SAN MATEO COUNTY HEALTH
PUBLIC HEALTH, POLICY & PLANNING

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HEALTH ADVISORY:

Respiratory Virus Season 2022–23 Testing and Treatment Recommendations

December 22, 2022

This advisory is intended for emergency medicine, urgent care providers, infectious disease, primary care, internal medicine, family practice, pediatric, and OB/GYN providers. Please distribute as appropriate.

Situational Update:

COVID-19, influenza, and Respiratory Syncytial Virus (RSV) have been circulating at high levels in California. Hospitalizations of vulnerable populations including children and the elderly remain high and are straining our healthcare systems. Symptoms of influenza, RSV, COVID-19, and other respiratory viruses are often similar, and testing can be used to differentiate them. At this time, all individuals presenting with respiratory symptoms should be tested for both SARS-CoV-2 and influenza, as well as RSV if appropriate based on risk factors.

This is particularly important for patients at higher risk for severe illness from influenza or COVID-19 who are candidates for antiviral treatment. Many patients are not aware that they are at higher risk, and these patients can benefit from prompt treatment.

Testing:

Healthcare providers are encouraged to test patients presenting with respiratory symptoms for influenza, SARS-CoV-2, and RSV via multiplex assays when feasible, as testing may affect decisions regarding infection control, clinical management and treatment. In particular, healthcare providers caring for children and adults with respiratory illnesses in inpatient and congregate settings should test for respiratory viruses due to the risk of rapid spread and severe outcomes in these settings.

Of note, in the context of high clinical suspicion, a negative result from a rapid antigen test should be confirmed with a more sensitive (PCR/nucleic acid) test.

Treatment:

1. **COVID-19 Treatment**

   Once an individual is diagnosed with COVID-19, early treatment with COVID-19-specific agents is the only existing strategy to markedly decrease risk of serious illness. Patients with SARS-CoV-2 infection who meet age and timing requirements, including those presenting with mild, early symptoms, should be offered treatment unless a significant contraindication is present.

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At this time, there is **ample supply of COVID-19 therapeutic agents, but they have been underused – especially among populations disproportionately impacted by COVID-19,** including communities of color, low-income communities, and residents of long-term care facilities.

Studies have shown that:

- COVID-19 treatments reduce the risk for hospitalization and death by 50-88% among unvaccinated people and by 45–50% among vaccinated or previously infected people.[1,2,3]
- Early evidence suggests COVID-19 treatment may decrease the risk of developing post-COVID symptoms.[4,5,6,7]
- SARS-CoV-2 viral load decreases faster among people treated compared with people not treated, suggesting the potential for decreased transmission and isolation time for test-result-based isolation protocols.[1]
- Prescribing options have been shown to be safe, including in the fragile, elderly population.[8] Risks are minimal, especially when weighed against benefits.

Preferred COVID-19 Treatments (listed in order of preference) are noted below. Regimens are current as of 11/28/2022. Please see NIH COVID-19 Treatment Guidelines and FDA authorization updates for the most current recommendations and regimens including updates related to subvariant susceptibilities. **Importantly, the agents below can prevent severe disease, hospitalization, and death. They retain full activity against the current variant mix in California**.

- Paxlovid orally twice daily for 5 days, initiated as soon as possible within 5 days of symptom onset in people aged ≥12years and weighing ≥40 kg; *or*
- Remdesivir 200 mg IV on Day 1, followed by remdesivir 100 mg IV once daily on Days 2 and 3, initiated as soon as possible within 7 days of symptom onset in people aged ≥12 years and weighing ≥40 kg. Indications and dosage for outpatients <12 years of age can be found in the remdesivir full prescribing information.

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[1] Hammond, Jennifer, et al. "Oral nirmatrelvir for high-risk, nonhospitalized adults with Covid-19." *New England Journal of Medicine* 386.15 (2022): 1397-1408.
[2] Ganatra, Sarju, et al. "Oral Nirmatrelvir and Ritonavir in Nonhospitalized Vaccinated Patients With Coronavirus Disease 2019 (COVID-19)." *Clinical Infectious Diseases* (2022).
[3] Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — United States, April–September 2022 | MMWR (cdc.gov)
[4] Yan, Xie et al. Nirmatrelvir and the Risk of Post-Acute Sequelae of COVID-19”.” MedRxiv Nov 3, 2022.
[5] Sudre, Carole H., et al. "Attributes and predictors of long COVID." *Nature medicine* 27.4 (2021): 626-631.
[6] Al-Aly, Ziyad, et al. "High-dimensional characterization of post-acute sequelae of COVID-19." *Nature* 594.7862 (2021): 259-264.
[7] Peluso, Michael J., et al. "Early clues regarding the pathogenesis of long-COVID." *Trends in Immunology* (2022).
[8] Zhong, Weijie, et al. "The efficacy of paxlovid in elderly patients infected with SARS-CoV-2 omicron variants: Results of a non-randomized clinical trial." *Frontiers in medicine* 9 (2022).

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- If neither of the preferred therapies for high-risk, non-hospitalized patients are available, feasible to deliver, or clinically appropriate, the NIH COVID-19 Treatment Guidelines outline additional options. **Of note, currently circulating Omicron subvariants are resistant to available monoclonal antibodies.**
  - As of 11/30/2022 Bebtelovimab is no longer authorized and should NOT be used due to viral resistance. For alternatives, see the NIH treatment recommendations.
  - The monoclonal antibody combination cilgavimab and tixagevimab (Evusheld™) is still authorized but >75% of circulating variants in California are resistant. At this point and until the EUA is revoked, NIH still recommends using it for PrEP.
  - **Antiviral therapeutics for the treatment of COVID-19, ritonavir-boosted nirmatrelvir (Paxlovid™), remdesivir (Veklury®), and molnupiravir (Lagevrio™), retain activity against currently circulating Omicron sublineages.**

2. **Influenza Treatment**

Ideally, high-risk patients with **suspected influenza** should be immediately started on antiviral treatment. Decisions about starting influenza antiviral treatment should not wait for laboratory confirmation. Once an individual is diagnosed with influenza, early treatment is recommended. If the patient tests negative for influenza, antiviral treatment can be discontinued.

- Available information suggests that current local antiviral availability issues are due to limited availability of *generic* oseltamivir.
  - If available, *brand-name* oseltamivir (Tamiflu) can be used to treat outpatients and hospitalized patients with influenza.
  - When there is limited availability of oseltamivir or other antivirals:
    - Antiviral treatment should target patients with influenza who are at the highest risk of severe disease and those who are hospitalized.
    - Patients with clinically mild influenza who are otherwise healthy and not at increased risk of influenza complications can be managed with supportive care without antiviral treatment.
    - Antiviral treatment of outpatients should be prioritized for persons who test positive for influenza within 2 days of illness onset.
  - If oseltamivir is unavailable, oral baloxavir, inhaled zanamivir, or intravenous peramivir can be used for early treatment of outpatients at increased risk for complications who present with uncomplicated influenza, depending upon age and contraindications.
- Considerations for Priority Groups
  - Children
    1. Oseltamivir is the only recommended oral antiviral for treatment of influenza in children less than 5 years of age.

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2. If oseltamivir suspension is unavailable for treating influenza in young children, clinicians can request that pharmacists compound a suspension from oseltamivir capsules.
3. In areas where generic oseltamivir is unavailable, baloxavir can be used for early treatment of influenza in otherwise healthy children aged 5 years and older, and for children aged 12 years and older with underlying conditions that increase their risk of influenza complications.

- Congregate Settings
  1. When an influenza outbreak is NOT occurring, prioritize oseltamivir for early treatment of influenza in residents of congregate settings such as long-term care facilities (LTCFs), who test positive for influenza.
  2. In the setting of laboratory confirmed influenza outbreaks in LTCFs:
     - Early empiric antiviral treatment of suspected influenza in residents is recommended. Once an influenza diagnosis is confirmed through testing, post-exposure antiviral chemoprophylaxis of exposed residents is recommended.
     - If oseltamivir is not available, baloxavir, zanamivir, or peramivir may be used for treatment of influenza.
     - Although baloxavir may be used for treatment, there are no available data on using baloxavir in LTCFs for treatment or post-exposure chemoprophylaxis.

3. **Influenza and COVID-19 Coinfection Treatment**

   High-risk patients **co-infected with influenza and SARS-CoV-2** should receive treatment for both viruses. There are no clinically significant drug-drug interactions between the antiviral agents or immunomodulators that are used to prevent or treat COVID-19 and the antiviral agents used to treat influenza.

Prevention:

RSV can cause serious disease in young children and in adults, especially the elderly. Per the American Academy of Pediatrics (AAP) guidance, healthcare providers should promptly administer **prophylactic palivizumab** to infants and young children at high risk for RSV.

The U.S. Centers for Disease Control (CDC) and California Department of Public Health (CDPH) recommend that everyone 6 months of age or older get an annual influenza vaccine and stay up to date with COVID-19 vaccines, including the bivalent booster that is now available for everyone 6 months of age or older.

Ideally, people aged 65 years and older should receive high-dose, recombinant, or adjuvanted influenza vaccines.

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It is strongly recommended that all staff working in healthcare facilities and congregate settings be vaccinated with both the annual influenza vaccine and the updated bivalent COVID-19 booster.

Reporting:

As a reminder, please use the SPOT Portal to report COVID-19 exposures, outbreaks, and case details to San Mateo County. COVID-19 questions and updates can also be sent through this portal.

For a **single case of influenza in a congregate setting**, **any pediatric influenza death**, and **any RSV death in an individual less than 5 years old**, please call the Communicable Disease Control Program at 650-573-2346 Monday through Friday between 8:00 am to 5:00 pm or fax a Confidential Morbidity Report (CMR) to 650-573-2919. Non-urgent questions and/or general inquiries may be directed to SMCCDControl@smcgov.org.

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Additional Resources:

1. COVID-19
   - **CDC Health Update: Important Updates on COVID-19 Therapeutics for Treatment and Prevention (12/20/2022)**
   - CDPH Health Advisory: Reminder to Lower Barriers to Prescribing COVID-19 Therapeutics to Mitigate Impact of COVID-19 (12/02/2022)
   - CDPH COVID-19 Therapeutics site: COVID-19 Treatments (ca.gov)
   - **NIH COVID-19 Treatment Guidelines: COVID-19 Treatment Guidelines (nih.gov)**
   - Health and Human Services ASPR COVID-19 Resources: COVID-19 Therapeutics | HHS/ASPR
   - ASPR Therapeutics Algorithm: Therapeutics Decision Aid (PDF)
   - ASPR Provider Information Sheet: Paxlovid Eligibility and Effectiveness (PDF)
2. Influenza
   - **CDPH Health Advisory: Early Respiratory Syncytial Virus and Seasonal Influenza Activity (11/12/2022)**
   - Influenza Vaccination | CDC
   - Influenza Testing | CDC
   - **Influenza Antiviral Medications: Summary for Clinicians | CDC**
   - Influenza and COVID-19 Testing, Treatment and Vaccination | NIH
   - Influenza Vaccine Promotional Materials Resources (eziz.org)
   - Influenza | CDPH (see Surveillance section for the weekly Flu and Respiratory Virus Report)
   - Detecting and Controlling Outbreaks | CDPH
   - Guidance for the Use of Face Masks | CDPH
3. RSV
   - CDPH Health Advisory: Early Respiratory Syncytial Virus and Seasonal Influenza Activity (11/12/2022)
   - RSV (Respiratory Syncytial Virus) | CDC
   - **Updated Guidance: Use of Palivizumab Prophylaxis to Prevent Hospitalization From Severe Respiratory Syncytial Virus Infection During the 2022-2023 RSV Season (aap.org)**
   - CDPH CAHAN: Early RSV Activity October 3, 2022
   - CDC HAN: Increased Respiratory Virus Activity, Especially Among Children, Early in the 2022-2023 Fall and Winter

The Communicable Disease Control Program is available to help meet the reporting needs of, and answer questions for, San Mateo County providers. To report a disease or outbreak, please call 650-573-2346, Monday through Friday, 8:00 am to 5:00 pm, or fax a Confidential Morbidity Report (CMR) to 650-573-2919. You may download an electronic copy of the CMR at smchealth.org/cmr. Web-based reporting via CalREDIE is also available. Please contact us if you would like to know more about, and sign up for, web-based reporting. Non-urgent questions and/or general inquiries may be directed to SMCCDControl@smcgov.org.

Categories of urgency levels:
Health Alert: conveys the highest level of importance; warrants immediate action or attention.
Health Advisory: provides important information for a specific incident or situation; may not require immediate action.
Health Update: provides information regarding an incident or situation; unlikely to require immediate attention.