



# Informing a Conceptual Framework for a Patient-Centered Value Assessment of Emerging Therapies for Mild/Moderate COVID-19

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## INTRODUCTION

- The COVID-19 pandemic gave rise to an array of therapeutics to treat mild to moderate COVID-19.
- Monoclonal antibody (mAb) and oral antiviral treatments received emergency use authorization (EUA) from the US Food and Drug Administration (FDA) to treat symptomatic, non-hospitalized individuals who are at high risk for progression to severe COVID-19.<sup>1</sup>
- Patient-centered perspective of the value of these treatments would inform future economic evaluation.
- The Patient-Driven Values in Healthcare Evaluation (PAVE) patient-informed value elements<sup>2</sup> can be applied to evaluate the potential for a patient-informed value assessment of these emerging mild/moderate COVID-19 treatments.

## STUDY OBJECTIVE

- This study aims to incorporate the PAVE patient-informed value element framework to evaluate potential areas for a value assessment of emerging therapies for mild/moderate COVID-19.

## METHODS

- Literature search:** Pubmed database was searched using the terms “(mild OR moderate) AND (COVID OR coronavirus 2019 OR COVID19) AND (bamlanivimab OR etesevimab OR Sotrovimab OR casirivimab OR imdevimab OR REGN-COV2) OR (paxlovid) OR (molnupiravir)”.
- The search retrieved 140 papers: 34 relevant papers were identified that had a primary focus on: a) mild-to-moderate COVID-19, b) non-hospitalized individuals, and c) approved under EUA by the US FDA.
- We included papers published in 2020 or later and in English.
- Papers that were not relevant to this review were those focused on therapies for severe COVID-19 in hospitalized individuals and therapies for which the FDA advised against for treatment of COVID-19.
- We extracted information on long and short-term treatment effects, treatment costs, social, and life impacts of treatments.

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## RESULTS

Figure 1: Timeline of Treatments for Mild to Moderate COVID-19

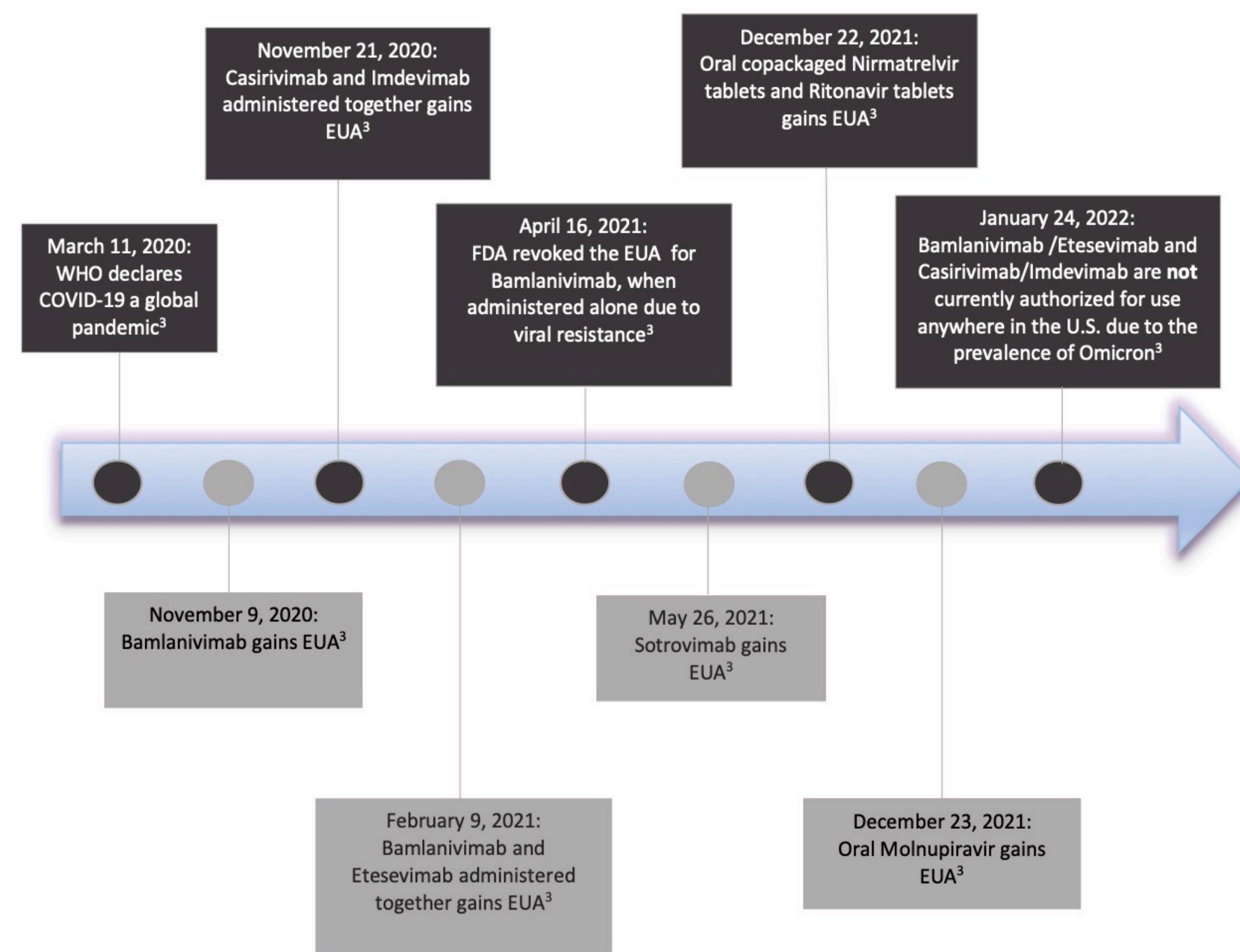


Table 1: Attributes of MAb and Oral Treatments for Mild to Moderate COVID-19 Mapped to Patient Driven Value Elements

Element Category	mAb	Oral	
	Sotrovimab	Molnupiravir	Nirmatrelvir/Ritonavir
<b>TOLERABILITY</b>			
<i>Frequency/Duration</i>	Single IV infusion x 15-30 mins <sup>4</sup> Post infusion monitor for 1 hour <sup>4</sup>	4 capsules twice daily x 5 days <sup>5</sup>	3 tablets twice daily x 5 days <sup>6</sup>
<i>Side Effects</i>	Common: cough, muscle aches or myalgia, headache, and fatigue <sup>7</sup> Risk of clinical worsening <sup>4</sup>	Common; headache, diarrhea, nausea, dizziness <sup>5,8</sup> Mutagenicity risk (low) <sup>9,10</sup>	Common: dysgeusia, diarrhea, hypertension, and myalgia <sup>11</sup>
	Orals and mAbs serious adverse effect: hypersensitivity (pruritus, flushing, rash, and facial swelling) <sup>4,7,8,11</sup>		

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Table 1: Attributes of MAb and Oral Treatments for Mild to Moderate COVID-19 Mapped to Patient Driven Value Elements (Cont.)

Element Category	mAb	Oral	
	Sotrovimab	Molnupiravir	Nirmatrelvir/Ritonavir
<b>DISEASE BURDEN</b>			
<i>Age of Onset</i>	Must be ≥12 years old or ≥40 kg <sup>4</sup>	Must be ≥18 years old; may affect bone & cartilage growth <sup>8</sup>	Must be ≥12 years old or ≥40 kg <sup>11</sup>
<i>Immediate/Surrogate Outcomes</i>	↓ risk of hospitalization or death by 85%% Mean decline in viral load at day 8 was - 2.610 log <sub>10</sub> copies/mL vs placebo was -2.358 <sup>12</sup> Active against Omicron variant <sup>3</sup>	↓ risk of hospitalization or death by ~50% in unvaccinated <sup>13,14</sup> ↓ viral load by 53% by day 5 with no positive PCR tests <sup>14,15</sup>	↓ risk of hospitalization or death 88% ↓ viral load 10-fold when treated within 3 days of symptom onset <sup>17</sup>

<b>ACCESSIBILITY</b>			
<i>Available treatment</i>	Outpatient infusion centers via physician referral Rural/underserved areas have longer travel to infusion clinics <sup>18</sup> Thousands of doses distributed per week <sup>19</sup> When supply is limited, priority is given to highest risk individuals <sup>20</sup>	May be taken at home	
<i>Appropriateness of Care</i>	Drug-drug interactions (DDIs) unlikely <sup>12</sup> May be used in pregnant and no data on lactation <sup>12</sup> Must treat within 7 days of symptom onset <sup>12</sup>	DDIs unlikely <sup>8</sup> Not recommended in pregnant or lactating <sup>8</sup>	Many DDIs with CYP3A substrate drugs <sup>11</sup> Not recommended in severe renal or hepatic impairment <sup>11</sup> Not studied in pregnant/lactating <sup>11</sup> Must treat within 5 days of symptom onset <sup>8,11</sup>
<b>PATIENT COSTS</b>			
<i>Affordability</i>	Out of pocket infusion related costs <sup>21</sup>		Federal government pays for antivirals while there is a COVID-19 public health emergency; uncertain how long this will last

Table 2: Summary of Pros and Cons of Mab vs Oral Treatments Mapped to Value Element Domains

Value Element Domain	Agent	Pros	Cons
Treatment effects	mAb	One time infusion Few/no drug-drug interactions Longer permissible window from symptom onset to treatment initiation	Generally mild side effects ↓ risk of hospitalization or death and viral load Active against variant of concern
	Oral	Molnupiravir has no DDIs Molnupiravir shows efficacy in unvaccinated	Pill burden, treatment duration and frequency Concern of mutagenicity with Molnupiravir Many DDIs with Nirmatrelvir/Ritonavir
Access	mAb	Ease of coordination between providers and infusion centers May be used in pregnant if benefits outweigh risks	Transportation/distance to infusion centers
	Oral	Home administration	Not indicated in pregnant
Cost	mAb	Drug products are currently free of charge	Infusion related costs
	Oral		Provider visit cost Possible future copays
Life Impact	mAb	Resume daily activities sooner	May need take day off from work/school
	Oral	No workday impact	

## CONCLUSION

- PAVE patient-informed value elements can be used to assess the potential impacts that EUA therapies for mild/moderate COVID-19 have on treatment effects, access, cost, and life impact.
- The possibility of needing ongoing COVID treatment due to emergence of resistant strains and the potential future costs of these treatments highlights the importance of patient values.

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