# Annexes to the recommendations for use of the Janssen AD26.COV2.S vaccine against COVID-19

Grading of evidence -
Evidence to recommendations tables

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## Background

These are the annexes to the Interim recommendations for use of the Janssen AD26.COV2.S vaccine.

Annexes 1–6 contain tables that summarize the grading of recommendations, assessment, development and evaluations (GRADE). Annexes 7–9 contain the SAGE evidence-to-recommendation framework tables (ETR tables). The ETR tables are based on the DECIDE Work Package 5: Strategies for communicating evidence to inform decisions about health system and public health interventions. Evidence to a recommendation (for use by a guideline panel) (www.decide-collaboration.eu/, accessed 9 December 2021).

## Contents

Annex 1. GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in adults ..... 2
Annex 2. GRADE table: Safety of Janssen AD26.COV2.S COVID-19 vaccine in adults..... 3
Annex 3. GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in older adults ..... 3
Annex 4. GRADE table: Safety of vaccine in older adults..... 5
Annex 5. GRADE table: GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in individuals with underlying conditions..... 6
Annex 6. GRADE table: Safety of Janssen AD26.COV2.S COVID-19 vaccine in individuals with underlying conditions..... 7
Annex 7. SAGE evidence-to-recommendation framework: Janssen AD26.COV2.S vaccine use in adults..... 8
Annex 8. SAGE evidence-to-recommendation framework: Janssen AD26.COV2.S vaccine use in older adults..... 17
Annex 9. SAGE evidence-to-recommendation framework: Janssen AD26.COV2.S vaccine use in individuals with comorbidities..... 26

**Annex 1. GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in adults**

| | |
|---|---|
| **Population:** | Adults (18–59 years) |
| **Intervention:** | Single dose of Janssen AD26.COV2.S vaccine |
| **Comparison:** | Placebo/active control |
| **Outcome:** | Moderate to severe/critical COVID-19 (PCR-confirmed) |

**What is the efficacy of a single dose of Janssen AD26.COV2.S vaccine compared with placebo/active control in preventing moderate to severe/critical PCR-confirmed COVID-19 in adults (18–59 years)?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 1/ RCT *(1)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Not serious | 0 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Not serious | 0 |
| | | Imprecision | Not serious | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **4** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).** |
| | **Conclusion** | | | We are very confident that a single dose of Janssen AD26.COV2.S vaccine is efficacious in preventing moderate to severe/critical PCR-confirmed COVID-19 in adults (18–59 years). |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

**Annex 2. GRADE table: Safety of Janssen AD26.COV2.S COVID-19 vaccine in adults**

| | |
|---|---|
| **Population:** | Adults (18–59 years) |
| **Intervention:** | Single dose of Janssen AD26.COV2.S vaccine |
| **Comparison:** | Placebo/active control |
| **Outcome:** | Serious adverse events following immunization |

**What is the risk of serious adverse events following Janssen AD26.COV2.S vaccination compared with placebo/active control in adults (18–59 years)?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 2/ RCT *(1, 2)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Serious[b] | -1 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Not serious | 0 |
| | | Imprecision | Not serious | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **3** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 3).** |
| | **Conclusion** | | | We are moderately confident that there is a very low risk of serious adverse events (Thrombosis with Thrombocytopenia Syndrome) following a single dose of Janssen AD26.COV2.S vaccine in adults (18–59 years) . |

**Annex 3. GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in older adults**

| | |
|---|---|
| **Population:** | Older adults (≥60 years) |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

[b] Downgraded for the following limitations. The trial was not adequately powered to detect rare adverse events (i.e. fewer than about 1 in 2000). Post-licensure data have identified the following safety signals following vaccination: a very rare syndrome of blood clotting combined with low platelet counts has been reported about 3 to 15 days following vaccination with the Ad26.COV2.S vaccine, described as Thrombosis with Thrombocytopenia Syndrome (TTS). Current evidence suggests a plausible causal association between the J&J COVID-19 vaccine and TTS. Further, Guillain-Barre Syndrome (GBS) and capillary leak syndrome (CLS) have been observed.. TTS was reported as one case in approximately 2 per million doses administered, GBS was reported as one case in 7-8 per million doses administered and CLS as 0.21 cases per million doses administered.

**Intervention:** Older adults (≥60 years)

**Comparison:** Single dose of Janssen AD26.COV2.S vaccine

**Outcome:** Moderate to severe/critical COVID-19 (PCR-confirmed)

**What is the efficacy of a single dose of Janssen AD26.COV2.S vaccine compared with placebo/active control in preventing moderate to severe/critical PCR-confirmed COVID-19 in older adults (≥60 years)?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 1/ RCT *(1)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Not serious[b] | 0 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Not serious | 0 |
| | | Imprecision | Not serious | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **4** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a high level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 4).** |
| | **Conclusion** | | | We are confident that a single dose of JANSSEN AD26.COV2.S vaccine is efficacious in preventing moderate to severe/critical PCR-confirmed COVID-19 in older adults (≥60 years), though vaccine effectiveness may wane over time. |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

[b] Observational and immunogenicity data suggest a decline in vaccine effectiveness and neutralizing antibodies over time in older adults.

**Annex 4. GRADE table: Safety of vaccine in older adults**

| | |
|---|---|
| **Population:** | Older adults (≥60 years) |
| **Intervention:** | Single dose of Janssen AD26.COV2.S vaccine |
| **Comparison:** | Placebo/active control |
| **Outcome:** | Serious adverse events following immunization |

**What is the risk of serious adverse events following Janssen AD26.COV2.S vaccination compared with placebo/active control in older adults (≥60 years)?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 1/ RCT*(1, 2)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Serious[b] | -1 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Not serious | 0 |
| | | Imprecision | Not serious[c] | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **3** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 3).** |
| | **Conclusion** | | | We are moderately confident that the risk of serious adverse events following a single dose of Janssen AD26.COV2.S vaccine in older adults (≥60 years) is low. |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

[b] Downgraded for the following limitations. The trial was not adequately powered to detect rare adverse events (i.e. fewer than about 1 in 2000).

[c] Approximately 40% of the trial participants were aged 60 years or over. This was not considered as constituting a limitation that leads to downgrading of the evidence.

**Annex 5. GRADE table: Efficacy of Janssen AD26.COV2.S COVID-19 vaccine in individuals with underlying conditions**

| | |
|---|---|
| **Population:** | Individuals with comorbidities or health states that increase risk for severe COVID-19 |
| **Intervention:** | Single dose of Janssen AD26.COV2.S vaccine |
| **Comparison:** | Placebo/active control |
| **Outcome:** | Moderate to severe/critical COVID-19 (PCR-confirmed) |

**What is the efficacy of a single dose of Janssen AD26.COV2.S vaccine compared with placebo/active control in preventing moderate to severe/critical PCR-confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 1/ RCT *(1)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Not serious | 0 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Serious[b] | -1 |
| | | Imprecision | Not serious[c] | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **3** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 3).** |
| | **Conclusion** | | | We are moderately confident that a single dose of Janssen AD26.COV2.S vaccine is efficacious in preventing moderate to severe/critical PCR-confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19, as included in the clinical trial. No data were obtained from the clinical trial on vaccination of pregnant or breastfeeding women, or persons who were immunocompromised. |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

[b] Trial excluded pregnant and breastfeeding women, and persons who were immunocompromised. This was considered as constituting a limitation that leads to downgrading of the evidence.

[c] Underlying comorbidities included BMI ≥ 30 kg/m2, cardiovascular disorder, respiratory disease and diabetes. Approximately 40% of the trial population had at least one comorbidity. This was considered as not constituting a limitation that would lead to downgrading of the evidence. Data on long-term protection emerging from the ongoing phase 3 clinical trial remain limited, as trial data have so far been reported only for a follow-up of approximately 2 months. This was considered as not constituting a limitation that would lead to downgrading of the evidence. SAGE will continue to review any emerging data and adjust its quality assessment as required.

**Annex 6. GRADE table: Safety of Janssen AD26.COV2.S COVID-19 vaccine in individuals with underlying conditions**

| | |
|---|---|
| **Population:** | Individuals with comorbidities or health states that increase risk for severe COVID-19 |
| **Intervention:** | Single dose of Janssen AD26.COV2.S vaccine |
| **Comparison:** | Placebo/active control |
| **Outcome:** | Serious adverse events following immunization |

**What is the risk of serious adverse events following Janssen AD26.COV2.S vaccination compared with placebo/active control in individuals with underlying conditions?**

| | | | Rating | Adjustment to rating |
|---|---|---|---|---|
| **Quality Assessment** | No. of studies/starting rating | | 1/ RCT*(1-3)* | 4 |
| | Factors decreasing confidence | Limitation in study design[a] | Serious[b] | -1 |
| | | Inconsistency | Not serious | 0 |
| | | Indirectness | Serious[c] | 0 |
| | | Imprecision | Not serious | 0 |
| | | Publication bias | Not serious | 0 |
| | Factors increasing confidence | Large effect | Not applicable | 0 |
| | | Dose-response | Not applicable | 0 |
| | | Antagonistic bias and confounding | Not applicable | 0 |
| | **Final numerical rating of quality of evidence** | | | **2** |
| **Summary of Findings** | **Statement on quality of evidence** | | | **Evidence supports a limited level of confidence that the true effect lies close to the estimate of the effect on the health outcome (level 2).** |
| | **Conclusion** | | | We have low confidence in the quality of evidence that there is a low risk of serious adverse events (Thrombosis with Thrombocytopenia Syndrome) in individuals with comorbidities or health states that increase risk for severe COVID-19 following a single dose of Janssen AD26.COV2.S vaccine. |

[a] For the risk of bias assessments using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2), please see www.covid-nma.com/vaccines.

[b] Downgraded for the following limitations. The trial was not adequately powered to detect rare adverse events (i.e. fewer than about 1 in 2000). Post-licensure data have identified the following safety signals following vaccination: a very rare syndrome of blood clotting combined with low platelet counts has been reported about 3 to 15 days, , mainly in younger individuals (18-59 years) following vaccination with the Ad26.COV2.S vaccine, described as Thrombosis with Thrombocytopenia Syndrome (TTS), Current evidence suggests a plausible causal association between the J&J COVID-19 vaccine and TTS. Further, Guillain-Barre Syndrome (GBS) and capillary leak syndrome (CLS) have been observed. TTS was reported as one case in approximately 2 per million doses administered, GBS was reported as one case in 7-8 per million doses administered and CLS as 0.21 cases per million doses administered.

[c] Trial excluded pregnant and breastfeeding women and persons who were immunocompromised. This was considered as constituting a limitation that leads to downgrading of the evidence.

**Annex 7. SAGE evidence-to-recommendation framework: Janssen AD26.COV2.S vaccine use in adults**

**Question:** Should Janssen AD26.COV2.S vaccine be administered to adults to prevent moderate to severe/critical COVID-19?

**Population:** Adults (18–59 years)

**Intervention:** Single dose of JANSSEN AD26.COV2.S vaccine

**Comparison(s):** Active control/placebo

**Outcome:** Moderate to severe/critical COVID-19 (PCR-confirmed)

**Background:** On 31 December 2019, WHO was alerted to several cases of pneumonia of unknown origin in Wuhan City, Hubei Province, China. The cause was found to be a novel coronavirus, SARS-CoV-2. The disease caused by this novel virus has been named COVID-19. The outbreak of COVID-19 was declared a public health emergency of international concern in January 2020. The disease has since spread, with an enormous impact on the health and well-being of individuals and populations worldwide. It has further caused major disruptions to various sectors of society and the economy across the globe.

Vaccines are a critical tool in combating the pandemic. In the rapidly evolving field of COVID-19 vaccines, WHO has issued to date interim recommendations on the use of a number of COVID-19 vaccines *(4)*.

| | | | | |
|---|---|---|---|---|
| | | | | **ADDITIONAL INFORMATION** |
| | | | | The COVID-19 situation is evolving rapidly; the most recent epidemiological situation can be found on the following website: https://covid19.who.int/table |
| | | | | |