|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Nirmatrelvir + ritonavir (Paxlovid)**  | * Limited supply available through **SPH Broadway Pharmacy.** The drug will be ordered using an order form **(NOT e-prescribed).**
 | * **Treatment** of mild-moderate COVID-19 in patients at risk of progression to severe COVID-19, including hospitalization or death.
 | * **First line if available**
* Adults or pediatrics 12 years or older weighing at least 40 kg
* Direct positive SARS-CoV-2 test
* **Tier 1-4** Risk Groups(see below)
* Treatment within **< 5 days of symptom onset**
* **\*\* Must screen for drug-drug interactions with ritonavir\*\***
 | * **Significant drug-drug interactions:** Co-administration with **CYP3A major substrates or inducers** is contraindicated
* Not recommended in patients were severe renal impairment **eGFR < 30 mL /min**
* Not recommended in patients with severe hepatic impairment (**CHILD-PUGH Class C**)

**Not authorized** for: * Patients requiring hospitalization due to severe or critical COVID-19
* Pre-exposure or post-exposure prophylaxis

 * Use longer than five consecutive days
 | * **Nirmatrelvir 300 mg** (two 150 mg tablets) by mouth + **ritonavir 100 mg** (one 100 mg tablet) by mouth twice daily (**total of three**

**tablets twice daily**) x **5 days** * eGFR 30-60 mL/min: dose reduce to nirmatrelvir 150 mg + ritonavir 100 mg by mouth twice daily
* May be taken with or without food
 | Phase 2/3 **EPIC-HR** (NCT #0496202) * Randomized, double-blind, placebo-controlled study
* Subjects: Non-hospitalized, symptomatic adults (symptom onset < 5 days) with laboratory confirmed diagnosis of COVID-19 and at least one risk for progression to severe COVID-19
* Primary endpoint: COVID-19 related hospitalization or all-cause mortality at day 28
* Efficacy: **88% relative risk reduction** in COVID-19 related hospitalization and all-cause mortality (95% CI: 75-94%, p<0.0001)
 |
| **Remdesivir (Veklury)**  | * Available to non-hospitalized patients through **SPH COVID infusion clinic**
* Because remdesivir has FDA approval (not EUA), there is no patient consent form for treatment
* Cost **$$$$$**: drug and infusion charge
 | * **Treatment** of mild-moderate COVID-19 in patients at risk of progression to severe COVID-19, including hospitalization or death
 | * Adults or pediatrics 12 years or older weighing at least 40 kg
* Direct positive SARS-CoV-2 test
* **Tier 1-4** Risk Groups Criteria (see below) **when Paxlovid unavailable** **or contraindicated**
* Treatment within **< 7 days of symptom onset**
 | * **Caution in renal impairment (eGFR < 30 mL/min)** as remdesivir contains the excipient SBECD which accumulates in renal dysfunction
 | * **Day 1**: remdesivir **200 mg** in 250 mL 0.9% sodium chloride administered over **30 minutes**
* **Days 2 and 3**: remdesivir **100 mg** in 250 mL 0.9% sodium chloride administered over **30 minutes**
* Monitor patient for at least 60 minutes after infusion complete
 | **PINE-TREE Trial** (NCT #04501952) * Randomized, double-blind, placebo-controlled trial.
* Subjects: Patients > 12 years with at least one symptom of COVID-19 (onset < 7 days) and at least one risk factor for progression to severe COVID-19
* Primary endpoint: COVID-19 related hospitalization or death by day 28
* Efficacy: **87% relative risk reduction** in COVID-19 related hospitalization and all-cause mortality (HR 0.13 [0.03-0.59]; p=0.008)
 |
| **Molnupiravir**  | * **Currently unavailable at SPH**
 | * **Treatment** of mild-moderate COVID-19 in patients at risk of progression to severe COVID-19, including hospitalization or death
 | * **Adults**
* Direct positive SARS-CoV-2 test
* Tier 1-4 Risk Groups when NONE of the above treatment options can be used
* Treatment within **< 5 days of symptom onset**
 | * Use in pregnancy not recommended
* Breastfeeding is not recommended during treatment and for 4 days after the last dose

**Not authorized** for: * Pediatric patients
* Patients requiring hospitalization due to severe or critical COVID-19
* Pre-exposure or post-exposure prophylaxis

 * Use longer than five consecutive days

**Warnings:** * Females of childbearing potential should use contraception during treatment and for 4 days after the last dose
* Males of reproductive potential who are sexually active with females of childbearing potential should use contraception during treatment and for 3 months after the last dose
 | * Molnupiravir **800 mg** (four 200 mg capsules) by mouth **twice daily x 5 days**
* May be taken with or without food
 | Phase 2/3 **MOVe-OUT** **Trial** (NCT #04575597) * Randomized, double-blind, placebo-controlled study
* Subjects: Non-hospitalized, symptomatic adults (symptom onset < 5 days) with laboratory confirmed diagnosis of COVID-19 and at least one risk for progression to severe COVID-19

(vaccinated patients excluded) * Primary endpoint: All-cause hospitalization or mortality at day 29
* Efficacy: **30% adjusted relative risk reduction** in all-cause hospitalization and mortality (95% CI: 1-51%)
 |

Additional resources:

* Patient Prioritization for Treatment:

|  |  |
| --- | --- |
| **Tier**  | **Risk Group**  |
| 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
	+ Patients within 1 year of receiving B cell depleting agents
	+ Patients receiving Bruton tyrosine kinase inhibitors
	+ Chimeric antigen receptor T cell recipients
	+ Post-hematopoietic cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
	+ Patients with hematologic malignancies who are on active therapy
	+ Lung transplant recipients
	+ Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
	+ Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
	+ Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm3
* Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
 |
| 2 | * Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
 |
| 3 | * Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors)

Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment. |
| 4 | * Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors)

Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment. |

* For more information about **management of Paxlovid drug-drug interactions** see the NIH COVID-19 Treatment Guidelines Panel’s Statement on Potential Drug-Drug Interactions: <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/>

Treatment Algorithm per NIH COVID-19 Treatment Guidelines Panel’s Statement on Therapies for High-Risk, Non-hospitalized Patients with Mild to Moderate COVID-19:

**References:**

1. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines (01/2022). National Institutes of Health website. Available at: https://www.covid19treatmentguidelines.nih.gov/. Accessed January 6, 2022.
2. Paxlovid [Emergency Use Authorization]. New York, NY: Pfizer; 2021 December.
3. Veklury [Emergency Use Authorization]. Gilead Sciences; 2020 October.
4. Gottlieb et. al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. N Engl J Med 2021.
5. Molnupiravir [Emergency Use Authorization]. Kenilworth, NJ: Merk & Co; 2020 October.