CMEO Snack

Guideline-Based Therapeutics for Hospitalized Patients with SARS-CoV-2 Infection

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LEARNING OBJECTIVE 1

Incorporate guideline-recommended SARS-CoV-2 therapies into the treatment of hospitalized patients to improve clinical outcomes and reduce mortality.

Gaps in Guideline-Directed Medical Therapy

Despite **five years of** established guidelines from major international organizations, **significant and measurable variability persists in the treatment of hospitalized patients with SARS-CoV-2**

Inconsistent patient stratification based on disease severity

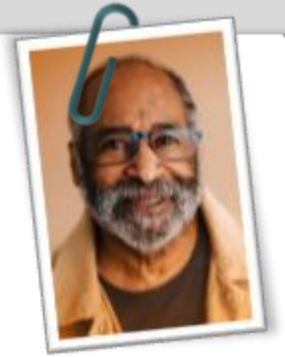
Limited oral antiviral awareness: eligibility, prescribing, benefits

Delayed application of immunomodulatory therapy

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Goldstein A, et al. *Sci Rep*. 2024;14(1). Chu K, et al. *BMJ Health Care Inform*. 2021;28(1).
Levy ME, et al. *Clinical Infectious Disease*. 2024; 78(6): 1531-1535.

Patient Case: DR



- DR is a 60-yr old male with multiple myeloma undergoing maintenance treatment for 5 years on lenalidomide.
- 3 days ago, he started feeling sick, with cough and at night developed low grade fever with the following vitals:

3 days ago
- Temp: 37.6°C *(99.7°F)*
- HR: 89 bpm
- BP: 130/85 mmHg
- RR: 20 breaths/min

Yesterday
- Temp: 38.5°C *(101.3°F)*
- HR: 92 bpm
- BP: 134/88 mmHg
- RR: 22 breaths/min

SARS-CoV-2 Self-Test (+)

This morning
- Experienced SOB
- Came to ER
- SpO2 **86%** on room air

History

- COPD
- Former smoker

- **What would be your first-line management option?**

BP = blood pressure; COPD = chronic obstructive pulmonary disease; ER = emergency room; HR = heart rate; RR = respiratory rate; SOB = shortness of breath; SpO2 = peripheral arterial oxygen saturation

Severity Thresholds: Foundational Comparison

Risk factors for severe disease progression: age > 65 years, obesity, diabetes, neoplastic disease, chronic heart failure, chronic lung disease, chronic kidney disease, cerebrovascular disease, immunodeficiencies, and immunosuppression

Mild-moderate

1. SpO2 **≥ 94%** in ambient air
2. Upper respiratory tract symptoms predominate
3. No signs of pneumonia on examination/imaging

Severe (not critical)

1. SpO2 **< 94%** in ambient air
2. Respiratory rate **> 30** breaths/min; lung infiltrates **> 50%**
3. Low-flow supplemental oxygen via nasal cannula or mask

Critical (non-invasive Support)

1. SpO2 **< 90%** in ambient air
2. Respiratory distress and signs of end-organ damage
3. High-flow nasal cannula (HFNC) or non-invasive ventilation (NIV)

Critical (invasive support)

1. Severe respiratory failure with multi-organ dysfunction
2. ARDS; possible vasopressor requirement
3. Invasive mechanical ventilation ± ECMO

ARDS = acute respiratory distress syndrome

Infectious Diseases Society of America (IDSA). 2025. https://www.idsociety.org/practice-guideline/SARS-CoV-2-guideline-treatment-and-management/.
GoodRx. 2025. https://www.goodrx.com/conditions/covid-19/coronavirus-treatments-on-the-way.

SARS-CoV-2 Therapeutics - Antivirals

Drug Name	Drug Class	Mechanism of Action	Clinical Indication
Remdesivir	Nucleoside analogue (adenosine)	Inhibits ribonucleic acid (RNA)-dependent RNA polymerase	• Treatment of SARS-CoV-2 in hospitalized adults and pediatric patients (≥ 28 days old, ≥ 3 kg) • Mild-to-moderate disease, outpatient, but at high risk for progression to severe SARS-CoV-2
Nirmatrelvir/Ritonavir	Protease inhibitor combination	Inhibits 3CLpro (main protease), blocking viral replication. Ritonavir boosts nirmatrelvir by inhibiting CYP3A metabolism.	• Mild-to-moderate disease in adults and children (≥ 12 years, ≥ 40 kg) at high risk for progression to severe disease
Molnupiravir†	Nucleoside analogue (cytidine)	Inhibits RNA-dependent RNA polymerase	• Mild-to-moderate disease in adults at high risk of severe illness
Ensitrelvir‡	Protease inhibitor	SARS-CoV-2 3C-like (3CL) protease inhibitor	• Mild-to-moderate disease in adults and adolescents (≥ 12 years)

† Molnupiravir does **not have a general EU marketing authorization**, but its availability for use in some European countries is possible through national-level emergency use or compassionate access programs

‡ Approved for use in Japan and Singapore

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GoodRx. 2025. https://www.goodrx.com/conditions/covid-19/coronavirus-treatments-on-the-way. Chen X, et al. *Immun Inflamm Dis.* 2025: 13(4).

SARS-CoV-2 Therapeutics - Immunomodulators

Drug Name	Drug Class	Mechanism of Action	Clinical Indication
Dexamethasone	Corticosteroids	Suppressing "cytokine storm", reducing inflammatory activity	• Severe or critical SARS-CoV-2 in hospitalized patients of all ages requiring supplemental oxygen
Tocilizumab	IL-6 receptor antagonist	Blocks **IL-6 receptors**, reducing inflammatory activity	• Severe or critical SARS-CoV-2 in pediatric (2+ yrs of age) and adults (requiring supplemental oxygen, ventilation, or ECMO) in combination with systemic corticosteroids
Baricitinib	JAK inhibitor	**JAK1/2 inhibitor** targeting immune dysregulation pathways	• Severe or critical SARS-CoV-2 in adults (requiring supplemental oxygen)

CTLA-4 = cytotoxic T-lymphocyte-associated protein 4; CYP3A = cytochrome P450 3A; ECMO = extracorporeal membrane oxygenation; IL-6 = interleukin 6; JAK = janus kinase

Infectious Diseases Society of America (IDSA). 2025. https://www.idsociety.org/practice-guideline/SARS-CoV-2-guideline-treatment-and-management/. GoodRx. 2025. https://www.goodrx.com/conditions/covid-19/coronavirus-treatments-on-the-way. Chen X, et al. *Immun Inflamm Dis.* 2025; 13(4).

SARS-CoV-2 Therapeutics – Alternative Immunomodulators

Drug Name	Drug Class	Mechanism of Action	Clinical Indication
Abatacept	T-cell costimulation modulator	Blocks T-cell activation via CTLA-4 pathway	• Severe or critical SARS-CoV-2 when other agents are unavailable
Infliximab	TNF-α inhibitor	Inhibits TNF-α inflammatory cascade	• Severe or critical SARS-CoV-2 when other agents are unavailable
Anakinra	Recombinant IL-1 receptor antagonist	Competitive inhibitor of the IL-1 receptor	• Severe or critical SARS-CoV-2 when other agents are unavailable

TNF-α = tumor necrosis factor-alpha

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GoodRx. 2025. https://www.goodrx.com/conditions/covid-19/coronavirus-treatments-on-the-way.

Framework for Inpatient Treatment

First-Line Intervention

- **Immediate assessment:** SpO2, respiratory rate, inflammatory markers
- **Severity classification** using appropriate regional criteria
- **Antiviral therapy** within 5-7 days for appropriate candidates
- **Corticosteroids** (dexamethasone 6mg daily) for severe/critical cases
- **Anticoagulation** with prophylactic LMWH for all hospitalized patients

Second-Line Intervention

- **High-flow nasal cannula** or **CPAP** for respiratory support before intubation
- **Immunomodulators** for severe cases with elevated CRP despite corticosteroids
- **Therapeutic anticoagulation** only for confirmed VTE or high-risk patients

Monitoring and Escalation

- **Daily assessment** of oxygen requirements and inflammatory markers
- **VTE screening** in high-risk patients
- **Bacterial co-infection/superimposition surveillance**

CPAP = continuous positive airway pressure; CRP = C-reactive protein; ICU = intensive care unit; LMWH = low molecular weight heparin; VTE = venous thromboembolism. World Health Organization (WHO). 2025. https://iris.who.int/server/api/core/bitstreams/d1021eff-f570-4c22-b630-a44bf4267a6c/content.

Framework for Inpatient Treatment: IDSA

Disease Severity	First-Line Treatment	Alternative Options	Monitoring Parameters	Special Considerations
Mild-Moderate	• **Nirmatrelvir/ritonavir** 300mg/100mg PO BID x 5 days (within 5 days)	• **Remdesivir** 200mg IV day 1, then 100mg IV days 2-3 • **Molnupiravir** 800mg PO BID × 5 days • High-titer convalescent plasma (immunocompromised only)	• Renal function (eGFR) • Drug interactions screening • Symptom progression • Vital signs	• High-risk patients only • **Avoid** systemic corticosteroids • Dose adjust for eGFR **30-60 mL/min** • Contraindicated if eGFR **< 30**
Severe (not critical)	• **Dexamethasone** 6mg IV/PO daily × 10 days PLUS **remdesivir** 200mg IV day 1, then 100mg IV × 4 days	• **Methylprednisolone** 32mg daily or **prednisone** 40mg daily • Add **Tocilizumab** 8mg/kg IV or **baricitinib** 4mg PO daily for high inflammatory state	• CRP levels (≥ **75** mg/L is the threshold for immunomodulators) • LFTs • Renal function • O_2 requirements	• Immunomodulators reserved for those with elevated inflammatory markers and progressive disease • Strong recommendation for **corticosteroids**
Critical (non-invasive support)	• **Dexamethasone** 6mg IV daily × 10 days PLUS **tocilizumab** 8mg/kg IV × 1 dose	• **Baricitinib** 4mg PO daily × 14 days for high inflammatory state • Abatacept or Infliximab (if standard agents unavailable)	• Inflammatory markers • Organ function • Ventilation parameters • Infection surveillance • Neutrophil count	• **Avoid** *remdesivir* • Strong recommendation for **corticosteroids** • *Requires ICU-level care*
Critical (invasive support)	• **Dexamethasone** 6mg IV daily × 10 days (up to 20mg if indicated) PLUS **tocilizumab** 8mg/kg IV × 1 dose	• **Baricitinib** 4mg PO/NG daily × 14 days	• Multi-organ function assessment • Ventilator parameters • Inflammatory markers • Infection monitoring • Coagulation studies	• **Avoid** *remdesivir* • Highest mortality risk population • Advanced life support required

BID = twice a day; eGFR = estimated glomerular filtration rate; IV = intravenous; NG = nasogastric; O_2 = oxygen; PO = per oral

Infectious Diseases Society of America (IDSA). 2025. https://www.idsociety.org/practice-guideline/SARS-CoV-2-guideline-treatment-and-management/.

Inpatient Treatment: Regional Variations

Organization	Severity Classifications	First-Line Treatments	Second-Line Treatments	VTE Prophylaxis
WHO	• Non-severe • Severe (SpO2 < 90%) • Critical (ARDS/sepsis/shock)	• Corticosteroids (dexamethasone) • Antivirals • Supportive care	• Tocilizumab/baricitinib for severe cases	• Standard prophylactic doses LMWH
NICE (UK)	• Similar to WHO classifications	• Corticosteroids • Antivirals • Oxygen therapy (CPAP/HFNC)	• Tocilizumab for severe cases	• Risk-based approach
IDSA (USA)	• Mild-Moderate (SpO2 > 94%) • Severe (SpO2 ≤ 94%) • Critical (mechanical ventilation/ECMO)	• Nirmatrelvir/ritonavir • Remdesivir • Corticosteroids	• Tocilizumab, baricitinib for severe cases	• ASH recommends prophylactic over intermediate doses
National Health Commission (China)	• Mild • Moderate • Severe • Critical (detailed Chinese criteria)	• Antivirals • TCM • Supportive care	• Immunomodulators • TCM injections	• Standard LMWH doses (now reduced use in practice)

HFNC = high-flow nasal cannula; TCM = traditional Chinese medicine

Infectious Diseases Society of America (IDSA). 2025. https://www.idsociety.org/practice-guideline/SARS-CoV-2-guideline-treatment-and-management/.
Zhang Z. *Health Care Science*. 2023;2(1):10-24; National Institute for Health and Care Excellence (NICE). 2021.
https://www.nice.org.uk/guidance/ng191/resources/covid19-rapid-guideline-managing-covid19-pdf-66142077109189. World Health Organization (WHO). 2025.
https://iris.who.int/server/api/core/bitstreams/d1021eff-f570-4c22-b630-a44bf4267a6c/content. Siegal et al. *Blood Advances*. 2025; 9(6):1247–1260.

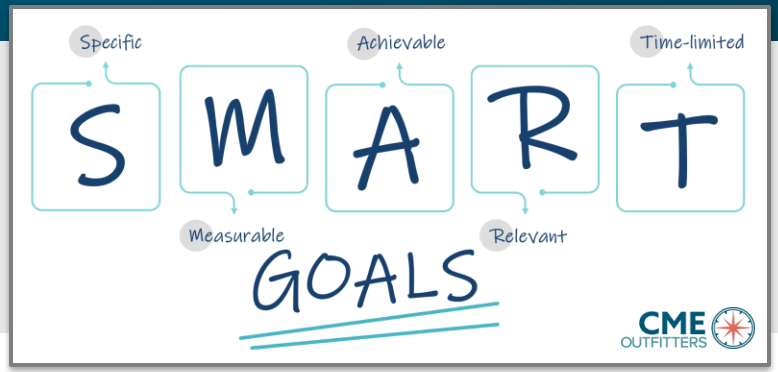
Key takeaways for Inpatient Care

Patient stratification by **disease severity** is the first and most critical step

Corticosteroids remain the cornerstone of therapy for hospitalized patients requiring oxygen

The choice of an antiviral and a potential immunomodulator depends on patient-specific factors

Be aware of your primary national guideline but understand the key differences in international recommendations



Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- Focus on early initiation of guideline-recommended corticosteroids the same day for inpatients requiring oxygen
- Implement initiation of antiviral therapy and potential immunomodulatory therapy among eligible encounters
- Ensure implementation of severity-based care pathways to initiate early supportive management for eligible SARS-CoV-2 patients

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

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Part 3:

Risk Stratification in Hospitalized SARS-CoV-2 Patients

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