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CLINICAL GUIDELINE

Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid, Living Practice Points From the American College of Physicians (Version 1)

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KEY QUESTION 1

What are the effectiveness and harms of remdesivir in patients with coronavirus disease 2019 (COVID-19)?

KEY QUESTION 2

Do effectiveness and harms vary by symptom duration, disease severity, and treatment duration?

BACKGROUND

Remdesivir, a broad-spectrum antiviral agent administered intravenously, was developed and studied as a potential treatment for Ebola virus disease and Marburg virus infection (1–3). In vitro and in vivo preclinical studies found antiviral activity for remdesivir against corona-like viruses, including Middle East respiratory syndrome coronavirus (4–6), severe acute respiratory syndrome coronavirus (SARS-CoV-1) (5), the circulating human coronaviruses HCoV-OC42 and HCoV-229E (7), and SARS-CoV-2 (8). Currently, the effectiveness of remdesivir is being tested as a treatment for patients infected with SARS-CoV-2 (COVID-19) and has been authorized for emergency use for treating COVID-19, by the U.S. Food and Drug Administration (9) in the United States, and in other countries (10–13).

The American College of Physicians (ACP) Scientific Medical Policy Committee (SMPC) based these rapid and living practice points (**Table 1**) on a systematic evidence review conducted by the U.S. Department of Veterans Affairs (VA) Evidence Synthesis Program in Minneapolis, Minnesota (14) (**Appendix**, available at Annals.org). This version of the practice points, based on a search completed on 3 June 2020 and updated through 31 August 2020, was approved by the ACP's Executive Committee of Board of Regents on behalf of the Board of Regents on 14 August 2020 and submitted to *Annals of Internal Medicine* on 13 August 2020. Because many studies are planned or under way, literature surveillance is ongoing, with updates currently planned for every 2 months through December 2021. The target audience for these practice points includes clinicians and the public. The target patient population includes all nonpregnant patients with COVID-19.

Critical and important outcomes were determined by the evidence review team in collaboration with methodological and content experts. The magnitude of the effect (such as little or no, slight, modest, or large) for critical

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Table 1. Practice Points

- Use remdesivir* for 5 days as a treatment for patients with moderate† COVID-19.
- Use remdesivir* for 5 days as a treatment for patients with severe† COVID-19 who do not require mechanical ventilation or extracorporeal membrane oxygenation (ECMO).
- Consider extending the use of remdesivir* to 10 days in patients with severe† COVID-19 requiring mechanical ventilation or ECMO within a 5-day course.

COVID-19 = coronavirus disease 2019.
* Remdesivir is not recommended for patients with an alanine aminotransferase level ≥5 times the upper limit of normal or an estimated glomerular filtration rate <30 mL/min/1.73 m^2 (see further details in **Table 3**).
† Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging or clinical assessment, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or the need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic evidence of pulmonary infiltrates and oxygen saturation >94% on room air; and mild COVID-19 was not defined (14).

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† Author (participated in discussion and voting).

‡ Nonauthor contributor (participated in discussion but excluded from voting).

§ Nonphysician public representative.

Update Alerts: The authors have specified in the Background section and the **Appendix** (available at Annals.org) the interval and stop date for updates to this Practice Points article. As *Annals* receives updates, they will appear in the Comments section of the article on Annals.org. Reader inquiries about updates that are not available at approximately the specified intervals should be submitted as comments to the article.

Table 2. Thresholds for Determining Magnitude of Effect*

Outcome	Little/No Effect	Small Effect†	Modest Effect‡	Large Effect§
Critical outcomes				
All-cause mortality, %	<1	1 to 2.9	3 to 4.9	≥5
Recovery, %	<2	2 to 4.9	5 to 9.9	≥10
Length of stay, *d*	<1	≥1 to 2	NA	≥3
Serious adverse event, %	<1	1 to 4.9	5 to 9.9	≥10
Important outcomes				
Time to recovery, *d*	<1	≥1 to 2	NA	≥3
Clinical improvement, %	<2	2 to 4.9	5 to 9.9	≥10
Time to clinical improvement, *d*	<1	≥1 to 2	>2 to <3	≥3
Mechanical ventilation or ECMO, %	<1	1 to 4.9	5 to 9.9	≥10
Nonserious/any adverse event, %	<2	2 to 4.9	5 to 19.9	≥20

ECMO = extracorporeal membrane oxygenation; NA = not applicable.
* Measured as absolute risk difference (when not otherwise specified).
† Described as "Slight increase or decrease."
‡ Described as "Modest increase or decrease."
§ Described as "Large increase or decrease."

and important outcomes was determined by applying thresholds prespecified by the evidence review team (Table 2). Table 3 presents clinical considerations, the Figure and Tables 4 and 5 summarize current evidence, and Table 6 identifies additional evidence gaps. Appendix Tables 1 and 2 (available at Annals.org) present the data estimates supporting the practice points.

RATIONALE

Use of Remdesivir in Patients With Moderate COVID-19

Table 4 summarizes the current evidence on the use of remdesivir in patients with moderate COVID-19.

Overall, the current evidence points toward a net benefit for remdesivir in patients with moderate COVID-19 and suggests that a shorter treatment period (5 days) is as effective as a longer one (10 days), with no increase in harms (16). Low-certainty evidence shows that the 5-day course may be superior for mortality, recovery, and clinical improvement; however, low-certainty evidence also shows improvement for several outcomes when comparing the 10-day course to placebo. Thus, the SMPC believes that it is reasonable to consider extending treatment to 10 days for patients whose condition does not improve during the initial 5 days. Because the overall certainty of evidence is low across the comparisons, the SMPC has flagged course duration as a particular area of interest for further discussion and close monitoring.

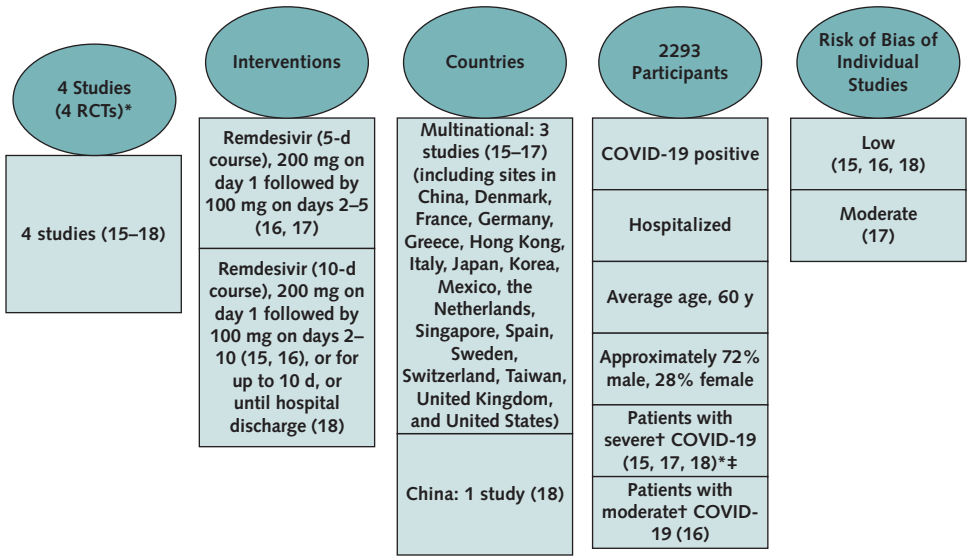
Evidence from 1 randomized controlled trial (RCT) (16) compared a 5- or 10-day course of remdesivir with standard care, although "standard care" was not defined. Among outcomes rated as critical, remdesivir (5- or 10-day course) may reduce mortality slightly and result in slightly fewer serious adverse events compared with standard care (low certainty). Evidence also showed a modest increase in recovery and clinical improvement with a 5-day course, and slight increases in recovery and clinical improvement with a 10-day course, compared with standard care (low certainty). A

Table 3. Clinical Considerations

- Remdesivir is currently administered only by IV infusion, generally in hospital settings.
- 5-d course in adults is 200 mg IV on day 1 followed by 100 mg/d for a total of 5 d (5 doses).
- 10-d course in adults is 200 mg IV on day 1 followed by 100 mg/d for a total of 10 d (10 doses).
- The practice points do not apply to pregnant women, because they were excluded from the studies included in the evidence review.
- A greater percentage of patients with severe COVID-19 (not requiring mechanical ventilation or ECMO) treated within 10 d of symptom onset vs. after 10 d of symptom onset with a 5- or 10-d course of remdesivir were discharged from the hospital (17).
- The effectiveness of a 10-d course of remdesivir in reducing time to recovery in patients with severe COVID-19 may not vary by age, sex, or race (15).
- Not enough information was reported in the studies included in the evidence review to determine what other treatment interventions, including experimental or off-label medications, were given in parallel to remdesivir.
- Currently, the cost of a 5-d course of remdesivir in the United States varies from $2340 (Indian Health Services and VA) to $3120 ($520/vial) (U.S. insurers, including Medicare and Medicaid). The cost for persons without insurance is currently $390/vial (14, 19).
- The FDA recommends that clinicians assess kidney and hepatic function at baseline and during treatment (8). The FDA recommends the following:
  - Not using remdesivir in patients with an eGFR <30 mL/min/1.73 m^2.
  - Discontinuing the use of remdesivir if ALT levels increase to ≥5 times the upper limit of normal or any ALT elevation is accompanied by signs or symptoms of liver inflammation, or increasing conjugated bilirubin levels, alkaline phosphatase levels, or INR.
- The FDA reports that hypersensitivity reactions, including infusion-related and anaphylactic reactions have been observed during and after remdesivir administration (9). Additional adverse events include endocrine and metabolic (hyperglycemia, increased serum glucose), hepatic (increased serum ALT and AST levels), and renal (renal toxicity) events (9, 20).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; FDA = U.S. Food and Drug Administration; INR = international normalized ratio; IV = intravenous; VA = U.S. Department of Veterans Affairs.

Figure. Evidence description.



The evidence search and assessment were conducted by the U.S. Department of Veterans Affairs Evidence Synthesis Program, Minneapolis, Minnesota (14). Current search for evidence, completed on 3 June 2020, aimed to identify RCTs evaluating remdesivir for treatment of patients with COVID-19. COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; RCT = randomized controlled trial.

* Patients requiring mechanical ventilation or ECMO were excluded from 1 RCT (17); therefore, despite a few patients (3.3%) developing a requirement for invasive mechanical ventilation between screening and the beginning of the treatment, this study is analyzed as being representative of patients with severe disease not requiring mechanical ventilation or ECMO at baseline.

† Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic infiltrates and oxygen saturation greater than 94% on room air; and mild COVID-19 was not defined (14).

‡ Most (88.7%) of the participants enrolled in 1 RCT (16) had severe disease, so this study is analyzed as being representative of patients with severe disease.

5-day course may also reduce time to recovery slightly (low certainty), but evidence is insufficient to make any conclusions about a 10-day course. Both courses of remdesivir (5- and 10-day) may slightly reduce the need for invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO) (low certainty). However, the occurrence of any adverse events may increase with a 5-day course (slight effect) and with a 10-day course (modest effect) compared with standard care (low certainty).

Evidence comparing a 5- versus 10-day course of remdesivir (16) showed that a 5-day course may reduce mortality slightly and may increase recovery (modest effect) and clinical improvement (slight effect) compared with a 10-day course (low certainty). However, evidence showed little to no difference between the 2 courses in reducing the need for invasive mechanical ventilation or ECMO (low certainty), and evidence is insufficient to show a difference in time to recovery. Evidence for potential harms showed that a 5-day course may result in fewer adverse events (any) compared with a 10-day course (modest effect), although the shorter course may not result in fewer serious adverse events (low certainty).

No evidence was found for any effect on other critical outcomes (hospital length of stay) or important outcomes (time to clinical improvement, nonserious adverse events) with either course in patients with moderate COVID-19. No evidence was identified as to whether outcomes vary by symptom duration in patients with moderate COVID-19.

Use of Remdesivir in Patients With Severe COVID-19

Table 5 summarizes the current evidence on the use of remdesivir in patients with severe COVID-19 (15, 17, 18).

Overall, the current evidence points toward a net benefit for a 10-day course of remdesivir in patients with severe COVID-19 (including those requiring mechanical ventilation or ECMO at baseline) compared with placebo (15, 18). No evidence was found comparing a 5-day course of remdesivir with placebo or standard care in patients with severe COVID-19. In the absence of this direct evidence, the SMPC looked at the indirect evidence that a 5-day course is as effective as a 10-day course of remdesivir with the same, or probably fewer, potential harms in patients with severe COVID-19 not requiring mechanical ventilation or ECMO at baseline (17). In addition, the compliance data showed that a 10-day course (10 doses) was used in 40.8% of patients with severe COVID-19 (including those requiring mechanical ventilation or ECMO at baseline), and 38.1% received fewer than 10 doses because they recovered and were discharged from the hospital (15). However, for a subgroup of patients with severe COVID-19 receiving mechanical ventilation or ECMO at day 5, extending treat-

Table 4. Evidence Summary for Patients With Moderate* COVID-19: What Information Does the Evidence Provide?

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence†
Remdesivir (5-d Course) vs. Placebo/Standard Care in Patients With Moderate* COVID-19			
Critical outcomes			
Mortality	1 RCT (391)	Remdesivir (5-d course) may reduce mortality slightly compared with standard care (16)	Low
Recovery‡	1 RCT (391)	Remdesivir (5-d course) may result in a modest increase in recovery compared with standard care (16)	Low
Hospital length of stay	NA	No evidence	No evidence
Serious adverse events§	1 RCT (391)	Remdesivir (5-d course) may reduce serious adverse events slightly compared with standard care (16)	Low
Important outcomes			
Time to recovery‡	1 RCT (391)	Remdesivir (5-d course) may reduce time to recovery slightly compared with standard care (16)	Low
Clinical improvement‖	1 RCT (391)	Remdesivir (5-d course) may result in a modest increase in clinical improvement compared with standard care (16)	Low
Time to clinical improvement‖	NA	No evidence	No evidence
Invasive mechanical ventilation/ECMO	1 RCT (391)	Remdesivir (5-d course) may reduce the need for invasive mechanical ventilation or ECMO slightly compared with standard care (16)	Low
Nonserious adverse events§	NA	No evidence	No evidence
Any adverse events§	1 RCT (391)	Remdesivir (5-d course) may increase adverse events slightly compared with standard care (16)	Low
Remdesivir (10-d Course) vs. Placebo/Standard Care in Patients With Moderate* COVID-19			
Critical outcomes			
Mortality	1 RCT (393)	Remdesivir (10-d course) may reduce mortality slightly compared with standard care (16)	Low
Recovery‡	1 RCT (393)	Remdesivir (10-d course) may increase recovery slightly compared with standard care (16)	Low
Hospital length of stay	NA	No evidence	No evidence
Serious adverse events§	1 RCT (393)	Remdesivir (10-d course) may reduce serious adverse events slightly compared with standard care (16)	Low
Important outcomes			
Time to recovery‡	1 RCT (393)	Very uncertain about the effect of remdesivir (10-d course) compared with standard care on time to recovery (16)	Insufficient
Clinical improvement‖	1 RCT (393)	Remdesivir (10-d course) may increase clinical improvement slightly compared with standard care (16)	Low
Time to clinical improvement‖	NA	No evidence	No evidence
Invasive mechanical ventilation/ECMO	1 RCT (393)	Remdesivir (10-d course) may reduce the need for invasive mechanical ventilation or ECMO slightly compared with standard care (16)	Low
Nonserious adverse events§	NA	No evidence	No evidence
Any adverse events§	1 RCT (393)	Remdesivir (10-d course) may result in a modest increase in adverse events compared with standard care (16)	Low
Remdesivir (5-d Course) vs. Remdesivir (10-d Course) in Patients With Moderate* COVID-19			
Critical outcomes			
Mortality	1 RCT (384)	Remdesivir 5-d course may reduce mortality slightly compared with remdesivir 10-d course (16)	Low
Recovery‡	1 RCT (384)	Remdesivir 5-d course may result in a modest increase in recovery compared with remdesivir 10-d course (16)	Low
Hospital length of stay	NA	No evidence	No evidence
Serious adverse events§	1 RCT (384)	Remdesivir 5-d course may not reduce serious adverse effects compared with remdesivir 10-d course (16)	Low
Important outcomes			
Time to recovery‡	NA	Very uncertain about the effect of remdesivir 5-d course compared with remdesivir 10-d course on time to recovery (16)	Insufficient
Clinical improvement‖	1 RCT (384)	Remdesivir 5-d course may increase clinical improvement slightly compared with remdesivir 10-d course (16)	Low
Time to clinical improvement‖	NA	No evidence	No evidence

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Table 4–Continued

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence†
Invasive mechanical ventilation/ECMO	1 RCT (384)	Remdesivir 5-d course may not reduce the need for invasive mechanical ventilation or ECMO compared with remdesivir 10-d course (16)	Low
Nonserious adverse events§	NA	No evidence	No evidence
Any adverse events§	1 RCT (384)	Remdesivir 5-d course may result in a modest reduction in adverse events compared with remdesivir 10-d course (16)	Low

COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; NA = not applicable; RCT = randomized controlled trial.
* Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic infiltrates and oxygen saturation >94% on room air; and mild COVID-19 was not defined (14).
† Certainty of evidence: insufficient, confidence is inadequate to assess the likelihood of benefit (benefit minus harm) of an intervention or its impact on a health outcome; low, confidence in the effect is limited because the true effect may be substantially different from the estimated effect; moderate, confidence in the effect is moderate because the true effect is probably close to the estimated effect, but a sizable possibility exists that it is substantially different; high, confidence that the true effect is close to the estimated effect.
‡ Recovery is defined as discharge from the hospital or hospitalization for infection control purposes only in 1 RCT (15, 18) and discharge from the hospital or hospitalized but not requiring supplemental oxygen or ongoing medical care in 3 RCTs (17).
§ Serious adverse events reported in studies included in the evidence review (15–17) were acute coronary syndrome, acute kidney injury, acute respiratory distress syndrome, acute respiratory failure, increased aminotransferase levels, atrial fibrillation, bronchitis, cardiac arrest, cardiopulmonary failure, increased D-dimer, deep venous thrombosis, diabetic ketoacidosis, dyspnea, endotracheal intubation, decreased glomerular filtration rate, hemorrhage of lower digestive tract, hypotension, hypoxia, ileus, lung abscess, mechanical ventilation, multiple organ dysfunction syndrome, respiratory distress, respiratory failure, pneumothorax, pulmonary embolism, pulmonary failure, recurrence of COVID-19, septic shock, sepsis, shock, tachycardia, thrombocytopenia, and viral pneumonia. Nonserious adverse events reported in studies included in the evidence review (16) were acidosis, acute kidney injury, alkalosis, increased aspartate aminotransferase, anemia, atrial fibrillation, decreased blood albumin, increased blood bilirubin, increased blood glucose, increased blood creatinine, deep venous thrombosis, delirium, dyspnea, decreased glomerular filtration rate, decreased hemoglobin, hyperglycemia, hypertension, hypoalbuminemia, hypotension, hypoxia, decreased lymphocyte count, lymphopenia, pneumonia, increased prothrombin time, pyrexia, respiratory distress, increased aminotransferase levels, and decreased urine creatinine clearance. Any adverse events reported in studies included in the evidence review (15, 17) were acute kidney injury, acute respiratory failure, increased alanine aminotransferase, anemia, increased aspartate aminotransferase, increased blood glucose, increased blood lipids, increased blood urea nitrogen, constipation, hyperlipidemia, hypoalbuminemia, hypokalemia, hypotension, insomnia, nausea, increased neutrophil count, rash, respiratory failure, increased serum potassium, reduced serum sodium, thrombocytopenia, increased total bilirubin, vomiting, and increased leukocyte count.
‖ Clinical improvement is defined as a 2-point reduction in patients' hospitalization status on a 6-point ordinal scale (1 = live discharge to 6 = death) or live discharge from the hospital, whichever came first (18), and as an improvement of at least 2 points from baseline on a 7-point ordinal scale (1 = death to 7 = discharged from hospital) (17).

ment to 10 days may be beneficial compared with discontinuing treatment on day 5 (17).

Evidence from 2 RCTs (15, 18) showed that among outcomes rated as critical, a 10-day course of remdesivir compared with placebo may slightly reduce mortality (low certainty) and probably increases recovery by a large effect (moderate certainty), and that there are probably fewer serious adverse events (modest effect, moderate certainty). Evidence from 1 RCT showed that a 10-day course may not reduce hospital length of stay (low certainty) (18). Low-certainty evidence also showed improvement with a 10-day course compared with placebo for the following important outcomes: time to recovery (large effect), clinical improvement (modest effect), time to clinical improvement (slight effect), the need for mechanical ventilation or ECMO (slight effect), and nonserious adverse events (slight effect). Evidence was insufficient regarding differences in any adverse events.

For a 10-day course of remdesivir compared with placebo, the outcomes of mortality (18), time to recovery (15), and time to clinical improvement (18) did not vary by symptom duration (≤10 days vs. >10 days), and time to recovery also did not vary by baseline oxygenation or ventilation requirements (15). No evidence was found on whether other outcomes vary by symptom duration.

Evidence from 1 RCT (17) that compared a 5-day course with a 10-day course of remdesivir showed that the 5-day course may reduce mortality slightly versus the 10-day course in patients with severe COVID-19 who did not require mechanical ventilation or ECMO at baseline (17). However, a post hoc analysis suggested that a 5- versus a 10-day course might result in a large increase in mortality among the most critical patients of those with severe COVID-19 (those receiving mechanical ventilation or ECMO at day 5) (17). Treatment beyond 5 days did not improve mortality among patients who were receiving noninvasive positive pressure ventilation or high-flow oxygen, those receiving low-flow oxygen, or those breathing ambient air. This finding suggests that extending treatment to 10 days for patients receiving mechanical ventilation or ECMO at day 5 may be beneficial (17). Compared with a 10-day course, a 5-day course shows a modest increase in recovery, a slight decrease in the time to recovery, and a modest reduction in the need for mechanical ventilation or ECMO (low certainty). Evidence for potential harms showed that a 5-day course of remdesivir results in fewer serious adverse events (large effect, low certainty) and a fewer number of any adverse events (slight effect, low certainty) compared with a 10-day course.

From American College of Physicians, Philadelphia, Pennsylvania (A.Q., I.E.); American College of Physicians, Philadelphia, and Villanova University, Villanova, Pennsylvania (J.Y.); University of Massachusetts Medical School and Saint Vincent

Table 5. Evidence Summary for Patients With Severe* COVID-19: What Information Does the Evidence Provide?

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence†
Remdesivir (5-d Course) vs. Placebo/Standard Care in Patients With Severe* COVID-19			
No evidence			
Remdesivir (10-d Course) vs. Placebo/Standard Care in Patients With Severe* COVID-19			
Critical outcomes			
Mortality	2 RCTs (1300)	Remdesivir (10-d course) may reduce mortality slightly compared with placebo (15, 18)‡ Note: The effect of remdesivir (10-d course) does not vary by symptom duration (≤10 vs. >10 d)§ (18)	Low
Recovery‖	2 RCTs (1300)	Remdesivir (10-d course) probably results in a large increase in recovery compared with placebo (15, 18)‡	Moderate
Hospital length of stay	1 RCT (237)	Remdesivir (10-d course) may not reduce hospital length of stay compared with placebo (15, 18)‡	Low
Serious adverse events¶	2 RCTs (1300)	Remdesivir (10-d course) probably results in a modest reduction in serious adverse events compared with placebo (15, 18)‡	Moderate
Important outcomes			
Time to recovery‖	1 RCT (1063)	Remdesivir (10-d course) may result in a large reduction in time to recovery compared with placebo (15)‡ Note: The effect of remdesivir (10-d course) does not vary by symptom duration (≤10 vs. >10 d) or baseline oxygenation/ventilation requirements§ (15)	Low
Clinical improvement**	1 RCT (237)	Remdesivir (10-d course) may result in a modest increase in clinical improvement compared with placebo (18)	Low
Time to clinical improvement**	1 RCT (237)	Remdesivir (10-d course) may reduce time to clinical improvement slightly compared with placebo (18) Note: The effect of remdesivir (10-d course) does not vary by symptom duration (≤10 vs. >10 d)§ (18)	Low
Invasive mechanical ventilation/ECMO	2 RCTs (1300)	Remdesivir (10-d course) may reduce the need for mechanical ventilation or ECMO slightly compared with placebo (15, 18)‡	Low
Nonserious adverse events¶	1 RCT (1063)	Remdesivir (10-d course) may reduce nonserious adverse events slightly compared with placebo (15)‡	Low
Any adverse events¶	1 RCT (237)	Very uncertain about the effect of remdesivir (10-d course) compared with placebo on adverse events (18)	Insufficient
Remdesivir (5-d Course) vs. Remdesivir (10-d Course) in Patients With Severe* COVID-19			
Critical outcomes			
Mortality	1 RCT (397)	Remdesivir 5-d course may reduce mortality slightly compared with remdesivir 10-d course (17)‡‡ Note: Remdesivir 5-d course compared with a 10-d course resulted in an increase in mortality in patients who progressed to require mechanical ventilation or ECMO at day 5§	Low
Recovery‖	1 RCT (397)	Remdesivir 5-d course may result in a modest increase in recovery compared with remdesivir 10-d course (17)‡‡	Low
Hospital length of stay	NA	No evidence	No evidence
Serious adverse events¶	1 RCT (397)	Remdesivir 5-d course may result in a large reduction in serious adverse events compared with remdesivir 10-d course (17)‡‡	Low
Important outcomes			
Time to recovery‖	1 RCT (397)	Remdesivir 5-d course may reduce time to recovery slightly compared with remdesivir 10-d course (17)‡‡	Low
Clinical improvement**	1 RCT (397)	Remdesivir 5-d course may result in a modest increase in clinical improvement compared with remdesivir 10-d course (17)‡‡	Low
Time to clinical improvement**	NA	No evidence	No evidence
Invasive mechanical ventilation/ECMO	1 RCT (397)	Remdesivir 5-d course may result in a modest reduction in the need for mechanical ventilation or ECMO compared with remdesivir 10-d course (17)‡‡	Low
Nonserious adverse events¶	NA	No evidence	No evidence
Any adverse events¶	1 RCT (397)	Remdesivir 5-d course may reduce adverse events slightly compared with remdesivir 10-d course (17)‡‡	Low

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***Table 5*–Continued**

COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; NA = not applicable; RCT = randomized controlled trial.
* Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or the need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic infiltrates and oxygen saturation >94% on room air; and mild COVID-19 was not defined (14).
† Certainty of evidence: insufficient, confidence is inadequate to assess the likelihood of benefit (benefit minus harm) of an intervention or its impact on a health outcome; low, confidence in the effect is limited because the true effect may be substantially different from the estimated effect; moderate, confidence in the effect is moderate because the true effect is probably close to the estimated effect, but a sizable possibility exists that it is substantially different; high, confidence that the true effect is close to the estimated effect.
‡ Most (88.7%) of the participants enrolled in 1 RCT (15, 18) had severe disease, so this study is analyzed as being representative of patients with severe disease.
§ Determined from a subgroup analysis; the certainty of evidence was not assessed for this comparison.
‖ Recovery is defined as discharge from the hospital or hospitalization for infection control purposes only in 1 RCT (15, 18) and as discharge from the hospital or hospitalized but not requiring supplemental oxygen or ongoing medical care in 3 RCTs (17, 18).
¶ Serious adverse events reported in studies included in the evidence review (15–17) were acute coronary syndrome, acute kidney injury, acute respiratory distress syndrome, acute respiratory failure, increased aminotransferase levels, atrial fibrillation, bronchitis, cardiac arrest, cardiopulmonary failure, increased D-dimer, deep venous thrombosis, diabetic ketoacidosis, dyspnea, endotracheal intubation, decreased glomerular filtration rate, hemorrhage of lower digestive tract, hypotension, hypoxia, ileus, lung abscess, mechanical ventilation, multiple organ dysfunction syndrome, respiratory distress, respiratory failure, pneumothorax, pulmonary embolism, pulmonary failure, recurrence of COVID-19, septic shock, sepsis, shock, tachycardia, thrombocytopenia, and viral pneumonia. Nonserious adverse events reported in studies included in the evidence review (16) were acidosis, acute kidney injury, alkalosis, increased aspartate aminotransferase, anemia, atrial fibrillation, decreased blood albumin, increased blood bilirubin, increased blood glucose, increased blood creatinine, deep venous thrombosis, delirium, dyspnea, decreased glomerular filtration rate, decreased hemoglobin, hyperglycemia, hypertension, hypoalbuminemia, hypotension, hypoxia, decreased lymphocyte count, lymphopenia, pneumonia, increased prothrombin time, pyrexia, respiratory distress, increased aminotransferase levels, and decreased urine creatinine clearance. Any adverse events reported in studies included in the evidence review (15, 17) were acute kidney injury, acute respiratory failure, increased alanine aminotransferase, anemia, increased aspartate aminotransferase, increased blood glucose, increased blood lipids, increased blood urea nitrogen, constipation, hyperlipidemia, hypoalbuminemia, hypokalemia, hypotension, insomnia, nausea, increased neutrophil count, rash, respiratory failure, increased serum potassium, reduced serum sodium, thrombocytopenia, increased total bilirubin, vomiting, and increased leukocyte count.
** Clinical improvement is defined as a 2-point reduction in patients' hospitalization status on a 6-point ordinal scale (1 = live discharge to 6 = death) or live discharge from the hospital, whichever came first (18), and as an improvement of at least 2 points from baseline on a 7-point ordinal scale (1 = death to 7 = discharged from hospital) (17).
‡‡ Patients requiring mechanical ventilation or ECMO were excluded from 1 RCT (17), so despite a few patients (3.3%) developing a requirement for invasive mechanical ventilation between screening and the beginning of the treatment, this study is analyzed as being representative of patients with severe disease not requiring mechanical ventilation or ECMO at baseline.

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Note: The Practice Points are developed by the SMPC of the ACP. The Practice Points are "guides" only and may not apply to all patients and all clinical situations. All Practice Points are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.

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Table 6. Evidence Gaps

- Additional rigorous studies are needed to assess the effectiveness of remdesivir to treat COVID-19 in patients with mild, moderate, and severe COVID-19.
- Additional rigorous studies are needed to assess the optimal treatment duration depending on COVID-19 disease severity.
- A need exists for studies assessing whether outcomes vary by symptom duration in patients with moderate COVID-19, and additional studies are needed to confirm existing findings in patients with severe COVID-19.
- Future studies should consider evaluating additional critical and important clinical outcomes, such as respiratory failure or duration of mechanical ventilation.

COVID-19 = coronavirus disease 2019.

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Appendix: Practice Points Development Process

The SMPC, in collaboration with staff from ACP's Department of Clinical Policy, developed these practice points on the basis of a rapid and living systematic evidence review conducted by the VA Evidence Synthesis Program, Minneapolis, Minnesota (14). The SMPC comprises 11 internal medicine physicians representing various clinical areas of expertise and 1 public (nonclinician) member, and includes members with expertise in epidemiology, evidence synthesis, health policy, and guideline development. In addition to contributing clinical, scientific, and methodological expertise, Clinical Policy staff provided administrative support and liaised among the SMPC, the evidence review funding entity and evidence team, and the journal. Clinical Policy staff and the SMPC reviewed and prioritized potential topic suggestions from ACP members, SMPC members, and ACP governance. A committee subgroup, including the SMPC chair, worked with staff to draft the key questions and led the development of the practice points. Clinical Policy staff worked with the subgroup and an independent evidence review team to refine the key questions and determine appropriate evidence synthesis methods for each key question. Via conference calls and e-mail, Clinical Policy staff worked with the committee subgroup to draft the practice points on the basis of the results of the rapid and living systematic evidence review. The full SMPC reviewed and approved the final practice points. Before journal submission, ACP's Executive Committee of the Board of Regents also reviewed and approved the practice points on behalf of the ACP Board of Regents. The evidence review team will continually update the evidence review. The ACP will update the practice points based on the evidence review by using the same process as the first version described above. Updates are currently planned for every 2 months through December 2021. The SMPC will continuously assess the priority of the topic and the overall state of evidence, including the anticipated rate of new evidence, and may choose to modify the update intervals accordingly (any modifications will be described in an Update Alert).

Appendix Table 1. Estimates: Patients With Moderate* COVID-19†

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence‡
Remdesivir (5-d Course) vs. Placebo/Standard Care in Patients With Moderate* COVID-19			
Critical outcomes			
Mortality (FU: 11 d)	1 RCT (391)	Remdesivir 5-d course, 0% (0/191), vs. standard care, 2% (4/200); ARD, −2.0% (95% CI, −4.2% to 0.2%) (16)	Low
Recovery§ (FU: 11 d)	**1 RCT (391)**	**Remdesivir 5-d course, 73.8% (141/191), vs. standard care, 64% (128/200); ARD, 9.8% (CI, 0.7% to 18.9%) (16)**	**Low**
Hospital length of stay	NA	No evidence	NA
Serious adverse events‖ (FU: 11 d)	1 RCT (391)	Remdesivir 5-d course, 4.7% (9/191), vs. standard care, 9.0% (18/200); ARD, −4.3% (CI, −9.3% to 0.7%) (16)	Low
Important outcomes			
Time to recovery§ (FU: 11 d)	**1 RCT (391)**	Remdesivir 5-d course, median 6 d (IQR, 5 to 10 d), vs. standard care, median 7 d (IQR, 4 to 15 d); HR, 1.18 (CI, 0.96 to 1.45) (16)	Low
Clinical improvement¶ (FU: 11 d)	**1 RCT (391)**	**Remdesivir 5-d course, 70.2% (134/191), vs. standard care, 60.5% (121/200); ARD, 9.7% (CI, 0.3% to 19%) (16)**	**Low**
Time to clinical improvement¶	NA	No evidence	NA
Invasive mechanical ventilation/ECMO (FU: 11 d)	1 RCT (391)	Remdesivir 5-d course, 0% (0/191), vs. standard care, 2.0% (4/200); ARD, −2.0% (CI, −4.2% to 0.2%) (16)	Low
Nonserious adverse events‖	NA	No evidence	NA
Any adverse events‖ (FU: 11 d)	1 RCT (391)	Remdesivir 5-d course, 51.3% (98/191), vs. standard care, 47.0% (93/200); ARD, 4.8% (CI, −5.1% to 14.7%) (16)	Low
Remdesivir (10-d Course) vs. Placebo/Standard Care in Patients with Moderate* COVID-19			
Critical outcomes			
Mortality (FU: 11 d)	1 RCT (393)	Remdesivir 10-d course, 1.0% (2/193), vs. standard care, 2.0% (4/200); ARD, −1.0% (CI, −3.4% to 1.4%) (16)	Low
Recovery§ (FU: 11 d)	1 RCT (393)	Remdesivir 10-d course, 68.4% (132/193), vs. standard care, 64% (128/200); ARD, 4.4% (CI, −4.9% to 13.7%) (16)	Low
Hospital length of stay	NA	No evidence	NA
Serious adverse events‖ (FU: 11 d)	**1 RCT (393)**	**Remdesivir 10-d course, 5.2% (10/193), vs. standard care, 9.0% (18/200); ARD, −3.8% (CI, −8.9% to −1.2%) (16)**	**Low**
Important outcomes			
Time to recovery§ (FU: 11 d)	1 RCT (393)	Remdesivir 10-d course, median 8 d (IQR, 4 to 13 d), vs. standard care, median 7 d (IQR, 4 to 15 d); HR, 1.11 (CI, 0.90 to 1.37) (16)	Insufficient
Clinical improvement¶ (FU: 11 d)	1 RCT (393)	Remdesivir 10-d course, 65.3% (126/193), vs. standard care, 60.5% (121/200); ARD, 4.8% (CI, −4.8% to 14.3%) (16)	Low
Time to clinical improvement¶	NA	No evidence	NA
Invasive mechanical ventilation/ECMO (FU: 11 d)	1 RCT (393)	Remdesivir 10-d course, 0.5% (1/193), vs. standard care, 2.0% (4/200); ARD, −1.5% (CI, −3.7% to 0.7%) (16)	Low
Nonserious adverse events‖	NA	No evidence	NA
Any adverse events‖ (FU: 11 d)	**1 RCT (393)**	**Remdesivir 10-d course, 58.5% (113/193), vs. standard care, 47% (93/200); ARD, 12.0% (CI, 2.2% to 21.9%) (16)**	**Low**
Remdesivir (5-d Course) vs. Remdesivir (10-d Course) in Patients With Moderate* COVID-19			
Critical outcomes			
Mortality (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, 0% (0/191), vs. remdesivir, 10-d course, 1.0% (2/193); ARD, −1.0% (CI, −2.8% to 0.7%) (16)	Low
Recovery§ (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, 73.8% (141/191), vs. remdesivir, 10-d course, 68.4% (132/193); ARD, 5.4% (CI, −3.6% to 14.5%) (16)	Low
Hospital length of stay	NA	No evidence	NA
Serious adverse events‖ (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, 4.7% (9/191), vs. remdesivir 10-d course, 5.2% (10/193); ARD, 0.5% (CI,−4.8% to 3.9%) (16)	Low

Continued on following page

Appendix Table 1–Continued

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence‡
Important outcomes			
Time to recovery§ (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, median 6 d (IQR, 5 to 10 d), vs. remdesivir 10-d course, median 8 d (IQR, 4 to 13 d); HR not reported (16)	Insufficient
Clinical improvement¶ (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, 70.2% (134/191), vs. remdesivir 10-d course, 65.3% (126/193); ARD, 4.9% (CI, −4.5% to 14.2%) (16)	Low
Time to clinical improvement¶	NA	No evidence	NA
Invasive mechanical ventilation/ECMO	1 RCT (384)	Remdesivir 5-d course, 0% (0/191), vs. remdesivir 10-d course, 0.5% (1/193); ARD, −0.5% (CI, −1.9% to 0.9%) (16)	Low
Nonserious adverse events‖	NA	No evidence	NA
Any adverse events‖ (FU: 11 d)	1 RCT (384)	Remdesivir 5-d course, 51.3% (98/191), vs. remdesivir 10-d course, 58.5% (113/193); ARD, −7.2% (CI, −17.2% to 2.7%) (16)	Low

ARD = absolute risk difference; COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; FU = follow-up; HR = hazard ratio; IQR = interquartile range; NA = not applicable; RCT = randomized controlled trial.

* Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or the need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic infiltrates and oxygen saturation >94% on room air; and mild COVID-19 was not defined (14).

† Statistically significant findings are in boldface.

‡ Certainty of evidence: insufficient, confidence is inadequate to assess the likelihood of benefit (benefit minus harm) of an intervention or its impact on a health outcome; low, confidence in the effect is limited because the true effect may be substantially different from the estimated effect; moderate, confidence in the effect is moderate because the true effect is probably close to the estimated effect, but a sizable possibility exists that it is substantially different; high, confidence that the true effect is close to the estimated effect.

§ Recovery is defined as discharge from the hospital or hospitalization for infection control purposes only in 1 RCT (15, 18) and as discharge from the hospital or hospitalized but not requiring supplemental oxygen or ongoing medical care in 3 RCTs (17, 18).

‖ Serious adverse events reported in studies included in the evidence review (15–17) were acute coronary syndrome, acute kidney injury, acute respiratory distress syndrome, acute respiratory failure, increased aminotransferase levels, atrial fibrillation, bronchitis, cardiac arrest, cardiopulmonary failure, increased D-dimer, deep venous thrombosis, diabetic ketoacidosis, dyspnea, endotracheal intubation, decreased glomerular filtration rate, hemorrhage of lower digestive tract, hypotension, hypoxia, ileus, lung abscess, mechanical ventilation, multiple organ dysfunction syndrome, respiratory distress, respiratory failure, pneumothorax, pulmonary embolism, pulmonary failure, recurrence of COVID-19, septic shock, sepsis, shock, tachycardia, thrombocytopenia, and viral pneumonia. Nonserious adverse events reported in studies included in the evidence review (16) were acidosis, acute kidney injury, alkalosis, increased aspartate aminotransferase, anemia, atrial fibrillation, decreased blood albumin, increased blood bilirubin, increased blood glucose, increased blood creatinine, deep venous thrombosis, delirium, dyspnea, decreased glomerular filtration rate, decreased hemoglobin, hyperglycemia, hypertension, hypoalbuminemia, hypotension, hypoxia, decreased lymphocyte count, lymphopenia, pneumonia, increased prothrombin time, pyrexia, respiratory distress, increased aminotransferase levels, and decreased urine creatinine clearance. Any adverse events reported in studies included in the evidence review (15, 17) were acute kidney injury, acute respiratory failure, increased alanine aminotransferase, anemia, increased aspartate aminotransferase, increased blood glucose, increased blood lipids, increased blood urea nitrogen, constipation, hyperlipidemia, hypoalbuminemia, hypokalemia, hypotension, insomnia, nausea, increased neutrophil count, rash, respiratory failure, increased serum potassium, reduced serum sodium, thrombocytopenia, increased total bilirubin, vomiting, and increased leukocyte count.

¶ Clinical improvement is defined as a 2-point reduction in patients' hospitalization status on a 6-point ordinal scale (1 = live discharge to 6 = death) or live discharge from the hospital, whichever came first (18), and as an improvement of at least 2 points from baseline on a 7-point ordinal scale (1 = death to 7 = discharged from hospital) (17).

Appendix Table 2. Estimates: Patients With Severe* COVID-19†

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence‡
Remdesivir (5-d Course) vs. Placebo/Standard Care in Patients With Severe* COVID-19			
No evidence			
Remdesivir (10-d Course) vs. Placebo/Standard Care in Patients With Severe* COVID-19			
Critical outcomes			
Mortality (FU: range, 14–28 d)	2 RCTs (1300)	**Remdesivir 10-d course, 5.9% (32/538), vs. placebo, 10.4% (54/521); ARD, −4.4% (95% CI, −7.7% to −1.1%) measured at 14 d (15)§** Remdesivir 10-d course, 13.9% (22/158), vs. placebo, 12.8% (10/78); ARD, 1.1% (CI, −8.1% to 10.3%) measured at 28 d (18) Note: The effect of remdesivir (10-d course) by symptom duration‖ (18): • ≤10 d of symptoms: remdesivir, 11% (8/71), vs. placebo, 15% (7/47); ARD, −3.6% (CI, −16.2% to 8.9%) • >10 d of symptoms: remdesivir, 14% (12/84), vs. placebo, 10%; ARD, 4.6% (CI, −8.2% to 17.4%)	**Low**
Recovery¶ (FU: range, 28–29 d)	**2 RCTs (1300)**	**Remdesivir 10-d course, 62.1% (334/538), vs. placebo, 52.4% (273/521); ARD, 9.7% (CI, 3.7% to 15.6%) measured at 29 d (15)§** Remdesivir 10-d course, 70.7% (106/150), vs. placebo, 63.6% (49/77); ARD, 7.0% (CI, −6.0% to 20.0%) measured at 28 d (18)	**Moderate**
Hospital length of stay (FU: 28 d)	1 RCT (237)	Remdesivir 10-d course, median 25 d (IQR, 16 to 38 d), vs. placebo, median 24 d (IQR, 18 to 36 d); MD, 0 d (CI, −4.0 to 4.0 d) (18)	Low
Serious adverse events** (FU: range, 28–29 d)	**2 RCTs (1300)**	**Remdesivir 10-d course, 21.1% (114/541), vs. placebo, 27.0% (141/522); ARD, −5.9% (CI, −11.1% to −0.8%) measured at 29 d (15)§** Remdesivir 10-d course, 18.1% (28/155), vs. placebo, 25.6% (20/78); ARD, −7.6% (CI, −19.0% to 3.9%) measured at 28 d (18)	**Moderate**
Important outcomes			
Time to recovery¶ (FU: 29 d)	**1 RCT (1063)**	**Remdesivir 10-d course, median 11 d (IQR, 9 to 12 d), vs. placebo, median 15 d (IQR, 13 to 19 d); *P* < 0.001 (15)§** Note: The effect of remdesivir (10-d course) by symptom duration‖ (15)§: • ≤10 d of symptoms: rate ratio, 1.28 (CI, 1.05 to 1.57) • >10 d of symptoms: rate ratio, 1.38 (CI, 1.05 to 1.81) Note: The effect of remdesivir (10-d course) by baseline oxygenation/ventilation requirements‖ (15)§: • Adjusted analysis by baseline ordinal score as a stratification variable: rate ratio, 1.31 (CI, 1.12 to 1.54)	**Low**
Clinical improvement†† (FU: 28 d)	1 RCT(237)	Remdesivir 10-d course, 65.2% (103/158), vs. placebo, 57.7% (45/78); ARD, 7.5% (CI, −5.7% to 20.7%) (18)	Low
Time to clinical Improvement†† (FU: 28 d)	1 RCT(237)	Remdesivir 10-d course, median 21 d (IQR, 13 to 28 d), vs. placebo, median 23 d (IQR, 18 to 36 d); HR, 1.23 (CI, 0.87 to 1.75) (18) Note: The effect of remdesivir (10-d course) by symptom duration‖ (18): • ≤10 d of symptoms: remdesivir, 18 d (IQR, 12 to 28 d), vs. placebo, 23 d (IQR, 15 to 28 d); HR, 1.52 (CI, 0.95 to 2.43) • >10 d of symptoms: remdesivir, 23 d, vs. placebo, 24 d; HR, 1.07 (CI, 0.63 to 1.83)	Low
Invasive mechanical ventilation/ECMO (FU: 28 d)	2 RCTs (1300)	Remdesivir 10-d course, 13.8% (60/434), vs. placebo, 17.6% (72/410); ARD, −3.7% (CI, −8.6% to 1.2%) measured at 15 d (15)§ Remdesivir 10-d course, 8.2% (13/158), vs. placebo, 12.8% (10/78); ARD, −4.6% (CI, −13.2% to 4.0%) (18)	Low
Nonserious adverse events** (FU: 29 d)	1 RCT (1063)	Remdesivir 10-d course, 28.8% (156/541), vs. placebo, 33.0% (172/522); ARD, −4.1% (CI, −9.7% to 1.4%) (15)§	Low
Any adverse events** (FU: 28 d)	1 RCT (237)	Remdesivir 10-d course, 65.8% (102/155), vs. placebo, 64.1% (50/78); ARD, 1.7% (CI, −11.3% to 14.7%) (18)	Insufficient
Remdesivir (5-d Course) vs. Remdesivir (10-d Course) in Patients With Severe* COVID-19			
Critical outcomes			
Mortality (FU: 14 d)	1 RCT (397)	Remdesivir 5-d course, 8.0% (16/200), vs. remdesivir 10-d course, 10.7% (21/197); ARD, −2.7% (CI, −8.4% to 3.1%) (17)‡‡ Note: Among patients receiving mechanical ventilation or ECMO at day 5‖ (17)‡‡: • Remdesivir 5-d course, 40% (10/25), vs. remdesivir 10-d course, 17% (7/41); ARD, 22.9% (CI, 0.5% to 45.3%) • Among patients who were receiving noninvasive positive pressure ventilation or high- or low-flow oxygen or breathing ambient air at 5 d, treatment beyond 5 d did not improve mortality	Low
Recovery¶ (FU: 14 d)	1 RCT (397)	Remdesivir 5-d course, 64.5% (129/200), vs. remdesivir 10-d course, 53.8% (106/197); baseline-adjusted ARD, 6.3% (CI, −2.8% to 15.4%) (17)‡‡	Low
Hospital length of stay	NA	No evidence	NA
Serious adverse events** (FU: 14 d)	**1 RCT (397)**	**Remdesivir 5-d course, 21.0% (42/200), vs. remdesivir 10-d course, 34.5% (68/197); ARD, −13.5% (CI, −22.2% to −4.8%) (17)‡‡**	**Low**

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Appendix Table 2–Continued

Outcome	Study Design (Patients, *n*)	Evidence	Certainty of Evidence‡
Important outcomes			
Time to recovery¶ (FU: 14 d)	1 RCT(397)	Remdesivir 5-d course, median 10 d (IQR, 6 to 18 d), vs. remdesivir 10-d course, median 11 d (IQR, 7 d to not estimable); HR, 0.81 (CI, 0.64 to 1.04) (17)‡‡	Low
Clinical improvement†† (FU: 14 d)	1 RCT(397)	Remdesivir 5-d course, 64.5% (129/200), vs. remdesivir 10-d course, 54.3% (107/197); baseline-adjusted ARD, 6.5% (CI, −2.8% to 15.7%) (17)‡‡	Low
Time to clinical improvement††	NA	No evidence	No evidence
Invasive mechanical ventilation/ECMO (FU: 14 d)	**1 RCT (397)**	**Remdesivir 5-d course, 8.0% (16/200), vs. remdesivir 10-d course, 16.8% (33/197); ARD, −8.8% (CI, −15.2% to −2.3%) (17)‡‡**	**Low**
Nonserious adverse events**	NA	No evidence	No evidence
Any adverse events** (FU: 14 d)	1 RCT (397)	Remdesivir 5-d course, 70.5% (141/200), vs. remdesivir 10-d course, 73.6% (145/197); ARD, −3.1% (CI, −11.9% to 5.7%) (17)‡‡	Low

ARD = absolute risk difference; COVID-19 = coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; FU = follow-up; HR = hazard ratio; IQR = interquartile range; MD = mean difference; NA = not applicable; RCT = randomized controlled trial.

* Within the evidence reviewed, severe COVID-19 is defined as hospitalized patients meeting ≥1 of the following criteria: radiographic infiltrates on imaging, an oxygen saturation level ≤94% on room air, tachypnea (respiratory rate >24 breaths per minute without supplemental oxygen), or the need for supplemental oxygen or mechanical ventilation; moderate COVID-19 is defined as hospitalized patients with radiographic infiltrates and oxygen saturation >94% on room air; and mild COVID-19 was not defined (14).

† Statistically significant findings are in bold.

‡ Certainty of evidence: insufficient, confidence is inadequate to assess the likelihood of benefit (benefit minus harm) of an intervention or its impact on a health outcome; low, confidence in the effect is limited because the true effect may be substantially different from the estimated effect; moderate, confidence in the effect is moderate because the true effect is probably close to the estimated effect, but a sizable possibility exists that it is substantially different; high, confidence that the true effect is close to the estimated effect.

§ Most of the participants (88.7%) enrolled in 1 RCT (15, 18) had severe disease, so this study is analyzed as being representative of patients with severe disease.

‖ The certainty of evidence was not assessed for this comparison determined from a subgroup analysis.

¶ Recovery is defined as discharge from the hospital or hospitalization for infection control purposes only in 1 RCT (15, 18) and as discharge from the hospital or hospitalized but not requiring supplemental oxygen or ongoing medical care in 3 RCTs (17, 18).

** Serious adverse events reported in studies included in the evidence review (15–17) were acute coronary syndrome, acute kidney injury, acute respiratory distress syndrome, acute respiratory failure, increased aminotransferase levels, atrial fibrillation, bronchitis, cardiac arrest, cardiopulmonary failure, increased D-dimer, deep venous thrombosis, diabetic ketoacidosis, dyspnea, endotracheal intubation, decreased glomerular filtration rate, hemorrhage of lower digestive tract, hypotension, hypoxia, ileus, lung abscess, mechanical ventilation, multiple organ dysfunction syndrome, respiratory distress, respiratory failure, pneumothorax, pulmonary embolism, pulmonary failure, recurrence of COVID-19, septic shock, sepsis, shock, tachycardia, thrombocytopenia, and viral pneumonia. Nonserious adverse events reported in studies included in the evidence review (16) were acidosis, acute kidney injury, alkalosis, increased aspartate aminotransferase, anemia, atrial fibrillation, decreased blood albumin, increased blood bilirubin, increased blood glucose, increased blood creatinine, deep venous thrombosis, delirium, dyspnea, decreased glomerular filtration rate, decreased hemoglobin, hyperglycemia, hypertension, hypoalbuminemia, hypotension, hypoxia, decreased lymphocyte count, lymphopenia, pneumonia, increased prothrombin time, pyrexia, respiratory distress, increased aminotransferase levels, and decreased urine creatinine clearance. Any adverse events reported in studies included in the evidence review (15, 17) were acute kidney injury, acute respiratory failure, increased alanine aminotransferase, anemia, increased aspartate aminotransferase, increased blood glucose, increased blood lipids, increased blood urea nitrogen, constipation, hyperlipidemia, hypoalbuminemia, hypokalemia, hypotension, insomnia, nausea, increased neutrophil count, rash, respiratory failure, increased serum potassium, reduced serum sodium, thrombocytopenia, increased total bilirubin, vomiting, and increased leukocyte count.

†† Clinical improvement is defined as a 2-point reduction in patients' hospitalization status on a 6-point ordinal scale (1 = live discharge to 6 = death) or live discharge from the hospital, whichever came first (18), and as an improvement of at least 2 points from baseline on a 7-point ordinal scale (1 = death to 7 = discharged from hospital) (17).

‡‡ Patients requiring mechanical ventilation or ECMO were excluded from 1 RCT (17), so despite a few patients (3.3%) developing a requirement for invasive mechanical ventilation between screening and the beginning of the treatment, this study is analyzed as being representative of patients with severe disease not requiring mechanical ventilation or ECMO at baseline.