The Medical Letter®
on Drugs and Therapeutics

Comparison Chart: ANTIVIRAL DRUGS FOR INFLUENZA FOR 2021-2022

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ANTIVIRAL DRUGS FOR INFLUENZA FOR 2021-2022

DRUG	FORMULATIONS	ROUTE	TREATMENT	CHEMOPROPHYLAXIS	COST[1]
NEURAMINIDASE INHIBITORS					
Oseltamivir – generic *Tamiflu* (Genentech)	30, 45, 75 mg caps; 6 mg/mL oral susp	Oral NG tube	▪ FDA-approved for treatment of acute uncomplicated influenza in patients ≥2 weeks old ▪ Preferred treatment for influenza in pregnant women, hospitalized patients, and outpatients with severe, complicated, or progressive illness	▪ FDA-approved for chemoprophylaxis of influenza in patients ≥1 year old	$32.00 151.90
Peramivir – *Rapivab* (BioCryst)	200 mg/20 mL single-use vials	IV	▪ FDA-approved for treatment of acute uncomplicated influenza in otherwise healthy patients ≥6 months old	▪ Not FDA-approved for chemoprophylaxis	950.00
Zanamivir – *Relenza* (GSK)	5 mg blisters of powder for inhalation	Inhalation	▪ FDA-approved for treatment of acute uncomplicated influenza in patients ≥7 years old ▪ Not recommended for use in patients with severe influenza or underlying airway disease	▪ FDA-approved for chemoprophylaxis of influenza in patients ≥5 years old	59.00
POLYMERASE ACIDIC (PA) ENDONUCLEASE INHIBITOR					
Baloxavir marboxil – *Xofluza* (Genentech)	40, 80 mg tabs; 40 mg/20 mL oral susp	Oral	▪ FDA-approved for treatment of acute uncomplicated influenza in patients ≥12 years ▪ No data in patients with severe influenza, hospitalized patients, or pregnant women ▪ Not recommended for use in severely immunosuppressed patients or pregnant women	▪ FDA-approved for post-exposure prophylaxis in patients ≥12 years old	154.50

RECOMMENDATIONS FOR ANTIVIRAL TREATMENT[2,3]

- Antiviral treatment should be started as soon as possible; it is most effective when started within 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.
- Antiviral treatment of suspected or confirmed influenza is recommended for hospitalized patients and for outpatients who are at increased risk for complications or have severe, complicated, or progressive illness, even if it is started >48 hours after illness onset.

PREGNANCY AND LACTATION

- Oseltamivir and zanamivir appear to be safe for use during pregnancy
- Oseltamivir is preferred for treatment of women who are pregnant, ≤2 weeks postpartum, or breastfeeding
- No data are available on use of baloxavir in pregnant or breastfeeding women
- Zanamivir may be preferred for chemoprophylaxis in pregnant women because of its limited systemic absorption, but oseltamivir is a reasonable alternative, especially in women at increased risk for respiratory problems

ANTIVIRAL DRUGS FOR INFLUENZA FOR 2021-2022 (continued)

DRUG	USUAL TREATMENT DOSAGE	USUAL CHEMOPROPHYLAXIS DOSAGE
OSELTAMIVIR *(TAMIFLU)*		
ADULT	75 mg PO bid x 5 days	75 mg PO once/day x 7 days
PEDIATRIC	**<2 wks old:** 3 mg/kg PO bid x 5 days (CDC)[4] **≥2 wks-<1 yr:** 3 mg/kg PO bid x 5 days (9-11 months: AAP recommends 3.5 mg/kg)[5] **1-12 yrs:** 30-75 mg PO bid x 5 days (≤15 kg: 30 mg; >15-23 kg: 45 mg; >23-40 kg: 60 mg; >40 kg: 75 mg) **≥13 yrs**: 75 mg PO bid x 5 days	**<3 mos:** not recommended **3 mos-1 yr:** 3 mg/kg PO once/day x 7 days (CDC & AAP)[6] **<1 yr:** 3 mg/kg PO once/day x 7 days **1-12 yrs:** 30-75 mg PO once/day x 7 days (≤15 kg: 30 mg; >15-23 kg: 45 mg; >23-40 kg: 60 mg; >40 kg: 75 mg) **≥13 yrs:** 75 mg PO once/day x 7 days
RENAL	**Adults and children >40 kg (CDC):** ▪ CrCl 31-60 mL/min: 30 mg bid ▪ CrCl 11-30 mL/min: 30 mg once/day ▪ HD: 30 mg after every HD (may be started immediately if influenza symptoms develop between HD sessions) ▪ CAPD: 30 mg once immediately ▪ ESRD (not on HD): not recommended	**Adults and children >40 kg (CDC):** ▪ CrCl 31-60 mL/min: 30 mg once/day ▪ CrCl 11-30 mL/min: 30 mg every other day ▪ HD: 30 mg after every other HD (initial dose can be given before start of HD) ▪ CAPD: 30 mg immediately and then once/week after exchange ▪ ESRD (not on HD): not recommended
PERAMIVIR *(RAPIVAB)*		
ADULT	600 mg IV over 15-30 minutes once	Not FDA-approved for chemoprophylaxis
PEDIATRIC	**6 months-12 yrs:** 12 mg/kg (max 600 mg) IV over 15-30 mins once **≥13 yrs:** 600 mg IV over 15-30 mins once	Not FDA-approved for chemoprophylaxis
RENAL	**2-12 yrs:** ▪ CrCl 30-49 mL/min: 4 mg/kg IV once ▪ CrCl 10-29 mL/min: 2 mg/kg IV once **≥13 yrs:** ▪ CrCl 30-49 mL/min: 200 mg IV once ▪ CrCl 10-29 mL/min: 100 mg IV once ▪ HD: administer dose after HD (based on CrCl)	
ZANAMIVIR *(RELENZA)*		
ADULT	2 inhalations bid x 5 days	2 inhalations once/day x 7 days
PEDIATRIC	**≥7 yrs:** 2 inhalations bid x 5 days	**≥5 yrs:** 2 inhalations once/day x 7 days
BALOXAVIR *(XOFLUZA)*		
ADULT	**<80 kg:** 40 mg PO once **≥80 kg:** 80 mg PO once	**<80 kg:** 40 mg PO once **≥80 kg:** 80 mg PO once
PEDIATRIC	**≥12 yrs and <80 kg:** 40 mg PO once **≥12 yrs and ≥80 kg:** 80 mg PO once	**≥12 yrs and <80 kg:** 40 mg PO once **≥12 yrs and ≥80 kg:** 80 mg PO once

DURATION OF THERAPY

TREATMENT:

- Oseltamivir or zanamivir should be given for 5 days; peramivir and baloxavir are given as single doses
- In hospitalized, critically ill, or immunocompromised patients, a longer treatment course of oseltamivir (e.g., 10 days) is often used. IV peramivir for at least 5 days may be considered for those who cannot tolerate or absorb oral or enterically administered oseltamivir because of gastric stasis, malabsorption, or GI bleeding

CHEMOPROPHYLAXIS:

- Oseltamivir or zanamivir should be continued for 7 days after the last known exposure
- For institutional outbreaks, 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

ADMINISTRATION

- Taking oseltamivir with food may minimize GI adverse effects
- Oseltamivir capsules can be opened and the contents mixed in a thick sweetened liquid to mask the bitter taste and consumed immediately
- Oseltamivir can be given by oro/nasogastric tube to patients who are unable to swallow
- Baloxavir suspension must be used within 10 hours after reconstitution

AAP = American Academy of Pediatrics; CAPD = continuous ambulatory peritoneal dialysis; CDC = Centers for Disease Control; ESRD = end-stage renal disease; HD = hemodialysis

ANTIVIRAL DRUGS FOR INFLUENZA FOR 2021-2022 (continued)

SOME ADVERSE EFFECTS

NEURAMINIDASE INHIBITORS AND BALOXAVIR:

- Neuropsychiatric events have been reported, but a causal relationship has not been established
- Neuropsychiatric dysfunction can be a complication of influenza itself

OSELTAMIVIR:

- Nausea, vomiting, headache

PERAMIVIR:

- Diarrhea, neutropenia

ZANAMIVIR:

- Diarrhea, nausea, sinusitis, fever, arthralgia
- Bronchospasm; not recommended in patients with underlying airway disease
- Contains lactose; contraindicated in patients with a history of milk protein allergy

BALOXAVIR:

- Nausea and vomiting; incidence appears to be lower than with oseltamivir

DRUG INTERACTIONS

With Intranasal Live-Attenuated Influenza Vaccine *(Flumist Quadrivalent)*:

- Antivirals could inhibit replication of vaccine virus and reduce vaccine efficacy
- Avoid **oseltamivir** or **zanamivir** within 48 hours before, **peramivir** within 5 days before, or **baloxavir** within 17 days before or <2 weeks after vaccine administration
- Revaccination with an inactivated or a recombinant influenza vaccine is recommended in persons who receive any one of these antiviral drugs within 2 weeks after receiving the intranasal influenza vaccine

With Polyvalent Cations:

- Coadministration of antacids, laxatives, multivitamins, or other products containing polyvalent cations, such as calcium, aluminum, iron, magnesium, selenium, or zinc, can reduce serum concentrations of **baloxavir** and should be avoided.

ACTIVITY/RESISTANCE

- Neuraminidase inhibitors and baloxavir have activity against influenza A and B viruses
- Over 99% of recently circulating influenza virus strains tested by the WHO have been susceptible to neuraminidase inhibitors
- Reduced susceptibility of some influenza virus strains, particularly influenza A(H1N1), to oseltamivir or peramivir can emerge during or after treatment, especially in immunocompromised patients with prolonged viral shedding and in young children
- Resistant isolates have generally remained sensitive to zanamivir, but reduced susceptibility to zanamivir has been reported
- Baloxavir monotherapy is not recommended for severely immunosuppressed patients because of concerns about emergence of resistance

References:

1. Approximate WAC for 5 days' treatment with oseltamivir capsules or zanamivir, or for a single treatment dose of peramivir or baloxavir, at the usual adult dosage. 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. December 5, 2021. Reprinted with permission by First Databank, Inc. All rights reserved. ©2021. www.fdbhealth.com/policies/drug-pricing-policy.
2. CDC. Influenza antiviral medications: summary for clinicians. Available at: https://bit.ly/34ieMdX. Accessed December 16, 2021.
3. Antiviral drugs for influenza 2021-2022. Med Lett Drugs Ther 2021; 64:1.
4. Although not FDA-approved for use in children <2 weeks old, the CDC recommends children <2 weeks old be treated with 3 mg/kg bid. For treatment of premature infants, refer to CDC recommendations (www.cdc.gov/flu).
5. 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).
6. Although not FDA-approved for chemoprophylaxis in children <1 year old, the American Academy of Pediatrics and 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.

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