University Health

COVID-19 Outpatient Therapeutics Overview

	Sotrovimab	Nirmatrelvir/ritonavir (Paxlovid®)	Molnupiravir (Lagevrio®)	Fluvoxamine	Remdesivir (Veklury®)
Manufacturer	GlaxoSmithKline	Pfizer	Merck	N/A	Gilead
Current EUA	Yes	Yes	Yes	No (submitted)	FDA approved[#]
Indication	At risk outpatients with mild-moderate COVID	At risk outpatients with mild-moderate COVID	At risk outpatients with mild-moderate COVID	At risk outpatients with mild-moderate COVID	At risk patients with COVID
Drug class	Monoclonal antibody	Protease inhibitor and CYP3A inhibitor	Nucleoside analogue	SSRI	RNA polymerase inhibitor
Mechanism of action	Neutralizing monoclonal antibody	Inhibits mPRO, preventing viral replication	Viral lethal mutagenesis	Anti-inflammatory, sigma-1 receptor	Inhibits viral replication
Delta variant activity	Yes	Yes	Yes	Expected	Expected
Omicron variant activity	Expected	Expected	Expected	Expected	Expected
Age limit	12 years or older	12 years or older	18 years or older	8 years or older	12 years or older
Weight limit	40 kg or more	40 kg or more	None stated	None stated	40 kg or more
Can initiate if hospitalized for COVID?	No	No	No	Currently non-formulary at UH	Yes
Can continue if hospitalized during therapy?	No	Yes, if available	Yes, if available	Currently non-formulary at UH	Yes
Authorized for pre-exposure or post-exposure prophylaxis?	No	No	No	No	No
When to start?	Within 10 days of symptom onset	Within 5 days of symptom onset	Within 5 days of symptom onset	Within 7 days of symptom onset	Within 7 days of symptom onset
Route	IV	Oral	Oral	Oral	IV
Dose	500 mg once over 30 minutes	300 mg nirmatrelvir + 100 mg ritonavir every 12 hours	800 mg every 12 hours	50 mg BID	200 mg on day 1, then 100 mg daily on day 2 & 3*
Pills per dose	N/A	3	4	1	N/A
Duration of therapy	One time infusion	5 days	5 days	10 days	3 days*
Okay to crush?	N/A	No	No	No	N/A
Renal and hepatic dose adjustments?	No	Yes	No	No	No

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Pregnancy and breastfeeding?	No data	No data	Not recommended	Not recommended	Risk vs benefit
Must provide patient fact sheet?	Yes	Yes	Yes	No	No
Drug interactions	No	Yes	No	Yes with melatonin	No
Warnings	Infusion related reactions	Hepatotoxicity, HIV-1 drug resistance	Embryo-fetal toxicity, bone and cartilage toxicity	Increased risk of suicidal thinking in children	Renal impairment (cyclodextrin)
Contraindications	None	Patients on drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions	Pregnancy	None	None
Most common adverse reactions	Infusion related reactions	Dysguesia, diarrhea, hypertension, myalgia	Diarrhea, nausea, dizziness	Headache, insomnia, nausea, weakness	Nausea, increased AST and ALT, prolonged prothrombin time
Efficacy in high risk patients compared to placebo: **Hospitalizations or deaths at ~28 days (%):**	79% reduction in hospitalization or death through day 29 SOT 1% vs PL 6%	88% reduction in hospitalization or death through day 28 PAX 0.8% vs PL 6.3%	30% reduction in hospitalization or death through day 29 MOL 6.8% vs PL 9.7%	32% reduction in hospitalization or >6 hrs in ED at 28 days FLU 11% vs PL 16%	87% reduction in hospitalization or death through day 28 REM 0.7% vs PL 5.3%

PL: placebo, [#]Remdesivir has EUA approval for pediatric patients who weigh 3.5 to less than 40 kg and are less than 12 years of age to support utilization in non-hospitalized patients with mild-to-moderate COVID-19 , and are at high risk for progression to severe COVID-19. *If being used outpatient, recommend total 3 day duration.

Citations:

1) Paxlovid EUA as of 1/2/22
2) Molnupiravir EUA as of 1/2/22
3) Sotrovimab EUA as of 1/2/22
4) Lenze EJ, Mattar C, Zorumski CF, et al. Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19: A Randomized Clinical Trial. JAMA. 2020;324(22):2292–2300. doi:10.1001/jama.2020.22760
5) Reis G, Dos Santos Moreira-Silva EA, Silva DCM, et al. Effect of early treatment with fluvoxamine on risk of emergency care and hospitalization among patients with COVID-19: the TOGETHER randomized, platform clinical trial. Lancet Glob Health. 2022 Jan;10(1):e42-e51. doi: 10.1016/S2214-109X(21)00448-4. Epub 2021 Oct 28. PMID: 34717820; PMCID: PMC8550952.
6) Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. N Engl J Med. DOI: 10.1056/NEJMoa2116846.

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