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SITUATION SUMMARY

Omicron is now estimated to be the dominant COVID-19 variant in both the United States and Region 8, which includes Wyoming. Bamlanivimab plus etesevimab and REGEN-COV are unlikely to retain activity against Omicron; sotrovimab appears to retain efficacy against Omicron. Two oral antiviral medications (PAXLOVID and Molnupiravir) have received emergency use authorization for use and will be distributed to Wyoming providers. The Centers for Disease Control and Prevention (CDC) has shortened isolation and quarantine recommendations and updated quarantine recommendations based on booster status.

OMICRON VARIANT

As of December 25, 2021, the Omicron variant is estimated to be the dominant variant in the United States, accounting for a predicted 58.6% of infections in the United States and 56.7% of infections in Region 8, which includes Wyoming. National estimates of variant proportions can be found here: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>. Omicron has been detected in Wyoming.

Initial data suggest that Omicron is highly infectious and has some ability to evade immunity from previous infection and vaccination and resistance to some available therapeutics. Current vaccines are expected to protect against severe illness, hospitalizations, and deaths due to infection with the Omicron variant. The Wyoming Department of Health (WDH) and CDC recommend that all individuals 5 years of age and older be vaccinated against COVID-19 using an mRNA COVID vaccine for which they are eligible (Pfizer or Moderna) and that all individuals 16 years of age and older receive a booster dose with an mRNA vaccine for which they are eligible. The Janssen (Johnson & Johnson) vaccine continues to be available to those patients who choose to receive it.

BAMLANIVUMAB PLUS ETESEVIMAB AND REGEN-COV DISTRIBUTION

Data show that it is unlikely that bamlanivimab plus etesevimab (bam/ete) and REGEN-COV will retain activity against the Omicron variant. As of January 3, 2022, Bam/ete and REGEN-COV will no longer be distributed to states in regions where the prevalence of Omicron is >80%. The current prevalence in Region 8 is estimated to be 56.7%.

Sotrovimab does appear to retain efficacy against the Omicron variant and will continue to be distributed to all locations. Supplies will likely be limited. Sotrovimab is authorized for the treatment of mild to moderate COVID-19 in adults and pediatric patients 12 years of age and older and weighing at least 40 kg with positive results of SARS-CoV-2 viral testing and who are at high risk for progression to severe COVID-19, including hospitalization and death. Sotrovimab is administered by intravenous infusion. Full details about sotrovimab can be found here: <https://www.fda.gov/media/149534/download>

While sotrovimab is the preferred monoclonal antibody moving forward, because there is still >20% delta variant circulating in Wyoming at this time, providers may choose to order and offer bam/ete or REGEN-COV to patients that may benefit, especially if sotrovimab is in short supply, with the understanding that the medications may be ineffective if the patient has Omicron.

Where Omicron is prevalent and sotrovimab is in short supply, the National Institutes of Health (NIH) also recommends the off-label use of remdesivir in nonhospitalized patients with mild to moderate COVID-19 who are at high risk of clinical progression. **Remdesivir is currently approved for use in hospitalized patients only; use of the drug for outpatient treatment would be an off-label indication.** NIH recommends a three day course of Remdesivir, with Remdesivir 200 mg IV on Day 1, then 100 mg once daily on Days 2 and 3 initiated as soon as possible and within 7 days of symptom onset. Remdesivir should be administered in a setting where management of severe hypersensitivity reactions, such as anaphylaxis, is possible. Patients should be monitored during the infusion and observed for at least 1 hour after the infusion. The complete NIH recommendations can be found here: <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-anti-sars-cov-2-mabs-and-rdv-and-omicron/>

In order to receive monoclonal antibodies, including sotrovimab, providers must use the WDH request process. Medications are currently being allocated on a biweekly basis. Requests must be submitted by Tuesday at 5PM for that week's allocation using this [request form](#). The next deadline for requests is December 28, 2021. The full URL for the request form is here: https://docs.google.com/forms/d/e/1FAIpQLSexmd-wm8QIZqMRX6ZoWkmQT0BCkentRdjYr0kQa-a_ef5bBw/viewform

To receive monoclonal antibodies, Wyoming healthcare providers must meet all federal criteria described in the U.S. Food and Drug Administration EUA Letters of Authorization and the Fact Sheets for Healthcare Providers. By submitting a request to WDH, providers are attesting that they meet all the requirements.

Sotrovimab is also available for purchase through the distributor AmerisourceBergen. Details about how to purchase Sotrovimab can be found here: <https://www.sotrovimab.com/hcp/access/>

SCARCE MONOCLONAL ANTIBODY ALLOCATION

Allocation Considerations

The following allocation procedure and administration recommendations are based on recommendations from the WDH Medical Ethics committee and draw upon the ethical guidance already developed by WDH in the Wyoming Department of Health Crisis Standards of Care Plan. This ethical framework is grounded in a commitment to transparency, consistency, fairness, and stewardship. It seeks to maximize the number of lives saved, based on clinical prognosis, while protecting against discrimination.

State Allocation Procedure:

1. State Allocation of if no shortage is present:
 - a. If requests, or demand, for monoclonal antibody drugs do not exceed the amount allocated by HHS to Wyoming, WDH will fulfill allocations fully based on the requests submitted.
2. State Allocation if shortage is present intrastate:
 - a. If the requests, or demand, for monoclonal antibody drugs exceed the amount allocated by HHS to Wyoming, WDH will allocate monoclonal antibodies to Wyoming providers based on their county's portion of the state's total reported 7-day average of active laboratory-confirmed COVID-positive patients. In assessing each provider's allocation, a proportionate reduction will be made for any unused courses of monoclonal antibody drugs currently in that provider's inventory.
 - b. For purposes of determining allocation in scarcity, the County Health Officer in each county without a monoclonal antibody provider may designate another county to receive its shares, if any, based on the location where residents are most likely to be sent to receive monoclonal antibodies

Recommendations for Allocation of Monoclonal Antibodies *Within Institutions*

These recommendations are provided for assistance after research and consultation with a broad spectrum of experts, but they are not mandatory. Institutions are free to develop different allocation plans for monoclonal antibody therapies consistent with legal and ethical duties. The best clinical judgement of providers should ground allocation decisions. No patient should receive monoclonal antibodies who does not meet all clinical inclusion criteria, as specified in the Emergency Use Authorization and Provider Fact Sheets.

When resources are scarce, providers should use their best clinical judgement and best available evidence to prioritize patients who are at high risk for progressing to severe COVID-19 complications, including hospitalization or death. Patients who appear to be roughly equivalent risk should be selected by lottery.

Monoclonal antibodies are **not** authorized for use in the following patient populations:

1. Adults or pediatric patients who are hospitalized due to COVID-19, or
2. Adults or pediatric patients who require oxygen therapy due to COVID-19, or

3. Adults or pediatric patients who require an increase in baseline oxygen flow rate due to COVID-19 in those patients on chronic oxygen therapy due to underlying non-COVID-19-related comorbidity.

Monoclonal antibodies may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Non-Discrimination

Allocation decisions should not consider or be based upon:

1. Judgments on “quality of life”;
2. Judgments on the “social value” of the patient;
3. Race, ethnicity, gender, gender identity, sexual orientation or preference, religion, citizenship or immigration status, or socioeconomic status;
4. Ability to pay;
5. Age as a criterion in and of itself; or
6. Disability status or comorbid condition(s) as a criterion in and of itself (this does not limit consideration of a patient’s physical condition in clinical prognostication of likelihood to survive).

NEW COVID-19 THERAPEUTICS

PAXLOVID

PAXLOVID is a combination of nirmatrelvir, a SARS-CoV-2 main protease inhibitor, and ritonavir, an HIV-1 protease and CYP3A inhibitor that is used to boost plasma levels of nirmatrelvir. PAXLOVID has received emergency use authorization for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct COVID-19 viral testing (molecular or antigen test) and who are at high risk of progression to severe COVID-19 including hospitalization or death.

PAXLOVID may only 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).

Dosage and Administration

PAXLOVID is nirmatrelvir tablets co-packaged with ritonavir tablets. Nirmatrelvir must be co-administered with ritonavir. The dosage for PAXLOVID is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet). All three tablets are taken together orally twice daily for 5 days. The 5-day treatment course should be initiated as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset.

No dosage adjustment is needed in patients with mild renal impairment (eGFR \geq 60 to $<$ 90 mL/min). In patients with moderate renal impairment (eGFR \geq 30 to $<$ 60 mL/min), the dosage of PAXLOVID is 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days. PAXLOVID is not recommended in patients with severe renal impairment (eGFR $<$ 30 mL/min) until more data

are available. The appropriate dosage for patients with severe renal impairment has not been determined.

No dosage adjustment is needed with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. No pharmacokinetic or safety data are available regarding the use of nirmatrelvir or ritonavir in subjects with severe hepatic impairment (Child-Pugh Class C); therefore, PAXLOVID is not recommended for use in patients with severe hepatic impairment. Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir. Caution should be exercised when administering PAXLOVID to patients with pre-existing liver diseases, liver enzyme abnormalities, or hepatitis.

Contraindications, Drug-Drug Interactions, Limitations, and Special Populations

PAXLOVID is contraindicated in patients with a history of clinically significant hypersensitivity reactions (e.g., toxic epidermal necrolysis or Stevens-Johnson syndrome) to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.

PAXLOVID is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions. PAXLOVID is also contraindicated with drugs that are 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 cannot be started immediately after discontinuation of certain medications due to the delayed offset of the recently discontinued CYP3A inducer. A list of clinically significant drug-drug interactions can be found in the healthcare provider fact sheet: <https://www.fda.gov/media/155050/download>.

PAXLOVID is not authorized for the initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19, for pre-exposure or post-exposure prophylaxis for prevention of COVID-19, or for use longer than 5 consecutive days.

Because nirmatrelvir is co-administered with ritonavir, there may be a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

At this time there are no available human data on the use of nirmatrelvir to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are also no available data on the presence of nirmatrelvir in human milk, the effects on the breastfed infant, or the effects on milk production. PAXLOVID may decrease the efficacy of combined hormonal contraceptives; patients should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception.

Providers are encouraged to reference the healthcare provider fact sheet for complete information on PAXLOVID: <https://www.fda.gov/media/155050/download>

Molnupiravir

Molnupiravir is a nucleoside analog that inhibits SARS-CoV-2 replication by viral mutagenesis. Molnupiravir has received emergency use authorization for the treatment of mild to moderate

COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing (molecular or antigen tests) who are at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by the FDA are not accessible or clinically appropriate. Prior to initiating treatment with molnupiravir, providers should carefully consider the known and potential risks and benefits.

Molnupiravir may only 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 molnupiravir belong (i.e., anti-infectives).

Dosage and Administration

The dosage in adult patients is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food. Molnupiravir should be taken as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset.

No dosage adjustment is recommended based on renal or hepatic impairment.

Contraindications, Drug-Drug Interactions, Limitations, and Special Populations

No contraindications have been identified based on the limited available data on the emergency use of molnupiravir.

No drug interactions have been identified based on the limited available data on the emergency use of molnupiravir. No clinical drug-drug interaction trials of molnupiravir with concomitant medications, including other treatments for mild-to-moderate COVID-19, have been conducted.

Molnupiravir is not authorized:

- For use in patients less than 18 years of age
- For initiation of treatment in patients requiring hospitalization due to COVID-19. Benefit of molnupiravir has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19
- For use longer than 5 consecutive days
- For pre-exposure or post-exposure prophylaxis for prevention of COVID-19

Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals. **Molnupiravir is not recommended for use during pregnancy. Breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the final dose.** Prior to initiating 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. In all other patients, assess whether the patient is pregnant based on the first day of the 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 the last menstrual period, or is not using effective contraception correctly and consistently.

It is recommended to advise females of childbearing potential to 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 molnupiravir. It is recommended to advise sexually active males with partners of childbearing potential to use a reliable method of contraception correctly and consistently during treatment and for at least three months after the last dose of molnupiravir.

Providers are encouraged to reference the healthcare provider fact sheet for complete information on molnupiravir: <https://www.fda.gov/media/155054/download>

EVUSHELD

EVUSHELD is authorized for the pre-exposure prophylaxis of COVID-19 in adults and pediatric individuals 12 years of age and older and weighing at least 40 kg and:

- Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 AND
 - Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination OR
 - For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine and/or COVID-19 vaccine components.

Medical conditions or treatments that may result in moderate to severe immune compromise and an inadequate immune response to COVID-19 vaccination include but are not limited to:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts $<200/\text{mm}^3$, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥ 20 mg prednisone or equivalent per day when administered for ≥ 2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

EVUSHELD is not authorized for use in individuals:

- For treatment of COVID-19
- For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2

EVUSHELD is administered by intramuscular injection. Individuals who qualify for EVUSHELD can be redosed every 6 months while COVID-19 is in circulation.

Further details about clinical considerations, storage, administration, and dosing can be found here: <https://www.fda.gov/media/154701/download>

Access to New Therapeutics

WDH expects PAXLOVID, molnupiravir, and EVUSHELD to arrive in Wyoming within the next week. Supplies of the medications will initially be extremely limited. WDH is working to register at least one provider in each county. Initial supplies may allow distribution only to a limited number of locations.

Initial allocations of these products will be allocated to registered providers on a pro rata basis using a pro rata allocation based on the county or regional case count, and the supply allocated to Wyoming from HHS.

Future allocations of these products will be allocated to registered providers on a requested basis using the Wyoming Department of Health’s COVID-19 Therapeutic Request form, which is located here:

https://docs.google.com/forms/d/e/1FAIpQLSexmd-wm8QIZqMRX6ZoWkmQT0BCkentRdjYr0kQa-a_ef5bBw/viewform. Allocations by the federal government are currently being made on a bi-weekly basis. Email reminders will be sent out regarding the next deadline to request an allocation. The next deadline to submit a request for an allocation of COVID-19 Therapeutics (monoclonal antibodies and antivirals) is Tuesday, December 28, 2021, by 5:00 p.m.

As medication supplies increase, WDH will register additional providers. If there is not a listed registered provider in your county and you are interested in becoming a registered provider for at least one of these medications, please contact Dr. Alexia Harrist at alexia.harrist1@wyo.gov.

The following locations are fully registered to receive at least one of these medications. Please note that because of limited supplies, not all locations may receive medication for the initial allocation:

County	Provider	PAXLOVID and/or Molnupiravir	EVUSHELD
Albany	Meredith and Jeannie Ray Cancer Center		X
Albany	Ivinson Memorial Hospital	X	
Big Horn	North Big Horn Hospital	X	
Campbell	Campbell County Memorial Hospital		X

Campbell	Campbell County Public Health	X	
Fremont	Lander Medical Clinic	X	
Johnson	Johnson County Healthcare Center	X	
Laramie	Cheyenne Regional Medical Center	X	X
Lincoln	South Lincoln Medical Center	X	
Natrona	Casper-Natrona County Health Department	X	X
Niobrara	Niobrara County Health District	X	
Park	West Park Hospital	X	X
Platte	Platte County Memorial Hospital	X	
Sheridan	Sheridan Memorial Hospital	X	X
Sweetwater	Sweetwater Memorial Hospital	X	X
Teton	St. John's Health	X	
Uinta	Evanston Regional Hospital	X	
Washakie	Washakie Medical Center	X	X
Weston	Weston County Pharmacy	X	

SHORTENED ISOLATION AND QUARANTINE GUIDANCE FOR COMMUNITY SETTINGS

Current data, including data on the Omicron variant, indicate that the majority of SARS-CoV-2 transmission occurs early in the course of illness, generally in the 1-2 days prior to onset of symptoms and the 2-3 days after. Therefore, CDC has shortened their isolation recommendations. People who test positive, regardless of vaccination status, should isolate at home for 5 days after symptom onset or, if asymptomatic, 5 days after the positive test . If after 5 days they are asymptomatic, or afebrile with improving symptoms, they may leave isolation. Strict masking when around others for an additional 5 days is recommended. Individuals who are still having fever after 5 days or whose symptoms are not improving should remain home until the fever has resolved and symptoms are improving.

CDC has also shortened quarantine recommendations for individuals who have been exposed to COVID-19 and updated quarantine recommendations based on vaccination status. The new quarantine recommendations are as follows:

Vaccination Status	Quarantine recommendations
Individuals 16 years of age and older who have completed a primary vaccination series and received a booster OR Individuals who are less than 16 years of age and have completed a primary series of Pfizer but are not eligible for a booster OR Individuals who have completed a primary series of Pfizer or Moderna within the last 6 months OR Individuals who have completed the primary series of the Janssen vaccine within the last 2 months	Quarantine at home not needed Wear a mask around others for 10 days after the exposure Test on day 5, if possible
Individuals 16 years of age and older who have completed a primary series of Pfizer or Moderna more than 6 months ago and are not boosted OR Individuals who have completed a primary series of Janssen more than 2 months ago and are not boosted OR Individuals of any age who are unvaccinated	Quarantine at home for 5 days after the exposure After quarantine, wear a mask around others for an additional 5 days If quarantine is not possible, wear a mask around others for 10 days Test on day 5 if possible
Individuals who have tested positive for COVID-19 on a molecular or antigen test within the past 90 days	Quarantine at home not needed Wear a mask around others for 10 days after the exposure

Anyone developing symptoms after an exposure should stay home and be tested.

These shortened isolation and quarantine guidelines are specific to community settings only. Individuals in healthcare settings should follow guidance specific to these settings.

CDC has updated isolation and quarantine guidance for healthcare workers, as well as provided strategies to mitigate staffing shortages in contingency and crisis situations. Links to that guidance are provided below:

- <https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html>
- <https://www.cdc.gov/coronavirus/2019-ncov/hcp/mitigating-staff-shortages.html>

Infection control recommendations for healthcare and long-term care facility settings can be found here here:

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html>

These recommendations may be updated as additional data on Omicron are collected.

CLINICAL RESOURCES

Clinical management guidance is available from the CDC (<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>), the NIH (<https://www.covid19treatmentguidelines.nih.gov/>), and the IDSA (<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>). CDC's Clinical Outreach and Communication Activity (COCA) calls and webinars offer the most up to date information and guidance for clinicians. COCA calls can be accessed at <https://emergency.cdc.gov/coca/calls/index.asp>. The Wyoming Medical Society website contains clinical resources from the University of Washington, including treatment guidelines and algorithms: <https://www.wyomed.org/resources/covid-19/>.

CONTACT INFORMATION

For questions about the COVID-19 vaccines, providers should visit the WDH Immunization Unit website at <https://health.wyo.gov/publichealth/immunization/wyoming-covid-19-vaccine-information/> or email WDH.immunization@wyo.gov.

For questions about monoclonal antibody therapies, please contact wdh.covid19@wyo.gov.

Wyoming healthcare providers and facilities are reminded to check COVID-19 resources available from WDH and CDC. Healthcare providers or facilities can contact WDH through the following channels:

- Please email questions about preparedness, PPE, infection control, or other non-urgent topics to wdh.covid19@wyo.gov.
- Please contact WPHL with questions about specimen collection, storage, or shipping at 307-777-7431 or WPHL@wyo.gov.
- **Please use the WDH Public Health Emergency Line (1-888-996-9104) for urgent questions. This line is intended ONLY for healthcare providers. Do not share this number with the public.**

Please refer questions from the general public to 211 or to the WDH email box (wdh.covid19@wyo.gov).