	System Wide
	Oral Antivirals for the Treatment of COVID-19
	Version 2.0 **Effective Date**: 01/05/2022

PURPOSE: To outline the mandated requirements in accordance with the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUA), for the use of oral antiviral therapies for the treatment of SARS-CoV-2. Omicron is now the dominant variant in the United States. The FDA issued Emergency Use Authorization (EUA) for two novel antiviral agents, nirmatrelvir/ritonavir (Paxlovid) and molnupiravir, for the treatment of mild-to-moderate COVID-19 in non-hospitalized patients at high risk of progression to severe disease. Both of these agents are investigational drugs and are not currently approved for any indication. The patient must have a confirmed (+) SARS-CoV-2 test prior to initiating therapy. SARS-CoV-2 antivirals should be administered as soon as possible, at least within at least 5 days of symptom onset. Please review each indication and exclusion, per the EUA, to ensure patient eligibility. Both of these agents are primarily indicated for us in outpatient high risk patients. Patients hospitalized due to severe/critical COVID-19 should **NOT** receive either oral antiviral agent.

- Outpatient use of nirmatrelvir/ritonavir and molnupiravir will be at the responsibility of the prescriber to comply and acknowledge all the requirements per the issued EUA.
- Infectious Diseases (ID) will **NOT** be responsible for the compliance of EUA requirements, dispensing, reporting side effects, or follow up. Outpatient use does **NOT** require ID approval. This guideline is intended to serve as a resource for outpatient prescribers.
- CHKD inpatient pharmacy, per Virginia law, CANNOT dispense nirmatrelvir/ritonavir (Paxlovid) or molnupiravir for outpatient use.

Outpatient:

- Use of oral antivirals in the outpatient setting are at the discretion of the prescriber and does **NOT** require infectious diseases (ID) approval.
- The prescriber is thereby responsible for compliance with EUA requirement.
- Drug supply for outpatient cannot be supplied by the CHKD inpatient pharmacy and must be obtained from an outpatient pharmacy per Virginia law.

Inpatient:

- High-risk patients admitted for non-COVID-19 illness, who are COVID-19 (+) and meet EUA criteria, may qualify for inpatient treatment.
- Inpatient use of oral antivirals **ARE** restricted to ID. Eligibility criteria should be reviewed and confirmed prior to contacting ID.

Table 1: FDA Approved Oral Antiviral Agents for the Treatment of COVID-19

Drug	EUA Criteria
Nirmatrelvir/ritonavir (Paxlovid)	Mild-moderate COVID-19 ***High-Risk*** patients who are: ▪ ≥ 12 years and ≥ 40 kg, **AND** ▪ Confirmed (+) COVID-19 test, **AND** ▪ High risk for progression to severe COVID-19, **AND** ▪ Within 5 days of symptoms onset
Molnupiravir	Mild-moderate COVID-19 in ***High-Risk*** patients who are ▪ ≥ 18 years of age, **AND** ▪ Confirmed (+) COVID-19 test, **AND** ▪ High risk for progression to severe COVID-19, **AND** ▪ Within 5 days of symptoms onset
NOT authorized for hospitalized due to severe/critical COVID-19, for > 5 consecutive days, for pre or post-exposure prophylaxis	

Supply: Due to increased demand, the on-going supply chain, and manufacturing delays antivirals and monoclonal antibodies for the treatment of COVID-19 remain extremely limited. State and territorial health departments will allocate to healthcare facilities. Initial allocation is expect in early January 2022.

Prioritization: While the shortages continue, it is critical to prioritize the use of COVID-19 specific therapies to patients with the highest risks of progressing to severe illness. Initial allocations will be limited requiring even further narrowing of the EUA risk category. CHKD will utilize a tiered risk based approach prioritizing those at the highest risk of developing severe COVID-19, Table 3. Should the allocated supply increase, the prioritization tiers will broaden. CHKD's prioritization criteria are not dependent on vaccination status.

PROCEDURE:

I. **Confirm Patient Eligibility**: Review each indication and restriction to ensure patient eligibility per Table 1.

II. **Obtain ID Approval (Inpatient ONLY)**:
   a. Page Laura Sass, MD. via doctors direct at 668-9999 to obtain approval between the hours of (08:00-15:00) Monday-Friday
   b. DO **NOT** enter the medication order or schedule appointment or RSIU encounter until approved by ID
   c. Refer to section V. for additional provider requirements

III. **Confirm High Risk Criteria**:

Table 2. CHKD High Risk Patient Classification

High risk is defined as patients meeting ≥ 1 of the following:
Chronic kidney disease
Diabetes
Immunosuppressive disease
Currently on immunosuppressive treatment*
Are ≥65 years of age
Obesity
Pregnancy
Sickle cell disease
Congenital or acquired heart disease
Neurodevelopmental disorders
Medical technological dependence (trach, gastrostomy, or PPV (not related to COVID-19)
Asthma, reactive airway, or other chronic respiratory disease requiring daily controller medications

***Active treatment with: high-dose corticosteroids (≥20 mg/day prednisone or equivalent for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents (severely immunosuppressive), tumor-necrosis (TNF) blockers, any immunosuppressive or immunomodulatory biologic agent

For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19: https://www.cdc.gov/coronavirus/2019- ncov/need-extra-precautions/people-with-medical-conditions.html

IV. Prescribing Information

ID Restricted when utilized inpatient, approval is NOT required for outpatient use

<table>
<tr><th colspan="2">Paxlovid (Nirmatrelvir/Ritonavir)</th></tr>
<tr><td>Indication</td><td>EUA for the treatment of mild-to-moderate COVID-19 in high risk patients who are:
a. ≥ 12 years and ≥ 40 kg
b. Confirmed (+) COVID-19 test
c. High risk for progression to severe COVID-19
d. Within 5 days of symptoms onset
NOT authorized:
▪ Hospitalized due to severe/critical COVID-19
▪ Use for > 5 consecutive days
▪ Pre or post-exposure prophylaxis</td></tr>
<tr><td>Dosing</td><td>Nirmatrelvir 300 mg (two 150 mg tablets) + Ritonavir 100 mg (one 100 mg tablet), twice daily for a total of 5 days</td></tr>
<tr><td>Renal Dosing</td><td>Renal Dosing: Creatinine Clearance (CrCl)<table><tr><th>CrCl (mL/min)</th><th>Adjustment</th></tr><tr><td>≥ 60</td><td>None</td></tr><tr><td>≥ 30 to < 60</td><td>Nirmatrelvir 150mg + Ritonavir 100mg</td></tr><tr><td>< 30</td><td>Avoid</td></tr></table></td></tr>
<tr><td>Hepatic Dosing</td><td>Avoid in severe impairment (Child-Pugh Class C)</td></tr>
<tr><td>Pregnancy
Lactation</td><td>No data in pregnancy or breast feeding</td></tr>
<tr><td>Administration</td><td>▪ Take all 3 tabs together with fat containing meal
▪ If hospitalization occurs after starting treatment, complete the full 5-day course per the healthcare provider’s discretion
▪ If a dose is missed within an 8 hours window, take the missed dose as soon as possible
▪ If > 8 hours, do not take the missed dose and resume normal schedule</td></tr>
<tr><td>Contraindications</td><td>▪ History of significant hypersensitivity reactions to any ingredient
▪ <u>Significant CYP-3A4 inducers or substrates:</u> Ritonavir has many drug-drug and drug-herbal interactions of clinical importance and concomitant use is contraindicated</td></tr>
<tr><td>Monitoring</td><td>Current or the addition of significant medication resulting in drug-drug interactions</td></tr>
<tr><td>Drug Interactions</td><td>▪ Multiple significant drug-drug interaction of medication which are metabolized via or induce CYP3A.
▪ For inpatient use: prior to prescribing, obtain ID approval and consult the pharmacist to evaluate safety (steps not required for outpatient use).
▪ Drug Interaction Database: <u>https://www.hiv-druginteractions.org/checker</u></td></tr>
<tr><td>Side Effects</td><td>(< 5%) Dsygeusia, diarrhea, hypertension, myalgia</td></tr>
<tr><td>Warnings</td><td>Hepatotoxicity
HIV Resistance</td></tr>
</table>

IV. Prescribing Information

Molnupiravir	
Indication	***EUA*** for the treatment of mild-to-moderate COVID-19 in high risk patients who are: **a.** **≥ 18 years of age** **b.** Confirmed (+) COVID-19 test **c.** *High risk* for progression to severe COVID-19 **d.** Within 5 days of symptoms onset **NOT** authorized**:** ▪ Hospitalized due to severe/critical COVID-19 ▪ Use for > 5 consecutive days ▪ Pre or post-exposure prophylaxis ***Restricted to: ID Inpatient ONLY***
Dosing	800 mg (4 caps) every 12 hours for a total of 5 days Supplied as 200 mg capsules
Dose Adjustments	No renal or hepatic dose adjustments required
Pregnancy **Lactation**	Not recommended in pregnancy or breastfeeding *Pregnancy Surveillance Program***:** Voluntary long-term follow up program
Administration	▪ If hospitalization occurs after starting treatment, complete the full 5-day course per the healthcare provider's discretion ▪ If a dose is missed within an 10 hours window, take the missed dose as soon as possible ▪ If > 10 hours, do not take the missed dose and resume normal schedule
Monitoring	Pregnancy Screening prior to initiation
Contraindications	None known or reported
Drug Interactions	None known to date
Side Effects	(<2 %) Diarrhea, nausea, dizziness
Warnings	**Embryo-Fetal Toxicity:** ▪ Advise use of effective contraception correctly and consistently, for the duration of treatment and for 4 days after the last dose **Bone and Cartilage Toxicity:** ▪ Avoid age < 18 years may affect bone & cartilage growth

V. CHKD Step-by-Step Treatment Initiation per EUA Requirements

<table>
<tr><th>EUA Requirement</th><th colspan="2">Description</th></tr>
<tr><td rowspan="2">Confirm Qualification</td><td>Nirmatrelvir/ritonavir (Paxlovid)</td><td>Mild-moderate COVID-19 High-Risk patients who are:
▪ ≥ 12 years and ≥ 40 kg, AND
▪ Confirmed (+) COVID-19 test, AND
▪ High risk for progression to severe COVID-19, AND
▪ Within 5 days of symptoms onset</td></tr>
<tr><td>Molnupiravir</td><td>Mild-moderate COVID-19 in High-Risk patients who are
▪ ≥ 18 years of age, AND
▪ Confirmed (+) COVID-19 test, AND
▪ High risk for progression to severe COVID-19, AND
▪ Within 5 days of symptoms onset</td></tr>
<tr><td>Additional Requirements</td><td colspan="2">NOT Authorized for:
a. Hospitalized due to severe/critical COVID-19
b. Use > 5 consecutive day
c. Pre or post-exposure prophylaxis
Confirm therapy is not contraindicated per Table 3 & Table 5</td></tr>
<tr><td>Obtain ID Approval (Inpatient use ONLY)</td><td colspan="2">1. At CHKD, both oral antiviral agents are restricted to ID (Inpatient ONLY), Contact ASAP if use is anticipated
2. The ID attending will/will not approve
3. If approved, the ID physician will notify: Sarah Parsons Pharm. D., BCPPS (Simon 6491, 8-5447) 07:30-16:00, M-F</td></tr>
<tr><td>Education</td><td colspan="2">1. Prior to receiving, you MUST communicate & provide a printed copy of the Fact Sheet for Patients and Parents/Caregivers found at:
a. Nirmatrelvir/ritonavir: Fact Sheet for Patients, Parents and Parent/Caregivers:
▪ https://www.fda.gov/media/155051/download (English)
▪ https://www.fda.gov/media/155075/download (Spanish)
b. Molnupiravir: Fact Sheet for Patients, Parents and Parent/Caregivers:
▪ https://www.fda.gov/media/155055/download (English)
▪ https://www.fda.gov/media/155115/download (Spanish)
2. Counsel the patient or parent/caregiver, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” This education MUST include:
a) The FDA has authorized the emergency use of [------] for the treatment of COVID-19 in patients with [------]
b) The patient or parent/caregiver has the option to accept or refuse [-----] treatment
c) The known and potential risks and benefits of [------], and the extent to which such potential risks and benefits are unknown
d) Information on available alternative treatments (none currently available for this patient population)
e) Post treatment continued self-isolation and the use infection control measures according to CDC guidelines
f) Provide patient or parent/caregiver a hard copy of the “Fact Sheet for Patients, Parents and Caregivers”</td></tr>
<tr><td>Document Consent in EMR</td><td colspan="2">*Must be completed on each patient PRIOR to Administration*
Document in the EMR via progress note confirming that the patient/caregiver has been:
a) Given the “Fact Sheet for Patients, Parents and Caregivers” [-------]
b) Informed of alternatives to receiving authorized [---------]
c) Informed that is an unapproved drug that is authorized for use under this Emergency Use Authorization</td></tr>
</table>

Maintain Record Transparency	**1.** Healthcare facilities and prescribers will ensure any records associated with this EUA are maintained until notified by ____ and/or FDA **2.** Such records will be made available to ___, HHS, and FDA for inspection upon request
Tracking & Reporting Adverse Events	The prescribing healthcare provider/designee are responsible for **MANDATORY** reporting which includes: **a.** Completion of FDA MedWatch Form to report all medication errors and serious adverse events **b.** The prescribing healthcare provider and/or the provider's designee are/is responsible for the mandatory reporting of all medication errors and the following serious adverse events occurring during the use of the specific monoclonal antibody and considered to be potentially related **c.** These adverse events must be reported within 7 calendar days from the onset of the event: a) Death b) a life-threatening adverse event◊ c) inpatient hospitalization or prolongation of existing hospitalization d) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions e) a congenital anomaly/birth defect f) a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly **d.** Tracking of all serious medication errors and adverse events◊ that are considered to be potentially attributable to [--------] and must report to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit: a) MedWatch form www.fda.gov/medwatch/report.htm, or b) FDA Form 3500 by fax (1-800-FDA-0178) c) Call 1-800-FDA-1088 for questions d) Submitted reports should state, [-------] use for COVID-19 under Emergency Use Authorization" at the beginning of the question "Describe Event" for further analysis e) A copy of the completed FDA Form 3500 should also be provided to the manufacture via fax, per the instructions in the authorized labeling **e.** When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information, including: a) Patient demographics (e.g., patient initials, date of birth) b) Pertinent medical history c) Pertinent details regarding adverse events and course of illness d) Concomitant medications e) Timing of adverse event(s) in relationship to administration of [------] f) Pertinent laboratory and virology information g) Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report h) Subsequent reporting of follow-up information should be completed if additional details become available i) Include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the statement "[-------] use for COVID-19 under Emergency Use Authorization (EUA)" **f.** The following steps are highlighted to provide the necessary information for safety tracking: a) In section A, box 1, provide the patient's initials in the Patient Identifier b) In section A, box 2, provide the patient's date of birth c) In section B, box 5, description of the event: i. Write "[------] use for COVID-19 under Emergency Use Authorization (EUA)" as the first line

	ii. Provide a detailed report of medication error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved drug. Please see information to include listed above d) In section G, box 1, name and address: i. Provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report Provide the address of the treating institution (NOT the healthcare provider's office address)

VI. Prescriber Required Reporting & Record Maintenance

1. Prescribers **MUST** maintain records regarding the dispensed authorized[----------] including:
    a. Product specific information including: lot numbers, quantity, receiving site, receipt date, product storage
    b. Patient specific information including:
        - Patient name
        - Disease manifestation
        - Number of doses administered per patient
        - Other drugs administered
2. Providers must report therapeutics information and utilization data through HHS Protect, Teletracking or National Healthcare Safety Network (NHSN) as directed by the U.S. Department of Health and Human Services

VII. COVID-19 Oral Antiviral Comparison

Table 3. EUA Approved Oral Antivirals Comparison

EUA Approved Oral Antivirals Comparison		
Drug	**Nirmatrelvir/ritonavir (Paxlovid)**	**Molnupiravir**
EUA Approval	12/22/2021	12/23/2021
MOA	SARS-CoV-2 protease inhibitor/HIV-1 protease inhibitor & CYP3A inhibitor	Nucleoside analogue
Indication	High-risk COVID-19	High-risk COVID-19
Admission status	Outpatient*	Outpatient*
Age	≥ 12 years	≥ 18 years
Weight	≥ 40 kg	Not Stated
When to initiate?	Within 5 days symptom onset	Within 5 days symptom onset
Dosage Form	5 daily dose blister cards	40 count bottles
Standard Dose^	Nirmatrelvir 300 mg + Ritonavir 100 mg	800 mg
Frequency	Every 12 hours	Every 12 hours
Route	Oral	Oral
Pills per dose	3 pills	4 pills
Duration	5 days	5 days
Manufacture	Pfizer	Merck
Take w/ food?	High fat ↑ absorption ~15%	With or without
Can you crush?	No	No
Renal dose adjustment	Yes: CrCl ≥ 30 to < 60 ml/min Avoid use: CrCl < 30 ml/min	No
Hepatic dose adjustment	Avoid in severe (Child-Pugh Class C)	No
Pregnancy/Breastfeeding	No human data	**Not recommended** in pregnancy **Not recommended** if breastfeeding
Common side effects	Dysgeusia, diarrhea, hypertension, myalgia	Diarrhea, nausea, dizziness
Contraindications	Hypersensitivity to drug Use with CYP3A4 significant drugs	None identified
Warnings	**Drug interactions!!!** Hepatotoxicity HIV resistance, if infected	Embryo-fetal toxicity Bone and cartilage toxicity
Drug Interactions	*Many*, refer to Table 4. https://www.hiv-druginteractions.org/checker	None identified
EUA Requirements	Yes (Section V.)	Yes (Section V.)

MOA, mechanism of action;
***** Non-hospitalized for COVID-19
^ Not renally adjusted

VIII. Common Ritonavir Drug-Drug Interaction

Table 4. Significant Drug Interactions

Class	Drug	Effect	Co-Administration Comments:
α 1-receptor antagonist	alfuzosin	↑ alfuzosin	Contraindicated due to potential hypotension
Analgesics	pethidine piroxicam propoxyphene	↑ pethidine ↑ piroxicam ↑propoxyphene	Contraindicated due to potential for serious respiratory depression or hematologic abnormalities
Antianginal	ranolazine	↑ ranolazine	Contraindicated due to potential for serious and/or life-threatening reactions
Antiarrhythmic	amiodarone dronedarone flecainide propafenone quinidine	↑ antiarrhythmic	Contraindicated due to potential for cardiac arrhythmias
	bepridil lidocaine	↑ antiarrhythmic	Contraindicated due to potential for cardiac arrhythmias
Anticancer drugs	apalutamide	↓ n/v	Contraindicated due to potential loss of virologic response and possible resistance
Anticancer drugs	abemaciclib ceritinib dasatinib encorafenib ibrutinib ivosidenib neratinib nilotinib venetoclax vinblastine vincristine	↑ anticancer drug	Avoid co-administration of encorafenib or ivosidenib due to potential risk of QT interval prolongation. Avoid use of neratinib, venetoclax or ibrutinib. Avoid co-administration of vincristine and vinblastine may lead to significant hematologic or gastrointestinal side effects.
Anticoagulants	warfarin rivaroxaban	↑↓ warfarin ↑ rivaroxaban	Closely monitor INR if co-administration with warfarin is necessary. Increased bleeding risk with rivaroxaban. Avoid concomitant use
Anticonvulsants	carbamazepine phenobarbital phenytoin	↓ n/v ↑ carbamazepine ↓ phenobarbital ↓ phenytoin	Contraindicated due to loss of virologic response
Antidepressants	bupropion trazodone	↓ bupropion ↑ trazodone	Decreased efficacy of bupropion. Nausea, dizziness, hypotension, and syncope have been observed following co-administration of trazodone and ritonavir. A lower dose of trazodone should be considered.
Antifungals	voriconazole ketoconazole isavuconazonium itraconazole	↓ voriconazole ↑ ketoconazole ↑isavuconazonium ↑ itraconazole ↑ n/v	Avoid concomitant use of voriconazole. Refer to specific product labels for further information.
Anti-gout	colchicine	↑ colchicine	Contraindicated due to potential for life-threatening reactions in renal and/or hepatic impairment
Protease inhibitors (PI)	amprenavir atazanavir darunavir fosamprenavir indinavir nelfinavir saquinavir tipranavir	↑ PI	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for increased adverse events with concomitant use of these PI
Anti-HIV	didanosine delavirdine efavirenz	↑ didanosine ↑ efavirenz ↑ maraviroc	Refer to specific anti-HIV prescribing information

	maraviroc nevirapine raltegravir zidovudine bictegravir- emtricitabine-tenofovir	↓ raltegravir ↓ zidovudine ↑ bictegravir ↔ emtricitabine ↑ tenofovir	
Anti-infective	clarithromycin erythromycin	↑ clarithromycin ↑ erythromycin	Refer to prescribing information for dose adjustment.
Antimycobacterial	rifampin	↓ n/v	Contraindicated due to potential loss of virologic response Rifabutin may be considered an alternative
Antimycobacterial	bedaquiline rifabutin	↑ bedaquiline ↑ rifabutin	Refer to product label for further information and rifabutin dose reduction.
Antipsychotics	lurasidone pimozide clozapine	↑ lurasidone ↑ pimozide ↑ clozapine	Contraindicated due to life-threatening reactions such as cardiac arrhythmias
	quetiapine	↑ quetiapine	If co-administration is necessary, reduce quetiapine dose and monitor for quetiapine-associated adverse reactions.
Calcium channel blockers (CCB)	Amlodipine diltiazem felodipine nicardipine nifedipine	↑ CCB	Caution is warranted and clinical monitoring is recommended. A dose decrease may be needed for these drugs when co-administered. Refer to specific product label for further information.
Cardiac glycosides	digoxin	↑ digoxin	Caution should be exercised when co-administering with digoxin, monitor of serum digoxin levels.
Endothelin receptor antagonists	bosentan	↑ bosentan	Discontinue use of bosentan at least 36 hours prior to initiation of n/v.
Ergot derivatives	dihydroergotamine ergotamine methylergonovine	↑ dihydroergotamine ↑ ergotamine ↑ methylergonovine	Contraindicated due to potential acute ergot toxicity
Hepatitis C antivirals	elbasvir/grazoprevir glecaprevir/pibrentasvir ombitasvir/paritaprevir/ritonavir + dasabuvir sofosbuvir/velpatasvir/voxilaprevir	↑ antiviral	Increased grazoprevir concentrations can result in ALT elevations. It is not recommended to co-administer ritonavir with glecaprevir/pibrentasvir. Refer to specific product label for further information. Patients on ritonavir-containing HCV regimens should continue their treatment as indicated. Monitor for increased n/v or HCV drug adverse events with concomitant use
Herbal products	St. John's Wort	↓ n/v	Contraindicated due to potential loss of virologic response
HMG-CoA reductase inhibitors	lovastatin simvastatin	↑ lovastatin ↑ simvastatin	Contraindicated due to potential for myopathy including rhabdomyolysis Discontinue use of lovastatin and simvastatin at least 12 hours prior to initiation of n/v.
	atorvastatin rosuvastatin	↑ atorvastatin ↑ rosuvastatin	Consider temporary discontinuation of atorvastatin and rosuvastatin during treatment with n/v.
Hormonal contraceptive	ethinyl estradiol	↓ ethinyl estradiol	Additional, non-hormonal contraception is recommended.
Immunosuppressants	cyclosporine tacrolimus sirolimus	↑ cyclosporine ↑ tacrolimus ↑ sirolimus	Therapeutic monitoring is recommended for immunosuppressants. Avoid concomitant use when monitoring is not feasible. Avoid concomitant use of sirolimus and n/v.

Long-acting β-agonist	salmeterol	↑ salmeterol	Co-administration is not recommended, increased risk of cardiovascular adverse events associated with salmeterol, including QT prolongation, palpitations, and sinus tachycardia.
Narcotic analgesics	fentanyl methadone	↑ fentanyl ↓ methadone	Careful monitoring of therapeutic and adverse effects is recommended when fentanyl is concomitantly administered. Monitor methadone-maintained patients closely for evidence of withdrawal.
PDE5 inhibitor	sildenafil	↑ sildenafil	Contraindicated due to sildenafil associated adverse events, including visual abnormalities hypotension, prolonged erection, and syncope
Sedative/hypnotics	triazolam midazolam (oral)	↑ triazolam ↑ midazolam	Contraindicated due to extreme sedation and respiratory depression
	midazolam (IV)	↑ midazolam	Co-administration of midazolam (IV) only when under close clinical monitoring in case of respiratory depression and/or prolonged sedation. Dosage reduction for midazolam should be considered, especially if more than a single dose of midazolam is administered.
Systemic corticosteroids	betamethasone budesonide ciclesonide dexamethasone fluticasone methylprednisolone mometasone prednisone triamcinolone	↑ corticosteroid	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.

n/v: nirmatrelvir/ritonavir

IX. Helpful Links: Emergency Use

Resources	
Nirmatrelvir/ritonavir (Paxlovid)	Website: **a)** Fact Sheet for Health Care Providers: ▪ https://www.fda.gov/media/155050/download **b)** Fact Sheet for Patients, Parents and Parent/Caregivers: ▪ https://www.fda.gov/media/155051/download (English) ▪ https://www.fda.gov/media/155075/download (Spanish) **c)** FDA Letter of Authorization: ▪ https://www.fda.gov/media/155049/download **d)** Important Dispensing Information [Moderate Renal Failure] ▪ https://www.fda.gov/media/155072/download **e)** Provider Letter ▪ https://www.fda.gov/media/155071/download
Molnupiravir	Merck Website: https://www.molnupiravir.com/ **a)** Fact Sheet for Health Care Providers: ▪ https://www.fda.gov/media/155054/download **b)** Fact Sheet for Patients, Parents and Parent/Caregivers: ▪ https://www.fda.gov/media/155055/download (English) ▪ https://www.fda.gov/media/155115/download (Spanish) **c)** FDA Letter of Authorization: ▪ https://www.fda.gov/media/155053/download

References:

1. Nirmatrelvir/ritonavir (Paxlovid) [EUA Fact Sheet]. Copyright © 2021, Pfizer. All rights reserved, issued 12/22/2021
2. Molnupiravir [EUA Fact Sheet]. Copyright © 2021, Merck & Co., Inc. All rights reserved, issued 12/23/2021
3. NIH COVID-19 Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/ (accessed 12/7/21)
4. Hanson KE. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19, last updated 5/27/21, [accessed 12/7/21]. [https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostic...]
5. Bhimraj A, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 [accessed 12/7/21]
6. Medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: https://www.cdc.gov/coronavirus/2019- ncov/need-extra-precautions/people-with-medical-conditions.html. Accessed 12/10//21

Created by: Sarah Parsons Pharm.D., BCPPS Laura Sass M.D.	
Originated: 01/05/2022	Last Revised: 5/5/2022
5/5/2022: updated interaction checker link, highlighted ID approval and restrictions for use are for inpatient only	