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
Characterizing COVID-19 by severity

Population

This recommendation applies only to people with these characteristics:

Patients with confirmed covid-19

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

- **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).

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

\begin{shaded}
\textbf{Conditional recommendation against}
\end{shaded}

\begin{itemize}
\item \textbf{We suggest not to use corticosteroids.}
\item \textbf{Remark:} This recommendation applies to patients with non-severe COVID-19 infection (absence of criteria for severe or critical infection).
\end{itemize}
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.
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:\textsuperscript{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.
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:

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

- **The BMJ**: https://doi.org/10.1136/bmj.m3379
- **MAGICApp**: https://app.magicapp.org/#/guidelines
- **WHO Therapeutics and COVID-19: Living Guideline**: https://apps.who.int/iris
References

2. RECOVERY trial homepage: https://www.recoverytrial.net
Acknowledgements

Contributors
Dr Janet Diaz, WHO, Geneva, Switzerland
Dr Pryanka Relan, WHO, Geneva, Switzerland
Dr Keegan Checkett, WHO Consultant, University of Chicago, USA