Therapeutic Essentials for the Long-Term Care Community – Paxlovid Highlights

The Centers for Disease Control (CDC) and National Institutes of Health (NIH) currently recommends one of two therapies in individuals who have COVID-19 in the outpatient setting who are at risk of progressing to severe disease:

1) nirmatrelvir-ritonavir (brand name Paxlovid)

2) remdesivir (brand name Velkury).[i,ii]

Paxlovid is given by mouth. Velkury is given intravenously. Of note, Velkury has historically been approved exclusively in the hospitalized population deemed to have severe disease. The recent PINETREE Trial[iii], however, moved the Food and Drug Administration (FDA) to authorize use in the outpatient setting for at-risk individuals – which includes the long-term care population. Of note, molnupiravir (brand name Lagevrio) is not currently a preferred therapy for at-risk populations due to the lack of efficacy recently shown in the PANORAMIC trial.[iv] According to NIH treatment guidelines, Lagevrio is recommended as an alternative only if Paxlovid or Velkury are not available or cannot be used, but these guidelines have not been updated since the release of the PANORAMIC trial.[v]

Here are a few key facts about Paxlovid:

- Paxlovid has not been FDA approved, but it is authorized under **emergency use authorization** by the FDA for adults and children ages 12 and over with mild-moderate COVID-19 who are at risk for progression to severe disease.[vi]

- Early evidence showing the significant benefit of Paxlovid came from the **EPIC-HR trial**,[vii] which showed an 89% relative risk reduction in progression to hospitalization or death among unvaccinated individuals at high-risk for disease progression. Recently, the CDC has also published data on the benefits of Paxlovid in preventing disease progression among vaccinated or previously infected COVID-19 populations.[viii]

- Paxlovid is a **two-drug combination** given orally twice daily for 5 days. At each dosing, two 150 mg tablets (300 mg total) of nirmatrelvir are given with one 100 mg tablet of ritonavir. Nirmatrelvir is a protease inhibitor targeted at the COVID virus, and ritonavir works by increasing the concentration of nirmatrelvir in the bloodstream.

- Paxlovid should be given **as soon as possible** after a diagnosis is made, works best when given early after diagnosis, and should certainly be given within 5 days of symptoms. It is not indicated in patients who have already progressed to severe disease (developed hypoxia) or have been hospitalized for COVID.

- Paxlovid in the general population may have a "**convenience benefit**" over Velkury since it can be given by mouth. But that can pose problems in the long-term care community - there are three pills per dose, and the pills cannot be crushed. Thus, individuals who cannot swallow pills cannot take Paxlovid.

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- Because of **significant drug-drug interactions**, Paxlovid is certainly not the right choice for every long-term care resident. Drug-drug interactions with Paxlovid are common, especially among medications that interact with the CYP3A metabolic pathway. When in doubt, **seek consultation with a pharmacist before prescribing**. Anticoagulants, statins, antiarrhythmics, antiepileptics, and antipsychotics commonly interact with Paxlovid. If contraindications exist, there should be a risk/benefit decision about holding the maintenance medication during Paxlovid treatment. If holding the contraindicated medication(s) is not an option, Velkury may be a therapeutic choice to consider for your patient.

- Paxlovid is generally **well-tolerated**. Side effects such as change in taste, body aches and gastrointestinal symptoms can occur.

- Paxlovid is **renally dosed** for individuals with eGFR <60 ml/min to one 150 mg tablet of nirmatrelvir given with one 100 mg tablet of ritonavir twice daily. It is not recommended for individuals with eGFR <30 ml/min, including dialysis patients, and is also not recommended for those with severe **hepatic impairment**.[ix]

- **Paxlovid rebound** is a clinical condition where COVID-symptoms or positive antigen testing recurs after a course or treatment. While this condition is usually self-limiting, it may require a longer period of isolation.

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[i] https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/outpatient-treatment-overview.html
[ii] https://www.covid19treatmentguidelines.nih.gov/therapies/
[iii] https://www.nejm.org/doi/full/10.1056/NEJMoa2116846
[iv] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02597-1/fulltext
[v] https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/nonhospitalized-adults--therapeutic-management/
[vi] https://www.pfizermedicalinformation.com/en-us/paxlovid
[vii] https://www.nejm.org/doi/full/10.1056/NEJMoa2118542
[viii] https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e2.htm
[ix] https://www.pfizermedicalinformation.com/en-us/paxlovid