تازه هاي مديريت و درمان كووید 19

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COVID-19 Treatment Guidelines (NIH)

Last Updated: August 4, 2021

Antiviral Drugs That Are Approved or Under Evaluation for the Treatment of COVID-19

- **Remdesivir is the only Food and Drug Administration-approved drug for the treatment of COVID-19**

Remdesivir

- Remdesivir is an intravenous nucleotide prodrug of an adenosine analog. Remdesivir binds to the viral RNA-dependent RNA polymerase and inhibits viral replication through premature termination of RNA transcription
- (FDA) for the treatment of COVID-19 in hospitalized adult and pediatric patients (aged ≥12 years and weighing ≥40 kg).
- It is also available through an FDA Emergency Use for the treatment of COVID-19 in hospitalized pediatric patients weighing 3.5 kg to <40 kg or aged <12 years and weighing ≥3.5 kg.
- Remdesivir should be administered in a hospital or a health care setting that can provide a similar level of care to an inpatient hospital.

- The safety and efficacy of combination therapy of remdesivir with corticosteroids have not been rigorously studied in clinical trials;
- however, there are theoretical reasons that combination therapy may be beneficial in some patients with severe COVID-19.

- Remdesivir can cause gastrointestinal symptoms (e.g., nausea), elevated transaminase levels, an increase in prothrombin time (without a change in the international normalized ratio), and hypersensitivity reactions.
- Liver function tests and prothrombin time should be obtained in all patients before remdesivir is administered and during treatment as clinically indicated.
- Remdesivir may need to be discontinued if alanine transaminase (ALT) levels increase to >10 times the upper limit of normal and should be discontinued if an increase in ALT level and signs or symptoms of liver inflammation are observed

- Remdesivir **is not recommended** for patients with an eGFR <30 mL/
- In two observational studies that evaluated the use of remdesivir in hospitalized patients with COVID-19, no significant differences were reported in the incidences of adverse effects or acute kidney injury between patients with an estimated creatinine clearance (CrCl) <30 mL/min and those with an estimated CrCl ≥30 mL/min

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Letters to the Editor

Remdesivir in COVID-19 Patients with Impaired Renal Function

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- a 5-day course of remdesivir in patients with an eGFR of ,30 ml/min per 1.73 m2 should be considered safe. Therefore, in their opinion, patients with coronavirus disease 2019 (COVID-19) who have impaired renal function should be offered remdesivir treatment, because this is a potentially life-saving treatment for such a vulnerable population

- Pregnant patients were excluded from the clinical trials that evaluated the safety and efficacy of remdesivir
- Among 86 pregnant and postpartum hospitalized patients with severe COVID-19 who received compassionate use remdesivir, the therapy was well tolerated, with a low rate of serious adverse events.
- Remdesivir should not be withheld from pregnant patients if it is otherwise indicated.

NICE

- Consider remdesivir for up to 5 days for COVID-19 pneumonia in adults, and young people 12 years and over weighing 40 kg or more, in hospital and needing low-flow supplemental oxygen.

Chloroquine or Hydroxychloroquine and/or Azithromycin

- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of chloroquine or hydroxychloroquine and/or azithromycin for the treatment of COVID-19 in hospitalized patients **(AI)** and in nonhospitalized patients **(AIIa)**.

Ivermectin

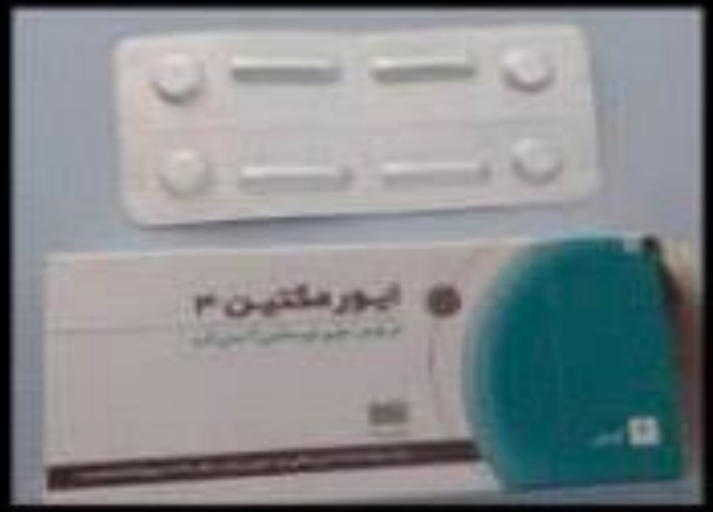
- Ivermectin is a Food and Drug Administration (FDA)-approved antiparasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiases, and scabies
- Ivermectin is not approved by the FDA for the treatment of any viral infection

- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of ivermectin for the treatment of COVID-19

- In animal studies, ivermectin was shown to be teratogenic when given in doses that were maternotoxic.
- These results raise concerns about administering ivermectin to people who are in the early stages of pregnancy (prior to 10 weeks gestation
- There are numerous reports of inadvertent ivermectin use in early pregnancy without apparent adverse effects.
- Therefore, there is insufficient evidence to establish the safety of using ivermectin in pregnant people, especially those in the later stages of pregnancy.

IVERMECTIN

- **Ivermectin dosing:** 150-200 ug/kg or fixed dose of 12 mg (≤ 80kg) or 18 mg (≥ 80kg). Depending on the manufacturer ivermectin is supplied as 3mg, 6 mg or 12 mg tablets.
  - 50-64.9 kg - 12mg
  - 65-79.9 kg - 15mg
  - 80-94.9 kg - 18mg
  - 95-109.9 kg - 21mg
  - ≥ 110 kg - 24mg



Lopinavir/Ritonavir and Other HIV Protease Inhibitors

- • The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of **lopinavir/ritonavir** and **other HIV protease inhibitors** for the treatment of COVID-19 in hospitalized patients **(AI)**. • The Panel **recommends against** the use of **lopinavir/ritonavir** and **other HIV protease inhibitors** for the treatment of COVID-19 in nonhospitalized patients **(AIII)**.

Nitazoxanide

- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of **nitazoxanide** for the treatment of COVID-19, except in a clinical trial **(BIIa)**.

Anti-SARS-CoV-2 Monoclonal Antibodies

- Monoclonal antibodies that target the spike protein have been shown to have a clinical benefit in treating SARS-CoV-2 infection
- Preliminary data suggest that monoclonal antibodies may play a role in preventing SARS-CoV-2 infection in household contacts of infected patients and during skilled nursing and assisted living facility outbreaks

Anti-SARS-CoV-2 Monoclonal Antibodies That Received Emergency Use Authorizations From the Food and Drug Administration

- Three anti-SARS-CoV-2 monoclonal antibody products currently have Emergency Use Authorizations (EUAs) from the Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in nonhospitalized patients with laboratory-confirmed SARS-CoV-2 infection who are at high risk for progressing to severe disease and/or hospitalization.

- *Bamlanivimab plus etesevimab:* These are neutralizing monoclonal antibodies that bind to different but overlapping epitopes in the spike protein RBD of SARS-CoV-2.
- *Casirivimab plus imdevimab:* These are recombinant human monoclonal antibodies that bind to nonoverlapping epitopes of the spike protein RBD of SARS-CoV-2.
- *Sotrovimab:* This monoclonal antibody was originally identified in 2003 from a SARS-CoV survivor. It targets an epitope in the RBD of the spike protein that is conserved between SARS-CoV and SARS-CoV-2.

- **Sotrovimab 500 mg intravenous (IV) infusion**
- **Casirivimab 600 mg plus imdevimab 600 mg IV infusion (AIIa)**
- If IV infusions are not feasible or would cause a delay in treatment, **casirivimab 600 mg plus imdevimab 600 mg** administered by four subcutaneous (SQ) injections (2.5 mL per injection) can be used as an alternative **(BIII)**

- When using monoclonal antibodies, treatment should be started as soon as possible after the patient receives a positive result test (NAAT) and within 10 days of symptom onset.

- The use of anti-SARS-CoV-2 monoclonal antibodies should be considered for patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 if they otherwise meet the EUA criteria for outpatient treatment.
- Anti-SARS-CoV-2 monoclonal antibodies are not currently authorized for use in patients who are hospitalized with severe COVID-19

Convalescent Plasma

- Plasma from donors who have recovered from COVID-19 may contain antibodies to SARS-CoV-2 that may help suppress the virus and modify the inflammatory response.
- [1] The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for convalescent plasma for the treatment of certain hospitalized patients with COVID-19

- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of **low-titer COVID-19 convalescent plasma** for the treatment of COVID-19 **(AIIb)**.
- •Low-titer COVID-19 convalescent plasma is no longer authorized through the convalescent plasma EUA

- On February 4, 2021, the FDA revised the convalescent plasma EUA to limit the authorization to high-titer COVID-19 convalescent plasma and only for the treatment of hospitalized patients with COVID-19 early in the disease course or hospitalized patients who have impaired humoral immunity.

Advers Effect

- serious adverse reactions following the administration of COVID-19 convalescent plasma are infrequent and consistent with the risks associated with plasma infusions for other indications.
- These risks include transfusion-transmitted infections (e.g., HIV, hepatitis B, hepatitis C), allergic reactions, anaphylactic reactions, febrile nonhemolytic reactions, transfusion-related acute lung injury, transfusion-associated circulatory overload, and hemolytic reactions. Hypothermia, metabolic complications, and post-transfusion purpura have also been described

Cell-Based Therapy Under Evaluation for the Treatment of COVID-19

- Mesenchymal Stem Cells :

The COVID-19 Treatment Guidelines Panel **recommends against** the use of **mesenchymal stem cells** for the treatment of COVID-19, except in a clinical trial **(AIIb)**.

Immunomodulators Under Evaluation for the Treatment of COVID-19

Colchicine

- Colchicine is an anti-inflammatory drug that is used to treat a variety of conditions, including gout, recurrent pericarditis, and familial Mediterranean fever
- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of colchicine for the treatment of nonhospitalized patients with COVID-19.
- The Panel **recommends against** the use of colchicine for the treatment of hospitalized patients with COVID-19
- some studies have reported higher discharge rates or fewer deaths among patients who received colchicine than among those who received comparator drugs or placebo

Advers Effect

- Common adverse effects of colchicine include diarrhea, nausea, vomiting, abdominal cramping and pain, bloating, and loss of appetite. In rare cases, colchicine is associated with serious adverse events, such as neuromyotoxicity and blood dyscrasias

Corticosteroids

- Patients with severe COVID-19 can develop a systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction.
- It has been proposed that the potent anti-inflammatory effects of corticosteroids might prevent or mitigate these deleterious effects.
- Both beneficial and deleterious clinical outcomes have been reported with use of corticosteroids (mostly prednisone or methylprednisolone) in patients with pulmonary infections.
- In patients with *Pneumocystis jirovecii* pneumonia and hypoxemia, prednisone therapy reduced the risk of death.
- However, in outbreaks of previous novel coronavirus infections (i.e., Middle East respiratory syndrome [MERS] and severe acute respiratory syndrome [SARS]), corticosteroid therapy was associated with delayed virus clearance.
- In severe pneumonia caused by influenza viruses, corticosteroid therapy appears to result in worse clinical outcomes, including secondary bacterial infection and death

- In the RECOVERY trial , dexamethasone was shown to reduce mortality in hospitalized patients with COVID-19 who required supplemental oxygen.
- In this trial, dexamethasone was stopped at the time of hospital discharge.
- Moreover, the use of corticosteroids can lead to adverse events (e.g., hyperglycemia, neuropsychiatric symptoms, secondary infections), which may be difficult to detect and monitor in an outpatient setting

- Recommendations on the use of corticosteroids for COVID-19 in hospitalized patients are largely based on data from the RECOVERY trial, a large, multicenter, open-label randomized trial performed in the United Kingdom.
- This trial randomized 6,425 hospitalized patients to receive up to 10 days of dexamethasone or standard of care. Mortality at 28 days was lower among the patients who received dexamethasone than among those who received the standard of care.[15] This benefit was observed in patients who were mechanically ventilated or required supplemental oxygen at enrollment. No benefit of dexamethasone was seen in patients who did not require supplemental oxygen at enrollment

Systemic Corticosteroids Other Than Dexamethasone

- If dexamethasone is not available, alternative glucocorticoids (e.g., prednisone, methylprednisolone, hydrocortisone) can be used.
- For these drugs, the total daily dose equivalencies to dexamethasone 6 mg (oral or intravenous)24 are:
- Prednisone 40 mg
- Methylprednisolone 32 mg
- Hydrocortisone 160 mg
- Half-life, duration of action, and frequency of administration vary among corticosteroids:
- *Long-acting corticosteroid:* Dexamethasone; half-life 36 to 72 hours, administer once daily.
- *Intermediate-acting corticosteroids:* Prednisone and methylprednisolone; half-life 12 to 36 hours, administer once daily or in two divided doses daily.
- *Short-acting corticosteroid:* Hydrocortisone; half-life 8 to 12 hours, administer in two to four divided doses daily

Inhaled Corticosteroids

- Budesonide is a synthetic, inhaled corticosteroid with potent glucocorticoid activity and weak mineralocorticoid activity.
- It has broad anti-inflammatory properties and has Food and Drug Administration-labeled indications in the management of chronic respiratory diseases including asthma and chronic obstructive pulmonary disease.
- Certain inhaled corticosteroids have been shown to impair viral replication of SARS-CoV and downregulate expression of the receptors used for cell entry
- These mechanisms support the potential of inhaled corticosteroids as therapeutic agents for COVID-19.
- However, observational studies of individuals who were chronic inhaled corticosteroid users have found that its use either had no effect on COVID-19 outcomes or increased risk of hospitalization
- There is insufficient evidence for the Panel to recommend either for or against the use of inhaled budesonide for the treatment of COVID-19

Adverse Effects

- Clinicians should closely monitor patients with COVID-19 who are receiving dexamethasone for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, avascular necrosis).
- The use of systemic corticosteroids may increase the risk of opportunistic fungal infections (e.g., mucormycosis, aspergillosis) and reactivation of latent infections (e.g., hepatitis B virus [HBV], herpesvirus infections, strongyloidiasis, tuberculosis)
- When initiating dexamethasone, clinicians should consider appropriate screening and treatment to reduce the risk of *Strongyloides* hyperinfection in patients at high risk of strongyloidiasis (e.g., patients from tropical, subtropical, or warm, temperate regions or those engaged in agricultural activities)or fulminant reactivations of HBV.
- Combining systemic corticosteroids with other immunosuppressants, such as tocilizumab or baricitinib, could theoretically increase the risk of secondary infections. However, this adverse effect has not been reported in clinical trials to date.
  .
- Dexamethasone should be continued for up to 10 days or until hospital discharge, whichever comes first

Considerations in Pregnancy

- A short course of betamethasone and dexamethasone, which are known to cross the placenta, is routinely used to decrease neonatal complications of prematurity in women with threatened preterm delivery.
- Given the potential benefit of decreased maternal mortality and the low risk of fetal adverse effects for a short course of dexamethasone therapy, the Panel recommends using **dexamethasone** in hospitalized pregnant patients with COVID-19 who are mechanically ventilated **(AIII)** or who require supplemental oxygen but who are not mechanically ventilated **(BIII)**.

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider in ED or an In-Person or Telehealth Visit	Anti-SARS-CoV-2 monoclonal antibody products are recommended for outpatients with mild to moderate COVID-19 who are at high risk of disease progression, as defined by the EUA criteria (treatments are listed in alphabetical order):[a] • **Casirivimab plus imdevimab**; *or* • **Sotrovimab** At this time, the Panel **recommends against** the use of **bamlanivimab plus etesevimab** in these patients due to an increase in the proportion of potentially resistant variants **(AIII)**.[a] See text for details. The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[b]
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[c]	There is insufficient evidence to recommend either for or against the continued use of remdesivir, dexamethasone, and/or baricitinib. Review the text below when considering the use of any of these agents after hospital discharge.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[d]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use should not exceed 10 days) with careful monitoring for adverse events **(BIII)**. There is insufficient evidence to recommend either for or against the use of remdesivir. When considering the use of remdesivir, review the text below for further discussion. The Panel **recommends against** the use of **baricitinib** in this setting, except in a clinical trial **(AIII)**.

Fluvoxamine

- In a murine sepsis model, fluvoxamine was found to bind to the sigma-1 receptor in immune cells, resulting in reduced production of inflammatory cytokines
- In an in vitro study of human endothelial cells and macrophages, fluvoxamine reduced the expression of inflammatory genes
- Further studies are needed to establish whether the anti-inflammatory effects of fluvoxamine observed in nonclinical studies also occur in humans beings and are clinically relevant in the setting of COVID-19.
- Recommendation: There is insufficient evidence for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of fluvoxamine for the treatment of COVID-19

Granulocyte-Macrophage Colony-Stimulating Factor Inhibitors

- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of GM-CSF inhibitors for the treatment of hospitalized patients with COVID-19

Immunoglobulins: Non-SARS-CoV-2 Specific

- The COVID-19 Treatment Guidelines Panel **recommends against** the use of non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific **intravenous immunoglobulin (IVIG)** for the treatment of COVID-19, except in a clinical trial **(AIII)**.
- This recommendation **should not preclude** the use of IVIG when otherwise indicated for the treatment of complications that arise during the course of COVID-19

- It is unknown whether products derived from the plasma of donors without confirmed SARS-CoV-2 infection contain high titer of SARS-CoV-2 neutralizing antibodies.
- Furthermore, although other blood components in IVIG may have general immunomodulatory effects, it is unclear whether these theoretical effects will benefit patients with COVID-19.

- A retrospective, non-randomized cohort study of IVIG for the treatment of COVID-19 was conducted across eight treatment centers in China between December 2019 and March 2020.
- The study showed no difference in 28-day or 60-day mortality between 174 patients who received IVIG and 151 patients who did not receive IVIG.
- More patients in the IVIG group had severe disease at study entry (71 patients [41%] with critical status in the IVIG group vs. 32 patients [21%] in the non-IVIG group).
- The median hospital stay was longer in the IVIG group (24 days) than in the non-IVIG group (16 days), and the median duration of disease was also longer (31 days in the IVIG group vs. 23 days in the non-IVIG group).
- A subgroup analysis that was limited to the critically ill patients suggested a mortality benefit at 28 days, which was no longer significant at 60 days.

Interferons (Alfa, Beta)

- Interferons are a family of cytokines with antiviral properties. They have been suggested as a potential treatment for COVID-19 because of their *in vitro* and *in vivo* antiviral properties.
- The COVID-19 Treatment Guidelines Panel **recommends against** the use of interferons for the treatment of patients with severe or critical COVID-19, except in a clinical trial **(AIII)**.
- There is insufficient evidence to recommend either for or against the use of **interferon beta** for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19.

Adverse Effects

- The most frequent adverse effects of interferon alfa include :
- flu-like symptoms
- nausea, fatigue, weight loss
- hematological toxicities
- elevated transaminases
- psychiatric problems (e.g., depression and suicidal ideation)
- Interferon beta is better tolerated than interferon alfa.

Interleukin-1 Inhibitors

- There is insufficient evidence to recommend for or against the use of interleukin (IL)-1 inhibitors, such as **anakinra**, for the treatment of COVID-19.
- There are case series data but no clinical trial data on the use of IL-1 inhibitors in patients with COVID-19.
- Endogenous IL-1 is elevated in patients with COVID-19 and other conditions, such as severe CAR T-cell-mediated CRS.
- Case reports and case series have described favorable responses to anakinra in patients with these syndromes, including a survival benefit in patients with sepsis and reversal of cytokine storm after tocilizumab failure in adults with MAS

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Adverse Effects

- Anakinra was not associated with any significant safety concerns when used in clinical trials for the treatment of sepsis.
- Increased rates of infection were reported with prolonged anakinra use in combination with tumor necrosis factor-alpha blockade, but not with short-term use.

Interleukin-6 Inhibitors

- Interleukin (IL)-6 is a pleiotropic, proinflammatory cytokine produced by a variety of cell types, including lymphocytes, monocytes, and fibroblasts.
- Infection by (SARS-CoV) induces a dose-dependent production of IL-6 from bronchial epithelial cells.
- COVID-19-associated systemic inflammation and hypoxic respiratory failure can be associated with heightened cytokine release, as indicated by elevated blood levels of IL-6, C-reactive protein (CRP), D-dimer, and ferritin
- It is hypothesized that modulating the levels of IL-6 or its effects may reduce the duration and/or severity of COVID-19 illness.
- (FDA)-approved IL-6 inhibitors:
- anti-IL-6 receptor monoclonal antibodies (e.g., sarilumab, tocilizumab)
- anti-IL-6 monoclonal antibodies (i.e., siltuximab)
- These drugs have been evaluated for the management of patients with COVID-19 who have systemic inflammation.

Recommendations

- The Panel recommends using **tocilizumab** (single intravenous [IV] dose of tocilizumab 8 mg/kg actual body weight up to 800 mg) **in combination with dexamethasone** (6 mg daily for up to 10 days) in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19. These patients are:

- Recently hospitalized patients (i.e., within first 3 days of admission) who have been admitted to the intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation, noninvasive ventilation, or high-flow nasal canula (HFNC) oxygen (>0.4 FiO2/30 L/min of oxygen flow)
- Recently hospitalized patients (i.e., within first 3 days of admission) not admitted to the ICU who have rapidly increasing oxygen needs and require noninvasive ventilation or HFNC oxygen and who have significantly increased markers of inflammation (CRP ≥75 mg/L) **(BIIa)**.

- For hospitalized patients with hypoxemia who require conventional oxygen therapy, there is insufficient evidence to specify which of these patients would benefit from the addition of tocilizumab.
- Some Panel members would also give tocilizumab to patients who are exhibiting rapidly increasing oxygen needs while on dexamethasone and have a CRP ≥75 mg/L, but who do not yet require noninvasive ventilation or HFNC oxygen as described above.
- The Panel **recommends against** the use of anti-IL-6 monoclonal antibody therapy (i.e., **siltuximab**) for the treatment of COVID-19, except in a clinical trial **(BI)**.

- Tocilizumab **should be avoided** in patients who are significantly :
- immunosuppressed, particularly in those with recent use of other biologic immunomodulating drugs
- in patients who have alanine aminotransferase >5 times the upper limit of normal
- high risk for gastrointestinal perforation
- an uncontrolled serious bacterial, fungal, or non-SARS-CoV-2 viral infection

- absolute neutrophil count <500 cells/µL
- platelet count <50,000 cells/µl
- known hypersensitivity to tocilizumab.
- Tocilizumab should only be given in combination with a course of dexamethasone (or an alternative corticosteroid at a dose equivalency to dexamethasone 6 mg) therapy.
- Some clinicians may assess the patient's clinical response to dexamethasone before deciding whether tocilizumab is needed.
- (RECOVERY) trial received a second dose of tocilizumab at the discretion of treating physicians, there is insufficient evidence to indicate which patients, if any, would benefit from an additional dose of tocilizumab
- Cases of severe and disseminated strongyloidiasis have been reported with use of tocilizumab and corticosteroids in patients with COVID-19
- Prophylactic treatment with ivermectin should be considered for patients who are from strongyloidiasis endemic areas

بسمه تعالی

راهنمای تجویز دارو

نام دارو	کاربرد دارو	افراد صاحب صلاحیت جهت تجویز	شرط تجویز		محل تجویز دارو	دوز و تواتر مصرف دارو	شرایط تجویز
			اندیکاسیون	کنترا اندیکاسیون			
Tocilizuma	بستری این دارو در بیماران سرپایی ممنوعیت مصرف دارد	متخصص داخلی متخصص عفونی فوق تخصص ریه فوق تخصص مراقبت ویژه	در بیماران مبتلا به کووید-۱۹ (بر اساس شواهد آزمایشگاهی، رادیولوژیک و بالینی) کاندید بستری و در فاز التهابی شدید، با هیپوکسمی مقاوم (نیاز به اکسیژن مکمل)، در صورت عدم پاسخ به کورتیکواستروئید و سیر شدیدا پیشرونده بیماری (با درنظر گرفتن شرایط بالینی بیمار و قضاوت درمانگر)	• سابقه حساسیت به دارو • پلاکت زیر ۵۰ هزار • شک به عفونت فعال ویرال (غیر کرونا)، باکتریال و قارچی • ANC زیر ۵۰۰ • شک به انسداد یا بیماریهای زمینه ای با خطر بالای پارگی احشا گوارشی • نارسایی کبدی زمینه ای (Child-Paugh	بیمارستان	دوز: ۸ میلی گرم بر کیلوگرم براساس وزن واقعی بدن (توصیه می گردد برای بیماران با وزن ۹۰ کیلوگرم و کمتر: یک ویال ۴۰۰ میلی گرمی و برای وزن بالاتر از ۹۰ کیلوگرم حداکثر دو ویال ۴۰۰ میلی گرمی) همراه با دوز استاندارد کورتیکواستروئید (معادل ۸ میلی گرم دگزامتازون وریدی)، در صورت عدم پاسخ مناسب(بهبود شرایط بالینی، وضعیت اکسیژناسیون و بیومارکرهای التهابی بخصوص CRP)، این دوز برای یکبار دیگر بعد از ۱۲ تا ۲۴ ساعت قابل تکرار است. *آماده سازی: توسیلیزوماب به صورت وریدی در ۱۰۰ سی سی سرم	شرایط تجویز: CRP بالا (ترجیحا به صورت کمی و بالای ۷۰mg/l) به همراه شواهد درگیری ریه در سی تی اسکن ریه به نفع بیماری کووید در بیماران بستری *تایید دو پزشک صاحب صلاحیت برای تجویز دارو الزامی می باشد. -درمان با توسیلیزوماب همراه با دوز پایین کورتیکواستروییدها (دوز معادل با ۸ میلی دگزامتازون وریدی) پیشنهاد می شود و درمان به تنهایی توصیه نشده است.

Adverse Effects

- elevated liver enzyme levels that appear to be dose dependent
- Neutropenia or thrombocytopenia are uncommon.
- Additional adverse effects, such as risk for serious infections (e.g., tuberculosis [TB], bacterial or fungal infections)
- bowel perforation, have been reported only in the context of tocilizumab use for the treatment of chronic disease

- Monoclonal antibodies are actively transported across the placenta as pregnancy progresses (with greatest transfer during the third trimester) and may affect immune responses in utero in the exposed fetus.
- Given the paucity of data, current recommendations advise against the use of tocilizumab during pregnancy.
- Decisions about tocilizumab administration during pregnancy must include shared decision-making between the pregnant individual and their health care provider, considering potential maternal benefit and fetal risks

Antithrombotic Therapy

- Monitoring Coagulation Markers in Patients With COVID-19:
- In nonhospitalized patients with COVID-19, markers of coagulopathy, such as D-dimer level, prothrombin time, fibrinogen level, and platelet count, should not routinely be obtained **(AIII)**.
- Although abnormalities in these coagulation markers have been associated with worse outcomes, prospective data demonstrating that the markers can be used to predict the risk of VTE in those who are asymptomatic or who have mild SARS-CoV-2 infection is lacking.
- In hospitalized patients with COVID-19, hematologic and coagulation parameters are commonly measured;
- however, there is currently insufficient evidence to recommend either for or against using such data to guide management decisions
- In hospitalized, critically ill patients, low molecular weight heparin or unfractionated heparin is preferred over oral anticoagulants because the two types of heparin have shorter half-lives, can be administered intravenously or subcutaneously, and have fewer drug-drug interactions

- COVID-19 outpatients receiving warfarin who are in isolation and thus unable to have international normalized ratio monitoring may be candidates for switching to direct oral anticoagulant therapy
- Patients receiving warfarin who have a mechanical heart valve, ventricular assist device, valvular atrial fibrillation, or antiphospholipid antibody syndrome or who are lactating should continue treatment with warfarin **(AIII)**.
- Hospitalized patients with COVID-19 who are taking anticoagulant or antiplatelet therapy for underlying medical conditions should continue this treatment unless significant bleeding develops, or other contraindications are present **(AIII)**.

Out patient

- For nonhospitalized patients with COVID-19, anticoagulants and antiplatelet therapy should not be initiated for the prevention of VTE or arterial thrombosis unless the patient has other indications for the therapy or is participating in a clinical trial

Hospitalized

- Hospitalized nonpregnant adults with COVID-19 should receive prophylactic dose anticoagulation **(AIII)**
- Anticoagulant or antiplatelet therapy should not be used to prevent arterial thrombosis outside of the usual standard of care for patients without COVID-19 **(AIII)**
- There is currently insufficient evidence to recommend either for or against the use of thrombolytics or higher than the prophylactic dose of anticoagulation for VTE prophylaxis in hospitalized COVID-19 patients outside of a clinical trial.
- Hospitalized patients with COVID-19 should not routinely be discharged from the hospital while on VTE prophylaxis **(AIII)**.
- Continuing anticoagulation with a Food and Drug Administration-approved regimen for extended VTE prophylaxis after hospital discharge can be considered for patients who are at low risk for bleeding and high risk for VTE, as per the protocols for patients without COVID-19
- There is currently insufficient evidence to recommend either for or against routine deep vein thrombosis screening in COVID-19 patients without signs or symptoms of VTE, regardless of the status of their coagulation markers.
- For hospitalized COVID-19 patients who experience rapid deterioration of pulmonary, cardiac, or neurological function, or of sudden, localized loss of peripheral perfusion, the possibility of thromboembolic disease should be evaluated **(AIII**).

- If antithrombotic therapy is prescribed during pregnancy prior to a diagnosis of COVID-19, this therapy should be continued **(AIII)**.
- For pregnant patients hospitalized for severe COVID-19, prophylactic dose anticoagulation is recommended unless contraindicated (**(BIII)**.

- Like for nonpregnant patients, VTE prophylaxis after hospital discharge **is not recommended** for pregnant patients **(AIII)**.
- Decisions to continue VTE prophylaxis in the pregnant or postpartum patient after discharge should be individualized, considering concomitant VTE risk factors.

- Unfractionated heparin, low molecular weight heparin, and warfarin do not accumulate in breast milk and do not induce an anticoagulant effect in the newborn; therefore, they can be used by breastfeeding individuals with or without COVID-19 who require VTE prophylaxis or treatment **(AIII)**.
- In contrast, use of direct-acting oral anticoagulants during pregnancy is not routinely recommended due to lack of safety data **(AIII)**.

Patients With COVID-19 Who Are Discharged from the Hospital

- VTE prophylaxis after hospital discharge **is not recommended** for patients with COVID-19
- For certain high-VTE risk patients without COVID-19, post-discharge prophylaxis has been shown to be beneficial. The Food and Drug Administration approved the use of rivaroxaban 10 mg daily for 31 to 39 days in these patients
- Any decision to use post-discharge VTE prophylaxis for patients with COVID-19 should include consideration of the individual patient's risk factors for VTE, including reduced mobility, bleeding risks, and feasibility. Participation in clinical trials is encouraged

Supplements

- Vitamin C:
- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of vitamin C for the treatment of COVID-19 in non-critically ill patients

Vitamin D

- There is insufficient evidence to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19.

zinc

- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of zinc for the treatment of COVID-19
- The Panel **recommends against** using **zinc** supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial **(BIII)**.

Famotidine

- Antiviral activity(the evidence is very uncertain).

- The guideline panel suggests against famotidine for the sole purpose of treating COVID-19, unless in the context of a clinical trial

Favipiravir

- Favipiravir is a purine analogue that inhibits the RNA dependent RNA polymerase of influenza and other RNA viruses.
- Should not be given during pregnancy.
- It is uncertain whether adequate drug levels can be achieved in vivo to inhibit SARS-CoV 2.
- There are ongoing clinical trials assessing favipiravir for treatment of COVID-19

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Short Communication

Effect of Ammonium Chloride in addition to standard of care in outpatients and hospitalized COVID-19 patients: A randomized clinical trial

Zeinab Siami[a], Sepehr Aghajanian[b], Somayeh Mansouri[b], Zakiye Mokhames[c], Reza Pakzad[d,e], Kourosh Kabir[f], Mehdi Norouzi[g,h], Alireza Soleimani[a], Mojtaba Hedayat Yaghoobi[a], Shahrzad Shadabi[b], Ramin Tajbakhsh[i], Ali Kargar Kheirabad[g,**], Sayed-Hamidreza Mozhgani[j,k,*]

- The findings of this trial suggest that the addition ofAmmonium Chloride to standard of care was not superior to standard of care alone in reducing mortality rate in COVID-19patients. Patients receiving Ammonium Chloride had shorter time to recovery and were more likely to have reduced viral load and clinical improvemen

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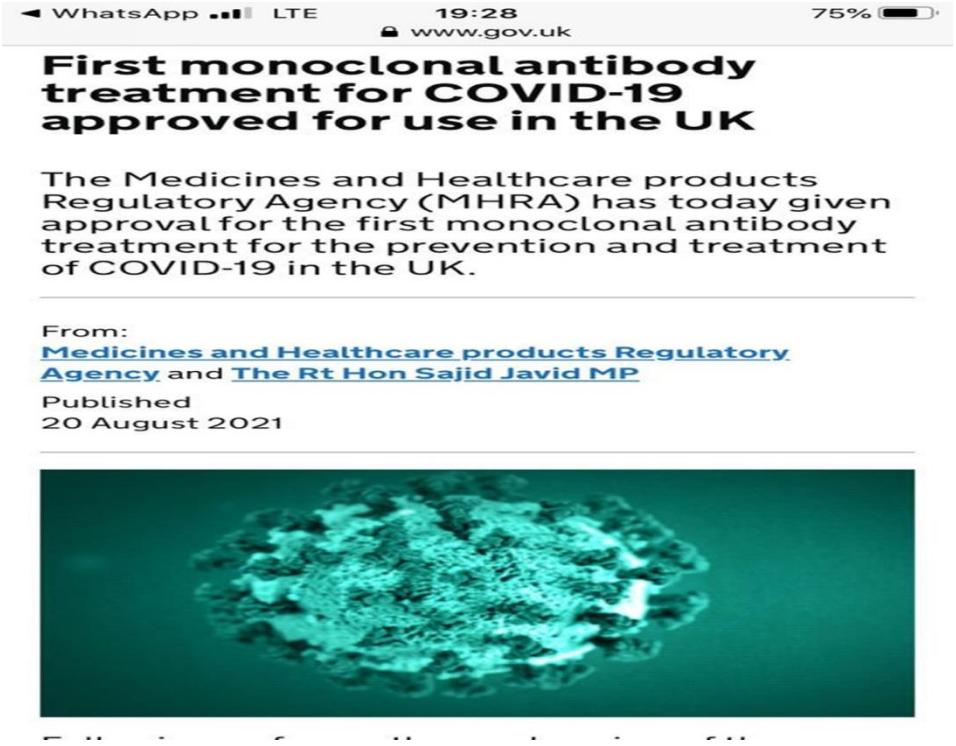
WhatsApp LTE 19:28 75%
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First monoclonal antibody treatment for COVID-19 approved for use in the UK
The Medicines and Healthcare products Regulatory Agency (MHRA) has today given approval for the first monoclonal antibody treatment for the prevention and treatment of COVID-19 in the UK.
From:
Medicines and Healthcare products Regulatory Agency and The Rt Hon Sajid Javid MP
Published
20 August 2021

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or other **corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients who are at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[d] **plus remdesivir**[b,c] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone**[d] (when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[d] **(AI)** • **Dexamethasone**[d] **plus remdesivir**[b,c] **(BIII)** For patients who were recently hospitalized[e] with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib**[f,g] **(BIIa)** or **tocilizumab**[f,h] **(BIIa)** to one of the two options above
Hospitalized and Requires IMV or ECMO	For most patients: • **Dexamethasone**[d,i] **(AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone**[d,i] **plus tocilizumab**[f,h] **(BIIa)**

Antibiotic

Out patient???

Hospitalazed???