ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

COVID-19 Vaccine Janssen suspension for injection
COVID-19 vaccine (Ad26.COV2-S [recombinant])

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

One dose (0.5 mL) contains:
Adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein* (Ad26.COV2-S), not less than 8.92 $\log_{10}$ infectious units (Inf.U).
* Produced in the PER.C6 TetR Cell Line and by recombinant DNA technology.

The product contains genetically modified organisms (GMOs).

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

Primary vaccination

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

Booster dose

A booster dose (second dose) of 0.5 mL of COVID-19 Vaccine Janssen may be administered intramuscularly at least 2 months after the primary vaccination in individuals 18 years of age and older (see also sections 4.4, 4.8 and 5.1).

A booster dose of the COVID-19 Vaccine Janssen (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with an approved mRNA COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorised for a booster dose of the vaccine used for primary vaccination (see also sections 4.4, 4.8 and 5.1).

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

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

Method of administration

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

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

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

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

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

4.3 Contraindications

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

A history of confirmed thrombosis with thrombocytopenia syndrome (TTS) following vaccination with any COVID-19 vaccine (see also section 4.4).

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 women 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).
- ***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

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

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 ≥ 38.0°C) was observed in 9% of participants. Most adverse reactions occurred within 1–2 days following vaccination and were mild to moderate in severity and of short duration (1–2 days).

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

The safety profile was generally consistent across participants with or without prior evidence of SARS-CoV-2 infection at baseline; a total of 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 (≥ 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).

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 thrombo-cytopenia
Immune system disorders				Hypersensitivity[a]; urticaria		Anaphylaxis[b]
Nervous system disorders	Headache		Tremor; dizziness; paraesthesia	Hypoaesthesia	Guillain-Barré syndrome	
Ear and labyrinth disorders				Tinnitus		
Vascular disorders				Venous thromboembolism	Thrombosis in combination with thrombo-cytopenia	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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

4.9 Overdose

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

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

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

Efficacy from a single-dose primary vaccination

Primary analysis

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

A total of 44325 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 21895 adults received COVID-19 Vaccine Janssen and 21888 adults received placebo. Participants were followed for a median follow-up of approximately 2 months after vaccination.

The primary efficacy analysis population of 39321 individuals included 38059 SARS-CoV-2 seronegative individuals at baseline and 1262 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/m^2 (27.5%), hypertension (10.3%), type 2 diabetes (7.2%), stable/well-controlled HIV infection (2.5%), serious heart conditions (2.4%) and asthma (1.3%). Other comorbidities were present in $\leq$ 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 after a single-dose

	COVID-19 Vaccine Janssen N=19630		**Placebo N=19691**		**% Vaccine Efficacy (95% CI)[c]**
Subgroup	**COVID-19 Cases (n)**	**Person-Years**	**COVID-19 Cases (n)**	**Person-Years**	
14 days post-vaccination					
All subjects[a]	116	3116.6	348	3096.1	66.9 (59.0; 73.4)
18 to 64 years of age	107	2530.3	297	2511.2	64.2 (55.3; 71.6)
65 years and older	9	586.3	51	584.9	82.4 (63.9; 92.4)
75 years and older	0	107.4	8	99.2	100 (45.9; 100.0)

28 days post-vaccination					
All subjects[a]	66	3102.0	193	3070.7	66.1 (55.0; 74.8)
18 to 64 years of age	60	2518.7	170	2490.1	65.1 (52.9; 74.5)
65 years and older	6	583.3	23	580.5	74.0 (34.4; 91.4)
75 years and older	0	106.4	3	98.1	–

[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 after a single-dose

	COVID-19 Vaccine Janssen N=19630		**Placebo N=19691**		**% Vaccine Efficacy (95% CI)[b]**
Subgroup	**COVID-19 Cases (n)**	**Person-Years**	**COVID-19 Cases (n)**	**Person-Years**	
14 days post-vaccination					
Severe	14	3125.1	60	3122.0	76.7 (54.6; 89.1)
28 days post-vaccination					
Severe	5	3106.2	34	3082.6	85.4 (54.2; 96.9)

[a] Final determination of severe COVID-19 cases was made by an independent adjudication committee, who also assigned disease severity according to the definition per FDA guidance.

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

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

Updated analyses

The updated efficacy analyses at the end of the double-blind phase (cut-off date 09 July 2021) were performed 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 the COVID-19 Vaccine Janssen.

Table 4: Analysis of vaccine efficacy against symptomatic[a] and severe[b] COVID-19 – 14 days and 28 days after a single-dose

Endpoint[c]	**COVID-19 Vaccine Janssen N=19577[d]**		**Placebo N=19608[d]**		**% Vaccine Efficacy (95% CI)**
	COVID-19 Cases (n)	**Person-Years**	**COVID-19 Cases (n)**	**Person-Years**	
14 days post-vaccination					
Symptomatic COVID-19	484	6685.6	1067	6440.2	56.3 (51.3; 60.9)
18 to 64 years of age	438	5572.0	944	5363.6	55.3

					(49.9; 60.2)
65 years and older	46	1113.6	123	1076.6	63.8
					(48.9; 74.8)
75 years and older	9	198.2	15	170.9	48.3
					(-26.1; 80.1)
Severe COVID-19	56	6774.6	205	6625.2	73.3
					(63.9; 80.5)
18 to 64 years of age	46	5653.8	175	5531.4	74.3
					(64.2; 81.8)
65 years and older	10	1120.8	30	1093.8	67.5
					(31.6; 85.8)
75 years and older	2	199.4	6	172.4	71.2
					(-61.2; 97.2)
28 days post-vaccination					
Symptomatic COVID-19	433	6658.4	883	6400.4	52.9
					(47.1; 58.1)
18 to 64 years of age	393	5549.9	790	5330.5	52.2
					(46.0; 57.8)
65 years and older	40	1108.5	93	1069.9	58.5
					(39.3; 72.1)
75 years and older	9	196.0	10	169.3	22.3
					(-112.8; 72.1)
Severe COVID-19	46	6733.8	176	6542.1	74.6
					(64.7; 82.1)
18 to 64 years of age	38	5619.2	150	5460.5	75.4
					(64.7; 83.2)
65 years and older	8	1114.6	26	1081.6	70.1
					(32.1; 88.3)
75 years and older	2	197.2	5	170.1	65.5
					(-110.7; 96.7)

[a] 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.

[b] 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.

[c] Co-primary endpoint as defined in the protocol.

[d] Per-protocol efficacy population

Beyond 14 days after vaccination, 18 vs. 74 cases of molecularly confirmed COVID-19 were hospitalised, respectively in the COVID-19 Vaccine Janssen vs. placebo group, resulting in 76.1% (adjusted 95% CI: 56.9; 87.7) vaccine efficacy. A total of 5 cases in the COVID-19 Vaccine Janssen group vs. 17 cases in the placebo group required Intensive Care Unit (ICU) admission and 4 vs. 8 cases in the COVID-19 Vaccine Janssen and placebo group respectively required mechanical ventilation.

Vaccine efficacy against asymptomatic infections at least 28 days after vaccination was 28.9% (95% CI: 20.0; 36.8) and against all SARS-CoV-2 infections was 41.7% (95% CI: 36.3; 46.7).

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.

A summary of vaccine efficacy by variant strain is presented in Table 5 below:

Table 5: Summary of vaccine efficacy against symptomatic[a] and severe[b] COVID-19 by variant strain following a single-dose

Variant	Onset	Severity	
		Symptomatic COVID-19 % Vaccine Efficacy (95% CI)	**Severe COVID-19 % Vaccine Efficacy (95% CI)**
Reference	At least 14 days after vaccination	71.5% (57.3; 81.4)	89.7% (57.3; 98.8)
	At least 28 days after vaccination	58.2% (35.0; 73.7)	93.1% (54.4; 99.8)
Alpha (B.1.1.7)	At least 14 days after vaccination	70.1% (35.1; 87.6)	51.1% (-241.2; 95.6)
	At least 28 days after vaccination	70.2% (35.3; 87.6)	51.4% (-239.0; 95.6)
Beta (B.1.351)	At least 14 days after vaccination	38.1% (4.2; 60.4)	70.2% (28.4; 89.2)
	At least 28 days after vaccination	51.9% (19.1; 72.2)	78.4% (34.5; 94.7)
Gamma (P.1)	At least 14 days after vaccination	36.4% (13.9; 53.2)	63.3% (18.3; 85.0)
	At least 28 days after vaccination	36.5% (14.1; 53.3)	63.6% (18.8; 85.1)
Zeta (P.2)	At least 14 days after vaccination	64.8% (47.3; 77.0)	91.1% (38.8; 99.8)
	At least 28 days after vaccination	64.1% (42.5; 78.3)	87.9% (9.4; 99.7)
Mu (B.1.621)	At least 14 days after vaccination	35.8% (1.5; 58.6)	79.4% (38.1; 94.9)
	At least 28 days after vaccination	35.9% (1.7; 58.7)	79.5% (38.5; 94.9)
Lambda (C.37)	At least 14 days after vaccination	10.0% (-39.5; 42.0)	67.4% (-30.6; 94.3)
	At least 28 days after vaccination	10.1% (-39.2; 42.1)	67.6% (-29.8; 94.4)
Delta (B.1.617.2/AY.1/AY.2)	At least 14 days after vaccination	-6.0% (-178.3; 59.2)	NE* NE*
	At least 28 days after vaccination	-5.7% (-177.7; 59.2)	NE* NE*
Other	At least 14 days after vaccination	73.2% (65.4; 79.4)	81.4% (59.8; 92.5)
	At least 28 days after vaccination	69.0% (59.1; 76.8)	75.7% (46.2; 90.3)

[a] 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.

[b] 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.

* If less than 6 cases are observed for an endpoint then the VE will not be shown. NE = not estimable.

Efficacy of two-doses of COVID-19 Vaccine Janssen administered 2 months apart

A final analysis (cut-off date 25 June 2021) of a multicenter, randomised, double-blind, placebo-controlled Phase 3 study (COV3009) was conducted in North and Latin America, Africa, Europe and Asia to assess the efficacy, safety, and immunogenicity of 2 doses of COVID-19 Vaccine Janssen administered with a 56-day interval. The study excluded individuals with abnormal function of the immune system resulting from a clinical condition, individuals who were 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 31300 individuals were randomised in the double-blind phase of the study. In total, 14492 (46.3%) individuals were included in the per-protocol efficacy population (7484 individuals received COVID-19 Vaccine Janssen and 7008 individuals received placebo). Participants were followed for a median of 36 days (range: 0-172 days) after vaccination.

Demographic and baseline characteristics were similar among individuals who received at least two doses of the COVID-19 Vaccine Janssen and those who received placebo. In the primary efficacy analysis population, among the individuals who received 2 doses of COVID-19 Vaccine Janssen, the median age was 50.0 years (range: 18 to 99 years); 87.0% (N=6512) of individuals were 18 to 64 years old [with 13.0% (N=972) aged 65 or older and 1.9% (N=144) aged 75 or older]; 45.4% of individuals were female; 37.5% were from North America (United States), 51.0% were from Europe (including UK), 5.4% were from South Africa, 1.9% from Philippines and 4.2% from Latin America. A total of 2747 (36.7%) individuals had at least one pre-existing comorbidity associated with increased risk of progression to severe COVID-19 at baseline. Comorbidities included: obesity defined as BMI ≥ 30 kg/m^2 (24.6%), hypertension (8.9%), sleep apnea (6.7%), type 2 diabetes (5.2%), serious heart conditions (3.6%), asthma (1.7%) and stable/well-controlled HIV infection (1.3%). Other comorbidities were present in $\leq 1\%$ of the individuals.

Vaccine efficacy against symptomatic COVID-19 and severe COVID-19 is presented in Table 6 below:

Table 6: Analysis of vaccine efficacy against symptomatic[a] and severe[b] COVID-19 – 14 days post-booster dose (second dose)

Endpoint	COVID-19 Vaccine Janssen N=7484[c]		Placebo N=7008[c]		% Vaccine Efficacy (95% CI)[d]
	COVID-19 Cases (n)	Person-Years	COVID-19 Cases (n)	Person-Years	
Symptomatic COVID-19	14	1730.0	52	1595.0	75.2 (54.6; 87.3)
Severe COVID-19	0	1730.7	8[e]	1598.9	100 (32.6; 100.0)

[a] 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.

[b] 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.

[c] Per-protocol efficacy population.

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

[e] Of the 8 participants with severe disease, 1 was admitted to an intensive care unit.

Approximately 68% of centrally confirmed strains have been sequenced as of this analysis (July 2021). Preliminary analysis results of variants with sufficient cases available for meaningful interpretations (Alpha [B.1.1.7] and Mu [B.1.621]) show that, after the first dose of COVID-19 Vaccine Janssen, efficacy 14 days post-dose 1 (Day 15-Day 56) for these 2 variants was 71.6% [95% CI: 43.2; 86.9] and 43.9% [95% CI: -43.4; 79.6], respectively. After the second dose (≥71 days), efficacy for Alpha and Mu was 94.2% [95% CI: 62.9; 99.9] and 63.1% [95% CI: -27.9; 91.6], respectively. Therefore, statistically significant efficacy for Mu was not demonstrated. There were only few Delta cases (2 and 1 in the COVID-19 Vaccine Janssen group and placebo group, respectively) and no reference strain cases in either the COVID-19 Vaccine Janssen or placebo group in the follow-up 14 days after the booster dose (≥71 days).

Vaccine efficacy against asymptomatic infections at least 14 days after second vaccination was 34.2% (95% CI: -6.4; 59.8).

Immunogenicity of a booster dose (second dose) following primary vaccination with COVID-19 Vaccine Janssen

It should be noted that there is no established immune correlate of protection. In a Phase 2 Study (COV2001), individuals 18 through 55 years of age and 65 years and older received a booster dose of the COVID-19 Vaccine Janssen approximately 2 months after the primary vaccination. Immunogenicity was assessed by measuring neutralising antibodies to SARS-CoV-2 Victoria/1/2020 strain using a qualified wild-type virus neutralisation assay (wtVNA). Immunogenicity data are available from 39 individuals, of whom 15 were 65 years of age and older, and are summarised in Table 7.

Table 7: SARS-CoV-2 Neutralisation Wild Type VNA-VICTORIA/1/2020 (IC50), Study COV2001 Group 1, Per-Protocol Immunogenicity Set*

	Baseline (Day 1)	**28 Days Post-Primary Vaccination (Day 29)**	**Pre-Booster Dose (Day 57)**	**14 Days Post-Booster Dose (Day 71)**	**28 Days Post-Booster Dose (Day 85)**
N	38	39	39	39	38
Geometric mean titre (95% CI)	<LLOQ (<LLOQ, <LLOQ)	260 (196; 346)	212 (142; 314)	518 (354; 758)	424 (301; 597)
Geometric mean fold increase (95% CI) from pre-booster	n/a	n/a	n/a	2.3 (1.7; 3.1)	1.8 (1.4; 2.4)

LLOQ = lower limit of quantification

* PPI set: The per-protocol immunogenicity population includes all randomised and vaccinated individuals for whom immunogenicity data are available excluding individuals with major protocol deviations expected to impact the immunogenicity outcomes. In addition, samples obtained after missed vaccinations or individuals with natural SARS-CoV-2 infection occurring after screening (if applicable) were excluded from the analysis.

Neutralising antibody and binding antibody increases against the reference SARS-CoV-2 strain were also observed in studies COV1001, COV1002 and COV2001 in a limited number of study participants after a boost given at 2, 3 and 6 months, when compared to pre-boost values. Overall, the increases of GMTs pre-boost to 1 month post-boost ranged from 1.5 to 4.4 fold for neutralising antibodies, and from 2.5 to 5.8 fold for binding antibodies. A 2-fold decrease in antibody levels was observed 4 months following 2-month booster dose, compared to 1 month following 2-month booster dose. Ab levels were still higher than antibody levels following a single-dose at a similar timepoint. These data support the administration of a booster dose when administered at an interval of 2 months or longer after primary vaccination.

Immunogenicity of a booster dose following primary vaccination with an approved mRNA COVID-19 vaccine

An independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a heterologous booster dose of the COVID-19 Vaccine Janssen. Immunogenicity was assessed by using a psVNA based on a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation. Due to the limited sample size, differences observed are only descriptive. In this study, adults who had completed primary vaccination with a Spikevax 2-dose series (N=151), a COVID-19 Vaccine Janssen single-dose (N=156), or a Comirnaty 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomised 1:1:1 to receive a booster dose of one of three vaccines: Spikevax, COVID-19 Vaccine Janssen, or Comirnaty. Neutralising antibody titres were assessed on Day 1 prior to administration of the booster dose and on Day 15 and Day 29 after the booster dose. A booster response to the COVID-19 Vaccine Janssen was demonstrated regardless of primary vaccination. The antibody level on Day 15 after a heterologous boost by COVID-19 Vaccine Janssen is lower than after a homologous boost by a licensed mRNA vaccine while on Day 29, neutralising antibody titers are roughly similar between

both regimens. Data indicate the homologous regimen with COVID-19 Vaccine Janssen induces lower antibody responses compared to heterologous boosting with a licensed mRNA vaccine. The clinical relevance of this is unknown. Only short-term immunogenicity data are available, long-term protection and immunological memory are currently unknown.

Elderly population

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

Paediatric population

The European Medicines Agency 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. The European Medicines Agency will review new information on this medicinal product 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 titres, 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. PHARMACEUTICAL PARTICULARS

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

20 vial pack

2-hydroxypropyl-β-cyclodextrin (HBCD)
Citric acid monohydrate
Ethanol
Hydrochloric acid
Polysorbate-80
Sodium chloride
Sodium hydroxide
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 or 20 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 or 20 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 sizes of 10 or 20 multi-dose vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions and administration

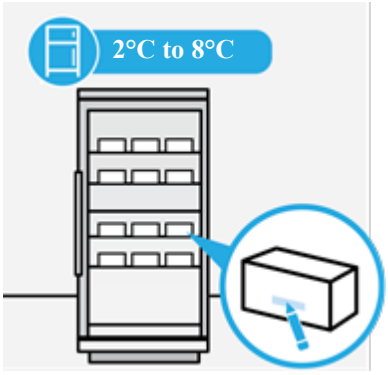
This vaccine should be handled by a healthcare professional using aseptic technique to ensure the sterility of each dose.

- 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



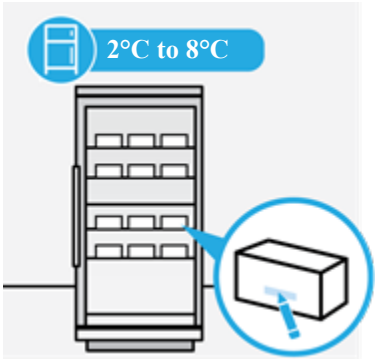
Store in a freezer

- 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).

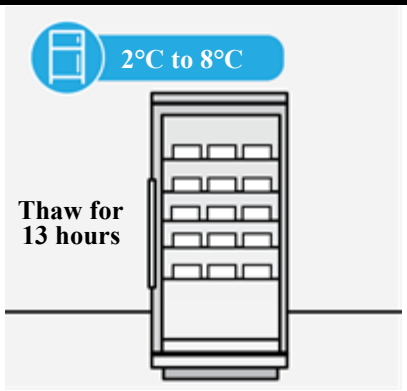
IF YOU RECEIVE YOUR VACCINE THAWED AT 2°C to 8°C you should store in a refrigerator:



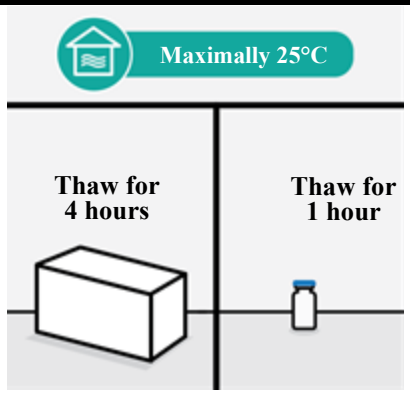
Do not re-freeze if the product is received already thawed at 2°C to 8°C.

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



OR



Thaw in refrigerator

- When stored frozen at -25°C to -15°C, a carton of 10 or 20 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.

Thaw at room temperature

- When stored frozen at **-25°C to -15°C**, a carton of 10 or 20 vials or individual vials should be thawed at room temperature maximally **25°C**.
- A carton of 10 or 20 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.

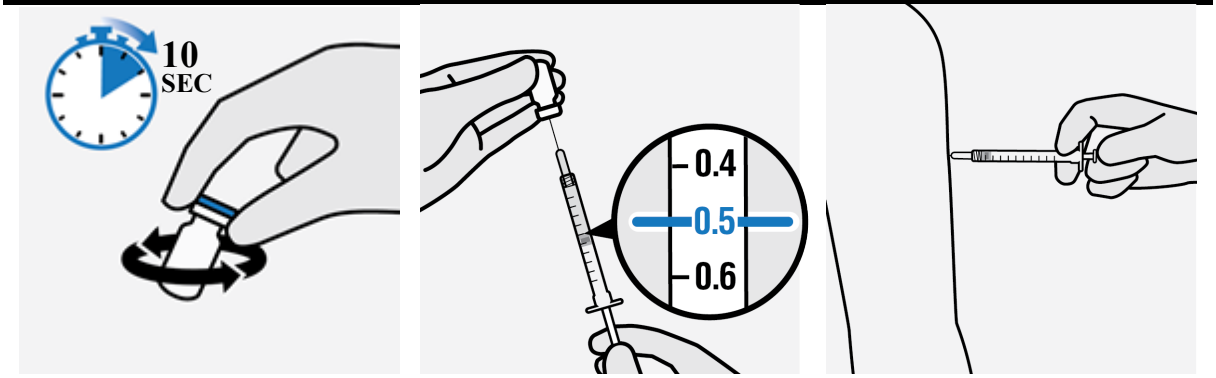
Do not re-freeze once thawed.

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

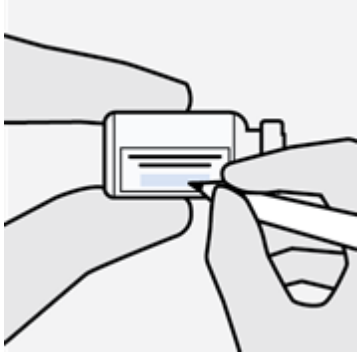
- Use a sterile needle and sterile syringe to extract a single-dose of **0.5 mL** from the multi-dose vial (see section 4.2).

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

Inject 0.5 mL

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

e. Storage after first puncture



Record date and time the vial should be discarded

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

Preferably, use immediately after first puncture.

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

OR

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

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 International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1525/001
EU/1/20/1525/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 March 2021

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

Janssen Biologics B.V.
Einsteinweg 101
2333 CB Leiden
The Netherlands

Emergent Manufacturing
Operations Baltimore LLC
5901 East Lombard Street
Baltimore, MD 21224
United States (USA)

Name and address of the manufacturers responsible for batch release

Janssen Biologics B.V.
Einsteinweg 101
2333 CB Leiden
The Netherlands

Janssen Pharmaceutica NV
Turnhoutseweg 30
2340 Beerse
Belgium

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

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

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

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

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

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

- **Risk management plan (RMP)**

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

An updated RMP should be submitted:

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

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to confirm the consistency of the active substance manufacturing process, the MAH should provide additional comparability and validation data.	30 November 2021 Interim report: 03 August 2021 Interim report: 13 August 2021
In order to confirm the consistency of the finished product manufacturing process, the MAH should provide additional comparability and validation data.	30 June 2022 Interim report: 15 December 2021 Interim report: 20 December 2021 Interim report: 31 January 2022 Interim report: 31 January 2022
In order to confirm the efficacy and safety of Ad26.COV2.S COVID-19 Vaccine, the MAH should submit the final Clinical Study Report for the randomised, placebo-controlled, observer-blind study VAC31518COV3001.	31 December 2023

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

COVID-19 Vaccine Janssen suspension for injection
COVID-19 vaccine (Ad26.COV2-S [recombinant])

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One dose (0.5 mL) contains not less than 8.92 $\log_{10}$ infectious units

Adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein (Ad26.COV2-S)

This medicine contains genetically modified organisms.

3. LIST OF EXCIPIENTS

10 vial pack

Excipients: 2-hydroxypropyl-β-cyclodextrin, citric acid monohydrate, ethanol, hydrochloric acid, polysorbate-80, sodium chloride, sodium hydroxide, trisodium citrate dihydrate, water for injections. See leaflet for further information.

20 vial pack

Excipients: 2-hydroxypropyl-β-cyclodextrin, citric acid monohydrate, ethanol, hydrochloric acid, polysorbate-80, sodium chloride, sodium hydroxide, water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
10 multi-dose vials
20 multi-dose vials
Each vial contains 5 doses of 0.5 mL

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use
For more information, scan this QR code or go to www.covid19vaccinejanssen.com.

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

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP when stored at -25°C to -15°C.
Write new expiry date at 2°C to 8°C (max 4.5 months): _____. Cross out former expiry date.

9. SPECIAL STORAGE CONDITIONS

Store and transport frozen at -25°C to -15°C.
Can also be stored at 2°C to 8°C for 4.5 months. Write new expiry date.
Do not refreeze once thawed.
Keep the vials in the original carton to protect from light.
For additional information on shelf-life and storage, see package leaflet.

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

Dispose of in compliance with the local guidance for pharmaceutical waste.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1525/001
EU/1/20/1525/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 1D & 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
MULTI-DOSE VIAL LABEL (5 DOSES OF 0.5 ML)

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

COVID-19 Vaccine Janssen injection
COVID-19 vaccine (Ad26.COV2-S [recombinant])
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 doses of 0.5 mL

6. OTHER

Discard date/time

B. PACKAGE LEAFLET

Package leaflet: Information for the user

COVID-19 Vaccine Janssen suspension for injection
COVID-19 vaccine (Ad26.COV2-S [recombinant])

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

Read all of this leaflet carefully before you are vaccinated because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What COVID-19 Vaccine Janssen is and what it is used for
2. What you need to know before you are given COVID-19 Vaccine Janssen
3. How COVID-19 Vaccine Janssen is given
4. Possible side effects
5. How to store COVID-19 Vaccine Janssen
6. Contents of the pack and other information

1. What COVID-19 Vaccine Janssen is and what it is used for

COVID-19 Vaccine Janssen is a vaccine used for preventing COVID-19 caused by the SARS-CoV-2 virus.

COVID-19 Vaccine Janssen is given to adults aged 18 years and older.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and specialised white blood cells that work against the virus, so giving protection against COVID-19. None of the ingredients in this vaccine can cause COVID-19.

2. What you need to know before you are given COVID-19 Vaccine Janssen

Do not have the vaccine if
- You are allergic to the active substance or any of the other ingredients of this vaccine (listed in section 6).
- 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 any COVID-19 vaccine.
- You have a previous diagnosis of capillary leak syndrome, (a condition causing fluid leakage from small blood vessels).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given COVID-19 Vaccine Janssen if:
- you have ever had a severe allergic reaction after injection of any other vaccine,
- you have ever fainted following any needle injection,
- you have a severe infection with a high temperature (over 38°C). However, you can have your vaccination if you have a mild fever or upper airway infection like a cold,
- you have a problem with bleeding or bruising, or if you are taking an anticoagulant medicine (to prevent blood clots),

- your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants or cancer medicines),
- you have risk factors for blood clots in your veins (venous thromboembolism (VTE)).

As with any vaccine, vaccination with COVID-19 Vaccine Janssen may not fully protect all those who receive it. It is not known how long you will be protected.

Blood disorders
- ***Venous thromboembolism:*** Blood clots in veins (venous thromboembolism (VTE)) have been observed rarely following vaccination with COVID-19 Vaccine Janssen.
- ***Thrombosis with thrombocytopenia syndrome:*** A combination of blood clots and low levels of 'platelets' in the blood has been observed very rarely following vaccination with COVID-19 Vaccine Janssen. This includes severe cases with blood clots, including in unusual locations, such as the brain, liver, bowel and spleen in some cases in combination with bleeding. These cases mostly occurred within the first three weeks following vaccination and in women below 60 years of age. Fatal outcome has been reported.
- ***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 COVID-19 Vaccine Janssen.

Seek immediate medical attention, if you experience symptoms that may be signs of blood disorders: severe or persistent headaches, seizures (fits), mental status changes or blurred vision, unexplained bleeding, unexplained skin bruising beyond the site of vaccination which appear a few days after vaccination, pinpoint round spots beyond the site of vaccination, develop shortness of breath, chest pain, leg pain, leg swelling, or persistent abdominal pain. Inform your healthcare provider that you have recently received COVID-19 Vaccine Janssen.

Capillary leak syndrome
Very rare cases of capillary leak syndrome (CLS) have been reported following vaccination with COVID-19 Vaccine Janssen. At least one affected patient 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 immediate medical attention if you develop these symptoms in the days following vaccination.

Guillain-Barré syndrome
Seek immediate medical attention if you develop weakness and paralysis in the extremities that can progress to the chest and face (Guillain-Barré syndrome, GBS). This has been reported very rarely after vaccination with COVID-19 Vaccine Janssen.

Risk of very rare events after a booster dose
The risk of very rare events (such as blood disorders including thrombosis with thrombocytopenia syndrome, CLS and GBS) after a booster dose of COVID-19 Vaccine Janssen is unknown.

Children and adolescents
COVID-19 Vaccine Janssen is not recommended for children aged below 18 years. Currently there is not enough information available on the use of COVID-19 Vaccine Janssen in children and adolescents younger than 18 years of age.

Other medicines and COVID-19 Vaccine Janssen
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines or vaccines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor, pharmacist or nurse for advice before you receive this vaccine.

Driving and using machines
Some of the side effects of COVID-19 Vaccine Janssen listed in section 4 (Possible side effects) may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

COVID-19 Vaccine Janssen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose of 0.5 mL, that is to say essentially 'sodium-free'.

COVID-19 Vaccine Janssen contains ethanol
This medicine contains 2 mg of alcohol (ethanol) in each dose of 0.5 mL. The amount of ethanol in this medicine is equivalent to less than 1 mL beer or wine. The small amount of alcohol in this medicine will not have any noticeable effects.

3. How COVID-19 Vaccine Janssen is given

Your doctor, pharmacist or nurse will inject the vaccine into the muscle - usually in the upper arm.

How much vaccine will you receive

A single-dose primary vaccination (0.5 mL) of COVID-19 Vaccine Janssen is injected.

A booster dose (second dose) of COVID-19 Vaccine Janssen may be given at least 2 months after the primary vaccination in individuals 18 years of age and older.

COVID-19 Vaccine Janssen may be administered as a single booster dose to eligible individuals who have completed primary vaccination with an approved mRNA COVID-19 vaccine. The dosing interval for the booster dose is the same as that authorised for a booster dose of the vaccine used for primary vaccination.

After the injection your doctor, pharmacist or nurse will watch over you for around 15 minutes to monitor for signs of an allergic reaction.

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

4. Possible side effects

Like all vaccines, COVID-19 Vaccine Janssen can cause side effects, although not everybody gets them. Most of the side effects occur in the 1 or 2 days of getting the vaccination.

Get medical attention immediately if within 3 weeks of vaccination you get any of the following symptoms:
- experience severe or persistent headaches, blurred vision, mental status changes or seizures (fits);
- develop shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain;
- notice unusual skin bruising or pinpoint round spots beyond the site of vaccination.

Get **urgent** medical attention if you get symptoms of a severe allergic reaction. Such reactions may include a combination of any of the following symptoms:
- feeling faint or light-headed
- changes in your heartbeat
- shortness of breath
- wheezing
- swelling of your lips, face, or throat

- hives or rash
- nausea or vomiting
- stomach pain

The following side effects can happen with this vaccine.

Very common: may affect more than 1 in 10 people
- headache
- nausea
- muscle aches
- pain where the injection is given
- feeling very tired

Common: may affect up to 1 in 10 people
- redness where the injection is given
- swelling where the injection is given
- chills
- joint pain
- cough
- fever

Uncommon: may affect up to 1 in 100 people
- rash
- muscle weakness
- arm or leg pain
- feeling weak
- feeling generally unwell
- sneezing
- sore throat
- back pain
- tremor
- excessive sweating
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)
- diarrhoea
- dizziness

Rare: may affect up to 1 in 1000 people
- allergic reaction
- hives
- swollen lymph nodes (lymphadenopathy)
- decreased feeling or sensitivity, especially in the skin (hypoaesthesia)
- persistent ringing in the ears (tinnitus)
- vomiting
- blood clots in veins (venous thromboembolism (VTE))

Very Rare: may affect up to 1 in 10000 people
- blood clots often in unusual locations (e.g., brain, liver, bowel, spleen) in combination with low level of blood platelets
- serious nerve inflammation, which may cause paralysis and difficulty breathing (Guillain-Barré syndrome (GBS))

Unknown (cannot be estimated from the available data)
- severe allergic reaction
- capillary leak syndrome (a condition causing fluid leakage from small blood vessels)

- low levels of blood platelets (immune thrombocytopenia) that can be associated with bleeding (see section 2, 'Blood Disorders')

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

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

5. How to store COVID-19 Vaccine Janssen

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

Store vial in the original carton to protect from light.

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

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".

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.

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 or 20 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 or 20 vials will take approximately 4 hours to thaw, and a single vial will take approximately 1 hour to thaw.

Do not re-freeze vaccine once thawed.

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.

6. Contents of the pack and other information

What COVID-19 Vaccine Janssen contains
- The active substance is Adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein*(Ad26.COV2-S) not less than 8.92 $\log_{10}$ infectious units (Inf.U) in each 0.5 mL dose.
  * Produced in the PER.C6 TetR Cell Line and by recombinant DNA technology.

  This product contains genetically modified organisms (GMOs).

- The other ingredients (excipients) are:
  - 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 (see section 2 COVID-19 Vaccine Janssen contains sodium and COVID-19 Vaccine Janssen contains ethanol).
- 20 vial pack: 2-hydroxypropyl-β-cyclodextrin (HBCD), citric acid monohydrate, ethanol, hydrochloric acid, polysorbate-80, sodium chloride, sodium hydroxide, water for injections (see section 2 COVID-19 Vaccine Janssen contains sodium and COVID-19 Vaccine Janssen contains ethanol).

What COVID-19 Vaccine Janssen looks like and contents of the pack
Suspension for injection (injection). The suspension is colorless to slightly yellow, clear to very opalescent suspension (pH 6-6.4).

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

COVID-19 Vaccine Janssen is available in a pack containing 10 or 20 multi-dose vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Janssen-Cilag International NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Manufacturer
Janssen Biologics B.V.
Einsteinweg 101
2333 CB Leiden
The Netherlands

Janssen Pharmaceutica NV
Turnhoutseweg 30
2340 Beerse
Belgium

For the specific manufacturer of the vaccine you have received, check the Lot number on the carton or vial and please contact the local representative of the Marketing Authorisation Holder.

For any additional information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Janssen-Cilag NV
Tel/Tél: +3233939323/0080056540088

България
„Джонсън & Джонсън България” ЕООД
Тел.: +35928008028/080018192

Česká republika
Janssen-Cilag s.r.o.
Tel: +420225296622/0080056540088

Danmark
Janssen-Cilag A/S
Tlf: +4535158573/0080056540088

Lietuva
UAB “JOHNSON & JOHNSON”
Tel: +37052142002/0080056540088

Luxembourg/Luxemburg
Janssen-Cilag NV
Tél/Tel: +35227302815/0080056540088

Magyarország
Janssen-Cilag Kft.
Tel.: +3614292336/0080056540088

Malta
AM MANGION LTD
Tel: +35627780004/80065007

Deutschland
Janssen-Cilag GmbH
Tel: +4932221863163/0080056540088

Eesti
UAB "JOHNSON & JOHNSON" Eesti filiaal
Tel: +3728804474/8002642

Ελλάδα
Janssen-Cilag Φαρμακευτική Α.Ε.Β.Ε.
Τηλ: +302119906006/0080056540088

España
Janssen-Cilag, S.A.
Tel: +34912158005/0080056540088

France
Janssen-Cilag
Tél: +33185169327/0080056540088

Hrvatska
Johnson & Johnson S.E. d.o.o.
Tel: +38518848011/0800806027

Ireland
Janssen Sciences Ireland UC
Tel: +353212356806/0080056540088

Ísland
Janssen-Cilag AB
c/o Vistor hf.
Sími: +3545390674/0080056540088

Italia
Janssen-Cilag SpA
Tel: +390699748520/0080056540088

Κύπρος
Βαρνάβας Χατζηπαναγής Λτδ
Τηλ: +35725654186/0080056540088

Latvija
UAB "JOHNSON & JOHNSON" filiāle Latvijā
Tel: +37163138821/0080056540088

Nederland
Janssen-Cilag B.V.
Tel: +31880030701/0080056540088

Norge
Janssen-Cilag AS
Tlf: +4723500417/0080056540088

Österreich
Janssen-Cilag Pharma GmbH
Tel: +43720380110/0080056540088

Polska
Janssen-Cilag Polska Sp. z o.o.
Tel.: +48225123915/0080056540088

Portugal
Janssen-Cilag Farmacêutica, Lda.
Tel: +351220608007/0080056540088

România
Johnson & Johnson România SRL
Tel: +40311305128/0800672516

Slovenija
Johnson & Johnson d.o.o.
Tel: +38616009336/0080056540088

Slovenská republika
Johnson & Johnson, s.r.o.
Tel: +421250112534/0080056540088

Suomi/Finland
Janssen-Cilag Oy
Puh/Tel: +358981710294/99080056540088

Sverige
Janssen-Cilag AB
Tfn: +46851992561/0080056540088

United Kingdom (Northern Ireland)
Janssen Sciences Ireland UC
Tel: +441494 567444

This leaflet was last revised in

This vaccine has been given ‘conditional approval’. This means that there is more evidence to come about this vaccine.
The European Medicines Agency will review new information on this vaccine at least every year and this leaflet will be updated as necessary.

Scan the QR code below (also available on the carton and QR card) to get the package leaflet in different languages.

Or visit the URL: www.covid19vaccinejanssen.com

Other sources of information

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

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

- As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of COVID-19 Vaccine Janssen. Individuals should be monitored by a healthcare professional after vaccination for at least 15 minutes.
- COVID-19 Vaccine Janssen must not be mixed with other medicinal products or diluted in the same syringe.
- COVID-19 Vaccine Janssen must not be administered by intravascular, intravenous, subcutaneous or intradermal injection under any circumstances.
- Immunisation should be carried out by intramuscular injection only, preferably in the deltoid muscle of the upper arm.
- Syncope (fainting) may occur with any injection, including COVID-19 Vaccine Janssen. Procedures should be in place to prevent injury from falling and to manage syncopal reactions.

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.

Instructions for administration and handling

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

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”.

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.

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 or 20 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 or 20 vials will take approximately 4 hours to thaw, and a single vial will take approximately 1 hour to thaw.

Do not re-freeze vaccine once thawed.

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.

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.

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.

Before administering a dose of vaccine, swirl the vial 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 into the deltoid muscle of the upper arm.

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.

After the first puncture of the vial the vaccine (vial) can be held at 2°C to 8°C for up to 6 hours or at room temperature (maximum 25°C) for a single period of up to 3 hours. Discard if vaccine is not used within this time. After the first puncture of the vial, record the date and time the vial should be discarded on each vial label.

Disposal

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