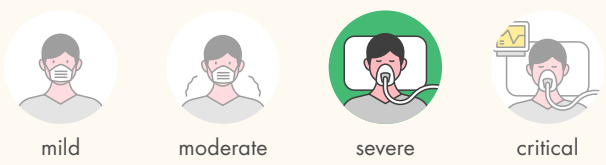
Summary of Pharmaceutical Recommendations

NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

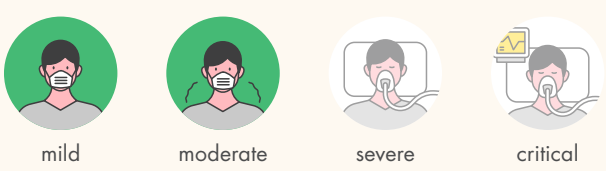
Remdesivir

Revision Jan 2023



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

1. For patients with severe COVID-19 who require oxygen therapy but do not require mechanical ventilation or extracorporeal membrane oxygenation, we suggest using remdesivir.



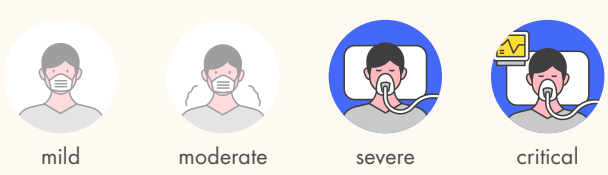
D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

2. For patients with mild or moderate COVID-19 who are at high risk for progression to severe COVID-19, we suggest using remdesivir.

Clinical considerations:
We recommend use within 7 days of symptom onset. When administering to patients with mild or moderate COVID-19, we recommend administration for 3 days. However, if the patient's condition progresses to severe COVID-19, the duration of remdesivir may be extended as recommended in severe COVID-19.

IL-6 inhibitor

Revision Jan 2023



D Strongly against | C Conditionally against | I Inconclusive | B Conditionally Recommend | **A Strongly recommended**

1. For patients with COVID-19 who require high-flow oxygen or invasive/non-invasive mechanical ventilation, we recommend using tocilizumab.

D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

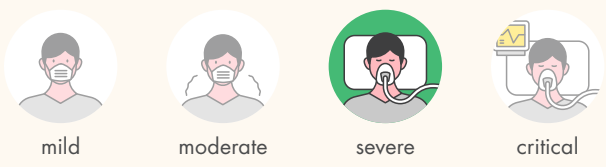
2. For patients with mild COVID-19, we suggest against the use of tocilizumab.

D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

3. We are unable to make a recommendation for or against the use of sarilumab for patients with COVID-19, in consideration of the situation in South Korea.

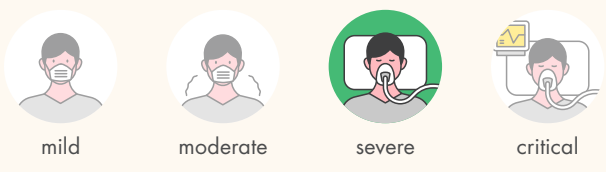
Selective JAK inhibitor

Revision Aug 2022



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

1. For patients with severe COVID-19 who require oxygen therapy but do not require mechanical ventilation, we suggest using baricitinib.



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

2. For patients with severe COVID-19 who require oxygen therapy but do not require mechanical ventilation, we suggest using tofacitinib.

Clinical considerations:
we suggest co-administration of standard treatments, such as antiviral agents and steroids, with baricitinib or tofacitinib as long as there are no contraindications.

D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

3. We are unable to make a recommendation for or against ruxolitinib for patients with COVID-19 due to insufficient evidence on its efficacy and safety.

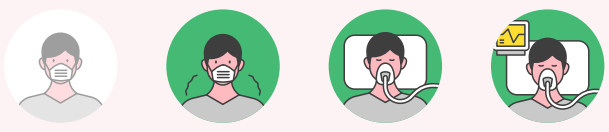
Summary of Recommendations for Respiratory/Intensive critical care

NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

Therapeutic dose of anticoagulant

Revision Dec 2022



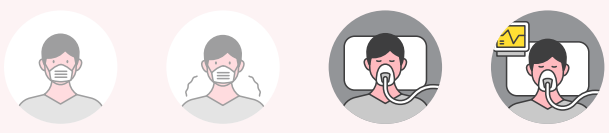
D	C	I	**B**	A
Strongly against	Conditionally against	Inconclusive	**Conditionally Recommend**	Strongly recommended

For severe patients with COVID-19 who require intensive care, we suggest the use of prophylactic-dose heparin (unfractionated or low molecular weight heparin). For patients who do not require intensive care, we suggest the use of therapeutic-dose heparin (unfractionated or low molecular weight heparin) unless a contraindication to such therapy exists.

Clinical considerations:
The anticoagulant dose should be determined based on the individual patient's risk of clot formation and bleeding.

Early intubation

Revision Apr 2022

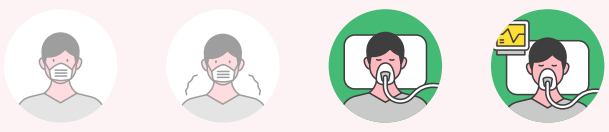


D	C	**I**	B	A
Strongly against	Conditionally against	**Inconclusive**	Conditionally Recommend	Strongly recommended

We are unable to make a recommendation for or against the early intubation in patients with COVID-19 who are admitted to the intensive care unit due to insufficient evidence on its efficacy and safety.

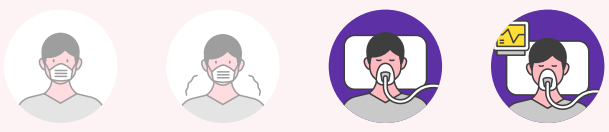
Extracorporeal membrane oxygenation (ECMO)

Revision Mar 2023



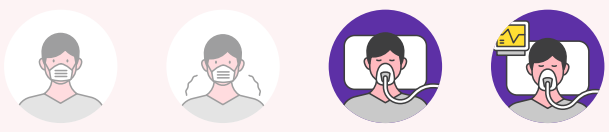
D	C	I	**B**	A
Strongly against	Conditionally against	Inconclusive	**Conditionally Recommend**	Strongly recommended

1. For patients with severe acute respiratory distress syndrome caused by COVID-19, we suggest veno-venous ECMO (vv-ECMO) if severe hypoxemia fails to improve despite appropriate lung-protective ventilation strategies and prone positioning*.
   * The decision to place a patient in a prone position before ECMO should be based on a consideration of the patient's benefits and harms of the procedure, as well as the intensive care unit resources resources.



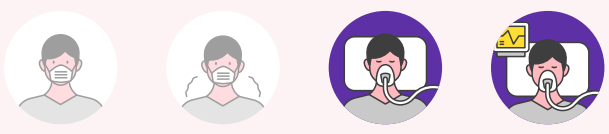
Expert consensus

2. For patients with COVID-19, we recommend vv-ECMO if the PaO_2/FiO_2 (P/F ratio) is < 50 mmHg for more than 3 hours or < 80 mmHg for more than 6 hours.



Expert consensus

3. For patients with COVID-19, we recommend transfer to a hospital capable of performing ECMO when hypoxemia (criteria: P/F ratio 150mmHg) is likely to deteriorate after appropriate treatments and ECMO is not available in the current center.

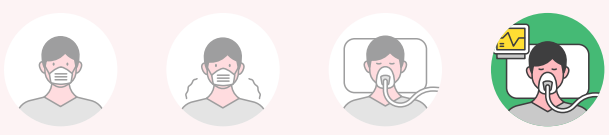


Expert consensus

4. For patients with COVID-19, age of 70 years or older, especially advanced frailty and comorbidities, are risk factors for death after ECMO. Therefore, we recommend to carefully consider the benefits and harms of ECMO application before deciding to apply ECMO.

Positive end expiratory pressure (PEEP)

Revision Oct 2022



D	C	I	**B**	A
Strongly against	Conditionally against	Inconclusive	**Conditionally Recommend**	Strongly recommended

For patients with severe acute respiratory distress syndrome caused by COVID-19, we suggest a high-PEEP strategy rather than low-PEEP strategy.

Summary of Recommendations for Respiratory/Intensive critical care

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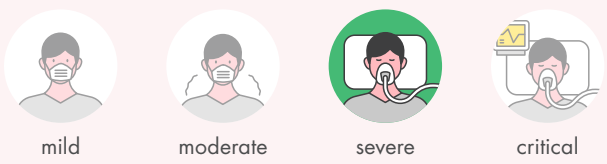
NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

Prone position

Revision Jan 2023



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

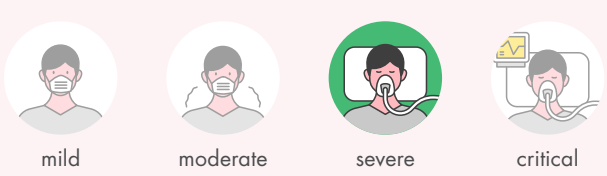
1. For patients with COVID-19 receiving high flow nasal cannula (without mechanical ventilation) or non-invasive ventilation, we suggest awake prone positioning.

Expert consensus

2. For patients with moderate-to-severe acute respiratory distress syndrome by COVID-19 who are receiving invasive mechanical ventilation, we recommend the application of prone positioning.

High-flow nasal cannula (HFNC)

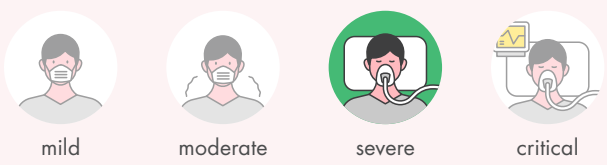
New Dec 2022



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

1. For patients with acute hypoxemic respiratory failure by COVID-19, we suggest the use of HFNC therapy, rather than conventional oxygen therapy.

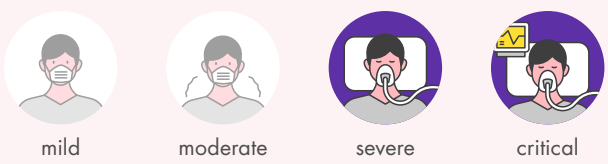
   Clinical considerations:
   The selection of an appropriate oxygen therapy modality for patients with acute hypoxemic respiratory failure by COVID-19, should be based on factors such as equipment availability, medical staff expertise, patient-specific considerations, and patient's convenience.



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

2. For patients with acute hypoxemic respiratory failure by COVID-19, we suggest the use of HFNC therapy or non-invasive mechanical ventilation as determined by medical staff, depending on the patient's condition.

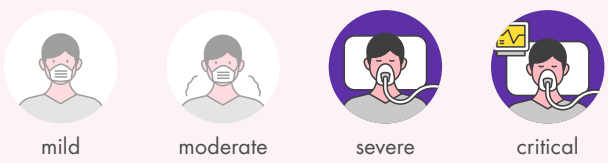
   Clinical considerations:
   In South Korea, HFNC may be the preferred treatment option for patients with acute hypoxemic respiratory failure due to greater medical staff experience with this modality, compared to Europe or China. However, non-invasive mechanical ventilation may be more appropriate for patients with respiratory failure accompanied by hypercapnia or pulmonary edema. The selection of an appropriate oxygen therapy modality should consider the experience of the medical staff, patient adaptability, and patient-specific considerations, such as the presence of claustrophobia.



Expert consensus

3-1. We recommend prompt initiation of invasive mechanical ventilation in patients with COVID-19 and progressive acute hypoxemic respiratory failure if their respiratory failure worsens despite HFNC therapy

   Clinical considerations:
   HFNC therapy is not a replacement for endotracheal intubation and mechanical ventilation in patients who require these procedures. Delaying endotracheal intubation due to HFNC use may increase mortality risk. If acute hypoxemia worsens with PaO_2/FiO_2 less than 150 mmHg despite HFNC therapy, prompt endotracheal intubation should be performed. Predictors such as the respiratory rate-oxygenation (ROX) index or modified ROX index can guide the decision to switch from HFNC to invasive mechanical ventilation, but continuous monitoring of the patient's condition is necessary due to the difficulty of predicting patient prognosis based on these predictors alone.



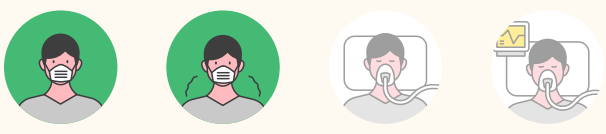
Expert consensus

3-2. We suggest HFNC therapy as an alternative to invasive mechanical ventilation in patients with acute hypoxemic respiratory failure by COVID-19 when a decision has been made to discontinue life-sustaining treatments and there are no indications for invasive mechanical ventilation.

Summary of Pharmaceutical Recommendations

Monoclonal antibody therapy

Revision Dec 2022

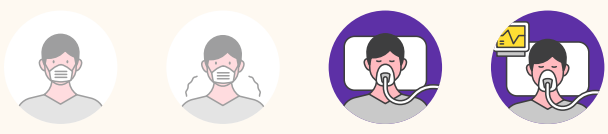


D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

1. For patients with mild or moderate COVID-19 at high risk for progression to severe disease who cannot use other antiviral agents, we suggest monoclonal antibody, in which case bebtelovimab.

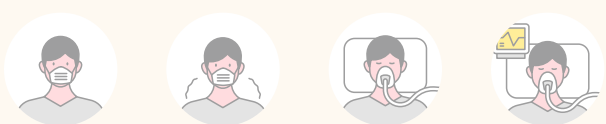
Clinical considerations:

1) Conditions associated with high risk for progression to severe COVID-19 are listed in Table 1.
2) Monoclonal antibody acts by specific binding to SARS-CoV-2. Thus, the choice of monoclonal antibody product should be guided by the current information on the SARS-CoV-2 variants circulating in Korea.



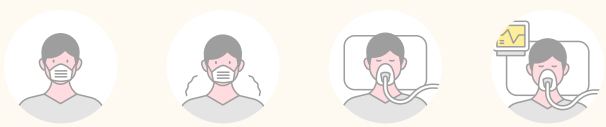
Expert consensus

2. For patients with severe or critical COVID-19, we recommend against using monoclonal antibody except for clinical trials.



Expert consensus

3. During Omicron and its subvariants are major variants circulating in Korea, we do not recommend monoclonal antibodies other than bebtelovimab, such as amubarvimab/romlusevimab, bamlanivimab, bamlanivimab/etesevimab, casirivimab/imdevimab, etesevimab, regdanvimab, and sotrovimab.

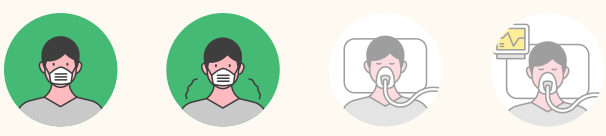


Expert consensus

4. For patients who are not expected to mount adequate immune response after vaccination or those who could not complete vaccination due to severe adverse reactions to the COVID-19 vaccine, we suggest using tixagevimab/cilgavimab for pre-exposure prophylaxis.

Paxlovid

New Nov 2022



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

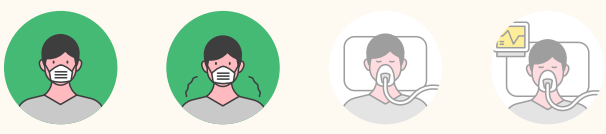
For patients with mild-to-moderate COVID-19 who are at least 12 years old, weigh more than 40 kg, and have risk factors for progression to severe COVID-19, we suggest using nirmatrelvir/ritonavir (Paxlovid).

Clinical considerations:

We recommend the use of nirmatrelvir/ritonavir (Paxlovid) within 5 days from symptom onset.

Molnupiravir

New Jan 2023



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

For patients 18 years or older with mild or moderate COVID-19 at high risk for progression to severe disease who cannot use other treatment options*, we suggest using molnupiravir.

* Paxlovid, remdesivir, or other monoclonal antibody effective against currently circulating variants

Clinical considerations:

We recommend use of molnupiravir within 5 days from symptom onset.

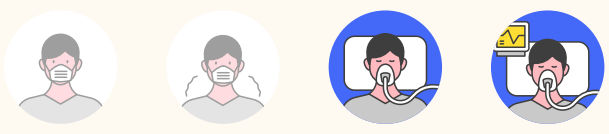
Summary of Pharmaceutical Recommendations

NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

Steroids

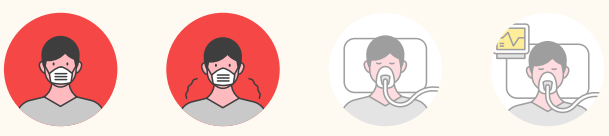
Revision Nov 2022



D Strongly against | C Conditionally against | I Inconclusive | B Conditionally Recommend | **A Strongly recommended**

1. For patients with severe or critical COVID-19, we recommend using steroids.

Clinical considerations:
The recommended dose of steroids is 6 mg of dexamethasone per day for up to 10 days (if discharged earlier than 10 days, then up to the day of discharge). Other steroids with similar potency may be administered as an alternative (160 mg of hydrocortisone, 40 mg of prednisone, or 32 mg of methylprednisolone).



D Strongly against | C Conditionally against | I Inconclusive | B Conditionally Recommend | A Strongly recommended

2. For patients with mild to moderate COVID-19, we recommend against the use of steroids.

Inhaled steroids

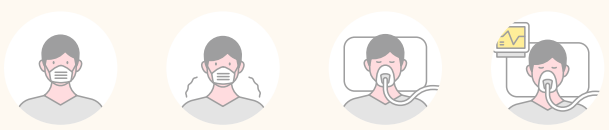
Revision Nov 2022

D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

For patients in early stage of COVID-19, we are unable to make a recommendation for or against inhaled steroids due to insufficient evidence on its efficacy and safety.

IL-1 inhibitor

Revision Nov 2022

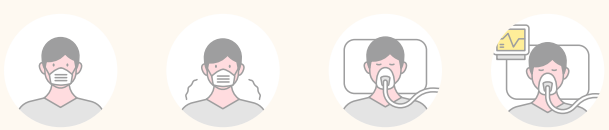


D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

We suggest against the use of anakinra (interleukin-1 inhibitor) for patients with COVID-19 except for clinical trials.

Specific IVIG

Revision Nov 2022

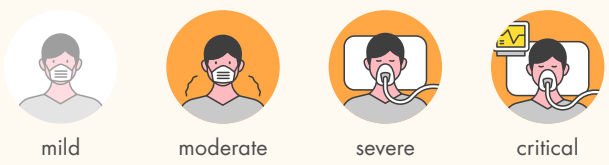


D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

We are unable to make a recommendation for or against the use of SARS-CoV-2 specific intravenous immunoglobulin (IVIG) due to insufficient evidence on its efficacy and safety.

Convalescent Plasma therapy

Revision 2023. Mar



D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

1. For patients with moderate-to-severe COVID-19, we suggest against the use of convalescent plasma.

D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

2. For patients with mild COVID-19, we are unable to make a recommendation for or against the use of convalescent plasma due to insufficient evidence on its efficacy and safety.

Non-specific IVIG

Dec 2021

D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

We suggest against the use of anti-SARS-CoV-2 non-specific IVIG for patients with COVID-19, except when indicated for treatment of complications.

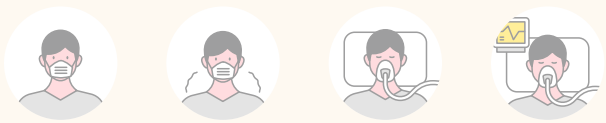
Summary of Pharmaceutical Recommendations

NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

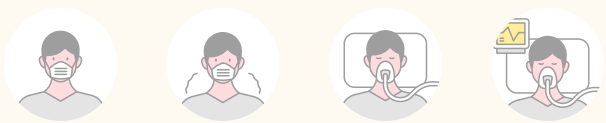
Protease inhibitors

Dec 2021



D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

1. We are unable to make a recommendation for or against the use of camostat for patients with COVID-19 due to insufficient evidence on its efficacy and safety.

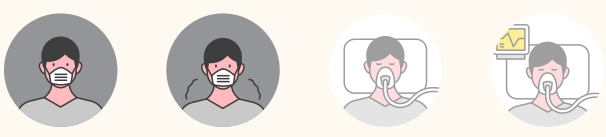


D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

2. We are unable to make a recommendation for or against the use of nafamostat for patients with COVID-19 due to insufficient evidence on its efficacy and safety.

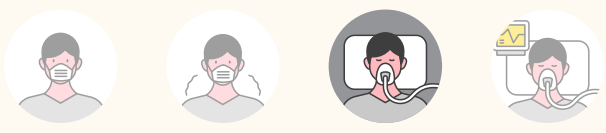
Ivermectin

Dec 2021



D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

1. We are unable to make a recommendation for or against the use of ivermectin for patients with mild to moderate COVID-19 due to insufficient evidence on its efficacy and safety.

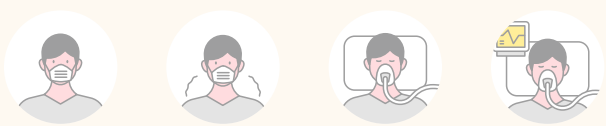


D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

2. We are unable to make a recommendation for or against the use of ivermectin for patients with severe COVID-19 due to insufficient evidence on its efficacy and safety.

Interferon

Dec 2021



D Strongly against | C Conditionally against | I Inconclusive | B Conditionally Recommend | A Strongly recommended

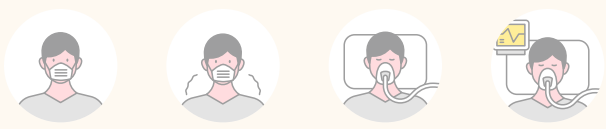
We recommend against the use of interferon for patients with COVID-19.

Other antiviral agents

Dec 2021

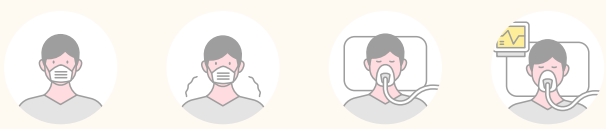
D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

1. We suggest against the use of favipiravir for patients with COVID-19 except for clinical trial.



D Strongly against | **C Conditionally against** | I Inconclusive | B Conditionally Recommend | A Strongly recommended

2. We suggest against the use of umifenovir for patients with COVID-19 except for clinical trial.



D Strongly against | C Conditionally against | **I Inconclusive** | B Conditionally Recommend | A Strongly recommended

3. We are unable to make a recommendation for or against the use of baloxavir marboxil for patients with COVID-19 due to insufficient evidence on its efficacy and safety.

Summary of Recommendations for Pediatric Infections

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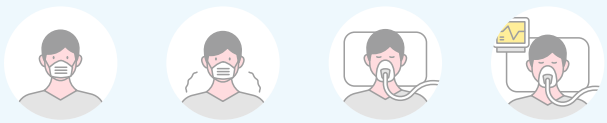
NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

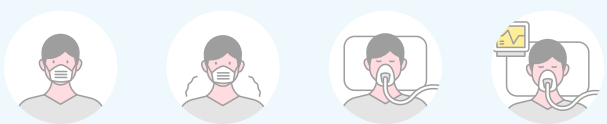
IVIG (alone or combined with steroids)

Revision Jan 2023



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

1. For the initial treatment of patients with multisystem inflammatory syndrome in children (MIS-C), we suggest the use of intravenous immunoglobulin (IVIG) combined with steroids rather than either IVIG alone or steroids alone.

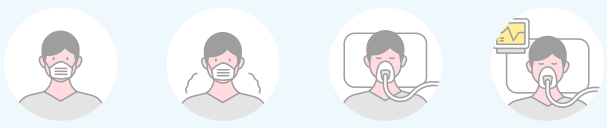


Expert consensus

2. We consider the use of steroids alone for the initial treatment of patients with MIS-C.

Other immunomodulators

Revision Feb 2023

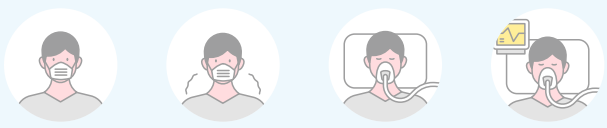


Expert consensus

For patients with MIS-C who do not respond to IVIG and/or steroid therapy, we suggest the use of other immunomodulators (e.g., interleukin-1 inhibitor, interleukin-6 inhibitor, TNF-α inhibitor).

Aspirin and anticoagulant therapy

Revision Jan 2023

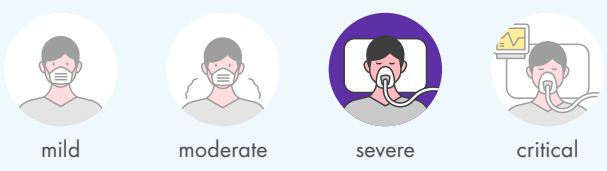


Expert consensus

We suggest the use of low-dose aspirin to prevent thrombosis in patients with MIS-C.

Pediatric drug therapy

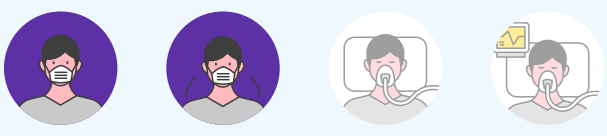
New Oct 2022



Expert consensus

1. We suggest the use of remdesivir in pediatric patients (aged 28 days and over and weighing at least 3 kg) with severe COVID-19 who require supplemental oxygen without mechanical ventilation or ECMO.

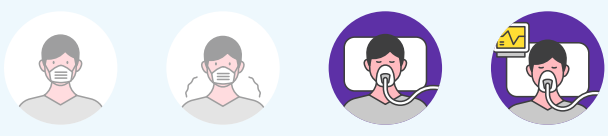
   Clinical considerations:
   We suggest treatment with five days of remdesivir in pediatric patients with severe COVID-19. If patients on remdesivir treatment progress to requiring mechanical ventilation or ECMO, the full course of remdesivir should still be completed. We recommend against the routine initiation of remdesivir in patients with COVID-19 on mechanical ventilation or ECMO.



Expert consensus

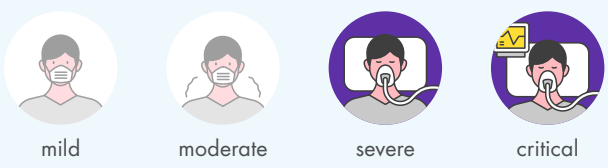
2. We suggest the use of remdesivir within seven days of symptom onset in pediatric patients (aged 12 years and over and weighing at least 40 kg) with mild-to-moderate COVID-19 who do not require supplemental oxygen at high risk for progression to severe disease.

   Clinical considerations:
   We suggest treatment with three days of remdesivir in patients with mild-to-moderate COVID-19. If these patients progress to severe COVID-19, five days of remdesivir treatment is suggested.



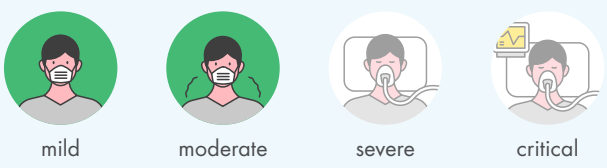
Expert consensus

3. We suggest the use of steroids (dexamethasone) in pediatric patients with severe-to-critical COVID-19 who require supplemental oxygen.



Expert consensus

4. In pediatric patients with severe or critical COVID-19 (≥2 years of age), we consider the use of tocilizumab in addition to steroids.



D Strongly against | C Conditionally against | I Inconclusive | **B Conditionally Recommend** | A Strongly recommended

5. We suggest the use of nirmatrelvir/ritonavir in pediatric patients (aged 12 years and over and weighing at least 40 kg) with mild-to-moderate COVID-19 at high risk for progression to severe disease.

   Clinical considerations:
   We recommend the use of nirmatrelvir/ritonavir within 5 days of symptom onset.

Summary of Recommendation for Emergency Care

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NECA National Evidence-based Healthcare Collaborating Agency

대한의학회 Korean Academy of Medical Sciences

Mechanical cardiopulmonary resuscitation

New Oct 2022

Expert consensus

We suggest the use of mechanical CPR devices for cardiac arrest in patients with suspected or confirmed COVID-19 to mitigate the potential spread of infection through aerosols.

Diagnostic test and Radiological examinations

Rapid antigen test (RAT)

Revision Feb 2023

Expert consensus

1. We recommend the rapid antigen test (RAT) be used in conjunction with the polymerase chain reaction (PCR) test for enhanced diagnostic accuracy.

D	C	I	B	A
Strongly against	**Conditionally against**	Inconclusive	Conditionally Recommend	Strongly recommended

2. For suspected COVID-19 cases, we generally do not recommend the RAT alone. However, as an exception, RAT may be used when the prevalence of COVID-19 increases and there are limitations in performing polymerase chain reaction (PCR) tests.

Clinical considerations:
While there are no significant differences in diagnostic accuracy based on virus variants, sensitivity tends to be lower in asymptomatic cases. However, additional studies are needed on newly emerging variants.

Contrast-enhanced chest CT scan

Revision Jan 2023

D	C	I	B	A
Strongly against	Conditionally against	Inconclusive	**Conditionally Recommend**	Strongly recommended

We suggest contrast-enhanced chest CT for patients with COVID-19 suspected of having a pulmonary embolism because of the elevated D-dimer level in a blood test and the presentation of suspicious symptoms, including dyspnea, hypoxia, and chest pain.

Chest X-ray follow-up

Dec 2021

D	C	I	B	A
Strongly against	Conditionally against	Inconclusive	**Conditionally Recommend**	Strongly recommended

We suggest chest X-ray follow-ups for patients with COVID-19 during the treatment course and after isolation treatment.

Chest CT using portable personal negative pressure isolation chamber (NPIC)

New Oct 2022

Expert consensus

We suggest utilizing the portable personal NPIC for patients at high risk of COVID-19 transmission who require a clinically necessary chest CT scan. This allows for the safe conduct of the chest CT examination in a CT room that lacks a negative pressure isolation system.

Clinical considerations:
COVID-19 is an infectious disease with a high risk of droplet transmission. Therefore, performing CT without preparation can cause contamination of the scan room, leading to secondary infection cases. Accordingly, using a negative-pressure chamber to isolate the patient from the outside environment is recommended for CT scans. Interference with X-ray penetration and degradation of CT image quality due to the use of a portal personal NPIC are determined to be at a level that would still allow CT images to be interpreted. More specific recommendations need on the confirmation of results from various studies, including different NPIC types used in clinical practice, the severity of the disease, and CT scan methods. However, even if used a NIPC, the other routine processes, including disinfection, cleaning, and ventilation, are essential before and after the CT examination.