North Collaborative Care

NORTH MEMORIAL HEALTH

MAPLE GROVE HOSPITAL

COVID-19 OUTPATIENT THERAPY FOR PREGNANT PATIENTS

April 2022—Version 2.0

The goal of outpatient therapy for COVID is to reduce progression of the disease, and therapy hospitalization, in populations at increased risk for progression. Limited data exist to inform clinical decision making in the setting of pregnancy This knowledge asset seeks to share current knowledge of available outpatient therapies.

KEY POINTS

- Pregnant individuals are at increased risk for severe COVID disease. Vaccination remains the most studied and most effective intervention to prevent severe COVID disease in pregnancy.
- As of 4/11/2022, therapeutics for outpatient COVID management include: Paxlovid™, remdesivir, monodonal antibodies and molnupiravir.
- MDH COVID therapy resources: https://www.health.state.mn.us/diseases/coronavirus/meds.html#pregnant
- **Paxlovid™** is a combination of protease inhibitors nirmatrelvir and ritonavir. Nirmatrelvir is a novel therapeutic and no human data currently exist. Ritonavir has been used by pregnant persons with HIV and has an acceptable safety profile. No adverse outcomes have occurred in animal reproduction models at doses 3x greater than the authorized human dose. **Pregnant persons may choose to participate in the EUA and receive therapy.**
- **Remdesivir** is an IV antiviral therapy administered daily for 3 days that may reduce progression of disease in some high risk populations and may be administered to pregnant patients. North Memorial Health does not presently have availability of outpatient remdesivir therapy.
- **Monoclonal antibody therapy** Monoclonal antibodies as a therapeutic class generally has acceptable risk in pregnancy although extent of fetal exposure to antibodies and benefit or risk to the fetus is unknown. **Effective 3/30/22, the FDA revoked authorization for sotrovimab in Minnesota due to lack of efficacy against the current variant.** Bebtelovimab is presently available.
- **Molnupiravir** is a nucleoside analog and is not recommended in pregnancy due to risk of genotoxicity when an alternative is available.

Based on present data and availability, North Memorial encourages consideration to Paxlovid for early mild-moderate COVID therapy in pregnancy.

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ORAL THERAPY FOR EARLY COVID-19

Paxlovid™ is a combination product of nirmatrelvir (SARS-CoV-2 protease inhibitor) and ritonavir (HIV protease inhibitor) taken twice daily for 5 days. This therapeutic demonstrated an 88% reduction in hospitalizations in emergency use authorization data (Table 1) (NNT = 16). There are presently no human pregnancy data on nirmatrelvir. Limited animal data has not revealed fetal impact. Ritonavir has been used successfully for HIV with an acceptable safety profile. Due to limited availability, an allocation framework has been created using the MASSBP tool (Figure 1). COVID positive patients with a score of 4 or greater and are appropriate for outpatient therapy are candidates for therapy, thus all pregnant individuals are candidates provided the patient consents to participation in the emergency use authorization. Adjusted dosing required for patient with renal dysfunction.

Eligibility: Mod-moderate disease within 5 days of symptoms and not requiring hospitalization for COVID.

Paxlovid™ has increased risk for drug-drug interactions thus partnership with the pharmacy team is key. Table 2 provides potential interactions with commonly used therapeutics in Obstetrics to include in consideration for recommendations for therapy. In accordance with MDH allocation framework, Paxlovid™ is available at the NMHH ED and Blaze Health clinics and urgent cares, including telehealth visits. Contact the inpatient pharmacy team for antepartum patients who are eligible and interested in therapy.

SMFM and ACOG support use of Paxlovid for the treatment of pregnant patient with COVID-19 and meeting clinical qualifications. Paxlovid should not be use concomitantly with sotrovimab.

Table 1. EUA data for Paxlovid.

	PAXLOVID(N=1,039)	PLACEBO(N=1,046)
Primary endpoint: COVID-19 related hospitalization or death from any cause through Day 28	8 (0.08%)	66 (6.3%)
All-cause mortality through Day 28	0	12 (1.1%)

Table 2. Potential impact of Paxlovid on common medications used in OB. Adapted from Paxlovid EUA

Drug Class	Drugs used in OB from this Class	Effect on Concentration	Clinical Comments
Calcium channel blockers	Nifedipine	Increased	Dose decrease may be needed when co-administered with Paxlovid.
Ergot derivatives	Methylergonovine	Increased	Co-administration may led to ergot toxicity due to vasospasm and ischemia.
Systemic corticosteroids	Betamethasone, Dexamethasone	Increased	Increase risk for Cushing's syndrome and adrenal suppression.

* Table adapted from FDA EUA summary for Paxlovid™.[3]

MASSBP SCORING

Monoclonal Antibody Screening Score – BIPOC + Pregnant (MASSBP)

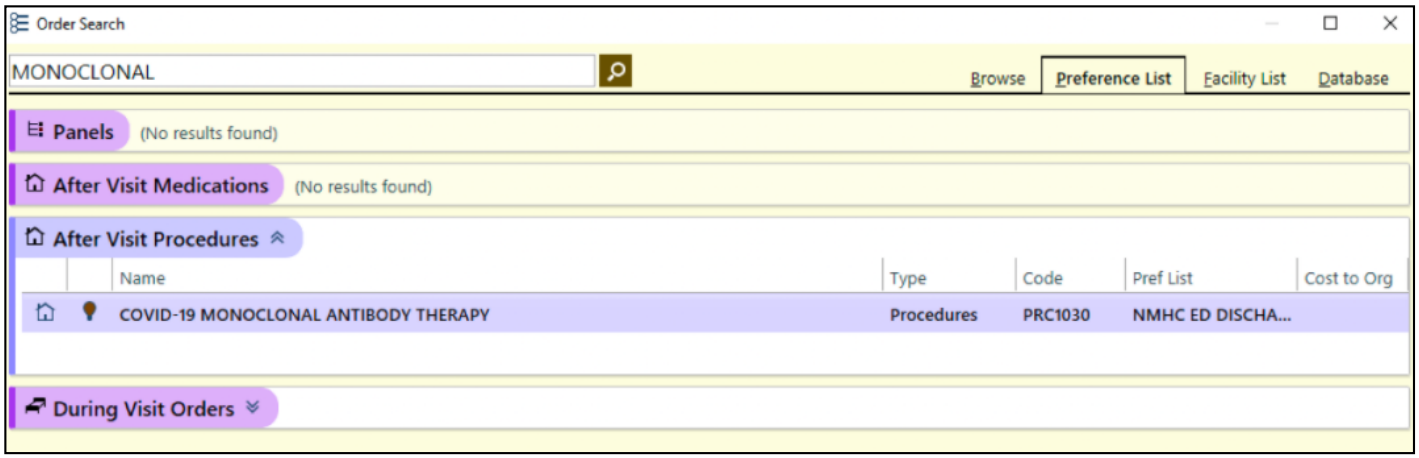
HIGH RISK PARAMETER	POINT VALUE
Age ≥ 65 years	2 points
BMI ≥ 35 kg/m^2	2 points
Diabetes Mellitus	2 points
Chronic kidney disease	3 points
Cardiovascular disease in a patient ≥ 55 years	2 points (0 if < 55 years)
Chronic respiratory disease in a patient ≥ 55 years	3 points (0 if < 55 years)
Hypertension in a patient ≥ 55 years	1 point (0 if < 55 years)
Immunocompromised status	4 points
Pregnancy	4 points
Member of the BIPOC community (black/African American, Hispanic/Latino, Asian, native Hawaiian or pacific islander, American Indian, Alaskan Native)	2 points

Monoclonal Antibody Treatment of Breakthrough COVID-19 in Fully Vaccinated Individuals with High-Risk Comorbidities | medRxiv

MONOCLONAL ANTIBODIES

Various monoclonal antibody therapies have been available during the course of COVID. Efficacy has varied between products and between COVID variants. As of 4/11/2022, sotrovimab does not have demonstrated efficacy against the prevailing variant. Bebtelovimab is presently available through the MDH MN RAP system. Data supporting efficacy of bebtelovimab are limited to unpublished data demonstrating reduction in duration of symptoms, but similar rate of hospitalization and death compared to placebo. Resource: Bebtelovimab EUA documentation: https://www.fda.gov/media/156152/download.

Monoclonal antibody therapy administration is not available at North Memorial Health sites. However, therapy is available to all NMH patients through the MN RAP (Resource Allocation Platform) system. MN RAP website: https://www.health.state.mn.us/diseases/coronavirus/mnrappeople.html. Providers may place an order for outpatient therapy in patients with COVID and mild-moderate symptoms. Therapy can be ordered at the time of hospital discharge (inpatient, ED and OB triage) as outlined in the screenshot below:



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2. SMFM Press release. FDA Issues EUA for the Treatment of Mild-to-Moderate COVID-19: Maternal-Fetal Medicine Subspecialists Support Use in Pregnant Patients. Dec 22, 2021. Accessed from ttps://s3.amazonaws.com/cdn.smfm.org/media/3287/Treatment_1.10.pdf on 1/27/2022.
3. FDA. Fact sheet for healthcare providers: emergency use authorization for Paxlovid™. Access from https://www.fda.gov/media/155050/download on 1/27/2022.
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6. MN Dept of Health. COVID-19 monoclonal antibody use in pregnancy: Joint statement from MDH, MN ACOG, Allina Health, Mayo Clinic, and University of Minnesota. Accessed from https://www.health.state.mn.us/diseases/coronavirus/hcp/jointmab.pdf on 1/27/2022.
7. NIH. The COVID-19 treatment guidelines panel's statement on therapies for high-risk, nonhospitalized patients with mild to moderate COVID-19. Last updated Jan 19, 2022. Access from https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/ on 1/27/2022.

This team represents expertise in Obstetrics, Acute Care Medicine and Pharmacy. If you would like further information, please contact the work group lead, Todd Stanhope, MD - todd.stanhope@northmemorial.com.

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Revision History

This document is active and further recommendations are forthcoming. It will be updated as additions develop.

Revision	Description of Changes	Approvals	Date
1.0	Initial Document	OB/GYN CPC; Acute Medicine CPC; Acute Medicine COVID-19 Workgroup	02-09-2022
2.0	Updated information on monoclonal antibody therapy	Acute Medicine COVID-19 Workgroup	04-12-2022