SEPTEMBER 2023

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.[1] 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).

PRODUCT	IV ANTIVIRALS Treatment: Veklury (remdesivir)	ORAL ANTIVIRALS Treatment: Paxlovid (nirmatrelvir co-packaged with ritonavir)	ORAL ANTIVIRALS Treatment: Lagevrio (molnupiravir)	BLOOD PRODUCTS Treatment COVID-19 Convalescent Plasma
Manufacturer	Gilead Sciences, Inc.	Pfizer, Inc.	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.	N/A
Product Websites	Veklury website	Paxlovid website	Lagevrio website	N/A
Package Insert	Veklury Prescribing Information	Paxlovid Prescribing Information Paxlovid distributed by the US Government was manufactured and packaged under the emergency use authorization (EUA) and must be prescribed in accordance with the EUA.	N/A	
Fact Sheets for Healthcare Providers (EUA)	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)	N/A	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)	N/A	Paxlovid Patient Fact Sheet (Spanish)	Lagevrio Patient Fact Sheet (Spanish)	Not Available
Mechanism of Action	Nucleotide analog ribonucleic acid (RNA) polymerase that inhibits viral replication	Viral protease inhibitor that inhibits 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	86% 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 Veklury Prescribing Information	See Section 12.4 of Paxlovid Healthcare Provider Fact Sheet or Section 12.4 of Paxlovid Prescribing Information	See Section 12.4 of Lagevrio Healthcare Provider Fact Sheet	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 (ages 12 and older) Approved for Treatment of mild to moderate COVID-19 (ages 18 and older)	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	**Paxlovid Packaged Under EUA:** 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 **FDA-approved for:** Adults 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	For non-hospitalized use, 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 prothrombin time Previous severe hypersensitivity reactions, including anaphylaxis, to Veklury (remdesivir)	Assessment of renal impairment Assessment of hepatic impairment Assessment of medication list 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.	**Product packaged under EUA is 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-19Use for longer than 5 consecutive days	**Not authorized for**: Treatment of immunocompetent patients with COVID-19

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Family Planning Considerations	**Pregnancy Exposure Registry**: There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to Veklury during pregnancy. Pregnant and recently pregnant individuals can go to https://covidpr.pregistry.com to enroll or call 1-800-616-3791 to obtain information about the registry. **Pregnancy**: Available data from published case reports and compassionate use of remdesivir in pregnant women are insufficient 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 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:** Available data on the use of nirmatrelvir during pregnancy are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published observational studies on ritonavir use in pregnant women have not identified an increase in the risk of major birth defects. Published studies with ritonavir are insufficient to identify a drug associated risk of miscarriage. 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 Registry**: There is a pregnancy registry that monitors pregnancy outcomes in individuals exposed to Lagevrio during pregnancy. The prescribing healthcare provider must document that a pregnant individual was made aware of the pregnancy registry at https://covid-pr.pregistry.com or 1-800-616-3791. **Pregnancy**: Not recommended for use during pregnancy because it 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. While the risk is regarded as low, nonclinical studies to fully assess the potential for Lagevrio to affect offspring of treated males have not been completed. Advise sexually active individuals with partners of childbearing potential to use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose. The risk beyond three months after the last dose is unknown. **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.

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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 life-threatening 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	IV Infusion	Oral	Oral	IV Infusion
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.

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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 (Adult & Pediatric):** No dosage adjustment of Veklury is recommended in patients with any degree of renal impairment, including those on dialysis. Veklury may be administered without regard to the timing of dialysis **Hepatic**: No dosage adjustment of Veklury is recommended for patients with mild, moderate, or severe hepatic impairment Perform hepatic laboratory testing in all patients before starting Veklury and during treatment as clinically appropriate	**Pediatric patients at least 12 years or older, and weighing at least 40 kg:** No dosage adjustment **(Product is authorized but not approved for pediatric patients 12 to <18)** **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.
Post-Administration Observation Period	One hour	None	None	One hour
Adverse Events (from Clinical Trials)[6]	**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%) *Emergency Use Authorization Experience in patients with COVID-19:* • General disorders and administration site conditions: Administration site extravasation • Skin and subcutaneous tissue disorders: Rash • Immune system disorders: Anaphylaxis, angioedema, infusion-related reactions, hypersensitivity • • Investigations: Transaminase elevations	**Adverse events** (incidence ≥1% and ≥5 patient difference) were dysgeusia (5%), and diarrhea (3%). **Other reactions noted:** Allergic reactions, abdominal pain, nausea, headache, and malaise (feeling generally unwell) *Post-Authorization Experience:* • Immune System Disorders: Anaphylaxis, hypersensitivity reactions • Skin and Subcutaneous Tissue Disorders: • Toxic epidermal necrolysis, Stevens-Johnson syndrome • Nervous System Disorders: Headache • Vascular Disorders: Hypertension • Gastrointestinal Disorders: Abdominal pain, nausea, vomiting • General Disorders and Administration Site Conditions: Malaise	**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:* • Gastrointestinal Disorders: vomiting • Immune System Disorders: hypersensitivity, anaphylaxis, angioedema • Skin and Subcutaneous Tissue Disorders: erythema, pruritus, 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.

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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)] [see Prescribing Information 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 ASPR's Veklury homepage.	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) **Product packaged under EUA 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 Therapeutic Management of Nonhospitalized Adults With COVID-19.

[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: Veklury (remdesivir), Paxlovid (nirmatrelvir co-packaged with ritonavir), Lagevrio (molnupiravir).

[3] For more details, see NCATS open data website and CDC Nowcast Projections.

[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 underlying medical conditions associated with higher risk for severe COVID-19.

[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 COVID-19 Therapeutics Locator.

[10] For more details on Test to Treat sites, see the Test to Treat Locator.