COVID-19 THERAPEUTIC FACTSHEET: NIRMATRELVIR-RITONAVIR (Paxlovid)

Use: FDA Emergency Use Authorization (EUA) for the treatment of mild to moderate COVID-19 in **adults and pediatric patients (12 years and older and weight at least 40 kg)** at risk for progression of disease.

Paxlovid Facts for Healthcare Providers - Summary	
Mechanism of Action	Viral protease inhibitor that inhibits SARS-CoV-2 replication plus a pharmacological booster (ritonavir)
Dosage/Administration	Nirmatrelvir 300mg (2 x 150mg tablets) plus Ritonavir 100mg (1 x 100mg tablet) PO Q12h x 5 days with/without food
EUA Inclusion Criteria (See UNC Healthcare current Criteria for Use)	• + for SARS CoV-2 • High risk for progression to severe COVID 19, including hospitalization and death • 12 years of age and older • Weight 40 kg or more • Outpatient status or not hospitalized due to COVID-19 • Symptom onset </= 5 days
Contraindications	Contraindicated concomitant medication that risks significant drug-drug interactions (find details here)
Adverse Effects (<1%)	• Diarrhea • Altered taste • Hypertension • Myalgias
Drug Interactions	Many (find details here)
Dose Adjustments	• In moderate renal impairment (eGFR ≥30 to <60 mL/min), reduce the dose to 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days • Not recommended in those with estimated GFR <30 mL/min. • Not recommended in those with severe hepatic impairment.

All patients should be provided with access to the **FDA Factsheet for Patients and Caregivers** and asked to review the information prior to starting treatment.

Renal Insufficiency

Laboratory testing prior to administration can lead to clinically significant delays in initiation of treatment, therefore, history should be obtained from the patient and available medical records reviewed for renal insufficiency including need for dialysis.

Hepatic Impairment

Laboratory testing prior to administration can lead to clinically significant delays in initiation of treatment, therefore, history should be obtained from the patient and available medical records reviewed for severe hepatic impairment including cirrhosis.

Considerations for People Who Can Become Pregnant

Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Advise patients using combined hormonal contraceptives to use an effective alternative contraceptive method or an additional barrier method of contraception.

Considerations for People Who Are Pregnant

Paxlovid can be used in pregnant individuals. There are no available human data on the use of nirmatrelvir during pregnancy 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

Considerations During Lactation

There are no available data on the presence of nirmatrelvir in human or animal milk, the effects on the breastfed infant, or the effects on milk production. There is no information on the effects of ritonavir on the breastfed infant or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for treatment and any potential adverse effects on the breastfed infant from Paxlovid or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Considerations for Those Younger than 18 Years of Age

Paxlovid is not authorized for use in patients younger than 12 years of age or weighing less than 40 kg. The authorized adult dosing regimen is expected to result in comparable serum exposures of nirmatrelvir and ritonavir in patients 12 years of age and older and weighing at least 40 kg as observed in adults.

Handling Missed Doses

- If the patient misses a dose of Paxlovid within 8 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule.
- If the patient misses a dose by more than 8 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time.

COVID-19 THERAPEUTIC FACTSHEET: BEBTELOVIMAB

Use: FDA Emergency Use Authorization (EUA) for the treatment of mild to moderate COVID-19 in **adults and pediatric patients (12 years and older and weight at least 40 kg)** at high risk for progression to severe COVID-19, including hospitalization or death.

Bebtelovimab Facts for Healthcare Providers - Summary

Mechanism of Action	Monoclonal antibody that binds to the spike receptor binding domain of SARS-CoV-2 interfering with cell entry. This monoclonal is predicted to be active against all SARS-CoV-2 variants identified to date including Omicron BA.1 and BA.2.
Dosage/Administration	175mg administered IV push over at least 30 seconds once
EUA Inclusion Criteria (See UNC Healthcare current Criteria for Use)	• Positive for SARS CoV-2 • High risk for progression to severe COVID 19, including hospitalization and death • 12 years of age and older • Weight 40 kg or more • Outpatient status or not hospitalized due to COVID-19 • Symptom onset </= 7 days
Contraindications	None
Adverse Effects (<1%)	• Infusion reactions • Hypersensitivity
Drug Interactions	None
Dose Adjustments	None

All patients should be provided with access to the **FDA Factsheet for Patients and Caregivers** and asked to review the information prior to starting treatment.

Considerations for People Who Can Become or Are Pregnant

Bebtelovimab can be used in pregnant individuals. There are no available human data on the use of bebtelovimab during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Nonclinical reproductive toxicity studies have not been performed with bebtelovimab. In tissue cross reactivity studies using human fetal tissues, no binding of clinical concern was detected for bebtelovimab. Human immunoglobulin G1 (IgG1) antibodies are known to cross the placental barrier; therefore, bebtelovimab has the potential to be transferred from the mother to the developing fetus. It is unknown whether the potential transfer of bebtelovimab provides any treatment benefit or risk to the developing fetus.

Considerations During Lactation

There are no available data on the presence of bebtelovimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for bebtelovimab and any potential adverse effects on the breastfed child from bebtelovimab or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Considerations for Those Younger than 18 Years of Age

The safety and effectiveness of bebtelovimab have not been established in pediatric patients younger than 12 years of age or weighing less than 40 kg.

COVID-19 Vaccination after Bebtelovimab

Patients can receive a COVID-19 vaccine after treatment with bebtelovimab. Earlier guidance suggested vaccination be delayed 90 days following administration given theoretical interaction between the monoclonal and the vaccine induced spike protein. Recent data indicates such interactions do not occur.

COVID-19 THERAPEUTIC FACTSHEET: REMDESIVIR (Veklury)

Use: FDA Emergency Use Authorization (EUA) and FDA approval for the treatment of **adults and pediatric patients (12 years of age and older and weighing at least 40 kg)** for the treatment of coronavirus disease 2019 (COVID-19) requiring hospitalization. Outpatient use to treat mild to moderate COVID-19 in those at risk of progression of disease is 'off-label.'

Remdesvir Facts for Healthcare Providers - Summary	
Mechanism of Action	Nucleoside analogue RNA polymerase inhibitor that inhibits SARS-CoV-2 replication.
Dosage/Administration	200mg IV day 1 followed by 100mg IV on days 2 and 3
EUA Inclusion Criteria (See UNC Healthcare current Criteria for Use)	• + for SARS CoV-2 • High risk for progression to severe COVID 19, including hospitalization and death • 12 years of age and older • Weight 40 kg or more • Outpatient status or not hospitalized due to COVID-19 • Symptom onset </= 7 days
Contraindications	Severe hepatic impairment
Adverse Effects (<1%)	• Elevated liver transaminases • Nausea
Drug Interactions	Reduced drug activity when co-administered with hydroxychloroquine or chloroquine
Dose Adjustments	• Not recommended in those with estimated GFR <30 mL/min. • Not recommended in those with severe hepatic impairment.

Renal Insufficiency

Laboratory testing prior to administration can lead to clinically significant delays in initiation of treatment, therefore, history should be obtained from the patient and available medical records reviewed for renal insufficiency including need for dialysis.

Hepatic Impairment

Laboratory testing prior to administration can lead to clinically significant delays in initiation of treatment, therefore, history should be obtained from the patient and available medical records reviewed for severe hepatic impairment including cirrhosis.

Considerations for People Who Can Become or Who Are Pregnant

Remdesivir can be used in pregnant individuals. 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. In nonclinical reproductive toxicity studies, remdesivir demonstrated no adverse effect on embryo-fetal development when administered to pregnant animals at systemic exposures (AUC) of the predominant circulating metabolite of remdesivir (GS-441524) that were 4 times (rats and rabbits) the exposure in humans at the recommended human dose (RHD)

Considerations During 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. In animal studies, remdesivir and metabolites have been detected in the nursing pups of mothers given remdesivir, likely due to the presence of remdesivir in milk *(see Data).* The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for remdesivir and any potential adverse effects on the breastfed child from remdesivir or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Considerations for Those Younger than 18 Years of Age

The safety and effectiveness of remdesivir have not been established in pediatric patients younger than 12 years of age or weighing less than 40 kg.

Handling Missed Doses

Three consecutive days of therapy is recommended. In cases where the second or third dose is missed, the clinician can decide whether to administer a 'make-up' dose of the medication based on the clinical circumstance and infusion center availability.

COVID-19 THERAPEUTIC FACTSHEET: MOLNUPIRIVIR (Lageviro)

Use: FDA Emergency Use Authorization (EUA) for the treatment of mild to moderate COVID-19 in **adults** at risk for progression of disease and for whom other authorized therapies are **not** readily available.

Molnupiravir Facts for Healthcare Providers - Summary	
Mechanism of Action	Nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis
Dosage/Administration	800mg (4 x 200mg capsules) PO Q12h x 5 days with/without food
EUA Inclusion Criteria (See UNC Healthcare current Criteria for Use)	• + for SARS CoV-2 • High risk for progression to severe COVID 19, including hospitalization and death • 18 years of age and older • Outpatient status • Symptom onset </= 5 days • Other authorized COVID-19 therapy not readily available
Contraindications	Not recommended with pregnancy and lactation Not authorized for PEP or PrEP
Adverse Effects (<1%)	• Diarrhea • Nausea • Dizziness
Drug Interactions	None Known
Dose Adjustments	No dosage adjustment is recommended based on renal or hepatic impairment or in geriatric patients

All patients should be provided with access to the **FDA Factsheet for Patients and Caregivers** and asked to review the information prior to starting treatment.

Considerations for People Who Can Become Pregnant

Molnupirivir causes viral mutations that inhibit replication. Based on findings from animal and laboratory studies there is a potential for fetal harm. Therefore, it is recommended by the FDA that molnupirivir not be used in pregnancy.

Prior to treatment with molnupiravir, assess whether an individual of childbearing potential is pregnant or not, if clinically indicated.

Pregnancy status does **not** need to be confirmed in patients who:

- Have undergone permanent sterilization,
- Are currently using an intrauterine system or contraceptive implant, or
- In whom pregnancy is not possible.

All other patients, assess whether the patient is pregnant based on:

- The first day of last menstrual period in individuals who have regular menstrual cycles, is using a reliable method of contraception correctly and consistently or have had a negative pregnancy test.

A pregnancy test is recommended if the individual:

- Has irregular menstrual cycles
- Is unsure of the first day of last menstrual period, or
- Is not using effective contraception correctly and consistently

Patient counseling:

- Use consistent contraception for the duration of treatment and for 4 days after last dose
- 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 of molnupiravir

Considerations for People Who Are Pregnant

If a clinical decision is made to use molnupirivir used during pregnancy, the patient must be informed of the potential benefits and risks of the medication during pregnancy and be made aware of Merck Sharp & Dohme's pregnancy surveillance program at 1-877-888-4231 or pregnancyreporting.msd.com.

If the pregnant individual agrees to participate in the pregnancy surveillance program and allows the prescribing healthcare provider to disclose patient specific information to Merck Sharp & Dohme, the prescribing healthcare provider must provide the patient's name and contact information to Merck Sharp & Dohme.

Considerations During Lactation

Breastfeeding is not recommended during treatment and for 4 days after the last dose of molnupiravir. 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 molnupiravir

Considerations for Those Younger than 18 Years of Age

Molnupiravir is not authorized for use in patients less than 18 years of age given bone and cartilage toxicity were observed in a 3-month, repeat-dose toxicology study in rats.

Handling Missed Doses

- </= 10 hours since time med usually taken, take it as soon as possible and resume normal dosing schedule
- > 10 hours since the time usually taken, do not take the missed dose and instead take the next dose at the regularly scheduled time. Do not double the dose to make up for a missed dose.

Provider Documentation

Providers must document the following:

- Assessment of potential for pregnancy, including confirmed negative pregnancy test when indicated
- If molnupiravir is prescribed during pregnancy, the provider must document that the known and potential benefits and potential risks of molnupiravir use during pregnancy, as outlined in "Fact Sheet for Patients and Caregivers" were discussed with the patient
- The provider must also document that a pregnant individual was made aware of Merck Sharp & Dohme's pregnancy surveillance program at 1-877-888-4231 or pregnancyreporting.msd.com