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The Medical Letter®

on Drugs and Therapeutics

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▶ Antiviral Drugs for Seasonal Influenza

Influenza is typically a self-limited illness, but complications including pneumonia, respiratory failure, and death can occur, especially in persons at increased risk (see Table 1). Influenza vaccination reduces the incidence of laboratory-confirmed influenza and the risk of complications associated with influenza illness. Annual vaccination should be offered to all persons ≥ 6 months old as long as influenza viruses are circulating in the community.¹

TREATMENT OF INFLUENZA – Antiviral treatment is recommended as soon as possible for any patient with suspected or confirmed influenza who is hospitalized, has severe, complicated, or progressive illness, or is at increased risk for complications (see Table 1), even if it is started >48 hours after illness onset.²⁻⁴ Such patients should receive antiviral treatment even if they test negative, especially when influenza viruses are known to be circulating in the community; false-negative results can occur with influenza tests, especially with rapid antigen tests and immunofluorescence assays.⁵

Guidelines for treatment of community-acquired pneumonia (CAP) recommend use of antiviral drugs in patients with CAP and confirmed influenza who are hospitalized, have severe or progressive illness, or are at an increased risk of complications, regardless of the time from illness onset.⁶

Table 1: Persons at Increased Risk for Influenza Complications¹

- ▶ Children <5 years old (especially <2 years old)
- ▶ Patients <19 years old receiving long-term treatment with aspirin or salicylate-containing drugs
- ▶ Adults ≥ 65 years old
- ▶ Persons with obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$)
- ▶ Women who are pregnant or ≤ 2 weeks postpartum
- ▶ Non-Hispanic Black persons, Hispanic/Latino persons, and persons of American Indian or Alaska Native heritage
- ▶ Residents of nursing homes or other long-term care facilities
- ▶ Patients who are immunosuppressed
- ▶ Patients with a chronic medical condition²

1. CDC. People at increased risk for flu complications. September 11, 2024. Available at: <https://bit.ly/3lxqzft>. Accessed October 22, 2026.

2. Including asthma, neurologic and neurodevelopmental conditions, stroke, chronic lung disease, heart or kidney disease, blood, endocrine, liver, or metabolic disorders, and certain disabilities (especially those affecting muscle or lung function or causing difficulty coughing, swallowing, or clearing fluids from airways).

Key Points: Antiviral Drugs for Seasonal Influenza

- ▶ Antiviral treatment is most effective when started ≤ 48 hours after illness onset.
- ▶ Antiviral treatment is recommended as soon as possible for patients with suspected or confirmed influenza who are hospitalized, have severe, complicated, or progressive illness, or are at increased risk for complications, even if it is started >48 hours after illness onset.
- ▶ Antiviral treatment can be considered for otherwise healthy symptomatic outpatients with suspected or confirmed influenza who are not at increased risk for complications if it can be started ≤ 48 hours after illness onset.
- ▶ Oseltamivir is preferred for treatment of children, pregnant women, hospitalized patients, and outpatients with severe, complicated, or progressive illness.
- ▶ Postexposure prophylaxis with oseltamivir, zanamivir, or baloxavir should be considered within 48 hours of exposure for persons at high risk of complications who have not received an annual influenza vaccine or when influenza vaccination may be ineffective; it is not recommended for healthy persons exposed to influenza.
- ▶ Postexposure prophylaxis with oseltamivir or zanamivir is recommended to control influenza outbreaks in institutional settings.

Antiviral treatment can be considered for otherwise healthy symptomatic outpatients with suspected or confirmed influenza who are not at increased risk for complications if it can be started ≤ 48 hours after illness onset.

Three neuraminidase inhibitors (oral oseltamivir, IV peramivir, and inhaled zanamivir) and the oral cap-dependent endonuclease inhibitor baloxavir marboxil are recommended for treatment of influenza in the US this season (see Table 2).² Oseltamivir is preferred for treatment of influenza in pregnant women, children, hospitalized patients, and outpatients with severe, complicated, or progressive illness.²⁻⁴

Effectiveness – Neuraminidase inhibitors and baloxavir are active against influenza A and B viruses. In adults and children with acute uncomplicated influenza, they shorten the duration of symptoms by about one day.⁵⁻

¹¹ Randomized trials directly comparing these drugs for **treatment** of influenza are lacking, but they appear to be similar in efficacy based on available data from observational studies.^{9,10,12,13} Although most controlled trials of antiviral drugs have not been powered to assess their efficacy in preventing serious influenza complications,

Table 2. Antiviral Drugs for Seasonal Influenza for 2026-2027

Drug/Formulations	Usual Dosage	Comments	Cost ¹
Neuraminidase Inhibitors			
Osetamivir – generic <i>Tamiflu</i> (Genentech) 30, 45, 75 mg caps; 6 mg/mL oral suspension ²	Treatment: <1 yr: 3 mg/kg PO bid ³ x 5 days ^{4,5} 1-12 yrs: 30-75 mg ⁶ PO bid x 5 days ^{4,5} ≥13 yrs: 75 mg PO bid x 5 days ^{4,5} Chemoprophylaxis: 3 months-<1 yr: 3 mg/kg PO once/day ⁷ x 7 days ⁸ 1-12 yrs: 30-75 mg ⁶ PO once/day x 7 days ⁸ ≥13 yrs: 75 mg PO once/day x 7 days ⁸	▶ FDA-approved for treatment of acute uncomplicated influenza in patients ≥2 weeks old who have been symptomatic for ≤48 hours ▶ FDA-approved for chemoprophylaxis of influenza in patients ≥1 year old ▶ Preferred for treatment of influenza in pregnant women, children, hospitalized patients, and outpatients with severe, complicated, or progressive illness	\$48.00 152.00
Peramivir – <i>Rapivab</i> (BioCryst) 200 mg/20 mL vials	Treatment: 6 months-12 yrs: 12 mg/kg (max 600 mg) IV over 15-30 minutes once ⁹ ≥13 yrs: 600 mg IV over 15-30 minutes once ⁹	▶ FDA-approved for treatment of acute uncomplicated influenza in patients ≥6 months old who have been symptomatic for ≤48 hours ▶ Not recommended for treatment of severe influenza¹⁰	950.00
Zanamivir – <i>Relenza</i> (GSK) 5 mg blisters of powder for inhalation	Treatment: ≥7 yrs: 2 inhalations bid x 5 days Chemoprophylaxis: ≥5 yrs: 2 inhalations once/day x 7 days ⁸	▶ FDA-approved for treatment of acute uncomplicated influenza in patients ≥7 years old who have been symptomatic for ≤48 hours ▶ FDA-approved for chemoprophylaxis of influenza in patients ≥5 years old	59.00
Cap-Dependent Endonuclease Inhibitor			
Baloxavir marboxil – <i>Xofluza</i> (Genentech) 40, 80 mg tabs	Treatment: ≥5 yrs and 20-<80 kg: 40 mg PO once ≥5 yrs and ≥80 kg: 80 mg PO once Chemoprophylaxis: ≥5 yrs and 20-<80 kg: 40 mg PO once ≥5 yrs and ≥80 kg: 80 mg PO once	▶ FDA-approved for treatment of acute uncomplicated influenza in patients ≥5 years old who are otherwise healthy or at high risk of developing influenza-related complications and have been symptomatic for ≤48 hours ▶ FDA-approved for postexposure prophylaxis in patients ≥5 years old ▶ Not recommended for use in pregnant women, severely immunocompromised patients, or patients who are hospitalized or have complicated or progressive illness	169.00 ¹¹
1. Approximate WAC for a single treatment course at the usual adult dosage and duration (single dose of baloxavir marboxil or peramivir or 5 days with osetamivir capsules or zanamivir). WAC = wholesaler acquisition cost, or manufacturer's published price to wholesalers; WAC represents published catalogue or list prices and may not represent an actual transactional price. Source: AnalySource® Monthly. October 5, 2026. Reprinted with permission by First Databank, Inc. All rights reserved. ©2026. www.fdbhealth.com/policies/drug-pricing-policy. 2. Contents of capsules can be mixed in a thick sweetened beverage (to mask the bitter taste) and consumed immediately. Osetamivir can be administered by oro/nasogastric tube. 3. The American Academy of Pediatrics has recommended a dose of 3.5 mg/kg for infants 9-11 months old based on the results of a study showing that a higher dose was needed to achieve the target exposure in this age group (DW Kimberlin et al. J Infect Dis 2013; 207:709). For treatment of premature infants, refer to CDC recommendations (www.cdc.gov/flu). 4. In hospitalized, critically ill, or immunocompromised patients, a longer treatment course (e.g., 10 days) is often used. 5. Osetamivir renal dosage adjustment for adults and children who weigh >40 kg (recommended by the CDC): CrCl 31-60 mL/min: 30 mg bid for treatment and 30 mg once/day for prophylaxis; CrCl 11-30 mL/min: 30 mg once/day for treatment and 30 mg every other day for prophylaxis; hemodialysis (HD): 30 mg x1 then 30 mg after every HD for duration of treatment (<5 days) and 30 mg after every other HD for prophylaxis; continuous ambulatory peritoneal dialysis (CAPD): 30 mg x1 immediately for treatment and 30 mg once/week after exchange for prophylaxis; end-stage renal disease (ESRD) not on HD: not recommended for treatment or prophylaxis. 6. FDA-approved doses for children 1-12 years old who weigh ≤15 kg: 30 mg; >15-23 kg: 45 mg; >23-40 kg: 60 mg; >40 kg: 75 mg. 7. Although not FDA-approved for chemoprophylaxis in children <1 year old, the American Academy of Pediatrics and the CDC recommend that children 3 months-<1 year old receive 3 mg/kg once/day. Chemoprophylaxis is generally not recommended for premature infants or infants <3 months old (refer to CDC recommendations at: www.cdc.gov/flu). 8. Duration of chemoprophylaxis recommended by the CDC is 7 days after the last known exposure. The recommended duration in the labeling of osetamivir and zanamivir is 10 days after the last known exposure. For control of outbreaks in institutional settings, the CDC recommends that chemoprophylaxis be given for at least 2 weeks and continued for up to 1 week after the end of the outbreak. Some experts would use twice-daily therapeutic doses for postexposure prophylaxis in highly immunocompromised patients. 9. Peramivir renal dosage adjustment for patients 2-12 years old: CrCl 30-49 mL/min: 4 mg/kg once; CrCl 10-29 mL/min: 2 mg/kg once. For patients ≥13 years old: CrCl 30-49 mL/min: 200 mg once; CrCl 10-29 mL/min: 100 mg once; hemodialysis (HD): administer dose (based on CrCl) after HD. 10. IV peramivir (for at least 5 days) may be considered for hospitalized, critically ill, or immunocompromised patients who cannot tolerate or absorb oral or enterically administered osetamivir because of gastric stasis, malabsorption, or GI bleeding. 11. Available for \$50 at select pharmacies through the manufacturer's direct-to-patient program.			

experts have generally concluded from the combined results of observational studies, controlled trials, and meta-analyses that early antiviral **treatment** of influenza in high-risk and hospitalized patients can reduce the risk of complications.^{7,9-12,14-19} In a randomized trial (available as a preprint, but not yet peer-reviewed) in critically-ill patients with severe influenza illness, use of oseltamivir was associated with a higher rate of mortality at 90 days compared to no antiviral treatment²⁰; formal peer review of the manuscript is needed.

Prompt treatment of an index patient with baloxavir can reduce the risk of influenza **transmission** to household contacts.²¹

Timing – Neuraminidase inhibitors are most effective when started ≤ 48 hours after illness onset, but the results of some observational studies in hospitalized and critically ill patients suggest that treatment started as late as 4-5 days after illness onset can shorten the duration of hospitalization and reduce the risk of pneumonia, respiratory failure, and death.²²⁻²⁴ No data are available on the efficacy of baloxavir when started >48 hours after illness onset.

In a retrospective cohort study of 26,233 hospitalized adults with laboratory-confirmed influenza and pneumonia, delayed initiation of antiviral treatment was associated with a higher risk of death; compared to patients who started antiviral treatment on day 0, the adjusted odds ratio for death was 1.14 (95% CI 1.01-1.27) in those who started treatment on day 1 and 1.40 (95% CI 1.17-1.66) in those who started on days 2-5.²⁵

In an observational study in 840 hospitalized adults with influenza, the risk of disease progression, ICU admission, and in-hospital death was lower with early use of oseltamivir than with no use or late use of the drug.²⁶

POSTEXPOSURE PROPHYLAXIS – Postexposure antiviral prophylaxis can be considered for persons who are at very high risk of developing influenza complications and have not or cannot receive an influenza vaccine for the current season or who are expected to have an inadequate response to vaccination. It may be considered for unvaccinated persons who are household contacts of persons at very high risk of influenza complications. Postexposure antiviral prophylaxis is not recommended for healthy persons exposed to influenza or when >48 hours have elapsed since exposure.²³

Antiviral prophylaxis with oral oseltamivir or inhaled zanamivir is recommended by the CDC for control of influenza outbreaks in institutional settings.²

Effectiveness – Postexposure prophylaxis of household contacts with oseltamivir, zanamivir, or baloxavir has reduced the risk of symptomatic influenza illness by about 70-90%, compared to placebo.^{2,27}

Timing – Antiviral prophylaxis with oseltamivir, zanamivir, or baloxavir should be started no later than 48 hours after exposure. Oseltamivir and zanamivir should be taken for 7 days after the last known exposure. Baloxavir is taken as a single dose.

The CDC recommends postexposure prophylaxis with oral oseltamivir or inhaled zanamivir for at least 2 weeks for institutional influenza outbreaks; it should be continued for up to 1 week after the end of the outbreak.

PREGNANCY AND LACTATION – Pregnant and postpartum women are at increased risk for complications of influenza. Empiric antiviral **treatment** should be started as soon as possible in those with suspected or confirmed influenza. Oseltamivir is preferred for women who are pregnant, postpartum (≤ 2 weeks), or breastfeeding. Zanamivir and peramivir are alternatives. Baloxavir is not recommended for use in pregnant or breastfeeding women because of a lack of data.²⁸⁻³²

Antiviral **postexposure prophylaxis** can be considered for pregnant women and those who are ≤ 2 weeks postpartum who cannot receive an influenza vaccine or are unlikely to respond to influenza vaccination. Oseltamivir is preferred.^{30,31}

RESISTANCE – Over 99% of recently circulating influenza virus strains tested by the World Health Organization have been susceptible to neuraminidase inhibitors and baloxavir.³³ Reduced susceptibility of some influenza virus strains, particularly influenza A(H1N1) viruses, to oseltamivir or peramivir can emerge during or after treatment, especially in young children and immunocompromised patients with prolonged viral shedding.³⁴⁻³⁹ Resistant isolates have usually remained susceptible to zanamivir, but reduced susceptibility to the drug has been reported.⁴⁰ In immunocompromised patients, a double dose of oseltamivir reduced the incidence of oseltamivir resistance compared to standard dosing, but it did not improve efficacy and caused more adverse effects.⁴¹

Amino acid substitutions associated with reduced susceptibility to baloxavir have occurred following treatment with a single dose of the drug.^{8,21,42} Reduced susceptibility to baloxavir appears to be more frequent in persons infected with influenza A(H3N2) or A(H1N1)pdm09 viruses, particularly children.^{33,43,44} Baloxavir monotherapy is not recommended for use in severely immunocompromised

patients because of concerns that prolonged viral replication in such patients could lead to emergence of resistance.² Oseltamivir and peramivir may be active against influenza virus strains with reduced susceptibility to baloxavir.⁴⁵ Baloxavir is active against neuraminidase inhibitor-resistant strains of influenza A and B viruses, including A(H1N1), A(H5N1), A(H3N2), and A(H7N9).

ADVERSE EFFECTS — Nausea, vomiting, and headache are the most common adverse effects of **oseltamivir**; taking the drug with food may minimize GI adverse effects. Oseltamivir has been associated with bradycardia in critically ill patients.⁴⁶ Headache, diarrhea, nausea, vomiting, bronchitis, cough, sinusitis, and ear, nose, and throat infections have been reported with **zanamivir**. Inhalation of zanamivir can cause bronchospasm; the drug should not be used in patients with underlying airway disease. Diarrhea, vomiting, and neutropenia have occurred with **peramivir**.⁴⁷ **Baloxavir** appears to cause less nausea and vomiting than oseltamivir.⁴⁸

Neuropsychiatric events, including self-injury and delirium, have been reported in patients taking **neuraminidase inhibitors** or **baloxavir**, but a causal relationship has not been established, and neuropsychiatric dysfunction can be a complication of influenza itself. In a retrospective cohort study of children 5-17 years old enrolled in Tennessee Medicaid during the 2016-2017 and 2019-2020 influenza seasons, oseltamivir use was associated with lower rates of neuropsychiatric events than untreated influenza (34.8% vs 59.9%; adjusted risk ratio 0.53, 95% CI 0.33-0.88).⁴⁹

Hypersensitivity reactions, including anaphylaxis, have been reported with all of these drugs.

DRUG INTERACTIONS — Coadministration of dairy products, beverages, antacids, laxatives, multivitamins, or other products containing polyvalent cations (e.g., calcium, aluminum, iron, magnesium, selenium, zinc) can reduce serum concentrations of **baloxavir** and should be avoided.

USE WITH THE LIVE-ATTENUATED VACCINE — Use of oseltamivir or zanamivir within 48 hours before, peramivir within 5 days before, or baloxavir within 17 days before administration of the live-attenuated intranasal influenza vaccine (*FluMist*, *FluMist Home*) could inhibit replication of the vaccine virus, reducing the vaccine's effectiveness, and is not recommended.¹ Persons who receive any of these antiviral drugs during these specified times or within 2 weeks after receiving the live-attenuated vaccine should be revaccinated with an injectable influenza vaccine.^{50,51} ■

Additional Content Available Online

Comparison Chart: Antiviral Drugs for Seasonal Influenza
<https://medicalletter.org/TML-article-1767c>

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