



MISSISSIPPI STATE DEPARTMENT OF HEALTH



COVID-19 Therapeutics: Oral Antivirals

**MISSISSIPPI STATE
DEPARTMENT OF HEALTH
REVISED: 19 July 2022**

Contents

- Medications and Dosing
- Target Population
- Safety Profile
- Drug/Drug Interactions
- Special Populations
- Accessibility



How to find this presentation on the MSDH website:

The screenshot shows the Mississippi State Department of Health website. The header includes the MSDH logo and navigation links: ABOUT, LOCATIONS, CONTACT, TOPICS A-Z, and a SEARCH button. A left-hand menu is visible with the following items: Menu, Disease Control, Coronavirus COVID-19 (highlighted with a red box), [Espanol, Tieng Viet, ASL], Charts, County COVID-19 Data, COVID-19 Data Reports, COVID-19 Epidemiological Briefs, Handouts and Posters, Healthcare Professionals (highlighted with a red box), Prevention and Treatment, School Cases and Outbreaks, Testing for COVID-19, and Vaccination Against COVID-19. The main content area is titled 'Coronavirus COVID-19 Guidance and Information for Healthcare Professionals' and is dated 'Updated May 2022'. It features a 'Select Language' dropdown and three main sections: 'Healthcare Guidance and case reporting' with a right arrow, 'MS-HAN Messages COVID-19 advisories' with a right arrow, and 'CDC Guidance Healthcare, EMS, etc.' with a right arrow. Below these are links for 'Guidance and resources', 'Health facilities', 'Therapeutics for COVID-19', 'Reporting COVID-19 cases', 'Specimen collection, reporting and delivery', 'Surveillance', and 'Vaccination providers'.

The screenshot shows the 'MS COVID-19 Therapeutics Locator' tool. It has a title bar with the text 'MS COVID-19 Therapeutics Locator *, **, ***'. Below the title bar are four dropdown menus: 'Available Therapies' (set to 'All'), 'Provider Type' (set to 'All'), 'City' (set to 'All'), and 'Zip' (set to 'All'). There is a 'RESET' button to the right of the 'Zip' dropdown. Below the dropdowns is a map of Mississippi showing various locations marked with colored dots. A legend on the right side of the map identifies the colors: Clinic (yellow), FQHC (purple), Hospital (blue), Infusion Center (green), and Pharmacy (brown). The map shows a high density of locations in the central and southern parts of the state. Below the map, there are three lines of text: '* Supply of treatments is changing rapidly. Please call the site to check availability.', '** Data updated on 7/8/2022.', and '*** Hold CTRL to select multiple items in drop-down menus.' At the bottom of the tool, there is a 'Microsoft Power BI' logo and a zoom control bar set to 80%.

Presentation: Oral Antiviral Therapeutics

Overview and details of use, safety, interactions, target population and more (May 12, 2022)



- ▶ View this video full screen
- ▶ Slides of this video PDF
- ▶ Online resources mentioned in this video
- ▶ COVID-19 Therapeutics Decision Aid (hhs.gov)

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>

Pharmacist Prescribing Requirements for Paxlovid

- Pharmacists may now prescribe Paxlovid under FDA authorization and MSDH standing order
 - MSDH Standing Order: [19176.pdf \(ms.gov\)](#)
- Patient consultation and counseling must be provided by a licensed pharmacist prior to dispensing Paxlovid.
- Patients must be given a copy of the “Fact Sheet for Patients, Parents, and Caregivers” prior to dispensing Paxlovid.
 - Paxlovid: <https://www.fda.gov/media/155051/download>
- Pharmacists may **NOT** prescribe Paxlovid renal dose packs

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

- PAXLOVID (nirmatrelvir co-packaged with ritonavir) is a **strong inhibitor of CYP3A** and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. Co-administration of PAXLOVID with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated. Co-administration with other CYP3A substrates may require a [dose adjustment or additional monitoring](#).
- Nirmatrelvir and ritonavir are CYP3A substrates; therefore, **drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations** and reduce PAXLOVID therapeutic effect
- **Prescribe alternative COVID-19 therapy for patients receiving any interacting medications that cannot be held during Paxlovid treatment.**



Drug Interactions: Paxlovid

For guidance on specific drug-drug interaction management, please refer to:

[Pfizer Paxlovid Fact Sheets for HCPs \(07052022\) \(fda.gov\)](#)

[Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](#)

[Drug Interaction Checker | Pfizer Medical Information - US](#)

[PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers \(fda.gov\)](#)

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

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:



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	***
bepidril	Antiarrhythmic	***
betamethasone	Systemic corticosteroid	***
bosentan	Endothelin receptor antagonist	***



MISSISSIPPI
STATE DEPARTMENT OF HEALTH

Drug Interactions: Paxlovid

If clinically appropriate, the following medications may be held while the patient is on Paxlovid. If 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
Calcium channel blockers:	Amlodipine, Diltiazem, Felodipine, Nicardipine, Nifedipine

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

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

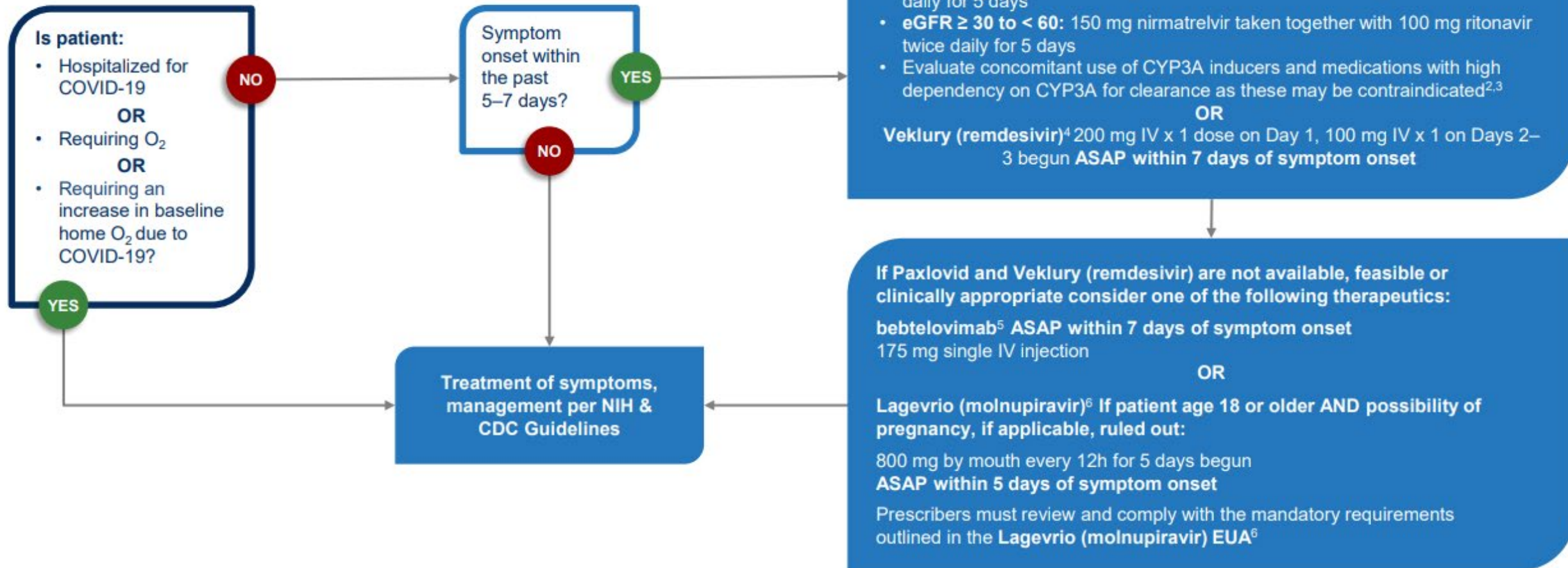
- [COVID-19 Therapeutics Decision Aid \(hhs.gov\)](https://www.hhs.gov/covid-19/therapeutics/decision-aid)



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>



April 18, 2022

Therapeutic Locator

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

MS COVID-19 Therapeutics Locator *

Available Therapies

Provider Type

City

Zip

RESET

All

All

All

All

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

Provider Type

FQHC

Hospital

Retail Pharmacy



Paxlovid Shelf-Life Extension

On April 4, 2022, the U.S. Food and Drug Administration (FDA) approved a shelf-life extension for PAXLOVID for lot numbers referenced below.

Lot/Batch#	Labeled Expiration date	Extended Expiration Date
FL4516	07/31/22	10/31/22
FL4517	07/31/22	10/31/22
FR7229	07/31/22	10/31/22
FR9088	08/31/22	11/31/22

Link: https://www.paxlovidhcp.com/files/hcp-letter-update-for-expiry-date_04Apr2022-003.pdf

How to find this presentation on the MSDH website:

The screenshot shows the Mississippi State Department of Health website. The header includes the MSDH logo and navigation links: ABOUT, LOCATIONS, CONTACT, TOPICS A-Z, and a SEARCH button. A left-hand menu is visible with the following items: Menu, Disease Control, Coronavirus COVID-19 (highlighted with a red box), [Espanol, Tieng Viet, ASL], Charts, County COVID-19 Data, COVID-19 Data Reports, COVID-19 Epidemiological Briefs, Handouts and Posters, Healthcare Professionals (highlighted with a red box), Prevention and Treatment, School Cases and Outbreaks, Testing for COVID-19, and Vaccination Against COVID-19. The main content area is titled 'Coronavirus COVID-19 Guidance and Information for Healthcare Professionals' and includes a 'Select Language' dropdown. Below this are three boxes: 'Healthcare Guidance and case reporting' with an arrow, 'MS-HAN Messages COVID-19 advisories' with an arrow, and 'CDC Guidance Healthcare, EMS, etc.' with an arrow. A list of 'Guidance and resources' is provided: Health facilities, Therapeutics for COVID-19, Reporting COVID-19 cases, Specimen collection, reporting and delivery, Surveillance, and Vaccination providers.

The screenshot shows the 'MS COVID-19 Therapeutics Locator' tool. It features a search interface with dropdown menus for 'Available Therapies' (set to 'All'), 'Provider Type' (set to 'All'), 'City' (set to 'All'), and 'Zip' (set to 'All'), along with a 'RESET' button. Below the search fields is a map of Mississippi with colored dots representing different provider types: Clinic (yellow), FQHC (purple), Hospital (blue), Infusion Center (green), and Pharmacy (red). The map shows a high density of providers in the central and southern parts of the state. Below the map, there are three lines of text: '* Supply of treatments is changing rapidly. Please call the site to check availability.', '** Data updated on 7/8/2022.', and '*** Hold CTRL to select multiple items in drop-down menus.' The bottom of the screenshot shows the 'Microsoft Power BI' logo.

Presentation: Oral Antiviral Therapeutics

Overview and details of use, safety, interactions, target population and more (May 12, 2022)



- ▶ View this video full screen
- ▶ Slides of this video PDF
- ▶ Online resources mentioned in this video
- ▶ COVID-19 Therapeutics Decision Aid (hhs.gov)

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?term=EPIC-HR&rank=1)
- 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?term=P002&rank=1)
- Paxlovid Fact Sheet for Patients, Parents, and Caregivers: <https://www.fda.gov/media/155051/download>
- Lagevrio Fact Sheet for Patients, Parents, and Caregivers: <https://www.fda.gov/media/155055/download>
- Paxlovid Drug-Drug Interactions:
 - <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/>
 - [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/us/druginfo/paxlovid)
- Clinical Decision Tool: [COVID-19 Therapeutics Decision Aid \(hhs.gov\)](https://www.hhs.gov/covid19/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>

C19therapeutics@msdh.ms.gov

601-713-3457



MISSISSIPPI
STATE DEPARTMENT OF HEALTH