Antimicrobial Treatment Guideline for COVID-19

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In December 2019, a novel coronavirus (2019-nCoV or SARS-CoV-2) was first identified as a cause of respiratory illness (coronavirus disease 2019, COVID-19) among patients in Wuhan, Hubei Province, China. Since that time, the spread of this virus has become a global health concern.

Currently, there are no medications licensed specifically for use against COVID-19, though several agents are undergoing evaluation in pre-clinical and clinical studies. In the absence of targeted therapies, several FDA-approved agents have been proposed as potential options to repurpose for use against COVID-19. The rationale for use of these agents is based mostly on data extrapolated from other viruses, including related coronaviruses such as those associated with Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS).

The recommendations below are meant to inform clinicians until further guidance becomes available from organizations such as the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Because the data surrounding COVID-19 treatment is rapidly evolving, these recommendations are subject to change. We continue to evaluate newly available studies on a daily basis and update this guideline accordingly. *Of note, the Infectious Diseases Society of America (IDSA) and National Institutes of Health (NIH) currently do not recommend the use of any specific antiviral therapy unless used in the context of a clinical trial.*
For additional up-to-date information, the CDC and WHO websites can be accessed via the links below:
CDC: https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html
WHO: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance

Recommended Therapies
Because there are currently no medication therapies directed specifically at COVID-19, the mainstay of treatment for most patients consists of supportive care and appropriate infection prevention and control measures.

- See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

Some additional therapies have demonstrated safety and may potentially be efficacious against COVID-19. However, these agents should be used with caution and reserved for critically ill patients or those deemed to be at higher risk for COVID-19 complications (Table 1). Use of these agents (Table 2) for the treatment of COVID-19 is restricted to ASP approval (via **pager #10307**) or ID consult **24 hours per day, 7 days per week.** Refer to Appendix C for additional details.

Table 1: Highly Suspected or Confirmed COVID-19 Treatment Recommendations Based on Treatment Setting and Illness Severity

Treatment Setting	Treatment Recommendations Regardless of Age, Comorbidities, or Immunocompromised Status
Outpatient Setting	Supportive Care
Inpatient Setting*	**Mild Disease** – Without pneumonia and requiring <4L of new O2
	Supportive Care
	Moderate Disease – Pneumonia requiring hospitalization, not meeting criteria for severe disease OR no evidence of pneumonia, but requiring ≥4L of new O2
	Consider Treatment**
	Severe Disease – Requiring mechanical ventilation OR impending respiratory failure requiring intubation (RR>30 breaths/min; O2 saturation ≤93% on room air; PaO2/FiO2 ratio ≤300mmHg)
	Consider Treatment**

*Treatment requires approval 24/7 – see Appendix C
**Strongly consider treatment if duration of illness ≥ 7 days

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patients Meeting Criteria for Treatment

Medication	Dose	Indication for Use	Other Information
If Patient Is Intubated			
Remdesivir	**200 mg IV x1 day, then 100 mg IV daily x4-9 days** No adjustment for renal impairment/ECMO	• Non-FDA-approved agent available via expanded access for a limited number of patients meeting inclusion criteria or via compassionate use available only to pregnant patients	• See Appendix A for inclusion/ exclusion criteria and additional information on how to obtain this product
Hydroxychloroquine* (Plaquenil®) PO suspension	**400 mg BID x1 day, then 200 mg PO BID x4 days**** No adjustment for renal impairment	• Consider use in patients who do not meet criteria for remdesivir or while awaiting remdesivir	• May cause QTc prolongation – See Appendix B
If Patient Is NOT Intubated			
Hydroxychloroquine* (Plaquenil®) PO tablets	**400 mg BID x1 day, then 200 mg PO BID x4 days**** No adjustment for renal impairment		• Tablets cannot be crushed – use hydroxychloroquine suspension for tube administration • May prolong QTc – See Appendix B

*If inadequate hydroxychloroquine supply, may substitute chloroquine 500 mg PO BID x5-10 days. See Appendix B.
**May extend hydroxychloroquine course up to 10 days based on clinical response.

Antimicrobial Therapies Not Currently Recommended

Due to lack of efficacy data and/or evidence of potential harm, the therapies below are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4). Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19.

Table 3: Therapies Not Currently Recommended

Medication	Comments
Azithromycin	Insufficient data to support use. Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or required oxygen. Previous study in MERS showed no benefit on mortality or viral clearance.
Baloxavir marboxil	No evidence to support use and potential for adverse effects, including severe and sometimes fatal hypersensitivity reactions
Interferon	No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects.
Ivermectin	In vitro activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy. Based on in vitro findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations.
Lopinavir/ritonavir	No definitive evidence of benefit against SARS-CoV-2 *in vivo*. Available data has shown high rates of patient intolerance. The NIH Guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial.
Nitazoxanide	In vitro activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19. Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses.
Oseltamivir	No in vitro activity against coronaviruses. Should only be used if influenza is suspected or confirmed.
Ribavirin	Some data from other coronaviruses suggest synergy when given with lopinavir/ritonavir. No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potential benefit.
Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	Ongoing clinical trials with darunavir/cobicistat but no in vitro or clinical outcomes data. Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time.

Other Therapies for Consideration

If convalescent plasma is being considered for COVID-19, with a recommendation provided by an Infectious Diseases provider, refer to the Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process.

Additional recommendations for non-antimicrobial medications associated with complications and comorbidities associated with COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) can be found in the Inpatient Evaluation and Management Guidelines for COVID-19.

Appendix A. Remdesivir Expanded Access and Compassionate Use How-To

Remdesivir is a non-FDA approved agent manufactured by Gilead Sciences.
OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition is via either compassionate use or expanded access. Compassionate use is only available for pregnant patients at this time. Remdesivir is now available via expanded access at OSU for a limited number of patients meeting inclusion criteria.
Inclusion/exclusion criteria for remdesivir compassionate use and expanded access as set forth by Gilead at this time are as follows (subject to change):

Inclusion Criteria:

- Hospitalization
- Confirmed SARS-CoV-2 by PCR
- Mechanical ventilation
- Pregnancy

Exclusion Criteria:

- Evidence of multi-organ failure
- Pressor requirements to maintain blood pressure
- ALT levels > 5 X ULN
- CrCl < 30 mL/min or dialysis or continuous veno-venous hemofiltration
- Remdesivir cannot be used in conjunction with other experimental antiviral agents for COVID-19

Use via expanded access program:

Under development

Obtaining drug via compassionate use:

If a patient warrants treatment according to Table 1 above and meets inclusion/exclusion criteria for use, the treating physician should submit a compassionate use request on behalf of the patient to Gilead at https://rdvcu.gilead.com/. Once the request is submitted, Gilead will be in communication with the provider to approve or decline use or to request additional information.
For shipment of remdesivir use the following information when completing the form:

Pharmacy/Hospital Name: The Ohio State University Medical Center
Pharmacist/pharmacy Contact Name: Investigational Drug Service
Address: Investigational Drug Service
460 W. 10th Ave, Room C150N
Columbus, OH 43210
E-mail: pharmacy.ids@osumc.edu
Phone: 614-293-4560
Cell Phone: 614-293-3312 (central pharmacy)

For after-hours assistance with drug receipt, see service coverage for IDS on-call or page 614-730-4615.
For more information regarding the compassionate use process in general, please refer to the OSUWMC Expanded Use ("Compassionate Use") of Investigational Products guideline.

Appendix B. Cardiac Monitoring for Chloroquine (CQ)/Hydroxychloroquine (HCQ)

1. Place patients on telemetry and obtain baseline 12 lead ECG
2. Discontinue all QT-prolonging medication if possible. Consult medical specialty associated with medication for concerns with discontinuation risk or for alternatives. Consult pharmacy for assistance if needed for profile review to identify QT-prolonging medications.
3. Please correct electrolyte abnormalities, specifically potassium (> 4mmol/L) and magnesium (> 2mg/dL). We recommend that as you are starting to replete electrolytes, the drug therapy should not be delayed
4. Recognize that the likelihood for a malignant ventricular arrhythmia or a worrisome prolongation of the QTc is quite low (< 2%)
5. Regardless of the pre-drug / baseline QTc, give first dose
6. Obtain 6-lead telemetry or 12-lead ECG 2 hours after first dose
    a. If pre-drug QRS duration is < 120ms, can proceed with the second dose if the QTc < 520msec
    b. If pre-drug QRS duration is > 120ms, with native (meaning not paced) conduction, can proceed to give second dose if the QTc is < 570msec
    c. For paced QRS complex, QTc monitoring is not indicated, and thus would hold the medication and obtain an EP consult **only** if the patient experiences a ventricular arrhythmia
7. For concerns regarding ventricular arrhythmias or excessive QT prolongation, EP consult can be obtained to review the ECG
    a. Activation of a consult is completed using the usual protocol through IHIS
    b. For these consults, the primary team **must** upload each of the concerning telemetry strips and/or 12-lead ECG to the *Media tab* of the patient's IHIS chart
    c. The EP staff will complete a remote e-consult by reviewing the uploaded images in the *Media tab* of IHIS. The consult will provide an interpretation of the rhythm and QTc but cannot discern the risks/benefits of continued medical therapy
    d. EP staff will not be evaluating the patient with a face-to-face visit
    e. Overnight consultation will be reviewed the subsequent day and the e-consult will be completed in a timely manner
8. If any evidence of torsade de pointes on telemetry, discontinue CQ/HCQ and request EP consultation
9. Telemetry should be continued while the patient is receiving CQ/HCQ
10. Unless there is worrisome arrhythmia, the ECG needs to be obtained only at baseline and after the first dose of the medication

Appendix C. COVID-19 Medication Approval Process

		Day Response (0800-1700)	Night Response (1701-0759)
	Patient Scenario	**Who To Contact**	**Who To Contact**
COVID test pending	No ID consult or ID consult pending	On-Call ID Fellow	On-Call ID Fellow
COVID test positive	No ID consult, or ID consult pending **(placed after 1200)**	COVID Medication Approval Pager	COVID Medication Approval Pager
	ID consult pending **(placed before 1200)**	On-Call ID Fellow	On-Call ID Fellow
	ID actively following, review of ID note does not indicate need for therapy and COVID testing results **did not** return after ID note provided in chart	ID Service Fellow	On-Call ID Fellow
	ID actively following or suspect COVID note left, COVID positive result **did** return after ID note provided in chart	ID Service Fellow	COVID Medication Approval Pager
	ID actively following or suspect COVID note left, medication recommended but approval code not provided in note or order	ID Service Fellow	On-Call ID Fellow

Notes:

- Active/pending ID consults can be seen under the Referrals tab→IP Consult to Infectious Disease
- Remdesivir requests will be processed 0800-1700 each day
- Requests for emergent tocilizumab **must** be routed to the ID service fellow/on-call ID fellow (requires a conversation with the intensivist and ID attending)
- Discussion of the benefits vs risks of corticosteroids should be routed to the ID service fellow/on-call ID fellow

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COVID-19: Antimicrobial Treatment Guideline

- Recommendations below are meant to inform clinicians until further guidance becomes available from organizations such as the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Data surrounding treatment is rapidly evolving and these recommendations are subject to change.
- Of note, the *Infectious Diseases Society of America (IDSA)* and *National Institutes of Health (NIH)* currently do not recommend the use of any specific antiviral therapy unless used in the context of a clinical trial.
- Currently no medication therapies are directed specifically at COVID-19. The mainstay of treatment for most patients consists of supportive care and appropriate infection prevention and control measures
    - See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

Table 1: Treatment Recommendations for Highly Suspected / Confirmed COVID-19

Setting / Severity of Illness	Description	Treatment
Outpatients **Inpatients Mild Disease**	Inpatients without pneumonia and requiring < 4L of new O_2	• Supportive Care
Inpatients Moderate Disease	Pneumonia requiring hospitalization, not meeting criteria for severe disease OR no evidence of pneumonia, but requiring ≥ 4L of new O_2	• Strongly consider treatment if duration of illness ≥ 7 days • Inpatient Treatment requires approval 24/7 (Appendix C)
Inpatients Severe Disease	Requiring mechanical ventilation OR impending respiratory failure requiring intubation (RR > 30 breaths/minutes; O_2 saturation ≤ 93% on room air; PaO_2/FiO_2 ratio < 300 mmHg)	
Treatment recommendations regardless of age, comorbidities, or immunocompromised status		

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patient Meeting Criteria for Treatment

Medication	Dose	Indication for Use	Additional Information
Remdesivir	• **200 mg IV x 1 day** • **Then 100 mg IV daily x 4-9 days** • No adjustment for renal impairment/ ECMO	• Non-FDA-approved agent available via compassionate use, expanded access, and emergency use authorization	• See Appendix A for additional information on how to obtain this product • Baseline and daily hepatic function labs required
Hydroxychloroquine (Plaquenil®) PO Suspension (intubated) or Tablets (not intubated)	• **400 mg BID x 1 day** • **Then 200 mg PO BID x 4 days** • No adjustment for renal impairment • If inadequate supply, may substitute chloroquine 500 mg PO x 5-10 days (Appendix B) • May extend course up to 10 days based on clinical response	• Consider use in patients who do not meet criteria for remdesivir or while awaiting remdesivir	• May cause QTc prolongation (See Appendix B) • Tablets cannot be crushed – use suspension for tube administration
*Use of these agents to treat COVID-19 requires ASP approval **24 hours/day, 7 days/week** (Pager **#10307** or ID consult)*			

Table 3: Antimicrobial Therapies NOT Currently Recommended	
Medication	**Comments**
Azithromycin	• Insufficient data to support use • Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or required oxygen. • Previous study in MERS showed no benefit on mortality or viral clearance
Baloxavir marboxil	• No evidence to support use and potential for adverse effects, including severe and sometimes fatal hypersensitivity reactions
Interferon	• No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects
Ivermectin	• *In vitro* activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy • Based on *in vitro* findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations
Lopinavir/ritonavir	• No definitive evidence of benefit against SARS-CoV-2 *in vivo* • Available data has shown high rates of patient intolerance • The NIH guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial
Nitazoxanide	• *In vitro* activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19 • Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses
Oseltamivir	• No *in vitro* activity against coronaviruses • Should only be used in influenza is suspected or confirmed
Ribavirin	• Some data from other coronaviruses suggest synergy when given with lopinavir/ritonavir • No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potential benefit
Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	• Ongoing clinical trials with darunavir/cobicistat but no *in vitro* or clinical outcomes data • Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time
• *Due to lack of efficacy data and/or evidence of potential harm, the therapies above are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4)* • *Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19*	

Table 4: Other Therapies for Consideration	
Convalescent Plasma	• Refer to Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process for COVID-19 patients in whom this therapy is *recommended by an Infectious Disease provider*
Non-Antimicrobial Medications	• Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) refer to the Inpatient Evaluation and Management Guideline for COVID-19

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Appendix A: Request for Remdesivir Therapy

- Remdesivir is a non-FDA approved agent manufactured by Gilead Sciences.
- OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition via the compassionate use or expanded access protocol, or allocated supply under the emergency use authorization (EUA).
- The compassionate use program is an application process directly through the manufacturer and allows for single patient use of product. The manufacturer will ship medication to OSUWMC if approved.
- **Compassionate use is only available for pregnant patients with dyspnea** at this time.
- The expanded access protocol is offered through the manufacturer with multi-patient product use in select circumstances, with product storage at OSUWMC.
- **Expanded access protocol is only available for mechanically ventilated patients** and is not available to prisoners or patients located at the Ohio State University East Hospital.
- The emergency use authorization allows for use in adults with proven COVID-19 infections with O_2 < 94% on room air, requiring supplemental oxygen *or* mechanical ventilation *or* ECMO.
- Informed consent **is required** with all product pathways highlighted above.

Request Process	Additional Details
Treating physician determines if patient meets ineligibility criteria	**Ineligibility criteria:** • Known hypersensitivity to remdesivir • ALT ≥ 5 x UL of normal • eGFR < 30 mL/minute (unless benefit outweighs risk) • Symptoms of COVID-19 illness > 10 days • Mechanical ventilation > 14 days **AND** a negative current COVID-19 lower respiratory sample • Improving on current treatment/supportive regimen(s) as evidenced by improving oxygenation, and/or impending discharge • Patients in whom the clinical team believes death is in the immediate short-term and administration of remdesivir is unlikely to change the clinical outcome
Treating physician enters IHIS orders	• IP Infectious Diseases (if not already placed, reason for consult: "remdesivir") • IP Pharmacy (reason for consult: "other – please specify", specify "remdesivir")
Triage Team reviews requests *1-2 times daily* *7 days/week*	• Outcome will be provided in a written progress note *and* • Communicated directly to the primary team • See house staff announcement for further information on product screening and allocation • See expanded access or compassionate use sections for additional information if approved

Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	
Step	**Additional Details**

Informed Consent
Do not obtain consent until after approval
	• The treating physician must confirm consent with the patient or legally authorized representative and document all of the following in the chart:
	  ○ Patient given the Fact Sheet for Patients and Parents/Caregivers (English) or (Spanish)
	  ○ Patient was informed of alternatives to remdesivir
	  ○ Patient was informed that remdesivir is an unapproved drug authorized under EUA

Ordering Process	• After consent is documented, the treating physician should page the ASP pharmacist (x9394) to request placement of the remdesivir order • Remdesivir orders are only visible to pharmacists

Clinical Monitoring	• Baseline chemistries and hepatic function panel prior to beginning remdesivir therapy.
	  ○ Daily hepatic function panel throughout course
	  ○ Discontinue therapy if ALT > 5 x UL of normal OR ALT elevation with liver dysfunction
	• The Infectious Diseases team will assess the patient on treatment day 5 and recommend continuing or discontinuing therapy based on clinical response

Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	

Mandatory Medication Error and Adverse Event Reporting	• The treating physician is responsible for responding to requests from the FDA and reporting medication errors and adverse drug events **within 7 days** of the onset of the event
	• This report can be submitted online to FDA MedWatch **AFTER** a data release is granted by the institution. The description section of the report should denote "Remdesivir under EUA." A copy of the MedWatch form should also be forwarded to Gilead: safety_fc@gilead.com.
	• Adverse events that must be reported:
	  ○ Death or life-threatening adverse event
	  ○ Inpatient hospitalization or prolonging of existing hospitalization
	  ○ A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
	  ○ A congenital anomaly/birth defect
	  ○ A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly
	• An alternative to reporting to the FDA and manufacturer directly is allowing the medication safety team to do this on behalf of a provider. Submit a report in the Patient Safety Reporting System to initiate the process. Use the event type 'Adverse Drug Reaction'.

Table 6. Steps Alternative Programs *Following Approval*	
Expanded Access Protocol	• This program is directed by Dr. Kurt Stevenson and his team • The principal investigator will assist with patient enrollment, informed consent, product ordering, and ongoing monitoring for patients approved with this supply designated
Compassionate Use	• If the patient has been approved for compassionate use supply, the treating physician should submit a compassionate use request on behalf of the patient to Gilead at https://rdvcu.gilead.com/ • Once the request is submitted, Gilead will be in communication with the provider to approve or decline use and to request additional information ○ ASP/ID will assist the treating physician with these steps to ensure completeness and the requirements for ongoing data submission and adverse event reporting are met

	• For shipment of remdesivir use the following information when completing the form:
	  ○ Pharmacy/Hospital Name: The Ohio State University Medical Center
	  ○ Pharmacist/Pharmacy Contact Name: Investigational Drug Service
	  ○ Address:
	  ▪ Investigational Drug Service
	  460 W. 10th Avenue, Room C150N
	  Columbus, Ohio 43210
	  ○ Email: pharmacy.ids@osumc.edu
	  ○ Phone: 614-293-4560
	  ○ Cell Phone: 614-293-3312 (central pharmacy)

	• For after-hours assistance with drug receipt, see service coverage for IDS on-call or page 614-730-4615. • For more information regarding the compassionate use process in general, please refer to the OSUWMC Expanded Use ("Compassionate Use") of Investigational Products guideline

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Appendix B: Cardiac Monitoring for Chloroquine (CQ)/Hydroxychloroquine (HCQ)

☐	• Place patients on telemetry *and* • Obtain baseline 12 lead ECG
☐	• Discontinue all QT-prolonging medication if possible. ○ Consult medical specialty associated with medication for concerns with discontinuation risk or for alternatives • Consult pharmacy as needed for assistance with profile review to identify QT-prolonging medications

☐	• Correct electrolyte abnormalities, specifically
	  ○ Potassium (>4 mmol/L)
	  ○ Magnesium (>2 mg/dL)
	• Do not delay drug therapy as you replete electrolytes

☐	• The likelihood for a malignant ventricular arrhythmia or a worrisome prolongation of the QTc is low (<2%)
☐	• Regardless of the pre-drug / baseline QTc, give first dose

☐	• Obtain 6-lead telemetry or 12-lead ECG 2 hours after first dose:
	
	  ○ If pre-drug QRS duration is **< 120ms**, proceed with second dose if the QTc < 520msec
	  ○ If pre-drug QRS duration is **> 120ms**, with native (meaning not paced) conduction, proceed with second dose if the QTc is < 570msec
	
	• For paced QRS complex, QTc monitoring is not indicated, and thus would hold the medication and obtain an EP consult **only** if the patient experiences a ventricular arrhythmia

☐	• For concerns regarding ventricular arrhythmias or excessive QT prolongation, EP consult can be obtained to review the ECG
	  ○ Consult per usual via IHIS
	  ○ For these consults, the primary team **must** upload each of the concerning telemetry strips and/or 12-lead ECG to the *Media tab* of the patient's IHIS chart
	  ○ The EP staff will complete a remote e-consult by reviewing the uploaded images in the *Media tab* of IHIS. The consult will provide an interpretation of the rhythm and QTc but cannot discern the risks/benefits of continued medical therapy
	  ○ EP staff will <u>not</u> be evaluating the patient with a face-to-face visit
	  ○ Overnight consultation will be reviewed the subsequent day and the e-consult will be completed in a timely manner

☐	• If any evidence of torsade de pointes on telemetry, discontinue CQ/HCQ and request EP consultation
☐	• Telemetry should be continued while the patient is receiving CQ/HCQ
☐	• Unless there is worrisome arrhythmia, the ECG needs to be obtained only at baseline and after the first dose of the medication

Appendix C: COVID-19 Medication Approval Process

	Patient Scenario	Who to Contact Day Response (0800-1700)	Who to Contact Night Response (1701-0759)
COVID test pending	No ID consult or ID consult pending	On-Call ID Fellow	On-Call ID Fellow
COVID test positive	No ID consult or ID consult pending (**placed after 1200**)	COVID Medication Approval Pager	COVID Medication Approval Pager
	ID consulting pending (**placed before 1200**)	On-Call ID Fellow	On-Call ID Fellow
	ID actively following, review of ID note does not indicate need for therapy and COVID testing results **did not** return after ID note provided in chart	ID Service Fellow	On-Call ID Fellow
	ID actively following or suspect COVID note left, COVID positive result **did** return after ID note provided in chart	ID Service Fellow	COVID Medication Approval Pager
	ID actively following or suspect COVID note left, medication recommended but approval code not provided in note or order	ID Service Fellow	On-Call ID Fellow

Notes:
- Active/pending ID consults can be seen under the Referral tab → IP Consult to Infectious Disease
- Remdesivir requests are processed through IHIS consult orders and Triage Team review
- Requests for emergent tocilizumab **must** be routed to the ID service fellow/on-call ID fellow (requires a conversation with a critical care faculty attending and ID attending)
- Discussion of the benefits vs risks of corticosteroids should be routed to the ID service fellow/on-call ID fellow

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COVID-19: Antimicrobial Treatment Guideline

- Recommendations below are meant to inform clinicians until further guidance becomes available from organizations such as the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Data surrounding treatment is rapidly evolving and these recommendations are subject to change.
- Of note, the *Infectious Diseases Society of America (IDSA)* and *National Institutes of Health (NIH)* currently do not recommend the use of any specific antiviral therapy unless used in the context of a clinical trial.
- Currently no medication therapies are directed specifically at COVID-19. The mainstay of treatment for most patients consists of supportive care and appropriate infection prevention and control measures
    - See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

Table 1: Treatment Recommendations for Highly Suspected / Confirmed COVID-19

Setting / Severity of Illness	Description	Treatment
Outpatients	All outpatients	Supportive care
Inpatients Mild Disease	Inpatients without pneumonia and SpO_2 > 94% on room air	
Inpatients Severe Disease	Inpatients with $SpO_2 \leq 94\%$ on room air; requiring supplemental oxygen, mechanical ventilation, or ECMO	Consider treatment and/or enrollment in clinical trial(s)
Treatment recommendations regardless of age, comorbidities, or immunocompromised status		

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patient Meeting Criteria for Treatment

Medication	Dose	Indication for Use	Additional Information
Remdesivir	**200 mg IV for 1 day** **Then 100 mg IV daily for 4 – 9 days** No adjustment for renal impairment/ ECMO	• Non-FDA-approved agent available via compassionate use and emergency use authorization	• See Appendix A for additional information on how to obtain this product • Baseline and daily serum creatinine and hepatic function labs required

Table 3: Other Therapies for Consideration in Patients Meeting Criteria for Treatment

Convalescent Plasma	• Refer to Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process
Non-Antimicrobial Medications	• Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) refer to the Inpatient Evaluation and Management Guideline
Refer to the COVID-19 Clinical Trials Document for information regarding other potential therapies, including points of contact and inclusion/exclusion criteria.	

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Table 4: Antimicrobial Therapies NOT Currently Recommended	
Medication	**Comments**
Azithromycin	• Insufficient data to support use • Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or required oxygen • Previous study in MERS showed no benefit on mortality or viral clearance
Baloxavir marboxil	• No evidence to support use and potential for adverse effects, including severe and sometimes fatal hypersensitivity reactions
Interferon	• No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects
Ivermectin	• *In vitro* activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy • Based on *in vitro* findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations
Lopinavir/ritonavir	• No definitive evidence of benefit against SARS-CoV-2 *in vivo* • Available data has shown high rates of patient intolerance • The NIH guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial
Nitazoxanide	• *In vitro* activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19 • Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses
Oseltamivir	• No *in vitro* activity against coronaviruses • Should only be used in influenza is suspected or confirmed
Ribavirin	• Some data from other coronaviruses suggest synergy when given with lopinavir/ritonavir • No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potential benefit
Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	• Ongoing clinical trials with darunavir/cobicistat but no *in vitro* or clinical outcomes data • Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time

- *Due to lack of efficacy data and/or evidence of potential harm, the therapies above are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4)*
- *Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19*

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Appendix A: Request for Remdesivir Therapy

- Remdesivir is a non-FDA approved agent manufactured by Gilead Sciences.
- OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition via the compassionate use or allocated supply under the emergency use authorization (EUA).
- The compassionate use program is an application process directly through the manufacturer and allows for single patient use of product. The manufacturer will ship medication to OSUWMC if approved.
- **Compassionate use is only available for pregnant patients with dyspnea** at this time. Consideration will be made by the Triage Team for emergency use authorization supply to expedite therapy initiation in pregnant patients.
- The emergency use authorization allows for use in adults with proven COVID-19 infections with $O_2 \leq 94\%$ on room air, requiring supplemental oxygen *or* mechanical ventilation *or* ECMO.
- **Emergency use authorization *does* allow for inclusion in clinical trials (unless otherwise stated within the study protocol) and use of other COVID adjunctive therapies (e.g. convalescent plasma, tocilizumab).**

Request Process	Additional Details
Treating provider should follow each step below and then refer to Table 5 or 6 depending on approved supply.	
(1) Treating physician determines if patient meets ineligibility criteria	**Ineligibility criteria:** • Known hypersensitivity to remdesivir • ALT ≥ 5 x UL of normal • eGFR < 30 mL/minute (unless benefit outweighs risk) • Symptoms of COVID-19 illness > 10 days • Mechanical ventilation > 14 days **AND** a negative current COVID-19 lower respiratory sample • Improving on current treatment/supportive regimen(s) as evidenced by improving oxygenation, and/or impending discharge • Patients in whom the clinical team believes death is in the immediate short-term and administration of remdesivir is unlikely to change the clinical outcome
(2) Physician enters IHIS orders	• IP Infectious Diseases (if not already placed, reason for consult: "remdesivir") • IP Pharmacy (reason for consult: "other – please specify", specify "remdesivir")
(3) Triage Team reviews request *1-2 times daily 7 days/week*	• Outcome will be provided in a written progress note *and* • Communicated directly to the primary team • See house staff announcement for further information on product screening and allocation • See expanded access or compassionate use sections for additional information if approved

Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	
Step	**Additional Details**
(1) Informed Consent *Do not obtain consent until after approval*	• The treating physician must confirm *verbal* consent with the patient or legally authorized representative (LAR). A prisoner can provide *verbal* consent if able, if unable to consent, the warden may be contacted to consider consent. The following specific verbiage should be documented in the chart: ○ Patient/LAR given the Fact Sheet for Patients and Parents/Caregivers (English/Spanish) ○ Patient/LAR was informed of alternatives to remdesivir ○ Patient/LAR was informed that remdesivir is an unapproved drug authorized under EUA
(2) Ordering Process	• After verbal consent is documented, the treating physician should page the ASP pharmacist (x9394) to request placement of the remdesivir order • Remdesivir orders are only visible to pharmacists
(3) Clinical Monitoring	• Baseline chemistries and hepatic function panel prior to beginning remdesivir therapy. ○ Daily serum creatinine and hepatic function panel throughout course ○ Discontinue therapy if ALT > 5 x UL of normal OR ALT elevation with liver dysfunction • The Infectious Diseases team will assess the patient on treatment day 5 and recommend continuing or discontinuing therapy based on clinical response

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Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	

(4) Mandatory Medication Error and Adverse Event Reporting	• The treating physician is responsible for responding to requests from the FDA and reporting adverse drug events **within 7 days** of the onset of the event
	• This report can be submitted online to FDA MedWatch **AFTER** a data release is granted by the institution. The description section of the report should denote "Remdesivir under EUA." A copy of the MedWatch form should also be forwarded to Gilead: safety_fc@gilead.com.
	• Adverse events that must be reported:
	  ○ Death or life-threatening adverse event
	  ○ Inpatient hospitalization or prolonging of existing hospitalization
	  ○ A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
	  ○ A congenital anomaly/birth defect
	  ○ A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly
	• An alternative to reporting to the FDA and manufacturer directly is allowing the medication safety team to do this on behalf of a provider. Submit a report in the Patient Safety Reporting
	• System to initiate the process. Use the event type 'Adverse Drug Reaction'.
	• Medication errors should be reported through the Patient Safety Reporting System as well.

Table 6. Steps for Remdesivir Compassionate Use Ordering and Monitoring *Following Approval*	
Compassionate Use	• If the patient has been approved for compassionate use supply, the treating physician should submit a compassionate use request on behalf of the patient to Gilead at https://rdvcu.gilead.com/ • Once the request is submitted, Gilead will be in communication with the provider to approve or decline use and to request additional information ○ ASP/ID will assist the treating physician with these steps to ensure completeness and the requirements for ongoing data submission and adverse event reporting are met

	• For shipment of remdesivir use the following information when completing the form:
	  ○ Pharmacy/Hospital Name: The Ohio State University Medical Center
	  ○ Pharmacist/Pharmacy Contact Name: Investigational Drug Service
	  ○ Address:
	  ▪ Investigational Drug Service
	  460 W. 10th Avenue, Room C150N Columbus,
	  Ohio 43210
	  ○ Email: pharmacy.ids@osumc.edu
	  ○ Phone: 614-293-4560
	  ○ Cell Phone: 614-293-3312 (central pharmacy)

	• For after-hours assistance with drug receipt, see service coverage for IDS on-call or page 614-730-4615 • For more information regarding the compassionate use process in general, please refer to the OSUWMC Expanded Use ("Compassionate Use") of Investigational Products guideline

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- Infectious Disease
- Pharmacy

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- Pharmacy & Therapeutics Executive/MUE

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COVID-19: Antimicrobial Treatment Guideline

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    - See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

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Setting / Severity of Illness	**Description**	**Treatment**
Outpatients	All outpatients	Supportive care
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Inpatients Severe Disease	Inpatients with $SpO_2 \leq 94\%$ on room air; requiring supplemental oxygen, mechanical ventilation, or ECMO	Consider treatment and/or enrollment in clinical trial(s)
Treatment recommendations regardless of age, comorbidities, or immunocompromised status		

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patient Meeting Criteria for Treatment			
Medication	**Dose**	**Indication for Use**	**Additional Information**
Remdesivir	**200 mg IV for 1 day** **Then 100 mg IV daily for 4 – 9 days** No adjustment for renal impairment/ ECMO	• Non-FDA-approved agent available via compassionate use and emergency use authorization	• See Appendix A for additional information on how to obtain this product • Baseline and daily serum creatinine and hepatic function labs required • Avoid combination therapy with hydroxychloroquine/ chloroquine due to in vitro antagonism • The clinical relevance of in vitro CYP drug-drug interactions has not been established.

Table 3: Other Therapies for Consideration in Patients Meeting Criteria for Treatment	
Convalescent Plasma	• Refer to Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process

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Non-Antimicrobial Medications	• Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) refer to the Inpatient Evaluation and Management Guideline
Refer to the COVID-19 Clinical Trials Document for information regarding other potential therapies, including points of contact and inclusion/exclusion criteria.	

Table 4: Antimicrobial Therapies NOT Currently Recommended

Medication	Comments
Azithromycin	• Insufficient data to support use • Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or required oxygen • Previous study in MERS showed no benefit on mortality or viral clearance
Baloxavir marboxil	• No evidence to support use and potential for adverse effects, including severe and sometimes fatal hypersensitivity reactions
Interferon	• No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects
Ivermectin	• *In vitro* activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy • Based on *in vitro* findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations
Lopinavir/ritonavir	• No definitive evidence of benefit against SARS-CoV-2 *in vivo* • Available data has shown high rates of patient intolerance • The NIH guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial
Nitazoxanide	• *In vitro* activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19 • Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses
Oseltamivir	• No *in vitro* activity against coronaviruses • Should only be used in influenza is suspected or confirmed
Ribavirin	• Some data from other coronaviruses suggest synergy when given with lopinavir/ritonavir • No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potential benefit

Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	• Ongoing clinical trials with darunavir/cobicistat but no *in vitro* or clinical outcomes data • Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time

- *Due to lack of efficacy data and/or evidence of potential harm, the therapies above are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4)*
- *Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19*

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Appendix A: Request for Remdesivir Therapy

- Remdesivir is a non-FDA approved agent manufactured by Gilead Sciences.
- OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition via the compassionate use or allocated supply under the emergency use authorization (EUA).
- The compassionate use program is an application process directly through the manufacturer and allows for single patient use of product. The manufacturer will ship medication to OSUWMC if approved.
- **Compassionate use is only available for pregnant patients with dyspnea** at this time. Consideration will be made by the Triage Team for emergency use authorization supply to expedite therapy initiation in pregnant patients.
- The emergency use authorization allows for use in adults with proven COVID-19 infections with $O_2 \leq 94\%$ on room air, requiring supplemental oxygen *or* mechanical ventilation *or* ECMO.
- **Emergency use authorization *does* allow for inclusion in clinical trials (unless otherwise stated within the study protocol) and use of other COVID adjunctive therapies (e.g. convalescent plasma, tocilizumab).**
- **Refer to the Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of Remdesivir for more information on this therapy.**

Request Process	Additional Details
Treating provider should follow each step below and then refer to Table 5 or 6 depending on approved supply.	
(1) Treating physician determines if patient meets ineligibility criteria	**Ineligibility criteria:** • Known hypersensitivity to remdesivir • ALT ≥ 5 x UL of normal • eGFR < 30 mL/minute calculated using the Cockcroft-Gault Equation (unless benefit outweighs risk) • Mechanical ventilation > 14 days **AND** a negative current COVID-19 lower respiratory sample • Improving on current treatment/supportive regimen(s) as evidenced by improving oxygenation, and/or impending discharge • Patients in whom the clinical team believes death is in the immediate short-term and administration of remdesivir is unlikely to change the clinical outcome
(2) Physician enters IHIS orders	• IP Infectious Diseases (if not already placed, reason for consult: "remdesivir") • IP Pharmacy (reason for consult: "other – please specify", specify "remdesivir")

(3) Triage Team reviews request
1-2 times daily
7 days/week
	• Patient eligibility is determined by the Team using the following criteria:
	  • Tier I. COVID+ patients with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) less than or equal to 10 days and:
	  • Pregnancy **OR**
	  • New and/or progressive requirement of supplemental oxygen defined as at least ≥4 LPM nasal cannula **OR**
	  • Mechanical ventilation ≤ 72 hours
	  • Tier II. When sufficient supply of 220 vials (i.e., 20 patients) on hand and uncertain supply chain:
	  • COVID+ patients **AND**
	  o Pregnancy with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) greater than 10 days **OR**
	  • Respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) for 10 to 14 days **AND** new and/or progressive requirement of supplemental oxygen defined as at least ≥4 LPM nasal cannula including ≤ 72 hours mechanical ventilation **OR**
	  • Any new and/or progressive supplemental oxygen requirement (including mechanical ventilation <72h) up to day 14 since respiratory symptom (e.g., new cough, dyspnea, or hypoxia) onset **AND**

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	○ High risk requiring a high-risk score determined by the Calculation Tool for Predicting Critically-Ill COVID-19 (http://118.126.104.170/) at Admission[1] **OR** ○ Identified as having two or more high risk factors as defined by the CDC for developing severe illness from COVID-19: • People age > 65 • People with chronic lung disease, including COPD, asthma, interstitial lung disease, cystic fibrosis • People with cardiac disease, including coronary artery disease, congestive heart failure, implanted cardiac device • People with BMI > 40 • People with DM • People who are immunocompromised (i.e., active chemotherapy, bone marrow or organ transplantation, immune deficiency, poorly controlled HIV or AIDS) • Tier III. When sufficient supply of 1100 vials (i.e., 100 patients) on hand and uncertain supply chain: • COVID+ patients at any illness duration with new or/and progressive requirement of supplemental oxygen defined as at least ≥4 LPM nasal cannula but NOT requiring mechanical ventilation. • Outcome will be provided in a written progress note *and* • Communicated directly to the primary team • Approval is valid for 24 hours, beyond which time re-evaluation by the Committee would be needed • See expanded access or compassionate use sections for additional information if approved

Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	
Step	**Additional Details**
(1) Informed Consent *Do not obtain consent until after approval*	• The treating physician must confirm *verbal* consent with the patient or legally authorized representative (LAR). A prisoner can provide *verbal* consent if able, if unable to consent, the warden may be contacted to consider consent. The following specific verbiage should be documented in the chart: ○ Patient/LAR given the Fact Sheet for Patients and Parents/Caregivers (English/Spanish) ○ Patient/LAR was informed of alternatives to remdesivir ○ Patient/LAR was informed that remdesivir is an unapproved drug authorized under EUA • If consent cannot be obtained from the patient and LAR cannot be identified, an ethics consult should be placed
(2) Ordering Process	• After verbal consent is documented, the treating physician should page the ASP pharmacist (x9394) to request placement of the remdesivir order • Remdesivir orders are only visible to pharmacists
(3) Clinical Monitoring	• Baseline chemistries and hepatic function panel prior to beginning remdesivir therapy. ○ Daily serum creatinine and hepatic function panel throughout course ○ Discontinue therapy if ALT > 5 x UL of normal OR ALT elevation with liver dysfunction • The Infectious Diseases team will assess the patient on treatment day 5 and recommend continuing or discontinuing therapy based on clinical response

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Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*	
(4) Mandatory Medication Error and Adverse Event Reporting	• The treating physician is responsible for responding to requests from the FDA and reporting adverse drug events **within 7 days** of the onset of the event • This report can be submitted online to FDA MedWatch **AFTER** a data release is granted by the institution. The description section of the report should denote "Remdesivir under EUA." A copy of the MedWatch form should also be forwarded to Gilead: safety_fc@gilead.com. • Adverse events that must be reported: o Death or life-threatening adverse event o Inpatient hospitalization or prolonging of existing hospitalization o A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions o A congenital anomaly/birth defect o A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly • An alternative to reporting to the FDA and manufacturer directly is allowing the medication safety team to do this on behalf of a provider. Submit a report in the Patient Safety Reporting System to initiate the process. Use the event type 'Adverse Drug Reaction'. • Medication errors should be reported through the Patient Safety Reporting System as well.

Table 6. Steps for Remdesivir Compassionate Use Ordering and Monitoring *Following Approval*	
Compassionate Use	• If the patient has been approved for compassionate use supply, the treating physician should submit a compassionate use request on behalf of the patient to Gilead at https://rdvcu.gilead.com/ • Once the request is submitted, Gilead will be in communication with the provider to approve or decline use and to request additional information o ASP/ID will assist the treating physician with these steps to ensure completeness and the requirements for ongoing data submission and adverse event reporting are met
	• For shipment of remdesivir use the following information when completing the form: o Pharmacy/Hospital Name: The Ohio State University Medical Center o Pharmacist/Pharmacy Contact Name: Investigational Drug Service o Address: ▪ Investigational Drug Service 460 W. 10th Avenue, Room C150N Columbus, Ohio 43210 o Email: pharmacy.ids@osumc.edu o Phone: 614-293-4560 o Cell Phone: 614-293-3312 (central pharmacy)
	• For after-hours assistance with drug receipt, see service coverage for IDS on-call or page 614-730-4615 • For more information regarding the compassionate use process in general, please refer to the OSUWMC Expanded Use ("Compassionate Use") of Investigational Products guideline

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Authors

- Antimicrobial Stewardship Program (ASP)

Department(s)

- Infectious Disease
- Pharmacy

Approved by

- Pharmacy & Therapeutics Executive/MUE

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COVID-19: Antimicrobial Treatment Guideline

- Recommendations below are meant to inform clinicians until further guidance becomes available from organizations such as the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Data surrounding treatment is rapidly evolving and these recommendations are subject to change.
- Currently no FDA-approved medication therapies are directed specifically at COVID-19. The mainstay of treatment for most patients consists of supportive care and appropriate infection prevention and control measures.
    - See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

Table 1: Treatment Recommendations for Highly Suspected / Confirmed COVID-19

Setting / Severity of Illness	Description	Treatment
Outpatients	All outpatients	Supportive care
Inpatients Mild Disease	Inpatients without pneumonia and SpO_2 > 94% on room air	
Inpatients Severe Disease	Inpatients with $SpO_2 \leq 94\%$ on room air; requiring supplemental oxygen, mechanical ventilation, or ECMO	Consider treatment and/or enrollment in clinical trial(s)
Treatment recommendations regardless of age, comorbidities, or immunocompromised status		

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patient Meeting Criteria for Treatment

Medication	Dose	Indication for Use	Additional Information
Remdesivir	**200 mg IV for 1 day** **Then 100 mg IV daily for 4 – 9 days** No adjustment for renal impairment/ ECMO	• Non-FDA-approved agent available via compassionate use and emergency use authorization	• See Appendix A for additional information on how to obtain this product • Baseline and daily serum creatinine and hepatic function labs required • Avoid combination therapy with hydroxychloroquine/ chloroquine due to in vitro antagonism • The clinical relevance of in vitro CYP drug-drug interactions has not been established.

Table 3: Other Therapies for Consideration in Patients Meeting Criteria for Treatment

Convalescent Plasma	• Refer to Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process
Non-Antimicrobial Medications	• Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) refer to the Inpatient Evaluation and Management Guideline
Refer to the COVID-19 Clinical Trials Document for information regarding other potential therapies, including points of contact and inclusion/exclusion criteria.	

Table 4: Antimicrobial Therapies NOT Currently Recommended	
Medication	**Comments**
Azithromycin	• Insufficient data to support use • Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or requiredoxygen • Previous study in MERS showed no benefit on mortality or viralclearance
Baloxavir marboxil	• No evidence to support use and potential for adverse effects, including severeand sometimes fatal hypersensitivity reactions
Interferon	• No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects
Ivermectin	• *In vitro* activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy • Based on *in vitro* findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations
Lopinavir/ritonavir	• No definitive evidence of benefit against SARS-CoV-2 *in vivo* • Available data has shown high rates of patient intolerance • The NIH guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial
Nitazoxanide	• *In vitro* activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19 • Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses
Oseltamivir	• No *in vitro* activity against coronaviruses • Should only be used in influenza is suspected or confirmed
Ribavirin	• Some data from other coronaviruses suggest synergy when given withlopinavir/ritonavir • No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potentialbenefit
Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	• Ongoing clinical trials with darunavir/cobicistat but no *in vitro* or clinical outcomes data • Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time
• *Due to lack of efficacy data and/or evidence of potential harm, the therapies above are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4)* • *Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19*	

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Appendix A: Request for Remdesivir Therapy

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- OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition via the compassionate use or allocated supply under the emergency use authorization (EUA).
- The compassionate use program is an application process directly through the manufacturer and allows for single patient use of product. The manufacturer will ship medication to OSUWMC ifapproved.
- **Compassionate use is only available for pregnant patients with dyspnea** at this time. Consideration will be made by the Triage Team for emergency use authorization supply to expedite therapy initiation in pregnant patients.
- The emergency use authorization allows for use in adults with proven COVID-19 infections with $O_2 \leq 94\%$ on room air, requiring supplemental oxygen *or* mechanical ventilation *or* ECMO.
- **Emergency use authorization *does* allow for inclusion in clinical trials (unless otherwise stated within the study protocol) and use of other COVID adjunctive therapies (e.g. convalescent plasma, tocilizumab).**
- **Refer to the Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of Remdesivir for more information on this therapy.**

Request Process

Treating provider should follow each step below and then refer to Table 5 or 6 depending on approved supply.

(1) Treating physician determines if patient meets ineligibility criteria

Ineligibility criteria:

- Known hypersensitivity to remdesivir
- ALT ≥ 5 x UL of normal
- eGFR < 30 mL/minute calculated using the Cockcroft-Gault Equation (unless benefit outweighs risk)
- Mechanical ventilation > 14 days **AND** a negative current COVID-19 lower respiratory sample
- Improving on current treatment/supportive regimen(s) as evidenced by improving oxygenation, and/or impending discharge
- Patients in whom the clinical team believes death is in the immediate short-term and administration of remdesivir is unlikely to change the clinical outcome

(2) Physician enters IHIS orders

- IP Infectious Diseases (if not already placed, reason for consult: "remdesivir")
- IP Pharmacy (reason for consult: "other – please specify", specify "remdesivir")

(3) Triage Team reviews request *1-2 times daily7 days/week*
Patient eligibility is determined by Team using the following criteria (Tier I, II, III)

- **Tier I**. COVID+ patients with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) less than or equal to 10 days **and**:
  - Pregnancy **OR** New and/or progressive requirement of supplemental oxygen defined as at least ≥ 4 LPM nasal cannula **OR** Mechanical ventilation ≤ 72 hours

- **Tier II.** When sufficient supply of 220 vials (i.e., 20 patients) on hand and uncertain supply chain:
  - COVID+ patients **AND** Pregnancy with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) greater than 10 days **OR**
  - Respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) for 10 to 14 days **AND** new and/or progressive requirement of supplemental oxygen defined as at least ≥4 LPM nasal cannula including ≤ 72 hours mechanical ventilation **OR**
  - Any new and/or progressive supplemental oxygen requirement (including
  - mechanical ventilation <72h) up to day 14 since respiratory symptom (e.g., new cough, dyspnea, or hypoxia) onset **AND** High risk requiring a high-risk score determined by the Calculation Tool for Predicting Critically-Ill COVID-19 (http://118.126.104.170/) at Admission[1] **OR**
  - Identified as having two or more high risk factors as defined by the CDC for developing severe illness from COVID-19:
    - People age > 65
    - People with chronic lung disease, including COPD, asthma, interstitial lung disease, cystic fibrosis
    - People with cardiac disease, including coronary artery disease, congestive heart failure, implanted cardiac device
    - People with BMI > 30
    - People with DM
    - People who are immunocompromised (i.e., active chemotherapy, bone marrow or organ transplantation, immune deficiency, poorly controlled HIV or AIDS)
    - People with hemoglobin disorders such as sickle cell disease and thalassemia

Request Process
• **Tier III.** When sufficient supply of 1100 vials (i.e., 100 patients) on hand and uncertain supply chain: ○ COVID+ patients at any illness duration with new or/and progressive requirement of supplemental oxygen defined as at least ≥ 4 LPM nasal cannula but NOT requiring mechanical ventilation.
• Outcome will be provided in a written progress note *and* • Communicated directly to the primary team • Approval is valid for 24 hours, beyond which time re-evaluation by the Committee would be needed • See expanded access or compassionate use sections for additional information if approved

Table 5: Steps for Remdesivir EUA Ordering and Monitoring *Following Approval*
(1) Informed Consent *(Do not obtain consent until after approval)*

• The treating physician must confirm *verbal* consent with the patient or legally authorized representative (LAR). A prisoner can provide *verbal* consent if able, if unable to consent, the warden may be contacted to consider consent. The following specific verbiage should be documented in the chart:
  ○ Patient/LAR given the Fact Sheet for Patients and Parents/Caregivers (English/Spanish)
  ○ Patient/LAR was informed of alternatives to remdesivir
  ○ Patient/LAR was informed that remdesivir is an unapproved drug authorized under EUA
• If consent cannot be obtained from the patient and LAR cannot be identified, an ethics consult should be placed

(2) Ordering Process
• After verbal consent is documented, the treating physician should page the ASP pharmacist (x9394) to request placement of the remdesivir order • Remdesivir orders are only visible to pharmacists
(3) Clinical Monitoring

• Baseline chemistries and hepatic function panel prior to beginning remdesivir therapy.
  ○ Daily serum creatinine and hepatic function panel throughout course
  ○ Discontinue therapy if ALT > 5 x UL of normal OR ALT elevation with liver dysfunction
• The Infectious Diseases team will assess the patient on treatment day 5 and recommend continuing or discontinuing therapy based on clinical response

(4) Mandatory Medication Error and Adverse Event Reporting

• The treating physician is responsible for responding to requests from the FDA and reporting adverse drug events **within 7 days** of the onset of the event
• This report can be submitted online to FDA MedWatch **AFTER** a data release is granted by the institution. The description section of the report should denote "Remdesivir under EUA." A copy of the MedWatch form should also be forwarded to Gilead: safety_fc@gilead.com.
• Adverse events that must be reported:
  ○ Death or life-threatening adverse event
  ○ Inpatient hospitalization or prolonging of existing hospitalization
  ○ A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
  ○ A congenital anomaly/birth defect
  ○ A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly
• An alternative to reporting to the FDA and manufacturer directly is allowing the medication safety team to do this on behalf of a provider. Submit a report in the Patient Safety Reporting
• System to initiate the process. Use the event type 'Adverse Drug Reaction'.
• Medication errors should be reported through the Patient Safety Reporting System as well.

Table 6. Steps for Remdesivir Compassionate Use Ordering and Monitoring *Following Approval*	
Compassionate Use	• If the patient has been approved for compassionate use supply, the treating physician should submit a compassionate use request on behalf of the patient to Gilead at https://rdvcu.gilead.com/ • Once the request is submitted, Gilead will be in communication with the provider to approve or decline use and to request additional information o ASP/ID will assist the treating physician with these steps to ensure completeness and the requirements for ongoing data submission and adverse event reporting are met

	• For shipment of remdesivir use the following information when completing the form:
	  o Pharmacy/Hospital Name: The Ohio State University Medical Center
	  o Pharmacist/Pharmacy Contact Name: Investigational Drug Service
	  o Address:
	  ▪ Investigational Drug Service
	  460 W. 10th Avenue, Room C150N Columbus,
	  Ohio 43210
	  o Email: pharmacy.ids@osumc.edu
	  o Phone: 614-293-4560
	  o Cell Phone: 614-293-3312 (central pharmacy)

	• For after-hours assistance with drug receipt, see service coverage for IDS on-call or page 614-730-4615 • For more information regarding the compassionate use process in general, please refer to the OSUWMC Expanded Use ("Compassionate Use") of Investigational Products guideline

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COVID-19: Antimicrobial Treatment Guideline

- Recommendations below are meant to inform clinicians until further guidance becomes available from organizations such as the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO). Data surrounding treatment is rapidly evolving and these recommendations are subject to change.
- Currently no FDA-approved medication therapies are directed specifically at COVID-19. The mainstay of treatment for most patients consists of supportive care and appropriate infection prevention and controlmeasures.
    - See the Inpatient Evaluation and Management Guidelines for COVID-19 for additional information

Table 1: Treatment Recommendations for Highly Suspected / Confirmed COVID-19

Setting / Severity of Illness	Description	Treatment
Outpatients	All outpatients	Supportive care
Inpatients Mild Disease	Inpatients without pneumonia and SpO_2 > 94% on room air	
Inpatients Severe Disease	Inpatients with $SpO_2 \leq 94\%$ on room air; requiring supplemental oxygen, mechanical ventilation, or ECMO	Consider treatment and/or enrollment in clinical trial(s)
Treatment recommendations regardless of age, comorbidities, or immunocompromised status		

Table 2: Adjunctive Antimicrobial Therapies to Consider in Patient Meeting Criteria for Treatment

Medication	Dose	Indication for Use	Additional Information
Remdesivir	**200 mg IV for 1 day** **Then 100 mg IV daily for 4 – 9 days (Refer to Table 5 in Appendix A)** No adjustment for renal impairment/ ECMO	• Non-FDA-approved agent available via emergency use authorization	• See Appendix A for additional information on how to obtain this product • Baseline and daily serum creatinine and hepatic function labs required • Avoid combination therapy with hydroxychloroquine/ chloroquine due to in vitro antagonism • The clinical relevance of in vitro CYP drug-drug interactions has not been established.

Table 3: Other Therapies for Consideration in Patients Meeting Criteria for Treatment

Convalescent Plasma	• Refer to Convalescent Plasma Expanded Access Program Workflow for information regarding eligibility, patient consent, and the approval process
Non-Antimicrobial Medications	• Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, tocilizumab, corticosteroids, ACEI/ARBs, NSAIDS, etc.) refer to the Inpatient Evaluation and Management Guideline
Refer to the COVID-19 Clinical Trials Document for information regarding other potential therapies, including points of contact and inclusion/exclusion criteria.	

Table 4: Antimicrobial Therapies NOT Currently Recommended	
Medication	**Comments**
Azithromycin	• Insufficient data to support use • Open label study (n=80) suggested benefit when given in combination with hydroxychloroquine, but many patients were asymptomatic or had upper respiratory symptoms only, and only 15% were febrile or required oxygen • Previous study in MERS showed no benefit on mortality or viral clearance
Baloxavir marboxil	• No evidence to support use and potential for adverse effects, including severe and sometimes fatal hypersensitivity reactions
Chloroquine/ Hydroxychloroquine	• Not recommended for prophylaxis or treatment of SARS-CoV-2 outside of a clinical trial
Interferon	• No definitive evidence of benefit against SARS-CoV-2 and other coronaviruses and significant potential for adverse effects
Ivermectin	• *In vitro* activity against SARS-CoV-2 and other viruses, but no clinical outcomes data specific to COVID-19 to suggest safety or efficacy • Based on *in vitro* findings, significantly higher doses than usually given would be required to achieve adequate serum concentrations
Lopinavir/ritonavir	• No definitive evidence of benefit against SARS-CoV-2 *in vivo* • Available data has shown high rates of patient intolerance • The NIH guidelines recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors for the treatment of COVID-19, except in the context of a clinical trial
Nitazoxanide	• *In vitro* activity against SARS-CoV-2 and other coronaviruses but no clinical outcomes data specific to COVID-19 • Failed to demonstrate benefit when added to standard care in randomized controlled trial of patients hospitalized with respiratory viral illness including small number with other coronaviruses
Oseltamivir	• No *in vitro* activity against coronaviruses • Should only be used in influenza is suspected or confirmed
Ribavirin	• Some data from other coronaviruses suggest synergy when given with lopinavir/ritonavir • No definitive evidence of benefit against SARS-CoV-2 *in vivo*, and risk of toxicity with higher doses that were used for SARS and MERS outweigh potential benefit
Other antiretrovirals (e.g. abacavir, boosted darunavir, tenofovir)	• Ongoing clinical trials with darunavir/cobicistat but no *in vitro* or clinical outcomes data • Other agents such as abacavir, tenofovir, and nelfinavir have been proposed, but not enough data to support use at this time • The NIH guidelines recommend against the use of these agents for the treatment of COVID-19, except in the context of a clinical trial

- *Due to lack of efficacy data and/or evidence of potential harm, the therapies above are not recommended for the specific treatment of COVID-19 at this time, unless otherwise indicated (Table 4)*
- *Of note, Vitamin C, Vitamin D, zinc, nor any medications listed in Tables 2-3 have been shown to prevent COVID-19*

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Appendix A: Remdesivir Approval Process

- Remdesivir is a non-FDA approved agent manufactured by Gilead Sciences.
- OSUWMC is not enrolled in remdesivir clinical trials; therefore, the mode of acquisition is via emergency use authorization (EUA).
- The emergency use authorization allows for use in adults with proven COVID-19 infections with $O_2 \leq 94\%$ on room air, requiring supplemental oxygen *or* mechanical ventilation *or* ECMO.
- **Emergency use authorization *does* allow for inclusion in clinical trials (unless otherwise stated within the study protocol) and use of other COVID adjunctive therapies (e.g. convalescent plasma, tocilizumab).**
- **Refer to the Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of Remdesivir for more information on this therapy.**

Approval Process

(1) Infectious Diseases Consult Team determines if patient meets ineligibility criteria

Ineligibility criteria:

- Known hypersensitivity to remdesivir
- ALT ≥ 5 x UL of normal
- eGFR < 30 mL/minute calculated using the Cockcroft-Gault Equation (unless benefit outweighs risk)
- Mechanical ventilation > 14 days **AND** a negative current COVID-19 lower respiratory sample
- Improving on current treatment/supportive regimen(s) as evidenced by improving oxygenation, and/or impending discharge
- Patients in whom the clinical team believes death is in the immediate short-term and administration of remdesivir is unlikely to change the clinical outcome

(2) Infectious Diseases Consult Team assesses eligibility against institutionally approved criteria for use and documents approval using templated progress note.

Tier I. COVID+ patients with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) ≤ to 10 days **AND**:

- Pregnancy **OR**
- New and/or progressive requirement of supplemental oxygen defined as at least ≥ 4 LPM nasal cannula **OR**
- Mechanical ventilation ≤ 72 hours

Tier II. When sufficient supply of 220 vials (i.e., 20 patients) on hand and uncertain supply chain:

- COVID+ patients **AND**
  - Pregnancy with respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) greater than 10 days **OR**
  - Respiratory symptoms (e.g., new cough, dyspnea, or hypoxia) for 10 to 14 days **AND** new and/or progressive requirement of supplemental oxygen defined as at least ≥ 4 LPM nasal cannula including ≤ 72 hours mechanical ventilation **OR**
  - Any new and/or progressive supplemental oxygen requirement (including mechanical ventilation <72h) up to day 14 since respiratory symptom (e.g., new cough, dyspnea, or hypoxia) onset **AND**
    - High risk requiring a high-risk score determined by the Calculation Tool for Predicting Critically-Ill COVID-19 (http://118.126.104.170/) at Admission[1] **OR**
    - Identified as having **2 or more high risk factors** as defined by the CDC for developing severe illness from COVID-19: Age > 65; Chronic lung disease, including COPD, asthma, interstitial lung disease, cystic fibrosis; Cardiac disease, including coronary artery disease, congestive heart failure, implanted cardiac device; BMI > 30; Diabetes Mellitus; Immunocompromised (i.e., active chemotherapy, bone marrow or organ transplantation, immune deficiency, poorly controlled HIV or AIDS)**;** Hemoglobin disorders such as sickle cell disease and thalassemia

Tier III. When sufficient supply of 1100 vials (i.e., 100 patients) on hand and uncertain supply chain:

- COVID+ patients at any illness duration with new or/and progressive requirement of supplemental oxygen defined as at least ≥ 4 LPM nasal cannula but NOT requiring mechanical ventilation.

(3) Remdesivir Approval Committee Role

- The Remdesivir Review Committee, a sub-committee of the OSUWMC Scarce Resource Allocation Committee, will evaluate remdesivir candidates for approval if the remdesivir supply reaches a critical level (e.g., 20 courses/220 doses) or in the following scenarios:
  - Patients questionably meeting institutional criteria at the request of the ID or primary team provider
  - Disagreements between primary and ID teams on appropriateness at the request of either provider
  - Transfers for RDV where patient doesn't meet institutional criteria at the request of either provider

Table 5: Steps for Remdesivir EUA Ordering, Monitoring and Duration of Therapy	
Step	**Additional Details**
(1) Informed Consent *Do not obtain consent until after approval*	• The treating physician must confirm *verbal* consent with the patient or legally authorized representative (LAR). A prisoner can provide *verbal* consent if able; if unable to consent, the warden may be contacted to consider consent. The following specific verbiage should be documented in the chart: ○ Patient/LAR given the Fact Sheet for Patients and Parents/Caregivers (English/Spanish) ○ Patient/LAR was informed of alternatives to remdesivir ○ Patient/LAR was informed that remdesivir is an unapproved drug authorized under EUA • If consent cannot be obtained from the patient and LAR cannot be identified, an ethics consult should be placed
(2) Ordering Process	• After verbal consent is documented, the remdesivir order can be placed by the treating physician • The verifying pharmacist will confirm chart documentation of (1) Infectious Diseases approval AND (2) verbal consent BEFORE verifying the order and dispending remdesivir
(3) Clinical Monitoring	• Baseline chemistries and hepatic function panel prior to beginning remdesivir therapy. ○ Daily serum creatinine and hepatic function panel throughout course ○ Discontinue therapy if ALT > 5 x UL of normal OR ALT elevation with liver dysfunction
(4) Duration of Therapy	• All patients meeting criteria for remdesivir should complete **at least 5 days of therapy**, with the following exceptions: ○ Contraindicated due to laboratory abnormalities or adverse drug event ○ Patient is well enough for hospital discharge prior to completing 5 days • Patients may receive **up to 10 days of remdesivir therapy** with duration to be determined based on clinical status and O2 requirements ○ Examples include ICU patients requiring high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO ○ If continued beyond 5 days in any patient, clinical status should be assessed daily thereafter with drug discontinuation occurring when clinical improvement is observed and the patient requires < 4 LPM nasal cannula for at least 24 hours.
(5) Mandatory Medication Error and Adverse Event Reporting	• The treating physician is responsible for responding to requests from the FDA and reporting adverse drug events **within 7 days** of the onset of the event • This report can be submitted online to FDA MedWatch **AFTER** a data release is granted by the institution. The description section of the report should denote "Remdesivir under EUA." A copy of the MedWatch form should also be forwarded to Gilead: safety_fc@gilead.com. • Adverse events that must be reported: ○ Death or life-threatening adverse event ○ Inpatient hospitalization or prolonging of existing hospitalization ○ A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions ○ A congenital anomaly/birth defect ○ A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly • An alternative to reporting to the FDA and manufacturer directly is allowing the medication safety team to do this on behalf of a provider. Submit a report in the Patient Safety Reporting System to initiate the process. Use the event type 'Adverse Drug Reaction'. • Medication errors should be reported through the Patient Safety Reporting System as well.

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