

Table 2e. Characteristics of Antiviral Agents That Are Approved or Under Evaluation for the Treatment of COVID-19

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Dosing Regimens <i>The doses listed here are for approved indications or from reported experiences or clinical trials.</i>	Adverse Events	Monitoring Parameters	Drug-Drug Interaction Potential	Comments and Links to Clinical Trials
Remdesivir				
<p>The doses and indications listed below come from the FDA product information. Please see Therapeutic Management of Hospitalized Adults With COVID-19 for the Panel's recommendations on when to use RDV.</p> <p>For Hospitalized Adults and Children (Aged ≥12 Years and Weighing ≥40 kg)</p> <p><i>For Patients Who Are Not Mechanically Ventilated and/or on ECMO:</i></p> <ul style="list-style-type: none"> • RDV 200 mg IV^a on Day 1, then RDV 100 mg IV on Days 2–5 • For patients who do not show clinical improvement after 5 days of therapy, treatment may be extended to up to 10 days. 	<ul style="list-style-type: none"> • Nausea • ALT and AST elevations • Hypersensitivity • Increases in prothrombin time • Drug vehicle is SBECD, which has been associated with renal and liver toxicity. SBECD accumulation may occur in patients with moderate or severe renal impairment. • Each 100 mg vial of RDV lyophilized powder contains 3 g of SBECD, and each 100 mg/20 mL vial of RDV solution contains 6 g of SBECD. • Clinicians may consider preferentially using 	<ul style="list-style-type: none"> • Infusion reactions • Renal function and hepatic function should be monitored before and during treatment as clinically indicated. • In the FDA product information, RDV is not recommended when eGFR is <30 mL/min. See the Remdesivir section for a discussion on using RDV in people with renal insufficiency. • RDV may need to be discontinued if ALT level increases to >10 times ULN and should be discontinued if there is an increase in ALT level and signs or symptoms of liver inflammation are observed.¹ 	<ul style="list-style-type: none"> • Clinical drug-drug interaction studies of RDV have not been conducted. • In vitro, RDV is a substrate of CYP3A4, OATP1B1, and P-gp and an inhibitor of CYP3A4, OATP1B1, OATP1B3, and MATE1.¹ • Minimal to no reduction in RDV exposure is expected when RDV is coadministered with dexamethasone (Gilead Sciences, written communication, July 2020). • CQ or HCQ may decrease the antiviral activity of 	<ul style="list-style-type: none"> • RDV should be administered in a hospital or a health care setting that can provide a similar level of care to an inpatient hospital. • RDV is approved by the FDA for the treatment of COVID-19 in hospitalized adult and pediatric patients (aged ≥12 years and weighing ≥40 kg). • An EUA^b is available for hospitalized pediatric patients

<p><i>For Mechanically Ventilated Patients and/or Patients on ECMO:</i></p> <ul style="list-style-type: none"> • RDV 200 mg IV^a on Day 1, then RDV 100 mg IV on Days 2–10 <p>Suggested Dose in EUA^b for Hospitalized Children</p> <p><i>For Patients Weighing 3.5 kg to <40 kg:</i></p> <ul style="list-style-type: none"> • RDV 5 mg/kg IV^a on Day 1, then RDV 2.5 mg/kg IV once daily starting on Day 2 • For patients who are not mechanically ventilated and/or on ECMO, the duration is 5 days. If patients have not shown clinical improvement after 5 days, treatment may be extended to up to 10 days. • For mechanically ventilated patients and/or patients on ECMO, the recommended treatment duration is 10 days. <p><i>For Patients Aged <12 Years and Weighing ≥40 kg:</i></p> <ul style="list-style-type: none"> • Same dose as for adults 	<p>the lyophilized powder formulation (which contains less SBECD) in patients with renal impairment.</p>		<p>RDV; coadministration of these drugs is not recommended.¹</p> <ul style="list-style-type: none"> • No significant interaction is expected between RDV and oseltamivir or baloxavir (Gilead Sciences, personal and written communications, August and September 2020). 	<p>weighing 3.5 kg to <40 kg or aged <12 years and weighing ≥3.5 kg.</p> <ul style="list-style-type: none"> • A list of clinical trials is available here: Remdesivir
<p>Ivermectin</p>				
<p>Adults:</p> <ul style="list-style-type: none"> • The dose most commonly used in clinical trials is IVM 0.2–0.6 mg/kg PO 	<ul style="list-style-type: none"> • Generally well tolerated • Dizziness • Pruritis 	<ul style="list-style-type: none"> • Monitor for potential AEs. 	<ul style="list-style-type: none"> • Minor CYP3A4 substrate • P-gp substrate 	<ul style="list-style-type: none"> • Generally given on an empty stomach with water; however,

<p>given as a single dose or as a once-daily dose for up to 5 days.</p>	<ul style="list-style-type: none"> • GI effects (e.g., nausea, diarrhea) • Neurological AEs have been reported when IVM has been used to treat parasitic diseases, but it is not clear whether these AEs were caused by IVM or the underlying conditions. 			<p>administering IVM with food increases its bioavailability.²</p> <ul style="list-style-type: none"> • A list of clinical trials is available here: Ivermectin
<p>Nitazoxanide</p>				
<p>Adults:</p> <ul style="list-style-type: none"> • Doses reported in COVID-19 studies range from NTZ 500 mg PO 3 times daily to 4 times daily.^{3,4} Higher doses are being studied (ClinicalTrials.gov Identifier NCT04746183). • Doses used for antiprotozoal indications range from NTZ 500 mg to 1 g PO twice daily. 	<ul style="list-style-type: none"> • Generally well tolerated • Abdominal pain • Diarrhea • Headache • Nausea • Vomiting • Urine discoloration • Ocular discoloration (rare) 	<ul style="list-style-type: none"> • Monitor for potential AEs. 	<ul style="list-style-type: none"> • Drug-drug interactions may occur if NTZ is administered concurrently with other highly plasma protein-bound drugs due to competition for binding sites.⁵ • If NTZ is coadministered with other highly protein-bound drugs with narrow therapeutic indices, monitor the patient for AEs. 	<ul style="list-style-type: none"> • NTZ should be taken with food. • The oral suspension is not bioequivalent to the tablet formulation. • A list of clinical trials is available here: Nitazoxanide

^a Infuse over 30–120 minutes.

^b The FDA EUA permits the emergency use of RDV for the treatment of suspected COVID-19 or laboratory-confirmed SARS-CoV-2 infection in hospitalized pediatric patients weighing 3.5 kg to <40 kg or aged <12 years and weighing ≥3.5 kg.⁶

Key: AE = adverse event; ALT = alanine transaminase; AST = aspartate aminotransferase; CQ = chloroquine; CYP = cytochrome P450; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; GI = gastrointestinal; HCQ = hydroxychloroquine; IV = intravenous; IVM =

ivermectin; LPV/RTV = lopinavir/ritonavir; MATE = multidrug and toxin extrusion protein; NTZ = nitazoxanide; OATP = organic anion transporter polypeptide; the Panel = the COVID-19 Treatment Guidelines Panel; P-gp = P-glycoprotein; PO = orally; RDV = remdesivir; SBECD = sulfobutylether-beta-cyclodextrin; ULN = upper limit of normal



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