



COVID-19 Therapy Update: Appropriate Referral

May 3, 2022

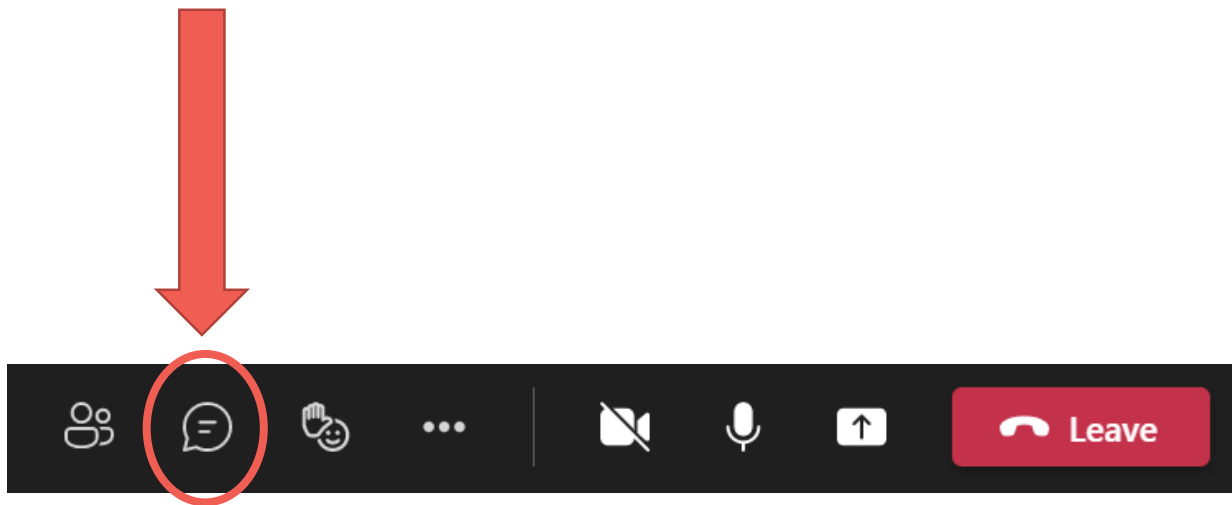


Welcome

Jennifer Khelil, DO, MBA
Senior VP and Chief Medical Officer

Housekeeping

- This program will be recorded
- All participants should have their microphones muted
- Please send questions for the presenters via the chat function





Covid-19 Outpatient Treatment

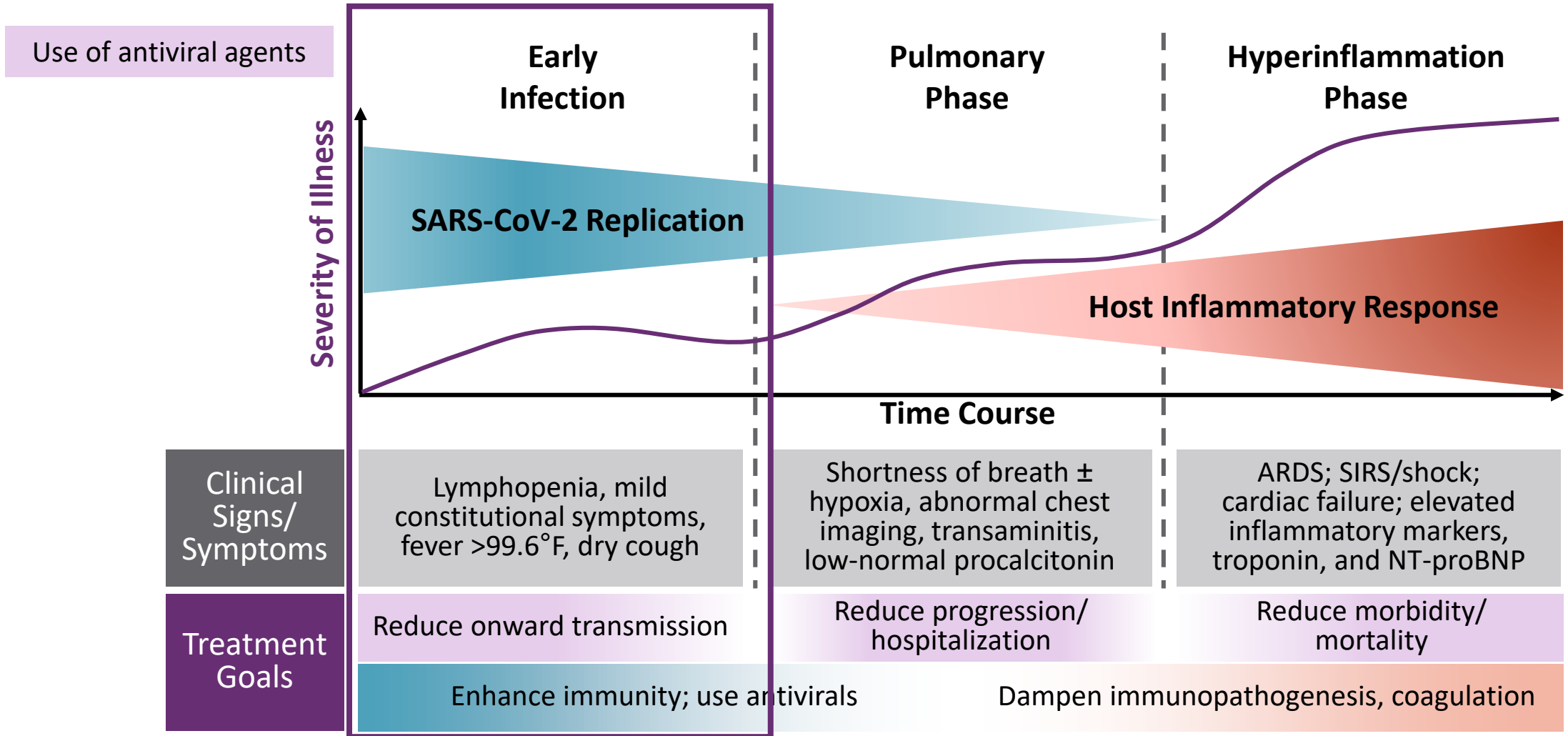
Marty Topiel, MD, FSHEA, Infection Prevention Officer

May 3, 2022

Links to Treatment Guidelines

- Below are links to updated treatment guidelines and recommendations:
- <https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf>
- <https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/>

Therapeutic Classes Dictated by SARS-CoV-2 Pathogenesis



Currently Available Anti-SARS-COV-2 Treatments: Antivirals

Drug	Route	Age groups authorized for treatment	Timing of Treatment	Effectiveness	Activity Against Variants Currently Circulating
Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid) Orally twice daily for 5 days	Oral	12 years and older and weighing at least 40 kg	As soon as possible, but within 5 days of symptom onset	Compared to placebo, a relative risk reduction of 89% in hospitalizations or deaths.	Effective against Delta and Omicron
Remdesivir (Veklury) 200 mg IV on Day 1, followed by 100 mg IV daily on Days 2 and 3	Intravenous	FDA approved in 12 years and older and weighing at least 40 kg; EUA for <12 years of age weighing 3.5 to 40 kg	As soon as possible, but within 7 days of symptom onset	Compared to placebo, a relative risk reduction of 87% in hospitalizations or deaths.	Effective against Delta and Omicron
Molnupiravir (Legevro) 800 mg Orally twice daily for 5 days	Oral	18 years and older	As soon as possible, but within 5 days of symptom onset	Compared to placebo, a relative risk reduction of 30% in hospitalizations or deaths.	Effective against Delta and Omicron

- [Merck and Biotherapeutics Molnupiravir Update](#)
- [Pfizer Paxlovid Study Interim Analysis](#)

Therapeutic Management of Non-hospitalized Adults w/COVID-19

PATIENT DISPOSITION

Does Not Require
Hospitalization or
Supplemental Oxygen

PANEL'S RECOMMENDATIONS

All patients should be offered symptomatic management **(AIII)**.

For patients who are at high risk of progressing to severe COVID-19,^a use 1 of the following treatment options:

Preferred Therapies

Listed in order of preference:

- Ritonavir-boosted nirmatrelvir (Paxlovid)^{b,c} **(AIIa)**
- Remdesivir^{c,d} **(BIIa)**

Alternative Therapies

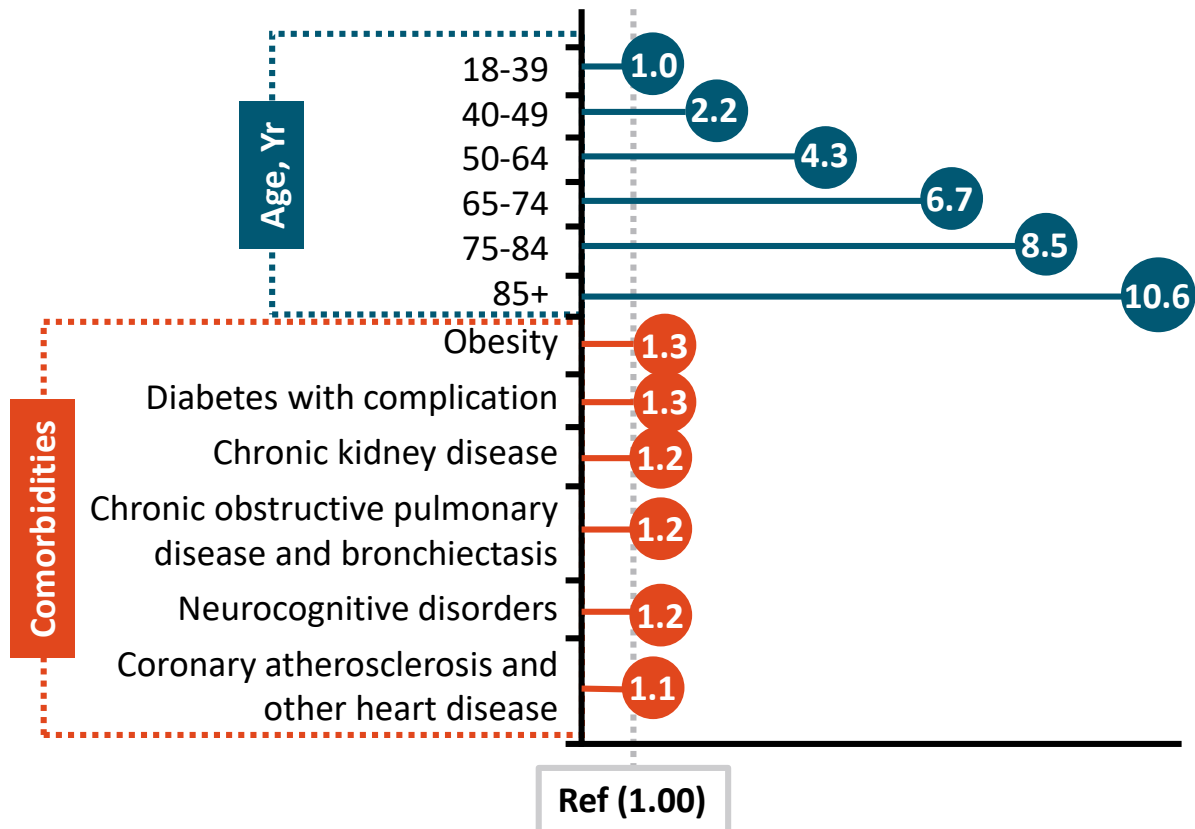
For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:

- Bebtelovimab^e **(CIII)**
- Molnupiravir^{c,f} **(CIIa)**

The Panel **recommends against** the use of **dexamethasone^g** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

Age Is an Important Risk Factor for Severe COVID-19

COVID-19 Death Risk Ratio for
Select Age Group and Comorbid Conditions



EPIC-HR and MOVE-OUT High-Risk Criteria:

- **≥60 yr of age**
- Tobacco smoker
- Chronic pulmonary disease
- Immunosuppression
- Overweight or obese
- Sickle cell disease
- Chronic kidney disease
- Diabetes
- Cardiovascular disease
- Active cancer
- Neurodevelopmental disorders
- Medically related technologic dependence

Preferred Anti-SARS-CoV-2 Treatment Options for Nonhospitalized Patients

- For nonhospitalized adult and adolescent patients with mild to moderate COVID-19 who are at high risk of progression to severe disease; **listed in order of preference**

Anti-SARS-CoV-2 Treatment (in Order of Preference)	Population	Clinical Considerations
Nirmatrelvir 300 mg (two 150-mg tablets) + 100 mg ritonavir tablet PO BID x 5 days	Age \geq 12 yr and weighing \geq 40 kg	<ul style="list-style-type: none">Use within 5 days of symptom onsetDrug interactionsRenal dosing if eGFR 30-59 mL/minHIV activity of ritonavir
Remdesivir 200 mg IV on Day 1, followed by remdesivir 100 mg IV daily on Days 2 and 3	Age \geq 12 yr and weighing \geq 40 kg	<ul style="list-style-type: none">Use within 7 days symptom onsetMust be administered in a healthcare setting

- Clinical trials are needed to determine whether combination therapy (with antivirals or antivirals with monoclonal antibodies) has a role in the treatment of SARS-CoV-2 infection
- For nonhospitalized **pediatric patients** age $<$ 12 yr or weighing $<$ 40 kg, can consider **IV remdesivir** if started within 7 days of symptom onset based on updated EUA

EPIC-HR: Day 28 Efficacy Analysis

- In nonhospitalized, at-risk patients with mild to moderate COVID-19, nirmatrelvir + RTV dosed every 12 hr for 5 days **reduced risk of hospitalization or death by 89%** ($P = .001$) when started within 3 days of symptom onset

Outcome	Started By Day 3			Started By Day 5		
	Nirmatrelvir + RTV (n = 697)	Placebo (n = 682)	P Value	Nirmatrelvir + RTV (n = 1039)	Placebo (n = 1046)	P Value
Hospitalization or death, n (%)	5 (0.72)	44 (6.45)	<.001	8 (0.77)	66 (6.31)	<.0001
Deaths, n (%)	0	9 (1.32)	NR	0	12 (1.15)	NR

- Safety analysis (N = 2224): fewer serious AEs and study drug discontinuation with nirmatrelvir + RTV vs placebo (1.6% vs 6.6% and 2.1% vs 4.2%, respectively)
- Due to positive interim results, DSMB stopped recruitment early
- EUA in nonhospitalized patients issued by the FDA on December 22, 2021

Interactions with Essential Medicines & Nirmatrelvir/ritonavir (NMV/r)

Please check www.covid19-druginteractions.org for updates.

Interaction tables - refer to page 2 for legend, notes and abbreviations

Please note that if a drug is not listed it cannot automatically be assumed it is safe to coadminister.

Drug interaction data for many agents are limited or absent; therefore, risk-benefit assessment for any individual patient rests with prescribers. Management of interactions with nirmatrelvir/ritonavir (Paxlovid) may be complex and full details should be obtained from the website where possible.

Analgesics	
<input type="checkbox"/>	Codeine
<input type="checkbox"/>	Diclofenac
<input type="checkbox"/>	Fentanyl
<input type="checkbox"/>	Hydromorphone
<input type="checkbox"/>	Ibuprofen
<input type="checkbox"/>	Mefenamic acid
<input type="checkbox"/>	Morphine
<input type="checkbox"/>	Oxycodone
<input type="checkbox"/>	Paracetamol
<input type="checkbox"/>	Tramadol
Antiarrhythmics	
<input type="checkbox"/>	Amiodarone
<input type="checkbox"/>	Lidocaine
Antibacterials	
<input type="checkbox"/>	Amikacin
<input type="checkbox"/>	Amoxicillin
<input type="checkbox"/>	Ampicillin
<input type="checkbox"/>	Bedaquiline
<input type="checkbox"/>	Cefalexin
<input type="checkbox"/>	Cefazolin
<input type="checkbox"/>	Cefixime
<input type="checkbox"/>	Cefotaxime
<input type="checkbox"/>	Ceftriaxone
<input type="checkbox"/>	Chloramphenicol
<input type="checkbox"/>	Ciprofloxacin
<input type="checkbox"/>	Clarithromycin (a)
<input type="checkbox"/>	Clindamycin
<input type="checkbox"/>	Clofazimine
<input type="checkbox"/>	Cloxacillin
<input type="checkbox"/>	Cycloserine
<input type="checkbox"/>	Dapsone
<input type="checkbox"/>	Delamanid
<input type="checkbox"/>	Doxycycline
<input type="checkbox"/>	Erythromycin
<input type="checkbox"/>	Ethambutol
<input type="checkbox"/>	Ethionamide
<input type="checkbox"/>	Gentamicin
<input type="checkbox"/>	Imipenem/cilastatin
<input type="checkbox"/>	Isoniazid
<input type="checkbox"/>	Kanamycin
<input type="checkbox"/>	Levofloxacin
<input type="checkbox"/>	Linezolid
<input type="checkbox"/>	Meropenem
<input type="checkbox"/>	Metronidazole
<input type="checkbox"/>	Moxifloxacin
<input type="checkbox"/>	Nitrofurantoin
<input type="checkbox"/>	Ofloxacin
<input type="checkbox"/>	Para-aminosalicylic acid
<input type="checkbox"/>	Penicillins
<input type="checkbox"/>	Piperacillin
<input type="checkbox"/>	Pyrazinamide
<input type="checkbox"/>	Rifabutin (b)
<input checked="" type="checkbox"/>	Rifampicin
<input checked="" type="checkbox"/>	Rifapentine
<input type="checkbox"/>	Spectinomycin
<input type="checkbox"/>	Streptomycin
<input type="checkbox"/>	Sulfadiazine
<input type="checkbox"/>	Tazobactam
<input type="checkbox"/>	Tetracyclines
<input type="checkbox"/>	Trimethoprim/sulfamethoxazole 12
<input type="checkbox"/>	Vancomycin

Anticoagulants/antiplatelets	
<input type="checkbox"/>	Apixaban
<input type="checkbox"/>	Aspirin (antiplatelet)
<input type="checkbox"/>	Clopidogrel (stented) (c)
<input type="checkbox"/>	Dabigatran (a)
<input type="checkbox"/>	Dalteparin
<input type="checkbox"/>	Edoxaban (d)
<input type="checkbox"/>	Enoxaparin
<input type="checkbox"/>	Heparin
<input type="checkbox"/>	Rivaroxaban
<input type="checkbox"/>	Streptokinase
<input type="checkbox"/>	Warfarin
Anticonvulsants	
<input checked="" type="checkbox"/>	Carbamazepine
<input type="checkbox"/>	Clonazepam
<input type="checkbox"/>	Ethosuximide
<input type="checkbox"/>	Lamotrigine
<input checked="" type="checkbox"/>	Phenobarbital
<input checked="" type="checkbox"/>	Phenytoin
<input type="checkbox"/>	Valproate
Antidepressants	
<input type="checkbox"/>	Amitriptyline
<input type="checkbox"/>	Clomipramine
<input type="checkbox"/>	Fluoxetine
<input type="checkbox"/>	Lithium
Antidiabetics	
<input type="checkbox"/>	Glibenclamide
<input type="checkbox"/>	Gliclazide
<input type="checkbox"/>	Insulin
<input type="checkbox"/>	Metformin
Antifungals	
<input type="checkbox"/>	Amphotericin B
<input type="checkbox"/>	Fluconazole
<input type="checkbox"/>	Flucytosine
<input type="checkbox"/>	Griseofulvin
<input type="checkbox"/>	Itraconazole (e)
<input type="checkbox"/>	Ketoconazole (e)
<input type="checkbox"/>	Nystatin
<input type="checkbox"/>	Voriconazole
Antimalarials	
<input type="checkbox"/>	Amodiaquine
<input type="checkbox"/>	Artemether
<input type="checkbox"/>	Artesunate
<input type="checkbox"/>	Atovaquone
<input type="checkbox"/>	Lumefantrine
<input type="checkbox"/>	Mefloquine
<input type="checkbox"/>	Piperaquine
<input type="checkbox"/>	Primaquine
<input type="checkbox"/>	Proguanil
<input type="checkbox"/>	Quinine
Antipsychotics	
<input type="checkbox"/>	Chlorpromazine
<input type="checkbox"/>	Clozapine
<input type="checkbox"/>	Fluphenazine
<input type="checkbox"/>	Haloperidol
<input type="checkbox"/>	Risperidone
Anxiolytics	
<input type="checkbox"/>	Diazepam
<input type="checkbox"/>	Lorazepam
<input type="checkbox"/>	Midazolam

Beta blockers	
<input type="checkbox"/>	Atenolol
<input type="checkbox"/>	Bisoprolol
<input type="checkbox"/>	Carvedilol
<input type="checkbox"/>	Metoprolol
<input type="checkbox"/>	Propranolol
<input type="checkbox"/>	Timolol
Bronchodilators	
<input type="checkbox"/>	Aminophylline
<input type="checkbox"/>	Ipratropium bromide
<input type="checkbox"/>	Salmeterol
Calcium channel blockers	
<input type="checkbox"/>	Amlodipine
<input type="checkbox"/>	Nifedipine
<input type="checkbox"/>	Verapamil
Cancer drugs	
<input type="checkbox"/>	Dasatinib (f)
<input type="checkbox"/>	Erlotinib (g)
<input type="checkbox"/>	Imatinib (h)
<input type="checkbox"/>	Methotrexate
<input type="checkbox"/>	Vinblastine (i)
Contraceptives	
<input type="checkbox"/>	Ethinylestradiol
<input type="checkbox"/>	Etonogestrel (IMP)
<input type="checkbox"/>	Etonogestrel (VR)
<input type="checkbox"/>	Levonorgestrel (COC)
<input type="checkbox"/>	Levonorgestrel (EC)
<input type="checkbox"/>	Levonorgestrel (IDU)
<input type="checkbox"/>	Levonorgestrel (POP)
<input type="checkbox"/>	Medroxyprogesterone (depot injection)
<input type="checkbox"/>	Norethisterone (COC)
<input type="checkbox"/>	Norethisterone (IM)
<input type="checkbox"/>	Norethisterone (POP)
<input type="checkbox"/>	Norgestrel (COC)
COVID19 therapies	
<input type="checkbox"/>	Budesonide (inhaled)
<input type="checkbox"/>	Convalescent plasma
<input type="checkbox"/>	Dexamethasone
<input type="checkbox"/>	Hydrocortisone
<input type="checkbox"/>	Infliximab
<input type="checkbox"/>	Methylprednisolone
<input type="checkbox"/>	COVID19 vaccines
Gastrointestinal agents	
<input type="checkbox"/>	Aprepitant
<input type="checkbox"/>	Domperidone
<input type="checkbox"/>	Lactulose
<input type="checkbox"/>	Loperamide
<input type="checkbox"/>	Mesalazine
<input type="checkbox"/>	Metoclopramide
<input type="checkbox"/>	Omeprazole
<input type="checkbox"/>	Ondansetron
<input type="checkbox"/>	Ranitidine
<input type="checkbox"/>	Senna
HCV antivirals	
<input type="checkbox"/>	Glecaprevir/pibrentasvir
<input type="checkbox"/>	Ledipasvir/sofosbuvir
<input type="checkbox"/>	Ombitasvir/paritaprevir/r
<input type="checkbox"/>	Sofosbuvir/velpatasvir
Herbals/supplements	
<input type="checkbox"/>	Folic acid
<input type="checkbox"/>	Magnesium
<input type="checkbox"/>	St John's Wort

HIV antiretrovirals	
<input type="checkbox"/>	Abacavir
<input type="checkbox"/>	Atazanavir/ritonavir
<input type="checkbox"/>	Darunavir/ritonavir
<input type="checkbox"/>	Dolutegravir
<input type="checkbox"/>	Efavirenz
<input type="checkbox"/>	Emtricitabine
<input type="checkbox"/>	Lamivudine
<input type="checkbox"/>	Lopinavir/ritonavir
<input type="checkbox"/>	Nevirapine
<input type="checkbox"/>	Raltegravir
<input type="checkbox"/>	Tenofovir alafenamide
<input type="checkbox"/>	Tenofovir-DF
<input type="checkbox"/>	Zidovudine
Hypertension/heart failure	
<input type="checkbox"/>	Amiloride
<input type="checkbox"/>	Digoxin
<input type="checkbox"/>	Dopamine
<input type="checkbox"/>	Enalapril
<input type="checkbox"/>	Furosemide
<input type="checkbox"/>	Hydrochlorothiazide
<input type="checkbox"/>	Isosorbide dinitrate
<input type="checkbox"/>	Lisinopril
<input type="checkbox"/>	Losartan
<input type="checkbox"/>	Methyldopa
<input type="checkbox"/>	Spirinolactone
Immunosuppressants	
<input type="checkbox"/>	Azathioprine
<input type="checkbox"/>	Ciclosporin
<input type="checkbox"/>	Everolimus
Lipid lowering agents	
<input type="checkbox"/>	Atorvastatin
<input type="checkbox"/>	Fluvastatin
<input type="checkbox"/>	Lovastatin
<input type="checkbox"/>	Simvastatin
Others	
<input type="checkbox"/>	Allopurinol
<input type="checkbox"/>	Ergometrine
<input type="checkbox"/>	Levodopa
<input type="checkbox"/>	Levothyroxine
Steroids	
<input type="checkbox"/>	Beclomethasone
<input type="checkbox"/>	Betamethasone
<input type="checkbox"/>	Fludrocortisone
<input type="checkbox"/>	Prednisolone
<input type="checkbox"/>	Testosterone
<input type="checkbox"/>	Triamcinolone

Interactions with Essential Medicines & Nirmatrelvir/ritonavir (NMV/r)

Please check www.covid19-druginteractions.org for updates.

Legend

Colour/Symbol	Recommendation for NMV/r use
! Do not co-administer	Do not use NMV/r ⇒ alternative COVID-19 therapy Risk of serious toxicity. Stopping the drug does not mitigate the interaction due to its prolonged half-life.
x Do not co-administer	Do not use NMV/r ⇒ alternative COVID-19 therapy Strong inducer can jeopardize NMV/r efficacy due to persisting induction after stopping the drug.
Do not co-administer	NMV/r use ONLY possible if drug is paused or replaced by a non-interacting drug Risk of serious toxicity. Only start NMV/r if the drug can be safely paused or replaced. Drug can be resumed 3 days after completing NMV/r therapy.
□ Potential interaction Dose adjustment and/or close monitoring required.	Stop or replace drug if possible or consult specialist for dose adjustment/monitoring to allow use with NMV/r Ideally, only start NMV/r if the drug can be safely paused or replaced. Alternatively, dose adjust/monitor. Refer to www.covid19-druginteractions.org for detailed information.
Potential interaction Manageable by counselling patient	Proceed with NMV/r Interaction manageable by counselling the patient about potential interaction and advising to temporarily stop the drug if feeling unwell.
Weak interaction No action needed	Proceed with NMV/r Drug metabolized partially by CYP3A4 or with low risk of adverse event from interaction.
No interaction expected	Proceed with NMV/r

Notes

- a No dose reduction or monitoring in patients with normal renal function.
- b Rifabutin dosed 150 mg once daily with NMV/r.
- c Ritonavir decreases clopidogrel efficacy therefore NMV/r cannot be prescribed in high risk situation (i.e. initial period (at least 6 weeks) post coronary stenting). NMV/r is allowed if clopidogrel is used outside this period or if clopidogrel is used as alternative to aspirin (intolerant patients).
- d The US product label for edoxaban advises no dose adjustment is needed for edoxaban in the presence of a P-gp inhibitor, such as ritonavir.
- e Itraconazole or ketoconazole should not be used at doses >200 mg/day.
- f The decision to pause or dose adjust dasatinib should be made in conjunction with the patient's oncologist.
Chronic phase chronic myelogenous leukaemia: pause dasatinib and restart 3 days after completing NMV/r. Alternatively, consider reducing dasatinib dose to 20 mg (in patients receiving 100 mg daily) or 40 mg (in patients receiving 140 mg daily) and monitor for toxicity.
Accelerated or blast phase chronic myelogenous leukaemia: do not coadminister, use alternative COVID-19 therapy.
- g The decision to pause or dose adjust erlotinib should be made in conjunction with the patient's oncologist.
If it is decided to pause treatment, restart erlotinib 3 days after completing NMV/r treatment. If pausing erlotinib treatment is not feasible, continue full dose erlotinib with patient self-monitoring for rash and diarrhoea. If these do occur, reduce erlotinib dose in 50 mg decrements or re-assess for a short pause.
- h The decision to pause imatinib should be made in conjunction with the patient's oncologist. If it is decided to hold treatment, restart imatinib 3 days after completing NMV/r treatment. Alternatively, imatinib may be coadministered with monitoring for adverse effects (fluid retention, nausea and neutropenia). NMV/r is expected to have a modest effect on imatinib exposure. Coadministration with ritonavir (600 mg once daily) for 3 days did not significantly alter imatinib exposure (*van Erp NP et al. Clin Cancer Res. 2007;13(24):7394-400*).
- i The decision to pause or dose adjust vinblastine should be made in conjunction with the patient's oncologist. Vinblastine may be paused in the context of acute infection. Restart vinblastine 3 days after completing NMV/r treatment. Alternatively, vinblastine may be coadministered with close monitoring for haematologic toxicity and neurotoxicity. Some providers may wish to empirically reduce vinblastine dose, especially in patients who have previously experienced or are at high risk for toxicity.

Contraceptive Abbreviations

COC = combined oral contraceptive
 EC = emergency contraception
 IDU = intrauterine device
 IM = intramuscular
 IMP = implant
 POP = progestin only contraceptive pill
 VR = vaginal ring.

nirmatrelvir-ritonavir (Paxlovid) 300 mg (150 mg x 2)-100 mg tab tablet therapy pack ✓ Accept ✗ Cancel

Order Inst: Per Dec 22 2021 EUA, Paxlovid is not indicated in patients weighing less than 40 kg, patients less than 12 years of age, or with eGFR < 30 mL/min.

For patients with eGFR => 60 mL/min, the recommended dose is 300 mg nirmatrelvir (2 tablets) + 100 mg ritonavir twice daily (1 tablet). (Order dose = 3 tablets)

For patients with eGFR => 30 to < 60 mL/min, the recommended dose is 150 mg nirmatrelvir (1 tablet) + 100 mg ritonavir (1 tablet) twice daily. (Order dose = 2 tablets)

Product: **NIRMATRELVIR 300 MG (150 MG X 2)-RITONAVIR 100 MG TABLET (EUA)**

Sig Method: **Specify Dose, Route, Frequency** Use Free Text Taper/Ramp Combination Dosage

Dose: 2 tablet **2 tablet** 3 tablet

Prescribed Dose: 2 tablet
Prescribed Amount: 2 tablet

Route: oral oral

Frequency: Every 12 hours scheduled q12h SCH

Duration: 5 Doses Days 30 days 2 months 1 year

Starting: 1/24/2022 Ending: 1/29/2022

Dispense: Days/Fill: Full (5 Days) 30 Days 90 Days

Quantity: 1 tablet Refill: 0 0 1 2 3 11

Total Supply: **Unable to calculate**

Do not send renewal requests to me
 Dispense As Written
 NIRMATRELVIR/RITONAVIR

Mark long-term:

⚠ Patient Sig: **Take 2 tablets by mouth every 12 (twelve) hours for 5 days. Take number of ordered nirmatrelvir (pink) tablets + ritonavir (white) tablet at the same time**

[Edit the additional information appended to the patient sig](#)

ⓘ The sig contains both discrete and free text elements. Please review the final sig above.

Report: Lab Test Results

Component	Time Elapsed	Value	Range	Status
eGFR	12 days (01/11/22 1605)	50.14 (L)	>=60.00 mL/min/1.73m ²	Final result

Comments: Calculation based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation refit without adjustment for race.

Class: Normal Normal Fax Print Phone In No Print Sample Downtime

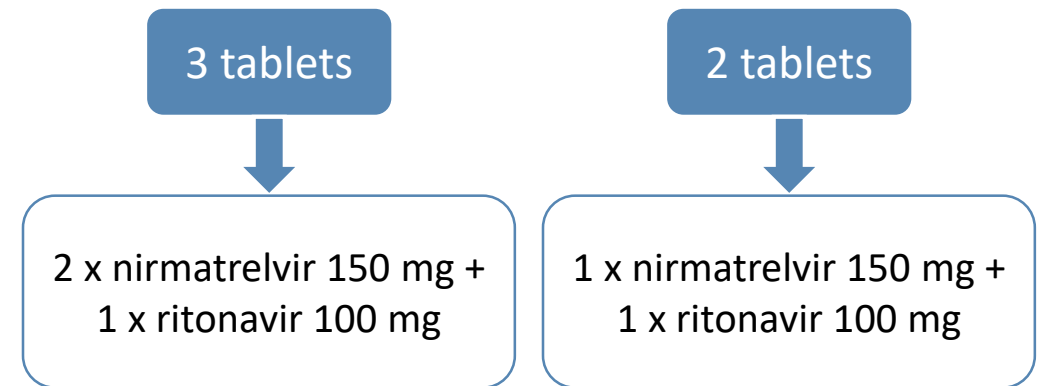
ⓘ This medication will not be e-prescribed. Invalid items: Patient Details...

Note to Pharmacy: **If the ordered dose is two tablets, dispense blister card to give only one nirmatrelvir (pink tablet) and one ritonavir (white tablet) per dose (dose for 30 <= eGRF < 60 mL/min)**

Renewal Provider:

[Show Additional Order Details](#)

ⓘ Next Required ✓ Accept ✗ Cancel



Drug-Drug: atorvastatin and nirmatrelvir-ritonavir

Concurrent use of nirmatrelvir-ritonavir may result in elevated levels of atorvastatin and rosuvastatin, which could result in rhabdomyolysis.(1-3)

nirmatrelvir-ritonavir (Paxlovid) 300 mg (150 mg x 2)-100 mg tab tablet therapy pack Remove
 Prescription. New.

atorvastatin (LIPITOR) 10 mg tablet Remove
 Prescription. New. Long-term.

[Details](#) ⓘ

Paxlovid

- COVID Therapy Locator Websites:
- <https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/>
- <https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8/data>

Inhibit CYP3A

- Alpha1-adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine, propoxyphene
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- Antipsychotics: lurasidone, pimozide, clozapine
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine • HMG-CoA reductase inhibitors: lovastatin, simvastatin
- PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH)
- Sedative/hypnotics: triazolam, oral midazolam

PINETREE: Day 28 Efficacy

- Baseline characteristics balanced across treatment arms
- In high-risk, nonhospitalized participants, **3-day course of remdesivir prevented COVID-19–related medically attended visits, hospitalization, or death**
- **No difference** between remdesivir vs placebo in TWA change in **viral load by NP swab** from Day 1-7

Outcome by Day 28	RDV, n/N (%)	PBO, n/N (%)	RR, %	HR (95% CI)	P Value
COVID-19–related hospitalization	2/279 (0.7)	15/283 (5.3)	87	0.13 (0.03-0.59)	.008
COVID-19–related medically attended visits	4/246 (1.6)	21/252 (8.3)	81	0.19 (0.07-0.56)	.002

- No deaths occurred in either arm by Day 28
- FDA approval updated to include nonhospitalized adult and adolescents and EUA extended to include nonhospitalized patients <12 yr old who are at high risk of disease progression

MOVE-OUT: Final Analysis in Nonhospitalized Adults

- In **nonhospitalized**, at-risk patients with mild to moderate COVID-19, molnupiravir 800 mg every 12 hr for 5 days **reduced risk of hospitalization or death by 30%** ($P = .0218$)

Outcome	Molnupiravir 800 mg Q12H (n = 709)	Placebo (n = 699)
Hospitalization or death, n (%)	48 (6.8)	68 (9.7)
Deaths, n	1	9

- AE profile consistent with the AE profile in the Day 29 interim analysis
- These additional data were presented to FDA's Antimicrobial Advisory Committee, and committee voted 13-10 that the known benefits outweigh potential risks
- EUA for nonhospitalized patients issued by the FDA on December 23, 2021, for use **when alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate**

Molnupiravir: Assessment and Counseling in Setting of Childbearing Potential

- Assess women for pregnancy
- Either
 - Report of LMP in an individual who has regular menstrual cycles, uses a reliable method of contraception correctly, and/or consistently has had a negative pregnancy test
 - Negative pregnancy test (recommended but not required if other criteria are not met)
- Reliable, correct, and consistent **contraception** required both for **men and women**
 - ♀ – **Women:** during treatment and for **4 days after the last dose** of molnupiravir
 - ♂ – **Men:** during treatment and for **at least 3 mo after the last dose** of molnupiravir

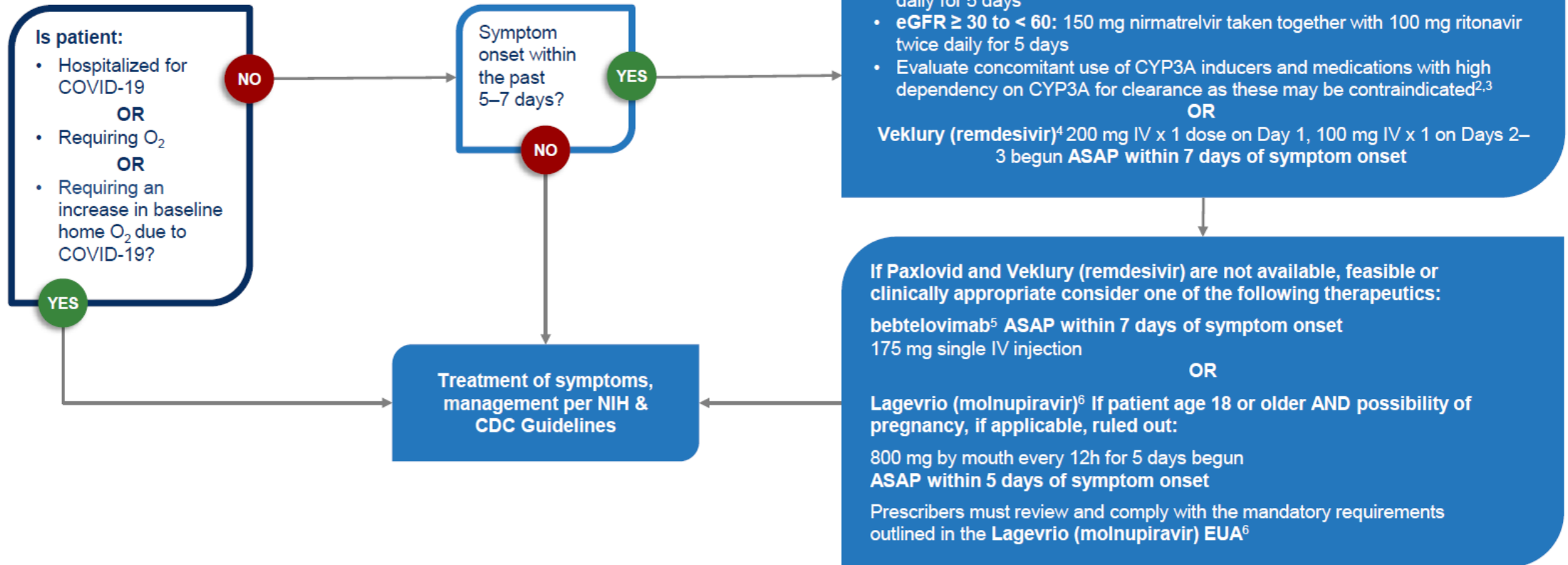
Pregnant recipients should join surveillance registry:
1-877-888-4231 or pregnancyreporting.msd.com

- Includes partners of men who took molnupiravir

COVID-19 Outpatient Therapeutics

Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease



Consider one of the following therapeutics, if available, feasible, and clinically appropriate¹:

Paxlovid² within 5 days of symptom onset If patient does not have severe renal impairment (eGFR <30mL/min OR severe hepatic impairment (Child-Pugh Class C))

- eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
- eGFR ≥ 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated^{2,3}

OR

Veklury (remdesivir)⁴ 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2-3 begun ASAP within 7 days of symptom onset

If Paxlovid and Veklury (remdesivir) are not available, feasible or clinically appropriate consider one of the following therapeutics:

bebtelovimab⁵ ASAP within 7 days of symptom onset
175 mg single IV injection

OR

Lagevrio (molnupiravir)⁶ If patient age 18 or older AND possibility of pregnancy, if applicable, ruled out:
800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Prescribers must review and comply with the mandatory requirements outlined in the Lagevrio (molnupiravir) EUA⁶

References:
¹ NIH's COVID-19 Treatment Guidelines Therapeutic Management of Nonhospitalized Adults With COVID-19. <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/>
² Paxlovid EUA. <https://www.fda.gov/media/155050/download>
³ NIH's COVID-19 Treatment Guidelines Panel: Ritonavir-Boosted Nirmatrelvir (Paxlovid). <https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid/>
⁴ Veklury (remdesivir) Prescribing Information. https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf
⁵ Bebtelovimab EUA. <https://www.fda.gov/media/158152/download>
⁶ Lagevrio EUA. <https://www.fda.gov/media/155054/download>



April 18, 2022



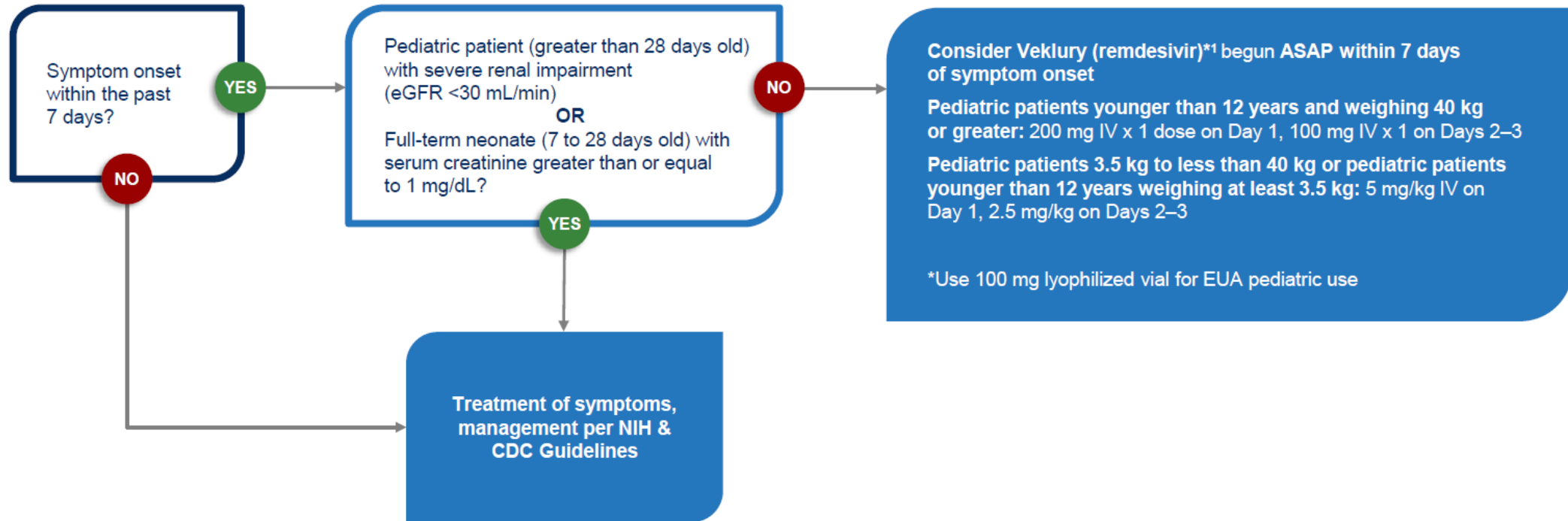
NIH Panel Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies When There Are Logistical or Supply Constraints

Tier	Priority Population
1	Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥ 75 yr or anyone aged ≥ 65 yr with additional risk factors)
2	Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥ 65 yr or anyone aged < 65 yr with clinical risk factors)
3	Vaccinated individuals at high risk of severe disease (anyone aged ≥ 75 yr or anyone aged ≥ 65 yr with clinical risk factors)
4	Vaccinated individuals at risk of severe disease (anyone ≥ 65 yr or anyone < 65 yr with clinical risk factors)

- Individuals in tiers 3 and 4 who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease and should be prioritized for treatment

Clinical Decision Aid for Pediatric Patients

Outpatient **3.5 kg to less than 40 kg** or **younger than 12 years of age**
weighing at least 3.5 kg, with mild to moderate COVID-19 and at high risk
for progression to severe disease



Reference:

¹[Veklury \(remdesivir\) EUA: https://www.fda.gov/media/137586/download.](https://www.fda.gov/media/137586/download)



April 18, 2022

Access

**Clinicians from outside of Virtua are directed to call
856-325-3150**

**Patients calling directly for information can be
directed to call the access center at 1 888 VIRTUA 3**

Treatment Links

- Below are links to updated treatment guidelines and recommendations:
- <https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf>
- <https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/>



Questions?



Thank You