



Response to ICER Special Assessment of Outpatient Treatments for COVID-19 Technical Brief (published December 20, 2022)

Dear Dr. Pearson,

Pfizer recognizes ICER's commitment to timely evidence updates to inform critical decisions regarding patient access to essential treatment options. We believe the December 2022 technical brief¹ could be improved by more closely following ICER's established methods and process for updating assessments^{2,3} and consideration of recently published real-world evidence:

- ICER selectively identified nirmatrelvir/ritonavir (Paxlovid™) alone for an update to its Health-Benefit Price Benchmark, based on updates to only two model inputs – Paxlovid effectiveness and the baseline risk of hospitalization – and based on a single CDC report which did not undergo peer-review.⁴ Sotrovimab, molnupiravir, and fluvoxamine were included in the original Evidence Report.⁵
- The process for identifying real-world evidence for the two model input updates was not systematic or transparent.
- There was no opportunity for patients and clinical stakeholders to provide feedback before the technical brief was released.

Using a single source of evidence for model input updates is problematic without critical evaluation of study quality, particularly when assessing non-randomized real-world evidence. Applying ICER's method for calculating the baseline risk of hospitalization to the US real-world evidence available in December 2022 results in hospitalization rates ranging from 1.0%-7.6%; the study used by ICER is an outlier and the lowest risk (1.0%, see Appendix for study details).

Additional analyses measuring Paxlovid effectiveness have since been published that could be considered, including a peer-reviewed real-world study⁶ that utilized a study design in line with the

¹ ICER. Special Assessment of Outpatient Treatments for COVID-19: Technical Brief. Accessed at [COVID-Technical-Brief.pdf \(icer.org\)](#) on 02 June 2023.

² ICER. Updating Assessments. Accessed at [Updating Assessments – ICER on 02 June 2023](#).

³ ICER. Methods & Process. Accessed at [Methods & Process | Our Approach | ICER on 02 June 2023](#).

⁴ Shah M, et al. Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — United States, April–September 2022. *MMWR* 2022;71(48):1531-7. Available at: <https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7148e2-H.pdf>

⁵ ICER. Special Assessment of Outpatient Treatments for COVID-19: Final Evidence Report and Meeting Summary. Accessed at [ICER COVID 19 Final Evidence Report_051022.pdf](#) on 02 June 2023.

⁶ Lewnard JA, McLaughlin JM, Malden D, et al. Effectiveness of nirmatrelvir-ritonavir in preventing hospital admissions and deaths in people with COVID-19: a cohort study in a large US health-care system. *The Lancet Infectious Diseases*. Mar 2023;15:S1473-3099. doi:10.1016/S1473-3099(23)00118-4.

Paxlovid label indication and EPIC-HR trial design.^{7,8} This study is the only to-date to evaluate the effectiveness of Paxlovid when administered within 5 days of symptom onset, reducing the potential for confounding by clinical severity.

Given the availability of additional recently published data across key model inputs (baseline hospitalization,⁶ treatment effectiveness,⁶ utility values⁹ and hospitalization costs⁹), we respectfully request that ICER conduct a full update of its analyses for all FDA-approved COVID-19 outpatient treatments and disseminate updated findings to ensure the communicated value-based price estimates reflect the accurate value of all treatment options.

Sincerely,

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⁷ Paxlovid – FDA Full Prescribing Information. Accessed at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217188s000lbl.pdf on 02 June 2023.

⁸ Hammond J, Leister-Tebbe H, Gardner A, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. *N Engl J Med* 2022; 386: 1397–408.

⁹ Goswami H, Alsumali A, Jiang Y, et al. Cost-Effectiveness Analysis of Molnupiravir Versus Best Supportive Care for the Treatment of Outpatient COVID-19 in Adults in the US. *Pharmacoeconomics*. Jul 2022;40(7):699-714. doi:10.1007/s40273-022-01168-0.



Appendix

Table 1 US-based studies available at the time of ICER Special Assessment on Outpatient Treatments for COVID-19 December 2022 Technical Brief

	Source/Sample	Publication Status (as of Dec 2022)	Index Period	All-Cause 30-day Hosp in Untreated	
US-based real-world studies with index period during Omicron wave	Shah et al. ⁴	EPIC Cosmos (≥18 y, n=693,084)	Published, not peer-reviewed	1 Apr – 31 Aug 2022	1.0%
	Dryden-Peterson et al. ¹⁰	Mass General/Brigham (MA/NH) (≥50 y, n=44,045)	Pre-print	1 Jan – 17 Jul 2022	1.0% [†]
	Aggarwal et al. ¹¹	medRx (CO) (78.9% ≥18 y, n=14,953)	Pre-print	26 Mar – 23 June 2022	2.0%
	Ganatra et al. ¹²	TriNetX (≥18 y, n = 2260, matched 1:1)	Published, peer-reviewed	1 Dec 2021 – 18 Apr 2022	2.1%
	Bajema et al. ¹³	VA+Medicare (≥18 y, n=112,380)	Pre-print	1 Jan – 28 Feb 2022	4.1%
	Zhou et al. ¹⁴	Optum (≥12 y, n=13,657, matched 1:≤4)	Pre-print	22 Dec 2021 – 8 May 2022	7.6%
	Lewnard et al. ¹⁵	Kaiser (CA) (≥12 y, n=133,426, matched 1:≤50)	Pre-print	31 Dec 2021 – 29 Jul 2022	4.6/100,000 person days
Overall Range				1.0% - 7.6%	

[†]Composite endpoint of hospitalization within 14 days or death within 28 days of incident SARS-CoV-2 infection

¹⁰ Dryden-Peterson S, Kim A, Kim AY, et al. Nirmatrelvir Plus Ritonavir for Early COVID-19 and Hospitalization in a Large US Health System. Accessed at <https://doi.org/10.1101/2022.06.14.22276393>

¹¹ Aggarwal NR, Molina KC, Beaty LE, Bennett TD, Carlson NE, Ginde AA. Real-world Use of Nirmatrelvir-Ritonavir in COVID-19 Outpatients During the Emergence of Omicron Variants BA.2/BA.2.12.1. Accessed at <https://doi.org/10.1101/2022.09.12.22279866>

¹² Ganatra S, Dani SS, Ahmad J, et al. Oral Nirmatrelvir and Ritonavir in Non-hospitalized Vaccinated Patients with COVID-19. Clin Infect Dis 2022;76(4):563-72.

¹³ Bajema KL, Berry K, Streja E, et al. Effectiveness of COVID-19 treatment with nirmatrelvir-ritonavir or molnupiravir among U.S. Veterans: target trial emulation studies with one-month and six-month outcomes. Accessed at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9774229/>

¹⁴ Zhou X, Kelly SP, Liang C, et al. Nirmatrelvir/Ritonavir in Preventing Hospitalization Among Patients With COVID-19 at High Risk for Severe Disease in the United States: A Nationwide Population-Based Cohort Study. Accessed at <https://doi.org/10.1101/2022.09.13.22279908>

¹⁵ Lewnard JA, Malden D, Hong V, et al. Effectiveness of nirmatrelvir-ritonavir against hospital admission: a matched cohort study in a large US healthcare system. Accessed at <https://www.medrxiv.org/content/10.1101/2022.10.02.22280623v1>