## Side-by-Side Overview of Therapeutics Authorized or Approved for the Prevention of COVID-19 Infection or Treatment of Mild-Moderate COVID-19

This table is a quick reference summarizing key information for available pre-exposure prophylaxis (PrEP) for preventing COVID-19 infection and for all outpatient therapies currently authorized or approved in the United States for treatment of mild-moderate COVID-19. This resource will be regularly reviewed and updated.

## For full details, please review the Fact Sheets for Healthcare Providers for each product (links below).

	MONOCLONAL ANTIBODIES (mAbs)		IV ANTIVIRALS	ORAL ANTIVIRALS	
	Preventative (PrEP)	Treatment	Treatment	Treatment	
PRODUCT	<u>Evusheld</u> (tixagevimab/cilgavimab)	<u>bebtelovimab</u>	<u>Veklury</u> <u>(remdesivir)</u>	<u>Paxlovid</u> (nirmatrelvir/ritonavir)	<u>Lagevrio</u> (molnupiravir)
Manufacturer	AstraZeneca Pharmaceuticals LP	Eli Lilly and Company	Gilead Sciences, Inc.	Pfizer, Inc.	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Product Websites	Evusheld website	bebtelovimab website	<u>Veklury website</u>	Paxlovid website	<u>Lagevrio website</u>
Package Insert	N/A	N/A	Veklury package insert	N/A	N/A
Fact Sheets for Healthcare Providers	Evusheld Healthcare Provider Fact Sheet	bebtelovimab Healthcare Provider Fact Sheet	Veklury Prescribing Information	Paxlovid Healthcare Provider Fact Sheet	Lagevrio Healthcare Provider Fact Sheet
Fact Sheets for Patients, Parents, and Caregivers (English)	Evusheld Patient Fact Sheet (English)	bebtelovimab Patient Fact Sheet (English)	Veklury Patient Information (English)	Paxlovid Patient Fact Sheet (English)	Lagevrio Patient Fact Sheet (English)
Fact Sheets for Patients, Parents, and Caregivers (Spanish)	Evusheld Patient Fact Sheet (Spanish)	bebtelovimab Patient Fact Sheet (Spanish)	N/A	Paxlovid Patient Fact Sheet (Spanish)	Lagevrio Patient Fact Sheet (Spanish)
Mechanism of Action	mAb against conserved epitope of spike protein; blocks viral entry	mAb against spike protein; blocks viral attachment to host cells	Nucleotide analog ribonucleic acid (RNA) polymerase inhibitor that halts viral replication	Viral protease inhibitor that halts viral replication	Nucleoside analog that inhibits viral replication by viral mutagenesis
Treatment Efficacy per Clinical Trials <sup>2</sup>	77% reduction in developing symptomatic COVID-19	Symptomatic improvement and Day 5 reduction in viral load vs. placebo <sup>3</sup>	87% reduction in hospitalizations/deaths4	88% reduction in hospitalizations/deaths	30% reduction in hospitalizations/deaths
Activity Against SARS-CoV- 2 Variants⁵	See Section 12.4 of <u>Evusheld Healthcare</u> <u>Provider Fact Sheet</u>	See Section 12.4 of <u>bebtelovimab</u> <u>Healthcare Provider Fact Sheet</u>	See Section 12.4 of Veklury package insert	See Section 12.4 of Paxlovid Healthcare Provider Fact Sheet	See Section 12.4 of <u>Lagevrio Healthcare</u> <u>Provider Fact Sheet</u>
Authorized Use(s)	Pre-exposure prophylaxis (PrEP)	Treatment of mild-moderate COVID-19	Treatment of mild-moderate COVID-19	Treatment of mild-moderate COVID-19	Treatment of mild-moderate COVID-19

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Eligible Population(s)	Adult and pediatric patients (at least 12 years of age and older weighing at least 40 kg) who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS CoV-2, and who have moderate to severe immune compromise or for those who any EUA or approved vaccine is not recommended.	Adult and pediatric patients (at least 12 years of age and older weighing at least 40 kg) at high risk <sup>6</sup> for progressing to severe COVID-19, including hospitalization or death, <b>and</b> for whom alternative COVID-19 treatment options approved or authorized by the U.S. Food and Drug Administration (FDA) are not accessible or clinically appropriate	FDA-approved for: Adults and pediatric patients (28 days of age and older and weighing at least 3 kg with positive results of direct severe acute respiratory SARS-CoV-2 viral testing who are (1) hospitalized or (2) not hospitalized and have mild-to-moderate COVID-19, and are at high risk <sup>6</sup> for progression to severe COVID-19, including hospitalization or death	Adults and pediatric patients (12 years of age and older weighing at least 40 kg) at high risk <sup>6</sup> for progressing to severe COVID-19, including hospitalization or death	Adult patients age 18 and older at high risk <sup>§</sup> for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate	
Prescribing Window	Pre-exposure	Initiate within 7 days of symptom onset	Initiate within 7 days of symptom onset	Initiate within 5 days of symptom onset	Initiate within 5 days of symptom onset	
Testing Requirements	None	Positive SARS-CoV-2 viral test	Positive SARS-CoV-2 viral test Baseline renal function required under EUA for pediatric patients Pediatric patients (greater than 28 days old and weighing at least 3 kg) must have an estimatedglomerular filtration rate (eGFR) determined. Before starting and during treatment as clinically appropriate, perform renal and hepatic laboratory testing Assess prothrombin time before starting and monitor as clinically appropriate	Positive SARS-CoV-2 viral test	Positive SARS-CoV-2 viral test	
History Requirements	Not specified	Not specified	Not specified	Not specified	Assessment of pregnancy status	
Limitations of Authorized Use	Not authorized for: • For treatment of COVID-19 • For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2. In individuals who have received a COVID-19 vaccine, Evusheld should be administered at least two weeks after vaccination.	Not authorized for: Patients less than 12 years of age and less than 40 kg Patients who are hospitalized due to COVID-19 Patients who require oxygen therapy due to COVID-19 OR Require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 and are on chronic oxygen therapy and/or respiratory support due to underlying non-COVID-19 related comorbidity	N/A	Not authorized for:  Patients requiring hospitalization due to severe or critical COVID-19.  Pre-exposure or post-exposure prophylaxis for prevention of COVID-19.  Use for longer than 5 consecutive days	Not authorized for:  Patients less than 18 years of age Initiation in patients who are hospitalized due to COVID-19.  Use for longer than 5 consecutive days.  Pre-exposure or post-exposure prophylaxis for prevention of COVID-19	

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Family Planning Considerations	None	None	None	Ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients should use an effective alternative contraceptive method or an additional barrier method of contraception.	Not recommended for use during pregnancy because may cause fetal harm when given to pregnant individuals based on animal reproduction studies. Authorized for use in pregnancy only if benefits would outweigh risks for the individual patient; documentation requirements apply.  Females of childbearing potential should be advised of potential risk to a fetus and should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of Lagevrio.  Males of reproductive potential who are sexually active with females of childbearing potential should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose.
Contraindications	Individuals with previous severe hypersensitivity reactions, including anaphylaxis, to any component of Evusheld	None	Patients with a history of clinically significant hypersensitivity reactions to Veklury or any components of the product.  Consider discontinuing Veklury if ALT levels increase to greater than 10 times the upper limit of normal. Discontinue Veklury if ALT elevation is accompanied by signs or symptoms of liver Inflammation.	Individuals with significant hypersensitivity reactions to any component of Paxlovid.  Co-administration with drugs highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or lifethreatening reactions.  Co-administration with potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance.	None
Administration Route(s)	IM Injection	IV Injection	IV Infusion	Oral	Oral

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Dosage	Initial Dose: 300 mg of tixagevimab and 300 mg of cilgavimab administered as two separate consecutive intramuscular injections (preferably one in each of the gluteal muscles, one after the other).  Dosing for those who initially received 150 mg of tixagevimab and 150 mg of cilgavimab  • Initial dose ≤ 3 months ago: 150 mg of tixagevimab and 150 mg of cilgavimab ASAP  • Initial dose > 3 months ago: 300 mg of tixagevimab and 300 mg of cilgavimab ASAP  Repeat Dose:  The SARS-CoV-2 variants that will be circulating in the US when Evusheld may need to be redosed are not known at this time and therefore repeat dosing recommendations cannot be made; the fact sheets will be revised with repeat dosing recommendations in the future when more data are available.	175 mg/2 mL (87.5 mg/mL) administered via IV injection over at least 30 seconds	For adults and pediatric patients weighing at least 40 kg:  A single loading dose of Veklury 200 mg on Day 1 via intravenous infusion followed by once-daily maintenance doses of Veklury 100 mg from Day 2 via IV infusion  For other non-hospitalized populations, see below	300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) with all three tablets taken together orally twice daily for 5 days, can be taken with or without food [see Clinical Pharmacology (12.3)]. The tablets should be swallowed whole and not chewed, broken, or crushed  For patients with renal impairment, see below	800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food	
Dosage for Special Populations	Pediatric patients at least 12 years or older, and weighing at least 40 kg: no dosage adjustment  Pregnancy or Lactation - No dosage adjustment  Geriatrics: No dosage adjustment  Renal: No dosage adjustment  Hepatic: Not specified	Pediatrics: If eligible, no dosage adjustment  Pregnancy or Lactation: No dosage adjustment  Geriatrics: No dosage adjustment  Renal: No dosage adjustment  Hepatic: No dosage adjustment for mild hepatic impairment	Pediatric patients 28 days of age and older and weighing at least 3 kg to less than 40 kg: a single loading dose of Veklury 5 mg/kg on Day 1 via intravenous infusion followed by once-daily maintenance doses of Veklury 2.5 mg/kg from Day 2 via intravenous infusion.  Renal: Not recommended in patients with eGFR less than 30 mL/min.	Pediatric patients at least 12 years or older, and weighing at least 40 kg, no dosage adjustment  Pregnancy or Lactation: No dosage adjustment  Renal: No dosage adjustment is needed in patients with mild renal impairment.  Dose reduction for moderate renal impairment (eGFR ≥30 to <60 mL/min): 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet), with both tablets taken together twice daily for 5 days.  Paxlovid is not recommended in patients with severe renal impairment (eGFR <30 mL/min).  Hepatic: No dosage adjustment for mild or moderate hepatic impairment.  Paxlovid is not recommended for use in patients with severe hepatic impairment.	Pediatrics: Not eligible, as it may affect bone and cartilage growth.  Pregnancy or Lactation: Not recommended for use during pregnancy. Breastfeeding not recommended during treatment or for 4 days after final dose.  Renal: No dosage adjustment  Hepatic: No dosage adjustment	

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Post-Administration Observation Period	One hour	One hour	One hour	None	None
Adverse Events (from Clinical Trials) <sup>2</sup>	Injection site reactions (1%); One case of anaphylaxis  Other adverse events: Headache (6%), fatigue (4%), and cough (3%) Injection site reactions (1%); One case of anaphylaxis  Other adverse events: Headache (6%), fatigue (4%), and cough (3%) Insomnia (1%), dizziness (1%)  Cardiac serious adverse events (SAE) were 0.6% vs 0.2% in the Evusheld and placebo groups, respectively.	Adverse reactions were infusion-related reactions (0.3%), pruritus (0.3%), and rash (0.8%)  Most common adverse events: nausea (0.8%) and vomiting (0.7%)  Infusion-related reactions may include fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia, chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions dizziness, and diaphoresis	Adverse events⁴ (incidence ≥1%) were nausea (10.8%), headache (5.7%), cough (3.6%), diarrhea (3.9%), dyspnea (2.5%), fatigue (3.6%), ageusia (2.9%), anosmia (3.2%), dizziness (1.8%), and chills (2.2%) Lab abnormalities⁴: All grade 3 or higher (10.8%)	Adverse events (incidence ≥1% and ≥5 patient difference) were dysgeusia (6%), diarrhea (3%), hypertension (1%), and myalgia (1%)	Adverse events (incidence ≥1%) were diarrhea (2%), nausea (1%), and dizziness (1%)  Lab abnormalities: Selected Grade 3 and 4 laboratory abnormalities in chemistry (ALT, AST, creatinine, and lipase) and hematology (hemoglobin, platelets, and leukocytes) parameters all occurred at a rate ≤2%  Post-Authorization Experience: Immune System Disorders: hypersensitivity, anaphylaxis, angioedema  Skin and Subcutaneous Tissue Disorders: erythema, rash, urticaria
Potential for Drug-Drug Interactions	Unlikely	Unlikely	Low Fact Sheet [Drug Interactions Section (10)] PI [See Section (7)]	Moderate/High [see Fact Sheet Drug Interactions Section (7)]	No drug interactions have been identified based on the limited available data
Potential for Patient Non-Compliance	Minimal	Minimal	Moderate	Moderate	Moderate
Cost to Patients for USG-Procured Drug <sup>8</sup>	Medicare/Medicaid <sup>8</sup> : \$0 Private insurers: \$0	Medicare/Medicaid <sup>8</sup> : \$0 Private insurers: \$0	Currently not procured by USG; cost to patient for drug product varies	Medicare/Medicaid <sup>§</sup> : \$0 Private insurers: \$0	Medicare/Medicaid <sup>8</sup> : \$0 Private insurers: \$0
Provider Payment (Administration or Dispensing Fee) <sup>8</sup> , <sup>9</sup> , <sup>10</sup> , <sup>11</sup> , <sup>12</sup>	Medicare: \$150.50 (most settings); \$250.50 (beneficiary's home or residence, in certain circumstances <sup>z</sup> )) Medicaid/Private insurers: Variable	Medicare: \$350.50 (healthcare settings); \$550.50 (beneficiary's home or residence, in certain circumstances <sup>2</sup> ) Medicaid/Private insurers: Variable	Medicare: For outpatient setting refer to COVID-19 Frequently Asked Questions (FAQs) on Medicare Fee-for-Service (FFS) Billing (ref Q30)  Medicaid/Private insurers: Variable	Provider may bill applicable insurance or program for dispensing fees. Medicare: CMS encourages Part D sponsors to pay higher than the usual negotiated dispensing fees given the unique circumstances of the PHE and administrative requirements associated with dispensing US Government-procured oral antivirals	Provider may bill applicable insurance or program for dispensing fees. Medicare: CMS encourages Part D sponsors to pay higher than the usual negotiated dispensing fees given the unique circumstances of the PHE and administrative requirements associated with dispensing US Government-procured oral antivirals
Product Availability	Variable by jurisdiction and healthcare facility	Variable by jurisdiction and healthcare facility	Commercially available, not subject to USG allocation limits	Variable by jurisdiction and healthcare facility	Variable by jurisdiction and healthcare facility
Other Considerations	Healthcare provider who can legally prescribe drugs, trained staff; immediate access to resuscitation meds;	Infusion supplies; trained staff; IV access; immediate access to resuscitation meds; ability to activate EMS	Infusion supplies; trained staff; IV access; immediate access to resuscitation meds; ability to activate EMS in outpatient settings	May only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Paxlovid belongs (i.e., anti-infectives).	May only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Lagevrio belongs (i.e., anti-infectives).

- 1 COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies is authorized for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment, in either the outpatient or inpatient setting. Fact Sheet for Healthcare Providers.
- 2 For more details on clinical trial results, see Section 18 of each respective product's Fact Sheet for Health Care Providers.
- The placebo-controlled phase 2 data are limited by enrollment of only subjects without risk factors for progression to severe COVID-19, and the trial was not powered or designed to determine a difference in the clinical outcomes of hospitalization or death between the placebo and bebtelovimab treatment arms [EUA Section 14.4].
- 4 For more details, see Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients | NEJM.
- 5 Reference NCATS open data website.
- See each product's Fact Sheet for Health Care Providers for additional details and criteria for identifying high risk patients/individuals. CDC also maintains a listing <u>underlying medical conditions associated with higher risk for severe</u>

  COVID-19.
- 7 For more details on adverse events from clinical trials, see Section 6 of each respective product's Fact Sheet for Health Care Providers. For more details on clinical worsening after administration, see Section 5.
- 8 For Medicaid resources, https://www.medicaid.gov/resources-for-states/coronavirus-disease-2019-covid-19/index.html.
- 9 For more details, see the CMS COVID-19 Monoclonal Antibodies Infographic and the https://www.cms.gov/monoclonal.
- Some patients/individuals may be responsible for co-pays, deductibles, and/or other charges.
- 11 CMS billing codes, Medicare allowances, and effective dates for COVID-19 vaccines and monoclonal antibodies.