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Antiviral Drugs for Seasonal Influenza for 2025-2026

Influenza is generally a self-limited illness, but complications including pneumonia, respiratory failure, and death can occur, especially in persons at increased risk (see Table 1).

TREATMENT OF INFLUENZA — Three neuraminidase inhibitors (oral oseltamivir, IV peramivir, and inhaled zanamivir) and the oral cap-dependent endonuclease inhibitor baloxavir marboxil are available in the US and are recommended for treatment of influenza this season (see Table 2).[1]

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.[1-3] False-negative results can occur with influenza tests, especially with rapid antigen tests; patients with suspected influenza in the aforementioned groups should receive antiviral treatment even if they test negative, especially when influenza viruses are known to be circulating in the community.[4]

Table 1: Persons at Increased Risk for Influenza Complications[1]

- 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 (BMI ≥40 kg/m^2)
- Women who are pregnant or ≤2 weeks postpartum
- Non-Hispanic Black persons, Hispanic or Latino persons, or 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 condition[2]

1. CDC. People at increased risk for flu complications. September 11, 2024. Availabale at: https://bit.ly/3lxqzft. Accessed October 8, 2025.
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 for 2025-2026

- Influenza antiviral drugs recommended for use this season include three neuraminidase inhibitors (oral oseltamivir, IV peramivir, and inhaled zanamivir) and the oral cap-dependent endonuclease inhibitor baloxavir marboxil. They are all active against influenza A and B viruses.
- Antiviral treatment is most effective when started within 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 more than 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 influenza complications if it can be started within 48 hours after illness onset.
- Oseltamivir is preferred for treatment of children, pregnant women, hospitalized patients, and outpatients with severe, complicated, or progressive illness.
- Post-exposure 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.
- Post-exposure 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 influenza complications if it can be started within 48 hours after illness onset.

Oseltamivir is preferred for treatment of influenza in pregnant women, children, hospitalized patients, and outpatients with severe, complicated, or progressive illness.[1,3]

Guidelines for treatment of community-acquired pneumonia (CAP) recommend antiviral treatment for patients with CAP who test positive for influenza regardless of the duration of illness before diagnosis.[5]

Effectiveness – Neuraminidase inhibitors and baloxavir are active against influenza A and B viruses.

In adults with acute uncomplicated influenza, they shorten the duration of symptoms by about one day.[6-8] Although most controlled trials of antiviral drugs have not been powered to assess their efficacy in preventing serious influenza complications, 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.[6,9-11]

Outpatients **–** In a randomized, double-blind trial (CAPSTONE-2) in 2184 high-risk outpatients ≥12 years old with uncomplicated influenza, the median time to symptom improvement was similar with a single dose of baloxavir or 5 days' treatment with oseltamivir (both started within 48 hours after illness onset) in the overall population and in those infected with influenza A(H3N2) virus, but was statistically significantly shorter with baloxavir in those infected with influenza B virus (74.6 vs 101.6 hours). Use of either drug was associated with a lower incidence of influenza-related complications and fewer antibiotic prescriptions compared to placebo.[8]

A meta-analysis of 73 randomized trials in patients with nonsevere influenza found that symptom duration was reduced by a mean of 1.02 days with baloxavir and 0.75 days with oseltamivir compared to placebo or standard care; baloxavir (but not oseltamivir) was associated with a possible reduction in the risk of hospitalization in high-risk patients.[12]

In a randomized, double-blind trial (miniSTONE-2) in 173 otherwise healthy children 1-11 years old with influenza, the median time to symptom improvement was similar with a single dose of baloxavir or 5 days' treatment with oseltamivir (138 vs 150 hours; both started within 48 hours after illness onset).[13]

A meta-analysis of five randomized trials in children with influenza found that starting oseltamivir within 48 hours after illness onset reduced illness duration by about 18 hours (by about 30 hours when trials that enrolled children with asthma were excluded) and decreased the risk of otitis media.[14]

Hospitalized Patients **–** In a retrospective cohort study in 11,073 adults hospitalized for influenza (mean age 73 years), oseltamivir treatment was associated with a lower risk of in-hospital death compared to supportive care (adjusted risk difference -1.8%, 95% CI -2.8 to -0.9%).[15]

In a meta-analysis of six randomized controlled trials in hospitalized patients with severe influenza (mean age 36-60 years), treatment with oseltamivir or peramivir was associated with small reductions in the duration of hospitalization compared to placebo or standard care (-1.63 days with oseltamivir and -1.73 days with peramivir).[16]

In an observational cohort study in hospitalized children (with underlying conditions or admitted to the ICU) with laboratory-confirmed influenza, the duration of hospitalization was shorter with antiviral treatment started within 48 hours after illness onset than with no antiviral treatment.[17]

In a retrospective cohort study in 542 adults hospitalized with laboratory-confirmed influenza, time to defervescence, durations of hospital and ICU stay, and mortality rates were similar with oral oseltamivir and IV peramivir.[18]

In a randomized, double-blind trial (FLAGSTONE) in 366 patients ≥12 years old hospitalized with severe influenza requiring ventilation or supplemental oxygen or with an influenza-related complication, the combination of a neuraminidase inhibitor (primarily oseltamivir) and baloxavir did not significantly improve median time to clinical improvement compared to a neuraminidase inhibitor alone (97.5 vs 100.2 hours).[19]

Timing – Neuraminidase inhibitors are most effective when started within 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.[20-22]

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.[23]

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 compared to late use or no use of the drug.[24]

Table 2. Antiviral Drugs for Seasonal Influenza

Drug/Formulations	Usual Dosage	Comments	Cost[1]
Cap-Dependent Endonuclease Inhibitor			
Baloxavir marboxil – *Xofluza* (Genentech) 40, 80 mg tabs	**Treatment:** ≥5 yrs and 20-<80 kg: 40 mg PO x 1 dose ≥5 yrs and ≥80 kg: 80 mg PO x 1 dose **Chemoprophylaxis:** ≥5 yrs and 20-<80 kg: 40 mg PO x 1 dose ≥5 yrs and ≥80 kg: 80 mg PO x 1 dose	▸ 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 post-exposure prophylaxis in patients ≥5 years old ▸ No data in patients with severe influenza ▸ Not recommended for use in severely immunocompromised patients or pregnant women ▸ Avoid coadministration of dairy products, calcium-fortified beverages, and products containing polyvalent cations	$169.00[11]
Neuraminidase Inhibitors			
Oseltamivir – generic *Tamiflu* (Genentech) 30, 45, 75 mg caps; 6 mg/mL oral suspension[2]	**Treatment:** ≥2 wks-<1 yr: 3 mg/kg PO bid[3] x 5 days[4] 1-12 yrs: 30-75 mg[5] PO bid x 5 days[4] ≥13 yrs: 75 mg PO bid x 5 days[4] Renal impairment: See footnote 6 **Chemoprophylaxis:** 3 months-<1 yr: 3 mg/kg PO once/day[7] x 7 days[8] 1-12 yrs: 30-75 mg[5] PO once/day x 7 days[8] ≥13 yrs: 75 mg PO once/day x 7 days[8] Renal impairment: See footnote 6	▸ 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 ▸ Taking oseltamivir with food may improve tolerability ▸ Contents of capsules can be mixed in a thick sweetened liquid to mask the bitter taste	46.40 152.00
Peramivir – *Rapivab* (BioCryst) 200 mg/20 mL single-use vials	**Treatment:** 6 months-12 yrs: 12 mg/kg (max 600 mg) IV over 15-30 minutes once ≥13 yrs: 600 mg IV over 15-30 minutes once Renal impairment: See footnote 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 influenza[10] ▸ Not FDA-approved for chemoprophylaxis	950.00
Zanamivir – *Relenza* (GSK) 5 mg blisters of powder for inhalation	**Treatment:** ≥7 yrs: 2 inh bid x 5 days **Chemoprophylaxis:** ≥5 yrs: 2 inh 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 ▸ Contraindicated for use in patients with lactose or milk protein allergy ▸ Not recommended for use in patients with underlying airway disease ▸ Insufficient data in patients with severe influenza	59.00

1. Approximate WAC for a single treatment course at the usual adult dosage and duration (single dose of peramivir or baloxavir marboxil or 5 days with oseltamivir 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, 2025. Reprinted with permission by First Databank, Inc. All rights reserved. ©2025. www.fdbhealth.com/policies/drug-pricing-policy.
2. Oseltamivir can be administered by oro/nasogastric tube.
3. Although not FDA-approved for use in children <2 weeks old, the CDC recommends that children <2 weeks old receive 3 mg/kg bid. 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 of oseltamivir (e.g., 10 days) is often used.
5. 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.
6. Oseltamivir 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 after every HD for treatment (may be started immediately if influenza symptoms develop between HD sessions) and 30 mg after every other HD for prophylaxis (initial dose can be given before start of HD); continuous ambulatory peritoneal dialysis (CAPD): single 30-mg dose after exchange 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.
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 oseltamivir and zanamivir is 10 days after the last known exposure. For control of outbreaks in institutions, 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 post-exposure 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 oseltamivir because of gastric stasis, malabsorption, or GI bleeding.
11. Available for $50 through the manufacturer's direct-to-consumer program.

CHEMOPROPHYLAXIS — Oseltamivir, zanamivir, and baloxavir are FDA-approved for chemoprophylaxis of influenza. Post-exposure prophylaxis should be considered within 48 hours of exposure for persons at high risk of complications who have not received an influenza vaccine for the current season, received one within the previous 2 weeks, or might not respond to vaccination, or when the match between the vaccine and circulating strains is poor. Post-exposure prophylaxis may be considered for unvaccinated persons who are in close contact with persons at high risk for influenza complications who are unable to be otherwise protected. It is not recommended for healthy persons exposed to influenza or when >48 hours have elapsed since exposure.[2,3]

Post-exposure prophylaxis with oral oseltamivir or inhaled zanamivir is recommended by the CDC for control of institutional influenza outbreaks.[1]

Effectiveness – Oseltamivir, zanamivir, and baloxavir have generally been about 70-90% effective in preventing influenza caused by susceptible strains of influenza A or B viruses.[1,25]

A meta-analysis of 33 trials found that prompt post-exposure prophylaxis with oseltamivir, zanamivir, or baloxavir can reduce the risk of symptomatic influenza in patients at high risk for severe disease.[26]

In a randomized, placebo-controlled trial, administration of a single dose of baloxavir to an index patient within 48 hours of symptom onset significantly reduced the incidence of laboratory-confirmed influenza transmission to household contacts (adjusted relative risk reduction 29%); transmission that resulted in symptoms in household contacts was not significantly lower with baloxavir (incidence 5.8% vs 7.6% with placebo).[27]

Timing – Prophylaxis with oseltamivir or zanamivir should be started no later than 48 hours after exposure and continued for 7 days after the last known exposure. A single dose of baloxavir taken within 48 hours of exposure is also an option.

For controlling institutional influenza outbreaks, the CDC recommends post-exposure prophylaxis with oral oseltamivir or inhaled zanamivir for at least 2 weeks; prophylaxis 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 severe complications of influenza. Empiric antiviral **treatment** should be started as soon as possible in those with suspected or confirmed influenza. Oseltamivir is preferred for treatment of pregnant or breastfeeding women. Zanamivir appears to also be safe for use during pregnancy. Data are insufficient on use of peramivir. Baloxavir is not recommended for treatment of pregnant or breastfeeding women because of a lack of data.[28-32]

Antiviral **post-exposure prophylaxis** can be considered for pregnant women and those who are ≤2 weeks postpartum who cannot receive an influenza vaccine or have severe immunodeficiencies or other medical conditions that make them 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.[7,27,42] 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.[1] 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).

The adamantanes amantadine and rimantadine are active against influenza A, but not influenza B, viruses. Resistance to these drugs has been reported in recent years and remains high (>99%) among circulating influenza A(H3N2) and A(H1N1)pdm09 viruses; neither amantadine nor rimantadine is recommended for treatment or chemoprophylaxis of influenza this season.

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] Diarrhea, nausea, sinusitis, fever, and arthralgia have been reported with **zanamivir**. Inhalation of zanamivir can cause bronchospasm; the drug should not be used in patients with underlying airway disease. Diarrhea and neutropenia have occurred with **peramivir**.[47] **Baloxavir** appears to cause less nausea and vomiting than oseltamivir.[48]

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

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 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]

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.[50] 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 inactivated or recombinant influenza vaccine.[51] ■

Additional Content Available Online

Comparison Table: Antiviral Drugs for Seasonal Influenza for 2025-2026
http://medicalletter.org/TML-article-1740d

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