COVID-19 Outpatient Treatment Reference

Additional detail can be accessed via the Banner Health COVID-19 Oral Antiviral and COVID-19 Monoclonal Antibody Guidelines and FDA Emergency Use Authorization

Outpatient COVID-19 Management, Clinical Summary

- **Oral Antiviral Medications for Treatment of COVID-19**
  - Two oral antiviral medications have received Emergency Use Authorization: nirmatrelvir/ritonavir (Paxlovid) and molnupiravir (Lagevrio)
  - ***Nirmatrelvir/ritonavir (Paxlovid)*** may decrease risk of hospitalization or death by 89% (NNT = 17.2)
    - Preferred Oral Antiviral
    - Safety concerns include significant drug-drug interactions, renal dosing adjustments, and contraindication in severe hepatic impairment
      - Review full medication list with potentially eligible patients to identify drug-drug interactions
      - Review renal function and reduce dose accordingly, if severe renal impairment (eGFR < 30 ml/min) do not use
  - ***Molnupiravir (Lagevrio)*** may decrease hospitalization or death by 30% (NNT = 34.5)
    - Safety concerns include contraindications in pregnancy and bone/cartilage toxicity in pediatric populations. Clinical data show declining efficacy (50% reduction in hospitalizations and death in interim analysis versus 30% in final analysis)
    - *Only use if nirmatrelvir/ritonavir (Paxlovid) or COVID-19 Monoclonal antibodies are contraindicated, or if either are unavailable*
  - **Ordering Oral Antivirals**
    - Orderable via standard prescribing workflows.
    - If within Maricopa County, you can confirm that the patient's pharmacy has the medication in stock via the Maricopa County Treatment locator tool. See below for additional information.
    - Note: *If ordering an oral antiviral, patient should not be prescribed a monoclonal antibody*
  - **Pharmacies Carrying Oral Antiviral Therapies**
    - Nirmatrelvir/ritonavir (Paxlovid) is available at all Banner Family Pharmacies
    - Providers in all care settings may write for either nirmatrelvir/ritonavir (Paxlovid) or molnupiravir (Lagevrio)
    - The number of retail pharmacies carrying oral antivirals continues to evolve.
      Note: It is strongly encouraged that prescribers call ahead to confirm product availability before prescribing. If the pharmacy is unable to fill a prescription due to supply issues, provider will need to cancel prescription prior to prescribing to an alternative location.

- **Monoclonal Antibodies for Treatment of COVID-19**
  - Omicron variant BA.2 is the dominant variant in the United States
  - Bebtelovimab demonstrates in vitro activity against BA.2
  - Banner Health currently administering bebtelovimab
  - *Note: if ordering a COVID-19 monoclonal antibody for treatment, patient should not be prescribed an oral antiviral*
- **Facilities Offering COVID Mab**
  - **All WR facilities with the exception of BFCMC and MMC**
  - **Phoenix Metropolitan Area**
    - Adults
      - BBMC Outpatient Infusion
      - BUMCP Outpatient Infusion
    - Peds
      - BTMC ED
      - BDMC ED

Drug Product Reference Sheet

Drug Name	Preference: 1st Line nirmatrelvir/ritonavir (Paxlovid)	Preference: 2nd Line Bebtelovimab	molnupiravir (Lagevrio) Note: Should only be considered when alternative options are unavailable or contraindications to other agents exist
Criteria for Use All require positive COVID-19 PCR or antigen test	• Within 5 days of symptom onset • 12 YOA and at least 40 kg • High Risk for severe COVID-19/hospitalization ▪ Age ≥ 65 years ▪ Cancer ▪ Chronic lung diseases ▪ Dementia or other neurological conditions ▪ Diabetes (type 1 or 2) ▪ Down syndrome ▪ Heart conditions ▪ HIV infection ▪ Immunocompromised state ▪ Mental health conditions ▪ Overweight and obesity ▪ Pregnancy ▪ Sickle cell disease or thalassemia ▪ Smoking & Tobacco Use ▪ Solid organ or blood stem cell transplant ▪ Stroke or cerebrovascular disease ▪ Substance use disorders ▪ Tuberculosis • High Risk criteria is different for 12-17 YOA and can be found in Banner Health Guidelines	• Within 7 days of symptom onset • 12 YOA and at least 40 kg • High Risk for severe COVID-19/hospitalization ▪ Age ≥ 65 years ▪ Major immune suppression (e.g., recently diagnosed hematologic malignancy, cancer chemotherapy, solid organ transplant on immune suppression) ▪ Obesity with BMI > 25 kg/m2 ▪ Cardiovascular disease (including hypertension) ▪ Pregnancy ▪ Diabetes ▪ Chronic kidney disease ▪ Chronic lung disease (e.g., COPD, cystic fibrosis) ▪ Sickle cell disease ▪ Neurodevelopment disorders or other conditions that confer medical complexity (e.g., genetic, or metabolic syndrome) ▪ Medical related technology dependence (e.g., gastrostomy) • High Risk criteria is different for 12-17 YOA and can be found in Banner Health Guidelines	• Within 5 days of symptom onset • 60 YOA and at least 40 kg • High Risk for severe COVID-19/hospitalization ▪ Age ≥ 65 years ▪ Cancer ▪ Chronic kidney disease ▪ Chronic liver disease ▪ Chronic lung diseases ▪ Dementia or other neurological conditions ▪ Diabetes (type 1 or 2) ▪ Down syndrome ▪ Heart conditions ▪ HIV infection ▪ Immunocompromised state ▪ Mental health conditions ▪ Overweight and obesity ▪ Sickle cell disease or thalassemia ▪ Smoking & Tobacco Use ▪ Solid organ or blood stem cell transplant ▪ Stroke or cerebrovascular disease ▪ Substance use disorders ▪ Tuberculosis
Efficacy Summary	• Reduces risk of hospitalization or death by 88% (NNT = 17) • Expect efficacy against Omicron variant • Clinical data not yet published	• Interim clinical trial results indicate patients who received bebtelovimab were less likely to advance to severe COVID-19. Results have not been published / peer reviewed • In-vitro data suggests that bebtelovimab has efficacy against Omicron BA.2 • Note: due to high prevalence of Omicron BA.2 variant, other COVID monoclonal antibodies should not be used	• Reduces risk of hospitalization or death by 30% (NNT = 34.5) • Expect efficacy against Omicron variant • Clinical data not yet published
Safety Summary	• Requires dose adjustment for eGFR < 60 mL/min • Not recommended for eGFR < 30 mL/min • Should not be used in severe hepatic impairment (Child-Pugh Class C) • Significant CYP3A4 drug-drug interactions See list below for list of common drug-drug interactions associated with nirmatrelvir/ritonavir	• No dosage adjustment recommended based on renal impairment, pregnancy, or while lactating • Hypersensitivity or infusion-related reactions may occur	• May cause fetal harm • Avoid use in pregnant/lactating patients • May cause disruption in bone/cartilage growth in younger patients • Specific counseling must be conducted per the EUA (see page 3 and 4)
Prescribing Information	Limited availability in pharmacies See above for additional information on locations.	Follow standard COVID-19 Mab order sets • Banner Health: Cerner Advisor • Non-Banner Health: Paper order set	Limited availability in pharmacies See above for additional information on locations
Fact sheet	nirmatrelvir + ritonavir EUA fact sheet for providers	Bebtelovimab EUA fact sheet for providers	molnupiravir EUA fact sheet for providers

Nirmatrelvir/ritonavir (Paxlovid) Drug-Drug Interactions Summary Table

- Below is a list of common interactions, and may not be inclusive
- Medications in red are contraindicated and should not be prescribed nirmatrelvir/ritonavir
- See FDA Emergency Use Authorization for detail regarding clinical effect of interaction and prescribing guidance

Class	Drug	Class	Drug
Alpha-1-adrenoreceptor antagonist	alfuzosin	**Antipsychotics**	lurasidone, pimozide, clozapine, quetiapine
Analgesics	pethidine, piroxicam propoxyphene	**Calcium channel blockers**	amlodipine, diltiazem, felodipine, nicardipine, nifedipine
Antianginal	ranolazine	**Cardiac glycosides**	digoxin
Antiarrhythmics	amiodarone, dronedarone flecainide, propafenone, quinidine	**Endothelin receptor antagonists**	bosentan
Antiarrhythmics	bepridil, lidocaine	**Ergot derivatives**	dihydroergotamine, ergotamine, methylergonovine
Anticancer Drugs	apalutamide, abemaciclib abemaciclib, ceritinib, dasatinib, encorafenib, ibrutinib, ivosidenib, neratinib, nilotinib, venetoclax, vinblastine, vincristine	**Hepatitis C direct acting antivirals**	elbasvir/grazoprevir, glecaprevir/pibrentasvir, ombitasvir/paritaprevir/ritonavir, dasabuvir, sofosbuvir/velpatasvir/voxilaprevir
Anticoagulants	warfarin, rivaroxaban	**Herbal products**	St. John's Wort
Anticonvulsants	carbamazepine, phenobarbital, phenytoin	**HMG-CoA reductase inhibitors**	lovastatin, simvastatin, atorvastatin, rosuvastatin
Antidepressants	Bupropion, trazodone	**Hormonal contraceptives**	ethinyl estradiol
Antifungals	voriconazole, ketoconazole, isavuconazonium sulfate itraconazole	**Immunosuppressants**	cyclosporine*, tacrolimus*, sirolimus *may use if close monitoring of immunosuppressed concentrations is feasible
Anti-gout	colchicine	**Long-acting beta-adrenoreceptor agonist**	salmeterol
Anti-HIV protease inhibitors	amprenavir, atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, saquinavir, tipranavir	**Narcotic analgesics**	fentanyl, methadone
Anti-HIV	didanosine, delavirdine, efavirenz, maraviroc, nevirapine, raltegravir, zidovudine, bictegravir/emtricitabine/ tenofovir	**PDE5 inhibitor**	sildenafil (Revatio®) when used for pulmonary arterial hypertension
Anti-infective	clarithromycin, erythromycin	**Sedative/hypnotics**	triazolam, oral midazolam
Antimycobacterial	rifampin, bedaquiline, rifabutin	**Systemic corticosteroids**	betamethasone, budesonide, ciclesonide, dexamethasone, fluticasone, methylprednisolone, mometasone, prednisone, triamcinolone