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

This table is a quick reference summarizing key information for all outpatient therapies currently authorized or approved in the United States for treatment of mild to moderate COVID-19. If Paxlovid and Veklury (remdesivir) are not available, feasible or clinically appropriate, consider Lagevrio. COVID-19 Convalescent plasma is an additional authorized therapy for specific immunocompromised patients. This resource will be regularly reviewed and updated.

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

	IV ANTIVIRALS	ORAL ANTIVIRALS		BLOOD PRODUCTS
	Treatment	Treatment		Treatment
PRODUCT	<u>Veklury</u> (<u>remdesivir)</u>	Paxlovid (nirmatrelvir co-packaged with ritonavir)	<u>Lagevrio</u> (molnupiravir)	COVID-19 Convalescent Plasma
Manufacturer	Gilead Sciences, Inc.	Pfizer, Inc.	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.	N/A
Product Websites	<u>Veklury website</u>	Paxlovid website	<u>Lagevrio website</u>	N/A
Package Insert	<u>Veklury Prescribing Information</u>	N/A	N/A	
Fact Sheets for Healthcare Providers	N/A	Paxlovid Healthcare Provider Fact Sheet	Lagevrio Healthcare Provider Fact Sheet	Convalescent Plasma EUA Fact Sheet for Healthcare Providers
Fact Sheets for Patients, Parents, and Caregivers (English)	Veklury Patient Information (English)	Paxlovid Patient Fact Sheet (English)	Lagevrio Patient Fact Sheet (English)	Convalescent Plasma EUA Fact Sheet for Patients and Parents/Caregivers
Fact Sheets for Patients, Parents, and Caregivers (Spanish)	Not Available	Paxlovid Patient Fact Sheet (Spanish)	Lagevrio Patient Fact Sheet (Spanish)	Not Available
Mechanism of Action	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	Possible mechanisms of action, to include direct neutralization of the virus, control of an overactive immune system (i.e., cytokine storm, Th1/Th17 ratio, complement activation) and immunomodulation of a hypercoagulable state.
Treatment Efficacy per Clinical Trials ²	87% reduction in hospitalizations/deaths	88% reduction in hospitalizations/deaths	30% reduction in hospitalizations/deaths	See FDA Convalescent Plasma EUA Letter of Authorization. Authorization is based on the totality of clinical evidence available in patients with immunosuppressive disease or receiving immunosuppressive treatment and remains limited, data from additional randomized, controlled trials is needed.
Activity Against SARS-CoV- 2 Variants ³	See Section 12.4 of <u>Veklury Prescribing Information</u>	See Section 12.4 of <u>Paxlovid Healthcare Provider Fact</u> <u>Sheet</u>	See Section 12.4 of <u>Lagevrio Healthcare Provider</u> <u>Fact Sheet</u>	Convalescent Plasma and Immune Globulins COVID-19 Treatment Guidelines
Authorized or Approved Use(s)	Approved for Treatment of mild to moderate COVID-19	Authorized for Treatment of mild to moderate COVID-19	Authorized for Treatment of mild to moderate COVID-19	Authorized for Treatment of Coronavirus Disease 2019 (COVID-19) in patients with immunosuppressive disease or receiving immunosuppressive treatment (outpatient and inpatient setting)

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Eligible Population(s) ^{4,5}	FDA-approved for: Adults and pediatric patients (28 days of age and older and weighing at least 3 kg who are (1) hospitalized or (2) not hospitalized and have mild-to-moderate COVID-19, and are at high risk 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) who have mild-to-moderate COVID-19 and are at high risk for progressing to severe COVID-19, including hospitalization or death	Adult patients (18 years of age and older) who have mild-to-moderate COVID-19, are at high risk 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	Adult and pediatric patients with immunosuppressive disease or receiving immunosuppressive treatment at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized/approved by FDA are not accessible or clinically appropriate
Prescribing Window	Initiate within 7 days of symptom onset	Initiate within 5 days of symptom onset	Initiate within 5 days of symptom onset	Not specified
History Requirements	Assessment of renal impairment Assessment of hepatic impairment Assessment of prothrombin time Previous severe hypersensitivity reactions, including anaphylaxis, to Veklury (remdesivir)	Assessment of renal impairment Assessment of hepatic impairment Previous severe hypersensitivity reactions, including anaphylaxis, to Paxlovid	Assessment of pregnancy status and contraceptive use Assessment of breastfeeding status Previous severe hypersensitivity reactions, including anaphylaxis, to Lagevrio	Assessment of prior history of severe allergic reactions or anaphylaxis to plasma transfusion.
Limitations of Authorized Use	This product has received FDA approval. Please refer to prescribing information for further information.	Not authorized for: Pediatric patients less than 12 years of age or weighing less than 40 kg Initiation in 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 Pre-exposure or post-exposure prophylaxis for prevention of COVID-19 Use for longer than 5 consecutive days	Not authorized for: Treatment of immunocompetent patients with COVID-19

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Family Planning Considerations	Pregnancy: Available data from published case reports and compassionate use of remdesivir in pregnant women are insufficient to evaluate for a drugassociated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy. Lactation: There are no available data on the presence of remdesivir in human milk, the effects on the breastfed infant, or the effects on milk production.	Ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients should use an effective alternative contraceptive method or an additional barrier method of contraception. Pregnancy: There is no available human data on the use of nirmatrelvir (a component of Paxlovid) during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy. Lactation: There is no available data on the presence of nirmatrelvir (a component of Paxlovid) in human or animal milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Paxlovid and any potential adverse effects on the breastfed infant from Paxlovid or from the underlying maternal condition.	Pregnancy: 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 Lactation: Based on the potential for adverse reactions in the infant from Lagevrio, breastfeeding is not recommended during treatment with Lagevrio and for 4 days after the final dose. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose of Lagevrio.	Pregnancy: There are insufficient data to evaluate the risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes associated with COVID-19 convalescent plasma. COVID-19 convalescent plasma should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus. Lactation: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COVID-19 convalescent plasma and any potential adverse effects on the breastfed infant from COVID-19 convalescent plasma.
Contraindications	Individuals with a history of clinically significant hypersensitivity reactions, including anaphylaxis, 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, including anaphylaxis, to any component of Paxlovid Co-administration with drugs highly dependent on CYP3A ⁵ 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 Paxlovid is contraindicated in patients with a history of clinically significant hypersensitivity reactions [e.g., toxic epidermal necrolysis (TEN) or Stevens-Johnson syndrome] to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.	Individuals with significant hypersensitivity reactions, including anaphylaxis, to any component of Lagevrio	Individuals with a history of severe allergic reactions or anaphylaxis to plasma transfusion.
Administration Route(s)	IV Infusion	Oral	Oral	IV Infusion

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			Treatment	
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Dosage	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. For administration via nasogastric (NG) or orogastric (OG) Tube (12F or Larger), refer to instructions within the EUA Fact Sheet, Section 2.3	Health care providers will administer COVID-19 convalescent plasma according to standard hospital procedures and institutional medical and nursing practices May first consider starting with one unit of COVID-19 convalescent plasma (about 200 mL), with administration of additional convalescent plasma units based on the prescribing physician's medical judgment and the patient's clinical response Patients with impaired cardiac function and heart failure may require a smaller volume or more prolonged transfusion times.
Dosage for Special Populations	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 under 18 years old: 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	Pediatric: Safety and effectiveness of COVID-19 convalescent plasma in the pediatric population has not been evaluated. The decision to treat patients <18 years of age with COVID-19 convalescent plasma should be based on an individual assessment of risk and benefit. Pediatric patients may be at an increased risk of transfusion associated circulatory overload (TACO) Geriatric: Safety and effectiveness of COVID-19 convalescent plasma has been evaluated in random clinicals trials indicating consistency with those expected for transfusion of blood components. Geriatric patients may be at increased risk of TACO.

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Post-Administration Observation Period	One hour	None	None	One hour
Adverse Events (from Clinical Trials)	Adverse events (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 abnormalities: 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%) Other reactions noted: Allergic reactions, abdominal pain, nausea, and malaise (feeling generally unwell)	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	Known side effects and hazards associated with plasma transfusion include transfusion-transmitted infections (e.g., HIV, hepatitis B, hepatitis C), allergic reactions, anaphylactic reactions, febrile nonhemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated cardiac overload (TACO), and hemolytic reactions. Hypothermia, metabolic complications, and posttransfusion purpura have also been described. Additional information on risks refer to Circular of information for the use of human blood and blood components.
Potential for Drug-Drug Interactions	Due to potential antagonism based on data from cell culture experiments, concomitant use of Veklury (remdesivir) with chloroquine phosphate or hydroxychloroquine sulfate is not recommended. Based on a drug interaction study conducted with Veklury (remdesivir), no clinically significant drug interactions are expected with inducers of cytochrome P450 (CYP) 3A4 or inhibitors of Organic Anion Transporting Polypeptides (OATP) 1B1/1B3, and P-glycoprotein (P-gp).	Paxlovid (nirmatrelvir co-packaged with ritonavir) is a strong inhibitor of CYP3A and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. Co-administration of Paxlovid with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated [see Fact Sheet Drug Interactions Section (7)]	No drug interactions have been identified based on the limited available data on the emergency use of Lagevrio authorized under the EUA. [see Fact Sheet Drug Interactions Section (7)]	COVID-19 convalescent plasma may be contraindicated in patients with a history of severe allergic reactions or anaphylaxis to plasma transfusion.
Potential for Patient Non-Compliance	Moderate	Moderate	Moderate	Minimal
Cost to Patients for USG-Procured Drug 7.8	Currently not procured by USG. For more information, refer to <u>ASPR's Veklury homepage</u> .	Medicare/Medicaid: \$0 Private insurers: \$0	Medicare/Medicaid: \$0 Private insurers: \$0	Currently not procured by USG. For more information, refer to MLN Connects®
Provider Payment (Administration or Dispensing Fee)-7.8	Medicare: For outpatient setting refer to Medicare FAQ Fee for Service Billing (ref Q30 on p.146) 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	Medicare: New COVID-19 Treatments Add-On Payment (NCTAP) CMS ICD-10-PCS Code: XW13325, XW14325 (Only applies to inpatient use) Addendum A and Addendum B Updates CMS APC Code: 9540 / HCPCS Code: C9507 (Only applies to outpatient use) Medicaid/Private insurers: Variable
Product Availability 9, 10	Commercially available	Widely available; no supply constraints	Widely available; no supply constraints	Variable by jurisdiction and healthcare facility; potential supply constraints

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Other Considerations	May 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 Veklury belongs (i.e., anti-infectives) Infusion supplies; trained staff in IV administration; IV access; immediate access to resuscitation meds; ability to activate EMS in outpatient settings	May 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 also be prescribed by a state-licensed pharmacist under the following conditions: Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction The state-licensed pharmacist should refer an individual patient for clinical evaluation (e.g., telehealth, in-person visit) with a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs, if any of the following apply: Sufficient information is not available to assess renal and hepatic function Sufficient information is not available to assess for a potential drug interaction Modification of other medications is needed due to a potential drug interaction	May 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)	See the Circular of Information for use of human blood and blood components.

¹ For more details on Therapeutic Management, see <u>Therapeutic Management of Nonhospitalized Adults With COVID-19</u>.

² For more details on clinical trial results, see Clinical Studies section of each respective product's Fact Sheet for Health Care Providers or, for approved products, see Clinical Studies section of Prescribing Information or see Prescribing Information for approved products. For the published literature referenced in each trial, please click on the following links: <u>Veklury (remdesivir)</u>, <u>Paxlovid (nirmatrelvir co-packaged with ritonavir)</u>.

³ For more details, see <u>NCATS open data website</u> and <u>CDC Nowcast Projections</u>.

⁴ For more details, see each product's Fact Sheet for Health Care Providers or Prescribing Information 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 COVID-19</u>.

⁵ For more details, see Paxlovid Patient Eligibility Checklist.

⁶ For more details on adverse events from clinical trials and details on clinical worsening after administration, see Sections 6 and 5 of each respective product's Fact Sheet for Health Care Providers or, for approved products, see respective product's Prescribing Information.

⁷ For more details on Medicaid resources, see Medicaid Coronavirus Disease 2019. For more details on Medicare FAQ Fee for Service, Medicare FAQ Fee for Service Billing.

⁸ Some patients/individuals may be responsible for co-pays, deductibles, and/or other charges.

⁹ For more details on where to find COVID-19 therapeutics, see <u>COVID-19 Therapeutics Locator</u>.

¹⁰ For more details on Test to Treat sites, see the <u>Test to Treat Locator</u>.