

Respiratory Pathogen Testing Considerations for Patients Presenting to Children's Hospital Colorado During the 2021-2022 Season

*This algorithm is intended for use in the Emergency Departments, Urgent Cares and inpatient units within the Children's Hospital Colorado system, and serves as an institutional complement to existing recommendations from the Centers for Disease Control, Infectious Diseases Society of America and the American Academy of Pediatrics. This guidance may also be relevant for providers in ambulatory settings. The contents were developed via a multidisciplinary collaboration between the Sections of Emergency Medicine, Epidemiology, Hospital Medicine, Microbiology and Infectious Diseases. These guidelines will apply during the influenza season, but testing for influenza will be available in **October 2021** for patients with compatible illness. The start of the influenza season varies from year to year, and providers in the CHCO system will be notified of the official start of the season by the CHCO Epidemiology/Microbiology Departments.*

Goals for respiratory pathogen testing during the respiratory season

- 1) Provide guidance to promote the judicious use of testing for influenza and SARS-CoV-2 testing at CHCO
- 2) Optimize outcomes through initiation of antiviral medication as early as possible for relevant high-risk groups in accordance with national recommendations
- 3) Minimize unnecessary testing and treatment, and associated side effects, costs, and impact on antimicrobial resistance
- 4) Minimize duplicative testing within our system
- 5) Enhance clinical management for patients and decrease transmission risks to team members
- 6) Support public health efforts to identify patients with SARS-CoV-2 to inform isolation and quarantine measures
- 7) Facilitate clinical and microbiology laboratory workflows

Important Updates to Testing

There will be three types of respiratory tests available for the upcoming respiratory season at the CHCO microbiology lab. All tests are run 24 hours a day, 7 days a week. Sample collection for these tests will be available at all CHCO locations.

SARS-CoV-2 PCR: tests for SARS-CoV-2 ONLY. There will be no expedited SARS-CoV-2 test during the respiratory season. See [COVID-19 policy](#) for more details.

SARS-CoV-2/Influenza/RSV PCR: The combined test for influenza A, influenza B, RSV as well as SARS-CoV-2 is NOT the same as the older influenza (RIDT) or RSV detection test and has higher sensitivity and specificity than rapid antigen/immunoassay tests. Testing platforms will be available at Anschutz, North at South Campus starting from October 2021, which will lead to faster turnaround time.

Respiratory pathogen panel PCR (RPP 2.1): The respiratory pathogen panel (RPP) is an updated version of the panel that includes SARS-CoV-2 and has a total of 22 pathogen targets.

The RPP also tests for adenovirus, coronaviruses HKU1, NL63, 229E and OC43, human metapneumovirus, rhinovirus/enterovirus, influenza A, A/H1-2009, A/H3, B, parainfluenza virus 1, 2, 3, and 4, RSV, *Bordetella pertussis* and *parapertussis*, *Chlamydomphila pneumoniae* and *Mycoplasma pneumoniae*.

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Information regarding cost and turnaround time for each test is shown in Table 1.

We will now accept mid-turbinate swabs for respiratory pathogen testing for all three test types. Information regarding sample types for each platform is outlined in Table 1.

Clinical considerations for testing

- Testing for influenza should be considered in situations when it will impact clinical care (e.g. help with decisions about starting an antiviral, avoid antibiotic use or other diagnostic evaluation) and in general does not need to be ordered for children who are being discharged home without risk factors outlined in Table 2.
- There are no stand-alone influenza tests this season- combined flu/RSV/SARS-CoV-2 and the respiratory pathogen panel will be the only tests available for influenza testing
- Given that the combined flu/RSV/SARS-CoV-2 test has a more rapid turnaround time than the SARS-CoV-2-only test, it will be recommended in situations in which more rapid test results for SARS-CoV-2 are required (e.g. preprocedural testing with high risk for SARS-CoV-2 transmission, admitted patients).
- Influenza and COVID-19 have overlapping signs and symptoms with other respiratory pathogens, and it may not be possible to differentiate them based on clinical features alone, and therefore testing for both (flu/RSV/SARS-CoV-2 testing) will be recommended in certain situations.
- Classic influenza symptoms usually seen with older children include: high fever, dry cough, chills, sweats, myalgia, photophobia, headache, which may be symptoms of SARS-CoV-2.
- Loss of taste or smell with or without respiratory symptoms are more common in children with SARS-CoV-2, but have been reported to occur in children with influenza.
- The pre-test probability for either influenza or SARS-CoV-2 is higher if there is exposure to a confirmed case.

Influenza treatment

Antiviral treatment is effective in reducing severity from influenza and illness duration, and is recommended as soon as possible for any patient with suspected or confirmed influenza who:

1. is hospitalized;
2. has severe, complicated, or progressive illness; or
3. is at higher risk for influenza complications (Table 2)

Note, for these scenarios, treatment is beneficial even if started after 48 hours of illness.

For other scenarios in ambulatory/outpatient settings, it is most effective if started within 48 hours.

First-line treatment for influenza is with a 5-day course of oseltamivir (trade name Tamiflu®). Dosing information is shown in Table 3. Baloxavir (trade name Xofluza™) was approved for use in 2018 in children 12 years and older. In contrast to other influenza medications which are neuraminidase inhibitors, Baloxavir is an endonuclease inhibitor. Baloxavir can be given as a single dose, but is not currently on formulary at CHCO. Inhaled zanamivir (trade name Relenza®) is also approved for use (but is not on formulary at CHCO) and IV peramavir is

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available for those who are unable to take oseltamivir enterally, and is not more efficacious than oseltamivir.

In general, asymptomatic patients who test positive for influenza do not need to be treated. However, there may be certain situations in which this may be considered, for example, immunocompromised patients, based on their reason for admission, level of immunosuppression and risk of developing more severe influenza illness.

SARS-CoV-2 testing

At the present time, testing all symptomatic individuals with compatible illness for SARS-CoV-2 is optimal for isolation practices, contact tracing, quarantine recommendations, and school/daycare considerations. All children admitted to a CHCO facility require SARS-CoV-2 testing. Best practices for the diagnosis of COVID-19 may evolve over time. Updated information regarding our testing platforms, PPE requirements, and other considerations for patients with SARS-CoV-2 is available in our [COVID-19 Policy](#), and [COVID-19 Resource Center](#).

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Respiratory Pathogen Panel (RPP) testing

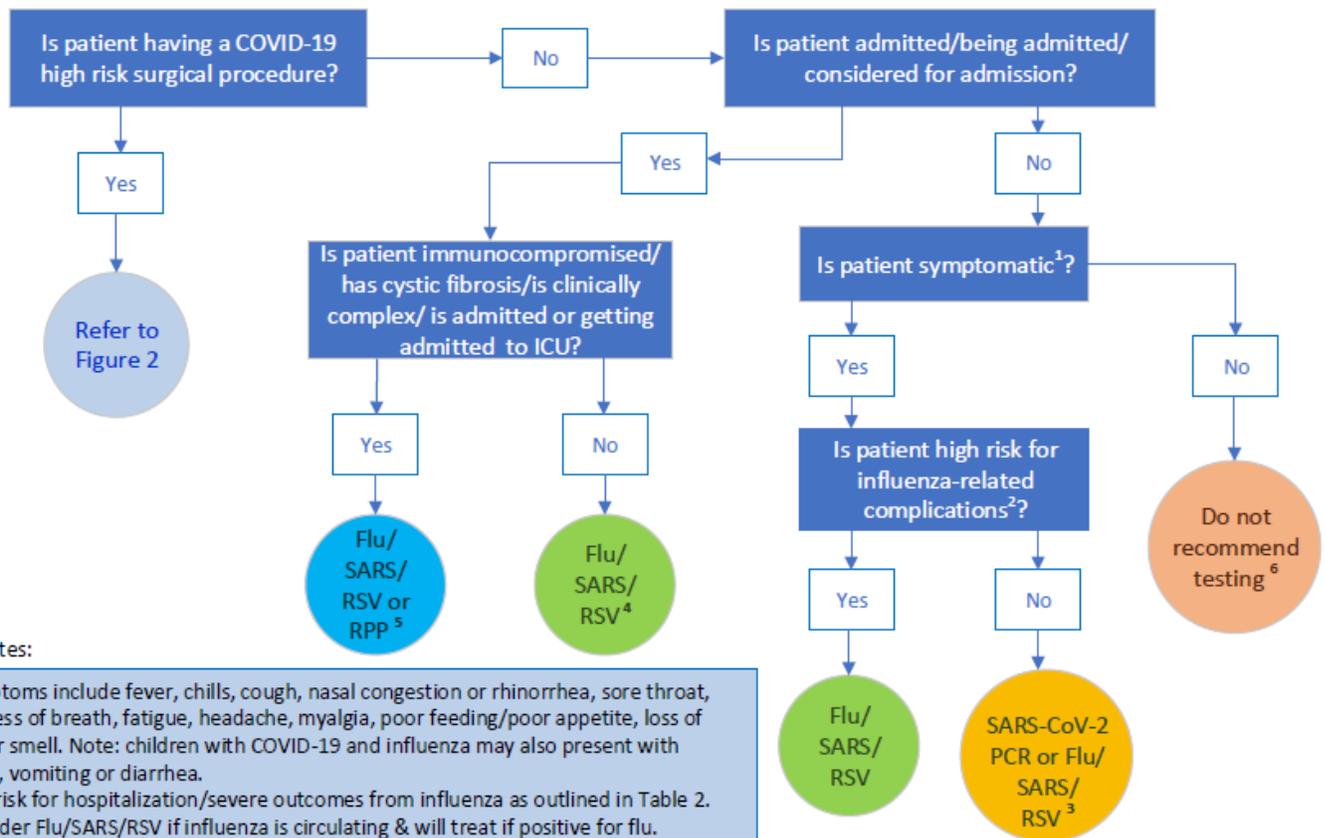
- We generally discourage the routine use of RPP testing for respiratory conditions given that it is an expensive test and may not change clinical outcomes. Respiratory pathogen testing should be reserved for critically-ill patients, immunocompromised patients, or patients admitted with cystic fibrosis exacerbations. Other scenarios in which it may be beneficial include: part of a fever of unknown origin workup, fever in a returning traveler, or scenarios in which it will help avoid other diagnostic evaluations.
- A summary of respiratory test considerations during the influenza season in children with respiratory symptoms is outlined below (Figure 1).

Information regarding drive-thru sample collection

We will offer all three tests for drive-through sample collection—SARS-CoV-2 testing, flu/SARS-CoV-2/RSV testing, and RPP testing—while supplies are available. However, RPP testing should only be limited to the clinical scenarios outlined above. Children who are not considered high risk and who do not have severe illness (ie. outpatients), do not require influenza testing since they will not benefit or only have modest benefits from treatment if within 48 hours of symptom onset.

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Figure 1. Respiratory Pathogen Testing Considerations for Children presenting to Children’s Hospital Colorado during 2021-22 season

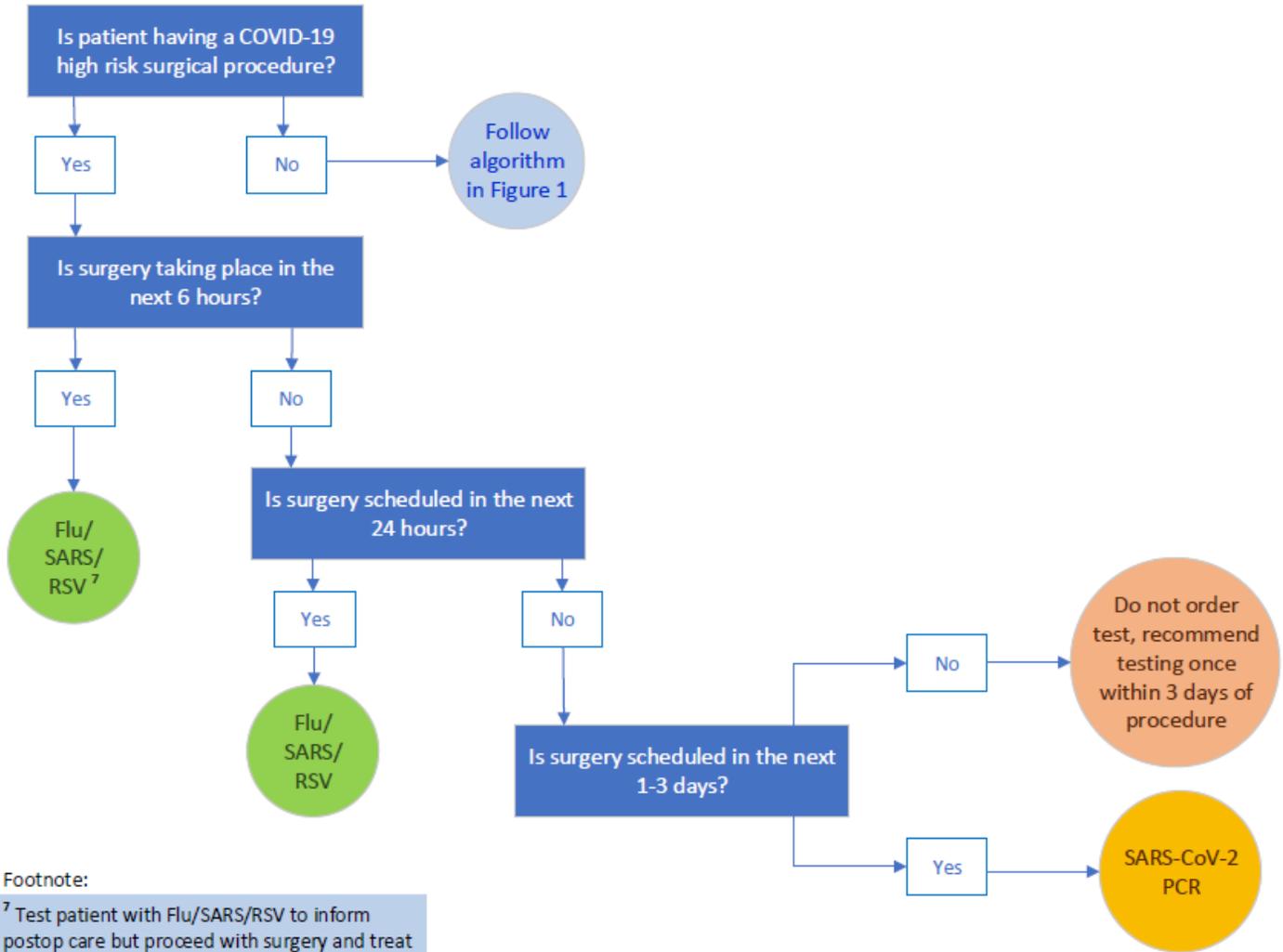


Footnotes:

- ¹ Symptoms include fever, chills, cough, nasal congestion or rhinorrhea, sore throat, shortness of breath, fatigue, headache, myalgia, poor feeding/poor appetite, loss of taste or smell. Note: children with COVID-19 and influenza may also present with nausea, vomiting or diarrhea.
- ² High risk for hospitalization/severe outcomes from influenza as outlined in Table 2.
- ³ Consider Flu/SARS/RSV if influenza is circulating & will treat if positive for flu.
- ⁴ Due to faster turnaround time, combination testing is recommended for admitted patients even if asymptomatic.
- ⁵ Can Consider Respiratory Pathogen Panel (RPP) for Symptomatic Patients who are immunocompromised, have CF or are admitted or getting admitted to the ICU.
- ⁶ Testing asymptomatic individuals may be required in certain situations, such as after exposure to COVID-19 positive cases, school/college requirements, etc. In those situations, SARS-CoV-2 testing is recommended.

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Figure 2. Respiratory Pathogen Testing Considerations for Children undergoing a COVID-19 High Risk Surgical procedure at Children’s Hospital Colorado during 2021-22 season



Footnote:

⁷ Test patient with Flu/SARS/RSV to inform postop care but proceed with surgery and treat patient as PUI as results will not be available prior to surgery.

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Table 1. Respiratory Pathogen testing information

	SARS-CoV-2 PCR	SARS-CoV-2/Flu/RSV PCR	Respiratory pathogen panel
Tests for	SARS-CoV-2	SARS-CoV-2, influenza A, influenza B, RSV	adenovirus, coronaviruses HKU1, NL63, 229E and OC43, human metapneumovirus, rhinovirus/enterovirus, RSV, influenza A, A/H1-2009, A/H3, B, parainfluenza virus 1, 2, 3, and 4, <i>Bordetella pertussis</i> and <i>parapertussis</i> , <i>Chlamydomphila pneumoniae</i> and <i>Mycoplasma pneumoniae</i>
Charge*	\$200	\$270	\$550
Procedure code	LAB 9100	LAB 9373	LAB 5595
Turnaround time for inpatients and ED patients from specimen arrival in the Microbiology Laboratory at Anschutz campus	24 hours	6 hours	6 hours
Other considerations	Expedited testing will no longer be available	Will only report flu A or B, does not provide subtype information	Panel includes SARS-CoV-2
Sample types	NP swabs, mid-turbinate swabs, saliva (for symptomatic children 4-18 years), NP washes, tracheal aspirates, broncho-alveolar lavages	NP swabs, mid-turbinate swabs, NP washes, tracheal aspirates, broncho-alveolar lavages	NP swabs, mid-turbinate swabs, NP washes, tracheal aspirates, broncho-alveolar lavages
*Pricing effective August 15, 2021. Please note that under federal mandate patients will NOT be billed for SARS-CoV-2 testing. However, depending on insurance coverage patients may still be billed for testing for other respiratory pathogens, including influenza.			

Table 2. Risk factors associated with complications or more severe disease from influenza

- Children aged <2 years
- Individuals <19 years receiving long-term aspirin
- Adults aged >65 years
- Persons of all ages with chronic pulmonary (including asthma), cardiovascular, renal, hepatic, metabolic (including diabetes) hematologic, neurologic and neurodevelopment conditions (including seizure disorders, developmental delay, muscular dystrophy, or spinal cord injury)
- Persons with immunosuppression
- Pregnant or recently post-partum women
- American Indians/Alaska Natives
- Persons who are morbidly obese (BMI >40)

Recommendations for the care of Patients with SARS-CoV-2 infection

The care of patients with SARS-CoV-2 including testing and treatment considerations is available on the [COVID-19 Resource Center](#).

Recommendations for ED Care of Patients in whom Influenza is High on Differential Diagnosis

Consider Influenza testing and treatment for the following patients:

Presentation consistent with influenza (e.g. high fever, cough, myalgias, fatigue) **AND** either one of the following:

1. Severe illness (hospitalized or requiring oxygen)
2. Risk factors outlined in Table 2

Any symptomatic patient requiring hospitalization from ED /Urgent care or patients being observed for home oxygen during influenza season:

Testing and treatment:

Scenario 1. Influenza/RSV/ SARS-CoV-2 PCR; one-time dose of oseltamivir given in ED; consider one-time dose of oseltamivir given in ED for high-risk or severely ill patients

Scenario 2. Respiratory pathogen panel if admitted to ICU, or for a CCBD patient or patient with a Cystic fibrosis exacerbation; one-time dose of oseltamivir given in ED for high-risk or severely ill patients

Follow up: Communicate with admitting team to continue or start oseltamivir course if patient is admitted and positive. Prescribe 5-day course of oseltamivir for those being discharged on oxygen with positive influenza results. Culture call back team will follow up on positive influenza results and SARS-CoV-2 results if patient is discharged before results are available. See culture call back process below for details.

Any patient with risk factors for more severe outcomes (see Table 2) who is being discharged home from the ED/Urgent care:

Testing and Treatment:

Send SARS-CoV-2/Flu/RSV PCR test and consider one-time dose of oseltamivir given in ED. Document in EHR that patient will require antiviral therapy if influenza test is positive.

Follow up: Culture call back team will follow up on positive influenza results and SARS-CoV-2 results if patient is discharged before results are available. See culture call back process below for details.

STANDARD RISK Patient who will be discharged home and presents within 48 hours of illness onset, and provider deems that results would influence clinical decision making

Treating with oseltamivir in this situation is not mandatory and can occur at the discretion of the treating provider. Consider treatment if clinically worsening.

Testing and Treatment Options:

Scenario 1. SARS-CoV-2 PCR (preferred)

*Scenario 2. **Consider** test for SARS-CoV-2/Flu/RSV PCR only if you will treat for influenza if test is positive. Provide family with prescription and instructions to fill if they receive a call that influenza test is positive. Document in EHR that patient will require treatment (oseltamivir or baloxavir) if influenza test is positive. Note that CDC and FDA recommend that for standard risk patient, treatment should be started within 48 hours of symptoms onset as clinical benefit is greatest when antiviral treatment is started as close to illness onset as possible.*

The Culture Call Back Team will be responsible for calling results of testing for the following scenarios:

SARS-CoV-2:

- Negative - No call
- Positive - Call and route to PCP

Influenza A/B:

- Negative - No call
- Positive - Call and instruct family to fill prescription (or prescribe if not already given). If there are family members with risk factors (see Table 2), provide information that these family members need to be followed up by their PCP (treatment and prophylaxis of family members is not part of CCB procedure)

RSV:

- Negative - No call
- Positive - No call and forward results to PCP given there is likely to be a follow up appointment.

Respiratory pathogen Panel:

Call if positive for any of the following pathogens: SARS-CoV-2, influenza A, influenza B, *Bordetella pertussis* or *parapertussis*, *Chlamydomphila pneumoniae*, or *Mycoplasma pneumoniae*

Recommendations for Ambulatory/Outpatient Office Care of Patients in whom Influenza is High on Differential Diagnosis

Testing and Treatment:

Scenario 1: no risk factors as outlined in Table 2: SARS-CoV-2 PCR

Scenario 2: a) risk factors present, or
b) worsening/progressive illness, or
c) within 48 hours of illness onset and considering treatment

Send test for SARS-CoV-2 PCR and influenza test (can send to mobile collection site for combined SARS-CoV-2/RSV/influenza testing and prescribe oseltamivir or baloxavir if test is positive for influenza).

Note: Influenza antigen testing is more reliable if sensitivity and specificity are > 80% and is during time of high influenza prevalence in the community. Children's Hospital Colorado does not offer antigen testing, and we do not recommend rapid SARS-CoV-2 antigen testing at this time given lower sensitivity and specificity.

Note: CDC and FDA recommend that for standard risk patients, treatment should be started within 48 hours of symptom onset as clinical benefit is greatest when antiviral treatment is started as close to illness onset as possible.

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Table 3: Medications for the treatment of Influenza

Drug	Dose (Treatment)	Duration (Treatment)	FDA Approval Age	Price*	Monitoring	Side effects and Considerations
Oseltamivir (oral) Only influenza medication on CHCO formulary	14 days – 3 months: 3 mg/kg/dose twice a day 3-12 months: 3 mg/kg/dose twice a day Children 1-12 years of age and weighing: ≤ 15 kg: 30 mg/dose twice a day > 15-23 kg: 45 mg/dose twice a day >23-40 kg: 60 mg/dose twice a day >40 kg: 75 mg/dose twice a day Children > 13 years of age and adults: 75 mg/dose twice a day Prophylaxis dosing – same dose as treatment except given once daily***	5 days	Treatment: 14 days and older Prophylaxis: 1 year and older	Capsule: \$154 Suspension: \$326	Renal function (Scr, BUN, urine output) Glucose in those with DM Behavioral changes	GI upset Insomnia Behavioral changes Requires renal dose adjustment
Zanamivir (inhaled)	Two inhalations (10 mg) twice daily	5 days	Treatment: 7 years and older Prophylaxis: 5 years and older	\$71	Behavioral changes	Headache, Sore throat Behavioral changes Not recommended in patients with underlying airway disease due to risk of bronchospasm. Contraindicated in those with milk-protein allergy
Peramivir (IV)	Children 2-12 years: 12 mg/kg once daily 13 years and older: 600 mg once daily	5-10 days (consult ID)	Treatment: 2 years and older	\$5500	Renal function (Scr, BUN, urine output) Behavioral changes Hypersensitivity reactions	Diarrhea Skin hypersensitivity reactions Behavioral changes Available as an intravenous infusion only Requires renal dose adjustment
Baloxavir (oral)	Children 12 years of age and older weighing 40 to < 80 kg: 40 mg as a single dose >80 kg: 80 mg as a single dose	1 day	Treatment: 12 years and older	\$90	Hypersensitivity reactions	Diarrhea Avoid administration with dairy, calcium fortified drinks or polyvalent cations

*Average Wholesale Price based a treatment course for a 40 kg child (exact pricing will vary depending on pharmacy)

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** Oral oseltamivir is approved by the FDA for treatment of acute uncomplicated influenza within 2 days of illness onset in people 14 days and older, and for chemoprophylaxis in people 1 year and older. Although not part of the FDA-approved indications, use of oral oseltamivir for treatment of influenza in infants less than 14 days old, and for chemoprophylaxis in infants 3 months to 1 year, is recommended by the CDC and the American Academy of Pediatrics at a dose of 3 mg/kg/dose twice daily.

***We do not recommend widespread or routine use of antivirals for chemoprophylaxis. Chemoprophylaxis is not recommended if more than 48 hours have elapsed since the last exposure to an infected person. Persons receiving chemoprophylaxis should be encouraged to seek medical attention as soon as they develop a febrile respiratory illness that might indicate influenza. For effective prophylaxis, an antiviral medication must be taken each day for the duration of potential exposure to a person with influenza, and continued for 7 days after the last known exposure.

References:

1. CDC website <https://www.cdc.gov/flu/professionals/diagnosis/index.htm>
2. Hanson et al. Molecular testing for acute respiratory tract infections: clinical and diagnostic recommendations from the IDSA's Diagnostics Committee; Clin Infect Dis. 2020 May
3. AAP, Committee on Infectious Diseases. Recommendations for Prevention and Control of Influenza in Children, 2020–2021 Pediatrics October 2020, 146 (4) e2020024588.