



# Considerations for Certain Concomitant Medications in Patients with COVID-19

## Summary Recommendations

### Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs):

- Persons with COVID-19 who are prescribed ACE inhibitors or ARBs for cardiovascular disease (or other indications) should continue these medications **(AIII)**.
- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of ACE inhibitors or ARBs for the treatment of COVID-19 outside of the setting of a clinical trial **(AIII)**.

### Corticosteroids

*For Critically Ill Patients with COVID-19:*

- The Panel **recommends against** the routine use of systemic corticosteroids for the treatment of mechanically ventilated patients with COVID-19 without acute respiratory distress syndrome (ARDS) **(AIII)**.
- For mechanically ventilated patients with ARDS, there is insufficient evidence to recommend for or against the use of systemic corticosteroids **(CI)**.
- For adults with COVID-19 and refractory shock, the Panel recommends using low-dose corticosteroid therapy (i.e., shock reversal) over no corticosteroids **(BII)**.

*For Hospitalized, Non-Critically Ill Patients with COVID-19:*

- The Panel **recommends against** the routine use of systemic corticosteroids for the treatment of COVID-19 in hospitalized patients, unless they are in the intensive care unit **(AIII)**.

*For Patients on Chronic Corticosteroids:*

- Oral corticosteroid therapy used prior to COVID-19 diagnosis for another underlying condition (e.g., primary or secondary adrenal insufficiency, rheumatological diseases) should not be discontinued **(AIII)**. On a case-by-case basis, supplemental or stress-dose steroids may be indicated **(AIII)**.
- Inhaled corticosteroids used daily for patients with asthma and chronic obstructive pulmonary disease for control of airway inflammation should not be discontinued in patients with COVID-19 **(AIII)**.

*Pregnancy Considerations:*

- The antenatal corticosteroids betamethasone and dexamethasone are known to cross the placenta and therefore are generally reserved for when administration is required for fetal benefit **(BIII)**. Other systemic corticosteroids do not cross the placenta, and pregnancy is not a reason to restrict their use if otherwise indicated **(CIII)**.
- The American College of Obstetricians and Gynecologists **recommends against** offering antenatal corticosteroids for fetal benefit in the late preterm period (34 0/7 weeks–36 6/7 weeks) because the benefits of antenatal corticosteroids in the late preterm period are less well established **(CIII)**.
- Modifications to care for these patients may be individualized, weighing the neonatal benefits of antenatal corticosteroid use with the risks of potential harm to the pregnant

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<p>patient <b>(CIII)</b>.</p> <p><b>HMG-CoA Reductase Inhibitors (Statins):</b></p> <ul style="list-style-type: none"><li>Persons with COVID-19 who are prescribed statin therapy for the treatment or prevention of cardiovascular disease should continue these medications <b>(AIII)</b>.</li><li>The Panel <b>recommends against</b> the use of statins for the treatment of COVID-19 outside of the setting of a clinical trial <b>(AIII)</b>.</li></ul> <p><b>Nonsteroidal Anti-Inflammatory Drugs (NSAIDs):</b></p> <ul style="list-style-type: none"><li>Persons with COVID-19 who are taking NSAIDs for a co-morbid condition should continue therapy as previously directed by their physician <b>(AIII)</b>.</li><li>The Panel recommends that there be no difference in the use of antipyretic strategies (e.g., with acetaminophen or NSAIDs) between patients with or without COVID-19 <b>(AIII)</b>.</li></ul>

## Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

### Recommendations:

- Persons with COVID-19 who are prescribed angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) for cardiovascular disease (or other indications) should continue these medications **(AIII)**.
- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of ACE inhibitors or ARBs for the treatment of COVID-19 outside of the setting of a clinical trial **(AIII)**.

Angiotensin-converting enzyme 2 (ACE2) is the cell surface receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has been hypothesized<sup>1</sup> that the modulation of ACE2 associated with these therapies could suppress or enhance SARS-CoV-2 replication.<sup>2</sup> Investigations of the role of ARBs and recombinant human ACE2 in treatment and prevention of SARS-CoV-2 infection are underway.<sup>3</sup>

Whether these medications are helpful, harmful, or neutral in the pathogenesis of SARS-CoV-2 infection is unclear. Currently, there is a lack of sufficient clinical evidence demonstrating that ACE inhibitors or ARBs have any impact on the susceptibility of individuals to SARS-CoV-2 or on the severity or outcomes of infection. This recommendation is in accord with a joint statement of the American Heart Association, the Heart Failure Society of America, and the American College of Cardiology.<sup>3</sup>

## Corticosteroids

Systemic corticosteroids can affect the pathogenesis of viral infections in various ways. In outbreaks of other novel coronavirus infections<sup>4, 5</sup> (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, corticosteroid therapy may worsen clinical outcomes, including secondary bacterial infection and mortality.<sup>6</sup> Conversely, the potent anti-inflammatory effects of corticosteroids are proposed to have a potential therapeutic role in suppressing cytokine-related lung injury.<sup>7</sup> Data on the use of corticosteroids in COVID-19 are limited. The recommendations for use of corticosteroids in patients with COVID-19 depend on the severity of illness, indication, and underlying medical conditions and should be considered on a case-by-case basis.

## Critically Ill Patients

For more information, see [Care of Critically Ill Patients with COVID-19](#)

### Recommendations:

- The Panel **recommends against** the routine use of systemic corticosteroids for the treatment of mechanically ventilated patients with COVID-19 without acute respiratory distress syndrome (ARDS) **(AIII)**.
- For mechanically ventilated patients with ARDS, there is insufficient evidence to recommend for or against the use of corticosteroids **(CI)**.
- For adults with COVID-19 and refractory shock, the Panel recommends using low-dose corticosteroid therapy (i.e., shock reversal) over no corticosteroids **(BII)**

## Hospitalized, Non-Critically Ill Patients

### Recommendation:

- The Panel **recommends against** the routine use of systemic corticosteroids for the treatment of COVID-19 in hospitalized patients, unless they are in the intensive care unit **(AIII)**.

Guidelines outside of the United States have proposed the use of low-dose, short-course corticosteroids in patients with progressive deterioration of oxygenation or elevated inflammatory markers.<sup>8,9</sup> Epidemiologic studies from China describe that a short course (median 5 to 7 days) of methylprednisolone has been used. Other retrospective studies and case series describe that methylprednisolone may be associated with improved symptom resolution and mortality. These results should be interpreted with caution, considering the limitations of uncontrolled study designs, use of a small sample size, subset analysis, and lack of detailed information on the dose and timing of methylprednisolone.<sup>10-12</sup> The decision to use corticosteroids in patients with early signs of cytokine storm should be balanced with the known adverse effects.<sup>13</sup>

## Patients on Chronic Systemic Corticosteroid Therapy

### Recommendation:

- Oral corticosteroid therapy used prior to COVID-19 diagnosis for another underlying condition (e.g., primary or secondary adrenal insufficiency, rheumatological diseases) should not be discontinued **(AIII)**.<sup>14</sup> On a case-by-case basis, supplemental or stress-dose steroids may be indicated **(AIII)**.

## Patients on Inhaled Corticosteroids

### Recommendation:

- Inhaled corticosteroids used daily for patients with asthma and chronic obstructive pulmonary disease for control of airway inflammation should not be discontinued in patients with COVID-19 **(AIII)**. No studies to date have investigated the relationship between inhaled corticosteroids in these settings and virus acquisition, severity of illness, or viral transmission.

## Pregnancy Considerations

The antenatal corticosteroids betamethasone and dexamethasone are known to cross the placenta and therefore are generally reserved for when administration is required for fetal benefits **(BIII)**. Other systemic corticosteroids do not cross the placenta, and pregnancy is not a reason to restrict their use if otherwise indicated.<sup>15</sup>

The American College of Obstetricians and Gynecologists suggests the following modifications regarding the use of antenatal corticosteroids for fetal benefit for patients with suspected or confirmed COVID-19:<sup>16</sup>

- *Before 37 0/7 Weeks of Gestation:* For pregnant patients with suspected or conformed COVID-19 between 24 0/7 weeks and 33 6/7 weeks of gestation who are at risk of preterm birth within 7 days, antenatal corticosteroids should continue to be offered as recommended. Modifications to care for these patients may be individualized, weighing the neonatal benefits with the risks of potential harm to the pregnant patient.
- *Between 34 0/7 Weeks and 36 6/7 Weeks of Gestation (Late Preterm):* The benefits of antenatal corticosteroids in the late preterm period are less well established. Weighing this against any potential harm to the pregnant patient, antenatal corticosteroids should

not be offered to pregnant patients with suspected or confirmed COVID-19 between 34 0/7 weeks and 36 6/7 weeks of gestation who are at risk of preterm birth within 7 days. Modifications to care for these patients may be individualized, weighing the neonatal benefits of antenatal corticosteroid use with the risks of potential harm to the pregnant patient.

## HMG-CoA Reductase Inhibitors (Statins)

### Recommendations:

- Persons with COVID-19 who are prescribed statin therapy for the treatment or prevention of cardiovascular disease should continue these medications **(AIII)**.
- The Panel **recommends against** the use of statins for the treatment of COVID-19 outside the setting of a clinical trial **(AIII)**.

HMG-CoA reductase inhibitors, or statins, affect ACE2 as part of their function in reducing endothelial dysfunction. It has been proposed that these agents have a potential role in managing patients with severe COVID-19.<sup>17</sup> Observational studies have reported that statin therapy may reduce cardiovascular morbidity in patients admitted with other respiratory infections, such as influenza and bacterial pneumonia.

## Nonsteroidal Anti-Inflammatory Drugs

### Recommendations:

- Persons with COVID-19 who are taking nonsteroidal anti-inflammatory drugs (NSAIDs) for a co-morbid condition should continue therapy as previously directed by their physician **(AIII)**.
- The Panel recommends that there be no difference in the strategy of antipyretic use (e.g., with acetaminophen or NSAIDs) as in patients with or without COVID-19 **(AIII)**.

In mid-March 2020, news agencies promoted reports that anti-inflammatory drugs may worsen COVID-19. It has been proposed that NSAIDs like ibuprofen can increase the expression of ACE2<sup>1</sup> and inhibit antibody production.<sup>18</sup> Shortly after these reports, the Food and Drug Administration stated that there is no evidence linking the use of NSAIDs with worsening of COVID-19 and advised patients to use NSAIDs as directed.<sup>19</sup>

## References

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