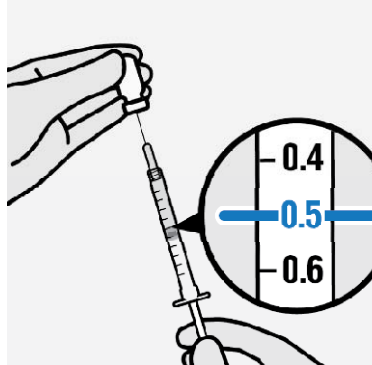
If any of these should exist, do not administer the vaccine.

d. Prepare and administer vaccine



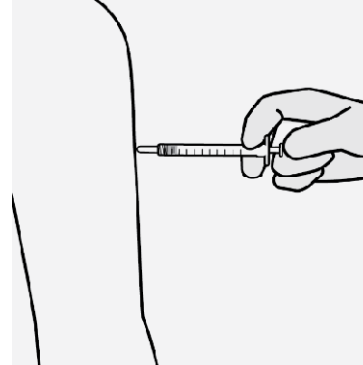
Swirl the vial gently

- 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 multi-dose vial (see section 4.2).

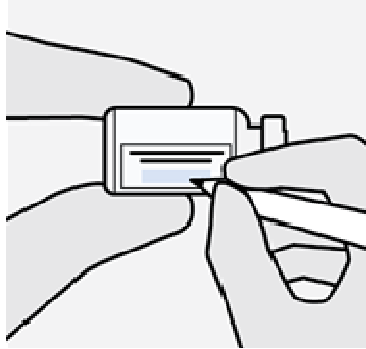



Inject 0.5 mL

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

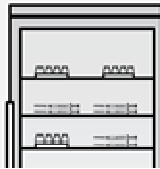
⚠ A maximum of 5 doses can be withdrawn from the multi-dose vial. Discard any remaining vaccine in the vial after 5 doses have been extracted.

e. Storage after first puncture



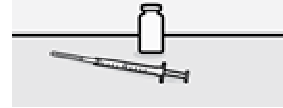
 **2°C to 8°C**

Store up to 6 hours



 **Maximally 25°C**


Store up to 3 hours



OR

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.

- 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.

f. 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 MARKETING AUTHORISATION HOLDER

Janssen-Cilag Ltd
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 00242/0742

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/03/2022

10 DATE OF REVISION OF THE TEXT

10/05/2022