

Clinical Management of COVID-19

INTRODUCTION TO THERAPEUTICS AND COVID-19

Learning objectives

At the end of this module, you will be able to relate the WHO recommendation for various therapeutics in the treatment of patients with COVID-19:

1. Systemic corticosteroids
2. Remdesivir
3. Hydroxychloroquine
4. Lopinavir/ritonavir
5. Ivermectin
6. IL-6 receptor blockers (tocilizumab or sarilumab)
7. Neutralizing monoclonal antibodies (casirivimab and imdevimab)

Background

- Current practice to treat COVID-19 is variable, reflecting large-scale uncertainty.
- Numerous randomized trials of many different drugs started early in the pandemic and continue.
- The results of these trials continue to inform clinical practice.
- The rapidly evolving evidence landscape requires trustworthy interpretation and expeditious clinical practice guidelines.
- The **WHO Living Guideline: Therapeutics and COVID-19** reflects innovation from the WHO and responds to the urgent need for global collaboration.¹

WHO recommendations on Therapeutics for COVID-19

last updated: November 2021



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Characterizing COVID-19 by severity

Population

This recommendation applies only to people with these characteristics:



Disease severity

Non-severe

Absence of signs of severe or critical disease

Severe

Oxygen saturation <90% on room air

Signs of pneumonia

Signs of severe respiratory distress ⁱ

Critical

Requires life sustaining treatment

Acute respiratory distress syndrome

Sepsis

Septic shock

Infographic co-produced by the BMJ and MAGIC; designer Will Stahl-Timmins (see [BMJ Rapid Recommendations](#)).

Infographic used with permission.

Corticosteroids in COVID-19 (1/2)

In September 2020, the following WHO recommendations regarding systemic corticosteroids for patients with COVID-19 were released:⁶

Recommended

We recommend systemic corticosteroids rather than no corticosteroids.

Remark: This recommendation applies to patients with severe or critical COVID-19 infection.

Corticosteroids in COVID-19 (2/2)

In September 2020, the following WHO recommendations regarding systemic corticosteroids for patients with COVID-19 were released:⁶

Conditional recommendation against

We suggest not to use corticosteroids.

Remark: This recommendation applies to patients with non-severe COVID-19 infection (absence of criteria for severe or critical infection).

Remdesivir in COVID-19

In November 2020, the following WHO recommendation regarding remdesivir for patients with COVID-19 was released:⁷

Conditional recommendation against

We suggest against administering remdesivir in addition to usual care.

Remark: This recommendation applies to hospitalized patients with COVID-19 infection, regardless of disease severity.

Hydroxychloroquine in COVID-19

In December 2020, the following WHO recommendation regarding hydroxychloroquine for patients with COVID-19 was released:⁸

Strong recommendation against

We recommend against administering hydroxychloroquine or chloroquine for treatment of COVID-19.

Remark: This recommendation applies to patients with any disease severity and any duration of symptoms.

Lopinavir/ritonavir in COVID-19

In December 2020, the following WHO recommendation regarding Lopinavir/ritonavir for patients with COVID-19 was released:⁸

Strong recommendation against

We recommend against administering lopinavir/ritonavir for treatment of COVID-19.

Remark: This recommendation applies to patients with any disease severity and any duration of symptoms.

Ivermectin in COVID-19

In March 2021, the following WHO recommendation regarding ivermectin for patients with COVID-19 was released:⁸

Only in research settings

We recommend not to use ivermectin in patients with COVID-19 except in the context of a clinical trial.

Remark: This recommendation applies to patients with any disease severity and any duration of symptoms.

IL-6 receptor blockers (tocilizumab or sarilumab) in COVID-19

In July 2021, the following WHO recommendations regarding systemic corticosteroids for patients with COVID-19 were released:⁶

Recommended

We recommend treatment with IL-6 receptor blockers (tocilizumab or sarilumab) for patients with severe or critical COVID-19 infection.

Remark: Corticosteroids have previously been strongly recommended in patients with severe and critical COVID-19, and we recommend patients meeting these severity criteria should now receive both corticosteroids and IL-6 receptor blockers.

Combination of neutralizing monoclonal antibodies (casirivimab and imdevimab) in COVID-19

In September 2021, the following WHO recommendation regarding neutralizing monoclonal antibodies for patients with COVID-19 was released:⁷

Conditional recommendation

We suggest treatment with casirivimab and imdevimab, conditional to those at highest risk of hospitalization.

Remarks: Whereas casirivimab and imdevimab achieves a substantial reduction in the relative risk of hospitalization, the absolute benefit will be trivial or unimportant in absolute terms for all but those at highest risk for which the intervention should be reserved. The panel identified a risk beyond 10% of being hospitalized for COVID-19 to represent a threshold at which most people would want to be treated with casirivimab and imdevimab. In the absence of credible tools to predict risk for hospitalization in people infected with COVID-19, typical characteristics of people at highest risk include lack of vaccination, older people, or those with immunodeficiencies and/or chronic diseases (e.g. diabetes).

Summary



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Summary

The [WHO Living Guideline: Therapeutics and COVID-19](#) seeks to provide trustworthy guidance, based on high quality research studies, to inform policy and practice worldwide

Existing recommendations can be found in the Living Guidelines and include:

1. Strong recommendation for corticosteroids in severe and critical COVID-19
2. Conditional recommendation against the use of corticosteroids in non-severe COVID-19
3. Conditional recommendation against the use of remdesivir in hospitalized patients with COVID-19
4. Strong recommendation against the use of hydroxychloroquine in patients with COVID-19, regardless of disease severity
5. Strong recommendation against the use of lopinavir/ritonavir in patients with COVID-19, regardless of disease severity
6. Strong recommendation to use IL-6 receptor blockers (tocilizumab or sarilumab) in patients with severe or critical COVID-19
7. Recommendation not to use ivermectin in patients with COVID-19 except in the context of a clinical
8. Conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab and imdevimab) in non-severe COVID-19 patients at the highest risk of severe disease
9. Conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab and imdevimab) in severe and critically ill COVID-19 patients with seronegative status

Visual summary

For further detail regarding guideline development process, see WHO Living Guideline, available at:

- [The BMJ](https://doi.org/10.1136/bmj.m3379): <https://doi.org/10.1136/bmj.m3379>
- [MAGICApp](https://app.magicapp.org/#/guidelines): <https://app.magicapp.org/#/guidelines>
- [WHO Therapeutics and COVID-19: Living Guideline](https://apps.who.int/iris): <https://apps.who.int/iris>

Population

This recommendation applies only to people with these characteristics:



Interventions

Disease severity		
Non-severe	Severe	Critical
Absence of signs of severe or critical disease	Oxygen saturation <90% on room air Signs of pneumonia Signs of severe respiratory distress	Requires life sustaining treatment Acute respiratory distress syndrome Sepsis Septic shock
Casirivimab and imdevimab Neutralising monoclonal antibodies	Recommendation in favour (conditional) For those with highest risk of hospitalisation	Recommendation in favour (conditional) For those with seronegative status Assessed by accurate and rapid testing
IL-6 receptor blockers Interleukin-6 receptor blockers		Recommendation in favour (strong)
Ivermectin	Recommendation against (except in clinical trials)	
Hydroxychloroquine	Recommendation against (strong)	
Lopinavir-ritonavir	Recommendation against (strong)	
Remdesivir	Recommendation against (weak)	
Corticosteroids	Recommendation against (weak)	Recommendation in favour (strong)

References

1. Rochwerg B, Agoritsas T, Lamotagne F, et al (2020). A living WHO guideline on drugs for covid-19. *BMJ* 2020;370:m3379. doi: <https://doi.org/10.1136/bmj.m3379>
2. RECOVERY trial homepage: <https://www.recoverytrial.net/>
3. SOLIDARITY trial homepage: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments>
4. Ader, F., & Discovery French Trial Management Team (2020). Protocol for the DisCoVeRy trial: multicentre, adaptive, randomised trial of the safety and efficacy of treatments for COVID-19 in hospitalised adults. *BMJ open*, 10(9), e041437. <https://doi.org/10.1136/bmjopen-2020-041437>
5. Siemieniuk RA, Bartoszko JJ, Ge L, Zeraatkar D, et al. Drug treatments for COVID-19: Living systematic review and network metanalysis. *BMJ (Clinical research ed.)* 2020;370:m2980. <https://doi.org/10.1136/bmj.m2980>
6. World Health Organization: Corticosteroids for COVID-19. Living guidance, 2 Sept 2020. <https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1>
7. WHO: Therapeutics and COVID-19, Living Guideline. 20 November 2020. <https://apps.who.int/iris/bitstream/handle/10665/336729/WHO-2019-nCov-remdesivir-2020.1-eng.pdf>
8. WHO: World Health Organization: Therapeutics and COVID-19: Living Guideline. 17 December 2020. <https://apps.who.int/iris/bitstream/handle/10665/337876/WHO-2019-nCoV-therapeutics-2020.1-eng.pdf>

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