



Special Assessment of Outpatient Treatments for COVID-19

Nirmatrelvir/Ritonavir (Paxlovid®) Health-Benefit Price Benchmark Update

Technical Brief

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Background

In May 2022, the Institute for Clinical and Economic Review (ICER) published a [special assessment](#) of several emerging outpatient treatment options for COVID-19. Since that time, the drug nirmatrelvir/ritonavir (Paxlovid[®], Pfizer) has become the leading treatment option. In addition, since May 2022, the viral epidemiology of COVID-19 has continued to evolve, increasing numbers of Americans have either been vaccinated and/or gained increased immunity from prior infections, and further evidence has been published on the relative effectiveness of treatment. It is also anticipated that in early-mid 2023 the payment for Paxlovid[®] for many patients will begin to shift from prior federal contracts over to new pricing and payment arrangements negotiated between Pfizer and commercial insurers. Although dominant viral variants, vaccination/prior infection status, and evidence on Paxlovid[®] will continue to evolve, and some questions, such as the relative impact on long COVID are still highly uncertain, we are presenting an update to our calculations of a health-benefit price benchmark range for Paxlovid[®] at this time to help inform new discussions on fair pricing for the dominant outpatient treatment option for COVID-19.

Objective

To update ICER's health-benefit price benchmark in the health care sector perspective for Paxlovid[®] using updated comparative clinical evidence.

Methods

We conducted an updated literature search on Paxlovid[®], limited to observational studies or randomized controlled trials published or available in pre-print between February and December 2022. Our search yielded 352 references. Following double-screening, we identified 12 studies meeting our criteria. Of the 12 studies, one was the publication of the pivotal randomized clinical trial of Paxlovid[®], conducted in an unvaccinated population with no previous COVID-19 infection before the predominance of the Omicron variant. The remaining 11 studies were retrospective observational studies, of which seven were conducted in the United States (US). Observational studies may include residual confounding that impacts the internal validity whereas the pivotal randomized trial suffers from external validity concerns that put into question the net clinical benefit of Paxlovid[®] use during the Omicron and future waves. Based on sample size and quality of evidence, we identified the [Shah et al. study](#) as the strongest source of comparative effectiveness evidence during the Omicron wave. The adjustment of population and clinical characteristics in the Shah et al. analysis supports internal validity whereas the large sample size supports external validity. Shah et al. was conducted in a large representative sample of those opting to take Paxlovid[®] during the Omicron variant predominance wave. Furthermore, Shah et al. enrolled patients from all US regions, making it more generalizable to the entire US population.

Shah et al. reported an adjusted hazard ratio of 0.49, (95% CI, 0.46 to 0.53) for Paxlovid®'s effectiveness in reducing hospitalization using a Cox proportional hazards model, adjusting for demographic characteristics, geographic location, vaccination, previous infection, and number of underlying conditions. The study sample of over 1.7 million people diagnosed with COVID-19 during the Omicron wave included both vaccinated and unvaccinated individuals. This study from Shah et al. represents the largest known sample of US patients who received Paxlovid® during the Omicron wave (N=198,927). The [Dryden-Peterson et al. publication](#) is the second largest-known published observational study of Paxlovid® during the Omicron wave (N=12,541 Paxlovid® treated). The Paxlovid® reduction in hospitalization from Dryden-Peterson et al. was an adjusted risk ratio of 0.60 (95% CI, 0.44 to 0.81), which is numerically less favorable compared to the Shah et al. study, but is also more uncertain due to a smaller sample size. We decided not to meta-analyze the Shah et al. relative treatment effectiveness estimate with that of other sources given the sample size magnitude (over 10 times more treated patients than other sources) that favors the use of the Shah et al. study and given concerns about differences in population characteristics across alternative studies (e.g., some studies only included the highest risk individuals). Additional peer-reviewed studies will emerge and may support further reductions in the uncertainty of treatment effectiveness.

From Shah et al., we abstracted the probability of hospitalization observed among patients that received Paxlovid® and the adjusted hazard ratio for Paxlovid®'s effect on hospitalization. Dividing the hospitalizations observed among patients that received Paxlovid® (0.47%) by the hospitalization hazard ratio for Paxlovid® (adjusted hazard ratio of 0.49) produced an adjusted estimate of hospitalization for those patients that do not receive Paxlovid® of 0.96%.

Using this new information, we updated the following inputs to the [previously detailed decision analytic model](#): 1) the risk of hospitalization among patients eligible for treatment with Paxlovid® who did not receive Paxlovid® (0.96%) and; 2) the effectiveness of Paxlovid® on reducing hospitalizations (hazard ratio of 0.49). Because mortality and long-term sequelae were modeled as consequences following a hospitalization, the updated relative treatment effect of Paxlovid® on hospitalization translates to an equivalent relative reduction in mortality and long-term sequelae associated with COVID-19 infection. Consistent with what was done in our prior assessment, no treatment benefit associated with reducing the level of respiratory support required once hospitalized was modeled. With these updated inputs, we generated updated health-benefit price benchmarks. Of note, we did not update the risk of mortality for hospitalized patients not treated with Paxlovid®, despite [some evidence](#) that mortality rates have declined. In addition, we did not update cost estimates for hospitalization, noting published studies with both lower and higher hospitalization cost estimates from those we used. We wish to emphasize that individual insurers and health systems can input their own specific cost structures when creating a customized version of the model and a user-specific health-benefit price benchmark.

Results

The updated health care sector health-benefit price benchmark for Paxlovid® is \$563 to \$906 per treatment course (Table 1).

Table 1. Updated Health-Benefit Price Benchmarks for Paxlovid®

	Health-Benefit Price Benchmark at \$100,000	Health-Benefit Price Benchmark at \$150,000
Per QALY	\$563	\$868
Per evLY	\$589	\$906

evLY: equal-value life year, QALY: quality-adjusted life year

Conclusions

The updated Paxlovid® health-benefit price benchmark range is lower than the prior estimate from our assessment in May 2022, due in part to new evidence of a lower risk of hospitalization for untreated patients during the Omicron wave of COVID-19. We wish to emphasize the ongoing evolution of the COVID-19 landscape, from population characteristics of patients treated with Paxlovid®, to advances in the care of hospitalized patients, to new evidence on the effects of treatment on long COVID. Our updated results should therefore be viewed as representing an evolving assessment of the value of treatment and of pricing that aligns with the benefits to patients. We acknowledge that there are other paradigms of fair pricing that can be applied, particularly in pandemic environments, including analyses of fair profit over and above the cost of production, and considerations of the impact of treatment on broader societal factors such as business activity and education. The federal government is currently paying approximately \$530 per treatment course of Paxlovid®. As negotiations ensue regarding the new pricing and payment arrangements for Paxlovid® within commercial insurance systems, we encourage all stakeholders, including patient groups, payers, and drug makers, to use the [ICER Analytics](#) platform to apply their own judgment of the emerging evidence in support of a transparent discussion around value and fair pricing.