Clinical Management of Adults Summary

Last Updated: February 29, 2024

Two main processes are thought to drive the pathogenesis of COVID-19. Early in the clinical course, the disease is primarily driven by the replication of SARS-CoV-2. Later in the clinical course, the disease is driven by a dysregulated immune/inflammatory response to SARS-CoV-2 infection that may lead to further tissue damage and thrombosis. Based on this understanding, therapies that directly target SARS-CoV-2 are anticipated to have the greatest effect early in the course of the disease, whereas immunosuppressive, anti-inflammatory, and antithrombotic therapies are likely to be more beneficial after COVID-19 has progressed to stages characterized by hypoxemia, endothelial dysfunction, and immunothrombosis.

The clinical spectrum of SARS-CoV-2 infection includes asymptomatic or presymptomatic infection and mild, moderate, severe, and critical illness. Table 2a provides guidance for clinicians on the therapeutic management of nonhospitalized adults. This includes patients who do not require hospitalization or supplemental oxygen and those who have been discharged from an emergency department or a hospital. Table 2c provides guidance on the therapeutic management of hospitalized adults according to their disease severity and oxygen requirements.

Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen

Patient Disposition	Panel's Recommendations
All Patients	• Symptom management should be initiated for all patients **(AIII)**. • The Panel **recommends against** the use of **dexamethasone**[a] or other systemic corticosteroids **(AIIb)**, unless these agents are being used to treat an underlying condition **(AIII)**.
Patients Who Are at High Risk of Progressing to Severe COVID-19[b,c,d]	*Preferred therapies. Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)**[e] **(AIIa)**. Start as soon as possible and within 5 days of symptom onset. See footnote on drug-drug interactions.[f] • **Remdesivir**[e,g] **(BIIa)**. Start as soon as possible and within 7 days of symptom onset. *Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate:*[h] • **Molnupiravir**[e,i] **(CIIa)**. Start as soon as possible and within 5 days of symptom onset. There is insufficient evidence for the Panel to recommend either for or against initiating these antiviral agents after the timeframes listed above.
Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.	

[a] There is currently a lack of safety and efficacy data on the use of dexamethasone in outpatients with COVID-19. Using systemic glucocorticoids in outpatients with COVID-19 may cause harm.

[b] For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19. When deciding whether to prescribe an antiviral agent to a patient who has been vaccinated, clinicians should be aware of the conditions associated with a high risk of disease progression. These conditions include older age, a prolonged amount of time since the most recent vaccine dose (e.g., >6 months), and a decreased likelihood of an adequate immune response to vaccination due to a moderate to severe immunocompromising condition or the receipt of immunosuppressive medications. The number and severity of risk factors also affects the level of risk.

[c] For a discussion of potential treatment options for patients who are immunocompromised and have prolonged COVID-19 symptoms and evidence of ongoing viral replication, see Special Considerations in People Who Are Immunocompromised.

[d] Concerns about viral rebound or the recurrence of symptoms should not be a reason to avoid using antiviral therapies when their use is indicated.

[e] If a patient requires hospitalization after starting treatment, the full treatment course can be completed at the health care provider's discretion.

[f] Ritonavir-boosted nirmatrelvir has significant drug-drug interactions. Clinicians should carefully review a patient's concomitant medications and evaluate potential drug-drug interactions. See Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications for more information.

[g] Administration of remdesivir requires an IV infusion once daily for 3 days.

[h] Molnupiravir appears to have lower efficacy than the other options recommended by the Panel.

[i] The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated **(AIII)**.

Key: CDC = Centers for Disease Control and Prevention; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel

Table 2c. Therapeutic Management of Hospitalized Adults With COVID-19

Disease Severity	Recommendations for Antiviral or Immunomodulator Therapy		Recommendations for Anticoagulant Therapy
	Clinical Scenario	Recommendation	
Hospitalized for Reasons Other Than COVID-19	Patients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19[a]	See Therapeutic Management of Nonhospitalized Adults With COVID-19.[b]	For patients without an indication for therapeutic anticoagulation: • **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients
Hospitalized but Does Not Require Supplemental Oxygen	All patients	The Panel **recommends against** the use of **dexamethasone (AIIa)** or other systemic corticosteroids **(AIII)** for the treatment of COVID-19.[c]	
	Patients who are at high risk of progressing to severe COVID-19[a]	**Remdesivir**[d] **(BIIb)** for patients who are immunocompromised; **(BIII)** for other high-risk patients	
Hospitalized and Requires Conventional Oxygen[e]	Patients who require minimal conventional oxygen	**Remdesivir**[d,f] **(BIIa)**	For nonpregnant patients with D-dimer levels above the ULN who do not have an increased bleeding risk: • **Therapeutic dose of heparin**[h] **(CIIa)** For other patients: • **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients
	Most patients	Use **dexamethasone plus remdesivir**[f] **(BIIa)**. If remdesivir cannot be obtained, use **dexamethasone (BI)**.	
	Patients who are receiving dexamethasone and who have rapidly increasing oxygen needs and systemic inflammation	Add 1 of the following immunomodulators:[g] *Preferred* • **PO baricitinib (BIIa)** • **IV tocilizumab (BIIa)** *Alternatives (Listed in Alphabetical Order)* • **IV abatacept (CIIa)** • **IV infliximab (CIIa)**	
Hospitalized and Requires HFNC Oxygen or NIV	All patients	**Dexamethasone** should be administered to all patients **(AI)**. If not already initiated, promptly add 1 of the following immunomodulators:[g,i] *Preferred* • **PO baricitinib (AI)** *Preferred Alternative* • **IV tocilizumab (BIIa)** *Additional Alternatives (Listed in Alphabetical Order)* • **IV abatacept (CIIa)** • **IV infliximab (CIIa)** Add remdesivir to 1 of the options above in certain patients (for examples, see footnote).[j]	For patients without an indication for therapeutic anticoagulation: • **Prophylactic dose of heparin**, unless contraindicated **(AI)**; **(BIII)** for pregnant patients For patients who start on a therapeutic dose of heparin in a non-ICU setting and then transfer to the ICU, the Panel recommends switching to a **prophylactic dose of heparin**, unless there is another indication for therapeutic anticoagulation **(BIII)**.
Hospitalized and Requires MV or ECMO	All patients	**Dexamethasone** should be administered to all patients **(AI)**. If the patient has not already received a second immunomodulator, promptly add 1 of the following (listed in alphabetical order):[i,k] • **PO baricitinib**[l] **(BIIa)** • **IV tocilizumab**[l] **(BIIa)** See footnote k for a discussion on the use of remdesivir.	

Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.

[a] For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19.

[b] If the patient is hospitalized for reasons other than COVID-19, the treatment duration for remdesivir is 3 days.

[c] Corticosteroids that are prescribed for an underlying condition should be continued.

[d] Evidence suggests that the benefit of remdesivir is greatest when the drug is given early in the course of COVID-19 (e.g., within 10 days of symptom onset).

[e] Conventional oxygen refers to oxygen supplementation that is not HFNC oxygen, NIV, MV, or ECMO.

[f] If these patients progress to requiring HFNC oxygen, NIV, MV, or ECMO, the full course of remdesivir should still be completed.

[g] If none of the preferred or alternative options are available or feasible to use, the JAK inhibitor **PO tofacitinib (CIIa)** or the IL-6 inhibitor **IV sarilumab (CIIa)** can be used in combination with dexamethasone. Sarilumab is only commercially available as a SUBQ injection; see Table 5e for information regarding the preparation of an IV infusion using the SUBQ product.

[h] Contraindications for the use of therapeutic anticoagulation in patients with COVID-19 include a PLT <50,000 cells/μL, Hgb <8 g/dL, the need for dual antiplatelet therapy, bleeding within the past 30 days that required an ED visit or hospitalization, a history of a bleeding disorder, or an inherited or active acquired bleeding disorder.

[i] Dexamethasone should be initiated immediately, without waiting until the second immunomodulator can be acquired. If other immunomodulators cannot be obtained or are contraindicated, use dexamethasone alone **(AI)**.

[j] Examples of patients who may benefit most from remdesivir include patients who are immunocompromised **(BIIb)**; patients with evidence of ongoing viral replication (e.g., those with a low Ct value, as measured by an RT-PCR result or with a positive rapid antigen test result) **(BIII)**; or patients who are within 10 days of symptom onset **(CIIa)**. For more information on using remdesivir in people with immunocompromising conditions, see Special Considerations in People Who Are Immunocompromised.

[k] There is insufficient evidence for the Panel to recommend either for or against the use of remdesivir in hospitalized patients with COVID-19 who require MV or ECMO. Some Panel members would add remdesivir to immunomodulator therapy in patients who have recently been placed on MV or ECMO, who are immunocompromised, who have evidence of ongoing viral replication, or who are within 10 days of symptom onset. See text for more information.

[l] If PO baricitinib and IV tocilizumab are not available or feasible to use, **PO tofacitinib** can be used instead of PO baricitinib **(CIIa)**, and **IV sarilumab** can be used instead of IV tocilizumab **(CIIa)**.

Key: CDC = Centers for Disease Control and Prevention; Ct = cycle threshold; ECMO = extracorporeal membrane oxygenation; ED = emergency department; HFNC = high-flow nasal cannula; Hgb = hemoglobin; ICU = intensive care unit; IL = interleukin; IV = intravenous; JAK = Janus kinase; MV = mechanical ventilation; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel; PLT = platelet count; PO = oral; RT-PCR = reverse transcription polymerase chain reaction; SUBQ = subcutaneous; ULN = upper limit of normal