



MISSISSIPPI STATE DEPARTMENT OF HEALTH



COVID-19 Therapeutics: Oral Antivirals

MISSISSIPPI STATE
DEPARTMENT OF HEALTH
12 May 2022

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Oral Antivirals

- **Paxlovid:** Nirmatrelvir + Ritonavir
 - Nirmatrelvir - a SARS-CoV-2 main protease inhibitor
 - Ritonavir - a CYP3A inhibitor included to increase nirmatrelvir plasma levels
 - Ritonavir alone has no activity against SARS-CoV-2
- **Lagevrio:** Molnupiravir
 - a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis



EUA- Authorized Use

Paxlovid:

- Treatment of mild-to-moderate COVID-19
- Adults and pediatric patients (12 years of age and older weighing at least 40 kg)
- Positive results of direct SARS-CoV-2 viral testing
- High risk for progression to severe COVID-19, including hospitalization or death
 - [People with Certain Medical Conditions | CDC](#)
- Must be started within 5 days of symptom onset
- EUA: [FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID \(fda.gov\)](#)

EUA- Authorized Use

Lagevrio:

- Treatment of mild-to-moderate COVID-19
- Adults (**18** years of age and older)
- Positive results of direct SARS-CoV-2 viral testing
- High risk for progression to severe COVID-19, including hospitalization or death
 - [People with Certain Medical Conditions | CDC](#)
- Alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate
- Must be started within 5 days of symptom onset
- EUA: [FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR MOLNUPIRAVIR \(fda.gov\)](#)

Limitations of Authorized Use

Paxlovid and Lagevrio are not authorized for:

- Initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
- Use as pre-exposure or post-exposure prophylaxis for COVID-19
- Use for longer than 5 consecutive days



Efficacy In Clinical Trials

- **Paxlovid:**
 - EPIC-HR: [EPIC-HR: Study of Oral PF-07321332/Ritonavir Compared With Placebo in Nonhospitalized High Risk Adults With COVID-19 - Full Text View - ClinicalTrials.gov](#)
 - Reduced COVID-19 related hospitalization and death by 88% when given within 5 days of symptom onset
- **Lagevrio:**
 - Trial P002 (MOVE-OUT): [Efficacy and Safety of Molnupiravir \(MK-4482\) in Non-Hospitalized Adult Participants With COVID-19 \(MK-4482-002\) - Full Text View - ClinicalTrials.gov](#)
 - Reduced COVID-19 related hospitalization and death by 30% when given within 5 days of symptom onset



Prescribing Requirements

- Paxlovid and Lagevrio require a prescription
- Prescribers must have an encounter with the patient prior to issuing a prescription
 - May be an in-person or virtual encounter
- Include the date of symptom onset on the prescription
 - Must be filled within 5 days of symptom onset
- Patients must be given a copy of the “Fact Sheet for Patients, Parents, and Caregivers”
 - Paxlovid: <https://www.fda.gov/media/155051/download>
 - Lagevrio: <https://www.fda.gov/media/155055/download>



Dosing

- Begin treatment as soon as possible after COVID-19 diagnosis and within 5 days of symptom onset
- **Paxlovid**
 - Two 150 mg tablets (300 mg) nirmatrelvir with one 100 mg tablet ritonavir orally twice daily for 5 days
 - May be taken with or without food
 - Dose reduction needed for moderate renal impairment
- **Lagevrio**
 - Four 200 mg capsules (800 mg) taken every 12 hours for 5 days
 - May be taken with or without food



Safety

Paxlovid:

- Adverse events (incidence $\geq 1\%$)
 - dysgeusia (6%)
 - diarrhea (3%)
 - hypertension (1%)
 - myalgia (1%)

Lagevrio:

- Adverse events (incidence $\geq 1\%$)
 - diarrhea (2%)
 - nausea (1%)
 - dizziness (1%)



Drug Interactions: Paxlovid

Prescribe alternative COVID-19 therapy for patients receiving any of the following:

Amiodarone	Propafenone
Carbamazepine	Ranolazine
Clopidogrel	Rifampin
Clozapine	Rivaroxaban
Dofetilide	Sildenafil for pulmonary HTN
Flecainide	St. John's wort
Phenobarbitol	Tadalafil for pulmonary HTN
Phenytoin	Ticagrelor

For full list see: [Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines \(nih.gov\)](#)

Drug Interactions: Paxlovid

If withholding any of the following medications is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy:

Benzodiazepines:	Alprazolam, Clonazepam, Diazepam, Triazolam
Erectile dysfunction:	Sildenafil, Tadalafil, Vardenafil
Pain:	Codeine, Fentanyl, Hydrocodone, Meperidine, Oxycodone, Tramadol
Prostate:	Alfuzosin, Silodosin, Tamsulosin
Statins:	Atorvastatin, Lovastatin, Rosuvastatin, Simvastatin

For full list see: [Statement on Paxlovid Drug-Drug Interactions | COVID-19 Treatment Guidelines \(nih.gov\)](#)

Drug Interactions: Paxlovid

- [PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers \(fda.gov\)](https://www.fda.gov/oc/ohrt/paxlovid-patient-eligibility-screening-checklist-tool-for-prescribers)
- [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://www.liverpooldruginteractions.org/covid19-interactions)
- [Drug Interaction Checker | Pfizer Medical Information - US](https://www.pfizer.com/medwatch/interaction-checker)

PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers

Other Drugs with Established and Other Potentially Significant Drug Interactions with PAXLOVID (listed alphabetically by generic name)

Interaction Codes:

XXX Coadministration of this drug with PAXLOVID is CONTRAINDICATED. For further information, refer to the Fact Sheet for Healthcare Providers and the individual Prescribing Information for the drug.

******* Coadministration of this drug with PAXLOVID should be avoided and/or holding of this drug, dose adjustment of this drug, or special monitoring is necessary. Consultation with the prescriber of the potentially interacting drug is recommended. For further information, refer to the Health Care Provider Fact Sheet and the individual Prescribing Information for the drug.

Drug	Drug Class	Interaction Code
abemaciclib	Anticancer drug	***
alfuzosin	Alpha 1-adrenoreceptor antagonist	XXX
amiodarone	Antiarrhythmic	XXX
amlodipine	Calcium channel blocker	***
apalutamide	Anticancer drug	XXX
bedaquiline	Antimycobacterial	***
bepidil	Antiarrhythmic	***
betamethasone	Systemic corticosteroid	***
bosentan	Endothelin receptor antagonist	***



Drug Interactions: Lagevrio

- No drug interactions have been identified based on the limited data available



Special Populations: Renal Impairment

Paxlovid:

eGFR	PAXLOVID Dose
>60 mL/min (normal renal function or mild renal impairment)	300 mg nirmatrelvir with 100 mg ritonavir, taken twice daily for 5 days
≥30 to ≤60 mL/min (moderate renal impairment)	150 mg nirmatrelvir with 100 mg ritonavir, taken twice daily for 5 days
<30 mL/min (severe renal impairment)	Not recommended

- Pharmacists can dispense the renal dose packaged form of Paxlovid, or,
- Can remove any unneeded tablets and dispose of per the site's standard policy
 - Instructions for pharmacists and sticker packs accompany each shipment of Paxlovid

Lagevrio:

- No adjustment is recommended in patients with any degree of renal impairment



Special Populations: Pregnancy

Paxlovid

- No available clinical data on pregnancy or with breast feeding
- Animal studies showed reduced body weights at ~10x the nirmatrelvir exposure seen in humans with the authorized dose

Lagevrio:

- Not recommended for use during pregnancy
 - Authorized for use in pregnancy only if benefits would outweigh risks for the individual patient
 - Documentation requirements apply



Family Planning Considerations

Paxlovid

- Ritonavir may reduce efficacy of combined hormonal contraceptives
 - Patients should use an effective alternative contraceptive method or an additional barrier method of contraception

Lagevrio

- Females of childbearing potential should be advised of potential risk to fetus
 - Alternate method of contraception should be used for the duration of the treatment and for 4 days after the last dose
- Males of reproductive potential who are sexually active with women of childbearing potential should use a reliable method of contraception during treatment and for at least 3 months after the last dose



Clinical Decision Tool

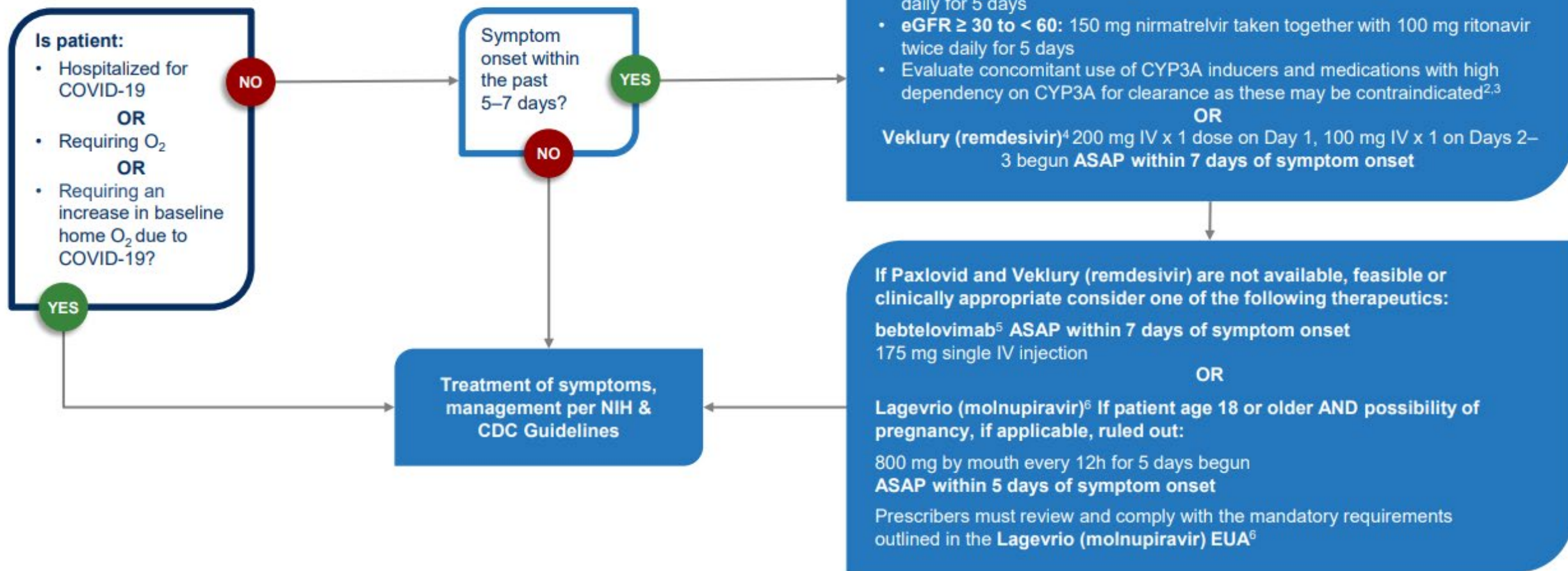
- [COVID-19 Therapeutics Decision Aid \(hhs.gov\)](https://www.hhs.gov)



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



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/156152/download>

⁶ Lagevrio EUA. <https://www.fda.gov/media/155054/download>



Therapeutic Locator

- Sites which dispense oral antivirals can be found on the MSDH website:
 - [MS COVID-19 Therapeutics Locator](#)
 - [17718.pdf \(ms.gov\)](#)

MS COVID-19 Therapeutics Locator *

Available Therapies: All | Provider Type: All | City: All | Zip: All | **RESET**

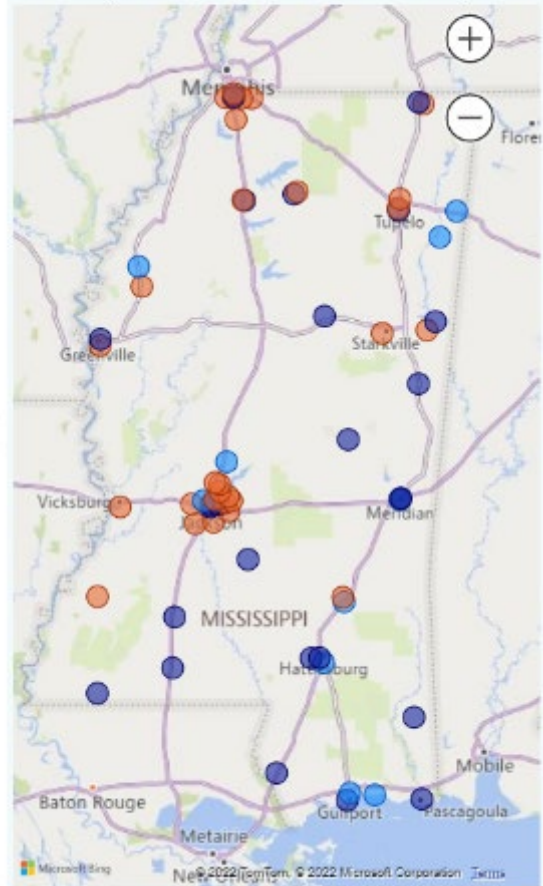
Provider Type ● FQHC ● Hospital ● Retail Pharmacy

Jackson-Hinds Comprehensive Health Center

Provider Type: FQHC
Available Therapies: Oral Antivirals
Location: 3502 West Northside Dr, Jackson, MS 39213
Phone: 601-362-5321

Kroger Food & Drug #404

Provider Type: Retail Pharmacy
Available Therapies: Oral Antivirals
Location: 465 State Line Rd., Southaven, MS 38671
Phone: 662-393-3426



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Resources

- Paxlovid Healthcare Provider Fact Sheet: <https://www.fda.gov/media/155050/download>
- Lagevrio Healthcare Provider Fact Sheet: <https://www.fda.gov/media/155054/download>
- Patients with Certain Medical Conditions: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>
- EPIC-HR Clinical Trial: [EPIC-HR: Study of Oral PF-07321332/Ritonavir Compared With Placebo in Nonhospitalized High Risk Adults With COVID-19 - Full Text View - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT04321332)
- Trial P002 (MOVE-OUT): [Efficacy and Safety of Molnupiravir \(MK-4482\) in Non-Hospitalized Adult Participants With COVID-19 \(MK-4482-002\) - Full Text View - ClinicalTrials.gov](https://www.clinicaltrials.gov/ct2/show/study/NCT04321332)
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- Lagevrio Fact Sheet for Patients, Parents, and Caregivers: <https://www.fda.gov/media/155055/download>
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 - [PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers \(fda.gov\)](https://www.fda.gov/paxlovid/patient-eligibility-screening-checklist-tool-for-prescribers)
 - [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://www.covid19-druginteractions.org/)
 - [Drug Interaction Checker | Pfizer Medical Information - US](https://www.pfizer.com/medinfo/us/drug-interaction-checker)
- Clinical Decision Tool: [COVID-19 Therapeutics Decision Aid \(hhs.gov\)](https://www.hhs.gov/therapeutics/decision-aid)
- Therapeutic Locator: https://msdh.ms.gov/msdhsite/_static/14,0,420,694.html - locator
- Health Partner Order Portal (HPoP): <https://vpop.cdc.gov/provider/signin/>
- Therapeutics Side-by-Side Overview: <https://www.phe.gov/emergency/events/COVID19/therapeutics/Documents/side-by-side-overview.pdf>

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