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| **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:

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| **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.