

Influenza Update and Best Practice

IDAT
12 OCT 2019

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Update and Best practice issue.

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- Clinical and laboratory diagnosis.
- Antiviral treatment
- Pre and post exposure antiviral chemoprophylaxis.
- Infection prevention and control.
- Vaccine

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Clinical Diagnosis :
Signs and Symptoms of Uncomplicated Influenzaa

General	Head, Eyes, Ears, Nose, Throat	Neuromuscular	Gastrointestinal	Pulmonary
Fever Chills Malaise Fatigue	Headache Nasal congestion Rhinitis Sore throat/hoarseness	Myalgia Arthralgia Weakness Chest pain	Abdominal pain Vomiting Diarrhea	Nonproductive cough Pleuritic chest pain

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Clinical Manifestations and Complications Associated With Influenza

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[illegible]

• Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press 2018.

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Clinical Manifestations and Complications Associated With Influenza

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Population	Clinical Manifestation/Complication
Infants and preschool children	<ul style="list-style-type: none"> Fever without respiratory complications, "sepsis-like syndrome" Otitis media Parotitis Bronchiolitis Croup Reactive airway disease Pneumonia Myocarditis, pericarditis Rhabdomyolysis Febrile seizures Encephalopathy and encephalitis Invasive bacterial coinfection Reye syndrome (with aspirin exposure) Sudden death Exacerbation of chronic disease

Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018.

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Clinical Manifestations and Complications Associated With Influenza

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Population	Clinical Manifestation/Complication
School-aged children	Otitis media Parotitis Bronchitis Sinusitis Reactive airway disease Pneumonia Myocarditis, pericarditis Myositis (bilateral gastrocnemius, soleus) Rhabdomyolysis Encephalopathy and encephalitis Invasive bacterial coinfection Reye syndrome (with aspirin use) Toxic shock syndrome Sudden death Exacerbation of chronic disease

Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018.

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Clinical Manifestations and Complications Associated With Influenza	
Population	Clinical Manifestation/Complication
Adults	Parotitis Bronchitis Sinusitis Reactive airway disease Pneumonia Myocarditis, pericarditis Myositis Rhabdomyolysis Invasive bacterial coinfection Invasive fungal coinfection (rare) Toxic shock syndrome due to <i>Staphylococcus aureus</i> or <i>Streptococcus pyogenes</i> Precipitation of acute cardiovascular events (eg, cardiac failure, myocardial infarction, heart failure, cerebrovascular accident) Acute kidney injury and acute renal failure (with rhabdomyolysis or multiorgan failure) Encephalopathy and encephalitis Exacerbation of chronic disease

Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018.

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Clinical Manifestations and Complications Associated With Influenza	
Population	Clinical Manifestation/Complication
Elderly patients	Pneumonia Invasive bacterial coinfection Myositis Exacerbation of chronic disease
Special groups: pregnant and postpartum women	Dehydration Pneumonia Cardiopulmonary disease Premature labor Fetal loss
Special groups: immunocompromised, immunosuppressed	Complications similar to immunocompetent patients, but severe pneumonia and acute respiratory distress syndrome may be more common.
All ages	Respiratory failure Acute respiratory distress syndrome Multiorgan failure Sepsis Liver inflammation

Adapted from Jani AA, Uyeki TM. Chapter 46. Influenza. In: Emergency management of infectious diseases. 2nd ed. Chin RL, ed. Cambridge, UK: Cambridge University Press, 2018.

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Persons Who Are at High Risk of Complications From Influenza

Children aged <5 years, and especially aged <2 years

Adults aged ≥65 years

Persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), or metabolic disorders (including diabetes mellitus) or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)

Persons with immunosuppression, including that caused by medications or by HIV infection^a

Women who are pregnant or postpartum (within 2 weeks after delivery)

Children and adolescents through 18 years who are receiving aspirin- or salicylate-containing medications and who might be at risk for experiencing Reye syndrome after influenza virus infection

American Indian/Alaska Native people^b

Persons with extreme obesity (ie, body mass index ≥40 kg/m²)

Residents of nursing homes and other chronic care facilities

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Interpretation of Influenza Testing Results on Respiratory Specimens

Test and Characteristics	Low Influenza Activity ^a		High Influenza Activity ^b	
	Negative result NPV is high: ➤ Likely to be a true-negative result if an upper respiratory tract specimen was collected <4 days after illness onset ➤ If epidemiologically linked to an influenza outbreak, consider confirming with molecular assay	Positive result PPV is low: ➤ Likely to be a false-positive result ➤ Confirm with molecular assay	Negative result NPV is low: ➤ May be a false-negative result, especially if upper respiratory tract specimen was collected >4 days after illness onset, cannot exclude influenza virus infection ➤ Do not withhold antiviral treatment if clinically indicated ➤ Confirm with molecular assay	Positive result PPV is high: ➤ Likely to be a true-positive result

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Interpretation of Influenza Testing Results on Respiratory Specimens	
Test and Characteristics	High Influenza Activity ^b
Molecular assay Nucleic acid detection: rapid molecular assay ^a Multiplex PCR, RT-PCR • High sensitivity • Very high specificity • Can be used for both outpatients and hospitalized patients ➤ RT-PCR assays should be used for hospitalized patients	Negative result NPV is high: ➤ Very likely to be a true-negative result, especially if an upper respiratory tract specimen was collected <4 days after illness onset Positive result PPV is low: ➤ False-positive result is possible ➤ Consider potential for a false-negative result, especially if an upper respiratory tract specimen was collected in a hospitalized patient ➤ For hospitalized patients on mechanical ventilation who tested negative on upper respiratory tract specimens, collect lower respiratory tract specimens (endotracheal aspirate, BAL fluid) for testing

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Diagnosis: Laboratory	
Which Patients Should Be Tested for Influenza?	Recommendations
• Which Patients Should Be Tested for Influenza? • Recommendations OPD (including ER), and IPD . During influenza activity who have (A–III). • Acute onset of respiratory symptoms, with or without fever (all ages) • Pneumonia (all ages)(A–II) • Acute exacerbation of underlying chronic lung disease (eg, chronic obstructive pulmonary disease, asthma), with or without fever (all ages)(A–III) • Fever without an obvious source (infants, young children) • New-onset neurologic signs and symptoms (eg, seizures, altered mental status), with or without fever (infants, young children) • Exacerbation or new onset of cardiovascular events (eg, heart failure, myocardial infarction or ischemia, cerebrovascular accident in adults) or altered mental status, with or without fever (all ages)(A–III) • Severe, complicated, or progressive (worsening) acute respiratory illness, without an alternative diagnosis (all ages)(A–III) • Hospitalized patients who develop new onset of acute respiratory symptoms, with or without fever (all ages)(A–II)	

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Diagnosis: Laboratory

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• Which Patients Should Be Tested for Influenza?

Recommendations OPD (including ER), and IPD. Year-round who have (A–III).

Acute onset of respiratory symptoms, **with or without fever**, especially those at high risk for influenza complications who are epidemiologically linked to recent influenza cases or outbreaks (all ages).....

- Healthcare personnel caring for influenza patients
- Healthcare personnel, residents, or visitors to an institution experiencing an influenza outbreak
- Close contacts of persons with suspected influenza (household or a congregate setting, such as daycare, school, or healthcare facility)
- Travelers who returned recently from areas where influenza viruses may be circulating
- Organized tour group participants
- Participants in international mass gatherings
- Summer camp attendees
- Cruise or military ship passengers

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Diagnosis

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What Specimen(s) Should Be Collected When Testing Patients for Influenza?

Recommendations NP > NS > Throat > MTNs > Throat

- **Nasopharyngeal specimens (NP)** should be collected over other upper respiratory tract specimens to increase detection of influenza viruses..... (A–II).
- If nasopharyngeal specimens are not available, **nasal swab (NS) and throat swab (TS) specimens should be collected and combine together** for influenza testing over single specimens from either site (particularly over throat swabs) to increase detection of influenza viruses.... (A–II).
- **Mid-turbinate nasal swab** specimens should be collected over throat swab specimens to increase detection of influenza viruses..... (A–II).
- **Flocked swab** specimens should be collected over nonflocked swab specimens to improve detection of influenza viruses..... (A–II).

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Diagnosis

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• What Specimen(s) Should Be Collected When Testing Patients for Influenza?

Recommendations

Clinicians should collect **endotracheal aspirate or bronchoalveolar lavage** fluid specimens from hospitalized patients for influenza testing in

- Respiratory failure receiving mechanical ventilation.
- Patients with negative influenza testing results on upper respiratory tract specimens, as soon as possible (A–II).

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The ways should not to practice.

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Collect or routinely test specimens for influenza from

- **Nonrespiratory sites** such as blood, plasma, serum, cerebrospinal fluid, urine, and stool (A–III).
- **Serum specimens**, including single or paired sera, for serological diagnosis of seasonal influenza virus infection for clinical management purposes (A–III).

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Clinical Infectious Diseases

IDSA GUIDELINE



Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza^a

Timothy M. Uyeki,¹ Henry H. Bernstein,² John S. Bradley,³ Janet A. Englund,⁴ Thomas M. File Jr.,⁵ Alicia M. Fry,⁶ Stefan Gravenstein,⁷ Frederick G. Hayden,⁸ Scott A. Hargrett,⁹ Jan Mock-Winkelmann,¹⁰ Michael G. Ison,¹¹ B. Lynn Johnston,¹² Shandra L. Knight,¹³ Allison McGuire,¹⁴ Laura E. Riley,¹⁵ Cameron R. Wolfe,¹⁶ Paul E. Alexander,¹⁷ and Andrew T. Pavia¹⁸

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Antiviral Agents and Dosing Recommendations for Treatment and Chemoprophylaxis of Influenza

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Antiviral Agents and Age Group	Treatment Dosing	Chemoprophylaxis Dosing
Oseltamivir		
Adults	75 mg twice daily	75 mg once daily
Pregnancy (any trimester) ^a	75 mg twice daily ^b	75 mg once daily ^b
Children 11 year or older ^c ≤15 kg	30 mg twice daily	30 mg once daily
Children >15–23 kg	45 mg twice daily	45 mg once daily
Children >23–40 kg	60 mg twice daily	60 mg once daily
Children >40 kg	75 mg twice daily	75 mg once daily
Infants 3–11 months	3.5 mg/kg per dose twice daily ^d	3.5 mg/kg per dose once daily ^d
Term infants 0–6 months	3 mg/kg per dose twice daily	3 mg/kg per dose once daily if <3 months; not recommended for infants <3 months unless the situation is judged critical due to lack of safety and efficacy data
Preterm infants	See details in footnote ^a	No data

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ตารางการให้ยาและผสม Oseltamivir suspension			
น้ำหนัก (กก.)	ขนาดที่ใช้	จำนวนเม็ด	น้ำเชื่อมที่มีสารกันเสีย
< 15 กก.	3 มล. วันละ 2 ครั้ง	6 เม็ด	45 มล.
> 15 กก. - 23 กก.	4.5 มล. วันละ 2 ครั้ง	8 เม็ด	60 มล.
> 23 กก. - 40 กก.	6 มล. วันละ 2 ครั้ง	10 เม็ด	75 มล.
> 40 กก.	1 แคปซูล วันละ 2 ครั้ง	ถ้าผู้ป่วยกลืนไม่ได้ ให้แกะแคปซูลผสมน้ำ	

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Antiviral Agents and Dosing Recommendations for Treatment and Chemoprophylaxis of Influenza		
Antiviral Agents and Age Group	Treatment Dosing	Chemoprophylaxis Dosing
Zanamivir		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children (>7 years)	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Peramivir		
Adults	600 mg intravenous infusion once, given over 15-30 minutes	NA
Children (2-12 years)	One 12 mg/kg dose, up to 600 mg maximum, intravenous, given over 15-30 minutes	NA
Children (13-17 years)	600 mg intravenous infusion once, given over 15-30 minutes	NA

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<p style="text-align: center;">Peramivir</p> <ul style="list-style-type: none"> Peramivir is the only FDA-approved IV antiviral drug for early treatment of uncomplicated influenza in OPD patients aged ≥2 years. Peramivir single-dose pharmacokinetics were studied in children ranging in age from ≥28 days to <16 years during the 2009 H1N1 pandemic and infants and children were treated on a compassionate use basis. Indication : IV peramivir can be considered for infants and children with influenza who cannot tolerate oral therapy, Intravenous zanamivir has been evaluated in adults and children but is not FDA approved and is currently available. <p>Marty FM, et al. Lancet Respir Med 2017; 5:135-46 Sugaya N, et al. Antimicrob Agents Chemother 2012; 56:369-77. Hernandez JE, et al. Clin Infect Dis 2011; 52:695-706. Bradley JS, et al. Pediatrics 2017; 140. doi:10.1542/peds.2016-2727.</p>

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<p style="text-align: center;">Lastest Antiviral</p> <p>Baloxavir Marboxil</p> <ul style="list-style-type: none"> A selective inhibitor of influenza cap-dependent endonuclease. It has shown therapeutic activity in preclinical models of influenza A and B virus infections. The activity including strains resistant to current antiviral agents.
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The new antiviral

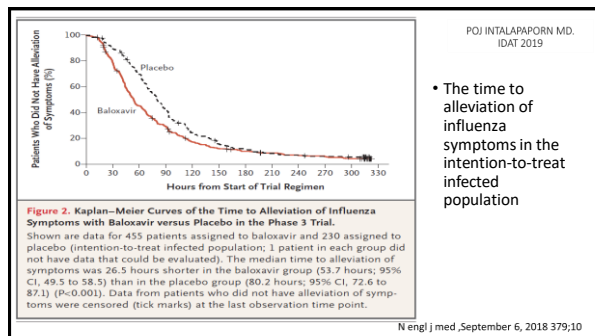
<p style="text-align: center;">The NEW ENGLAND JOURNAL of MEDICINE</p> <p>ESTABLISHED IN 1812 SEPTEMBER 6, 2018 VOL. 379 NO. 38</p> <p style="text-align: center;">Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents</p> <p>Frederick G. Hayden, M.D., Norio Sugaya, M.D., Nobuo Hirotsu, M.D., Ph.D., Nelson Lee, M.D., Menno D. de Jong, M.D., Ph.D., Aaron C. Hurt, Ph.D., Tadashi Ishida, M.D., Ph.D., Hirotaka Sakono, M.D., Ph.D., Kota Yamada, M.D., Simon Portsmouth, M.D., Keiko Kawaguchi, M.Sc., Takao Shishido, Ph.D., Masatsugu Arai, M.Sc., Kenji Tsuchiya, M.Sc., Takeli Uehara, Ph.D., and Akira Watanabe, M.D., Ph.D., for the Baloxavir Marboxil Investigators Group¹</p> <p style="text-align: center;">ABSTRACT</p> <p>BACKGROUND Baloxavir marboxil is a selective inhibitor of influenza cap-dependent endonuclease. It has shown therapeutic activity in preclinical models of influenza A and B virus infections, including strains resistant to current antiviral agents.</p> <p>METHODS We conducted two randomized, double-blind, controlled trials involving otherwise healthy outpatients with acute uncomplicated influenza. After a dose-ranging (10 to 40 mg) placebo-controlled trial, we undertook a placebo- and oseltamivir-controlled</p> <p>From the Department of Medicine, University of Virginia School of Medicine, Charlottesville (F.G.H.); the Department of Infectious, Kanto Hospital, Tokyo (N.S.); Hirotsu Clinic, Kawasaki (N.H.); the Department of Respiratory Medicine, Kurashiki Central Hospital, Kurashiki (T.U.); Sakano Hospital, Tokyo (H.S.); Tsuchiya Benji Clinic, Tsuchiura (K.T.).</p>

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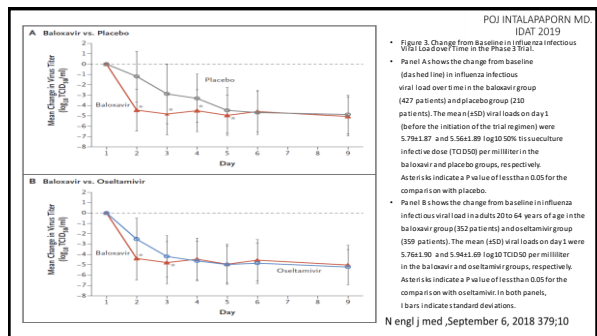
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<p style="text-align: center;">Baloxavir marboxil</p> <ul style="list-style-type: none"> Two randomized, double-blind, controlled trials involving otherwise healthy outpatients with acute uncomplicated influenza. After a dose-ranging (10 to 40 mg) placebo-controlled trial, then undertook a placebo- and oseltamivir-controlled trial of single, weight-based doses of baloxavir (40 or 80 mg) in patients 12 to 64 years of age during the 2016-2017 season. The dose of oseltamivir was 75 mg twice daily for 5 days. The primary efficacy end point was the time to alleviation of influenza symptoms in the intention-to-treat infected population. <p>N Engl J Med, September 6, 2018 379:10</p>

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Baloxavir marboxil POJ INTALAPORN MD, IDAT 2019

RESULTS

- In the phase 2 trial, the median time to alleviation of influenza symptoms was 23.4 to 28.2 hours shorter in the baloxavir groups than in the placebo group ($P < 0.05$).
- In the phase 3 trial, the intention-to-treat infected population included 1064 patients; 84.8 to 88.1% of patients in each group had influenza A(H3N2) infection.
- The median time to alleviation of symptoms was 53.7 hours (95% confidence interval [CI], 49.5 to 58.5) with baloxavir, as compared with 80.2 hours (95% CI, 72.6 to 87.1) with placebo ($P < 0.001$).
- The time to alleviation of symptoms was similar with baloxavir and oseltamivir.
- Baloxavir was associated with greater reductions in viral load 1 day after initiation of the regimen than placebo or oseltamivir.
- Adverse events were reported in 20.7% of baloxavir recipients, 24.6% of placebo recipients, and 24.8% of oseltamivir recipients.
- The emergence of polymerase acidic protein variants with I38T/M/F substitutions conferring reduced susceptibility to baloxavir occurred in 2.2% and 9.7% of baloxavir recipients in the phase 2 trial and phase 3 trial, respectively.

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Adverse Events during the Phase 3 Trial (Safety Population). * POJ INTALAPORN MD, IDAT 2019

Event	Baloxavir (n=455)		Placebo (n=230)		Oseltamivir (n=339)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Any adverse event	124 (28.7)	4 (1.0)	76 (24.6)	4 (1.3)	127 (24.8)	1 (0.3)
Adverse events reported in ≥1% of patients in any group						
Diarrhea	18 (4.0)	1 (0.2)	14 (6.3)	1 (0.3)	11 (2.1)	0
Headache	16 (3.6)	0	17 (7.5)	1 (0.3)	16 (3.3)	0
Nasopharyngitis	8 (1.3)	0	2 (0.4)	0	4 (0.8)	0
Nausea	8 (1.3)	1 (0.2)	4 (1.3)	1 (0.3)	16 (3.1)	0
Sinusitis	7 (1.1)	0	8 (2.4)	1 (0.3)	5 (1.0)	0
Increase in ALT level	4 (1.0)	0	4 (1.3)	0	7 (1.4)	0
Headache	5 (0.8)	1 (0.2)	3 (1.0)	0	4 (0.8)	0
Vomiting	5 (0.8)	1 (0.2)	2 (0.4)	0	4 (1.2)	0
Diarrhea	3 (0.3)	0	4 (1.3)	0	1 (0.2)	0
Lymphopenia	0	0	3 (1.0)	0	1 (0.2)	0
Constipation	0	0	3 (1.0)	0	0	0
Adverse event considered to be related to the trial regimen and reported in ≥1% of patients in any group	27 (4.4)	2 (0.3)	12 (3.1)	1 (0.3)	41 (8.4)	0
Diarrhea	11 (2.4)	1 (0.2)	4 (1.3)	0	7 (1.4)	0
Nausea	2 (0.3)	1 (0.2)	2 (0.4)	1 (0.3)	8 (1.4)	0
Serious adverse event	2 (0.3)	2 (0.3)	0	0	0	0
Adverse event leading to discontinuation of the trial regimen	2 (0.3)	0	1 (0.3)	1 (0.3)	2 (0.4)	0

* The severity of an event was categorized by the investigators according to definitions based on the Common Terminology Criteria for Adverse Events, version 4.0.
* ALT denotes alanine aminotransferase.
* No significant differences were noted between the groups except for the prespecified comparison of adverse events that were considered to be related to the trial regimen, which were more common in the oseltamivir group than in the baloxavir group ($P = 0.009$).
* Adverse events leading to discontinuation of the trial regimen occurred in two patients who received baloxavir (bronchitis and pneumonia in one patient and acute bronchitis in one patient), in one patient who received placebo (nausea, hip pain, low back pain, and jaw pain), and in two patients who received oseltamivir (nausea in one patient and pneumonia in one patient).

N engl j med, September 6, 2018 379;10

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CONCLUSIONS POJ INTALAPORN MD, IDAT 2019

- Single-dose baloxavir was without evident safety concerns, was superior to placebo in alleviating influenza symptoms, and was superior to both oseltamivir and placebo in reducing the viral load 1 day after initiation of the trial regimen in patients with uncomplicated influenza.
- Evidence for the development of decreased susceptibility to baloxavir after treatment was also observed.

N engl j med, September 6, 2018 379;10

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Which Patients With Suspected or Confirmed Influenza Should Be Treated With Antivirals? POJ INTALAPORN MD, IDAT 2019

Treatment Recommendations

Should start antiviral treatment as soon as possible for adults and children with documented or suspected influenza, irrespective of influenza vaccination history, who meet the following criteria:

- Hospitalized with influenza(A-II).
- Severe or progressive illness(A-III).
- High risk of complications from influenza(A-II).....
- Chronic medical conditions and immunocompromised patients ...(A-II).
- Children younger than 2 years and adults ≥65 years.....(A-III).
- Pregnant women and those within 2 weeks postpartum(A-III).

Uyeki et al CID 2019;68 (15 March)

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Treatment Recommendations (2)

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Consider antiviral treatment for adults and children **who are not at high risk of influenza complications, with documented or suspected influenza**, irrespective of influenza vaccination history, who are either:

- Outpatients with illness **onset ≤ 2 days** before presentation.....(C-I).
- **Symptomatic outpatients who are household contacts** of persons who are at high risk of developing complications from influenza, particularly those who are severely immunocompromised..... (C-II).
- **Symptomatic healthcare providers** who care for patient who are at high risk of developing complications from influenza, particularly those who are severely immunocompromised(C-III).

Uyeki et al CID 2019:68 (15 March)

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Which Antiviral Should Be Prescribed, at What Dosing, and for What Duration?

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Recommendation

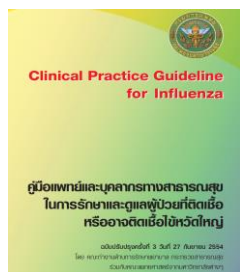
1. A single neuraminidase inhibitor (NAI) (either oral oseltamivir, inhaled zanamivir, or intravenous peramivir)(A-1).
2. Not use a combination of NAIs(A-1).
3. Should not routinely use higher doses of US FDA–approved NAI drugs for the treatment of seasonal influenza(A-II).
4. Should treat uncomplicated influenza in otherwise healthy ambulatory patients for **5 days** with oral oseltamivir or inhaled zanamivir, or a single dose of intravenous peramivir,(A-1).
5. Can consider **longer duration** of antiviral treatment for patients with a **documented or suspected immunocompromising condition** or patients requiring hospitalization for severe lower respiratory tract disease (especially pneumonia or ARDS), as influenza viral replication is often protracted(C-III).

Uyeki et al CID 2019:68 (15 March)

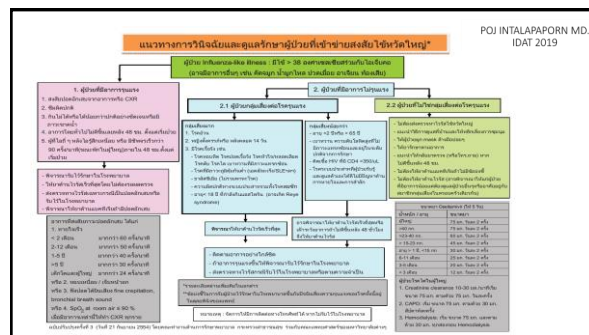
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จ. แนวทางการให้ยาต้านไวรัส Oseltamivir

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จ-1. การให้ยาเพื่อการรักษา

- ผลการรักษาที่ดีที่สุดเมื่อให้ยาภายใน 48 ชม.แรก อย่างไรก็ตามยังใช้ได้ผลเมื่ออาการป่วยไม่เกิน 5 วัน
- ให้ Oseltamivir เฉพาะผู้ป่วยที่เป็น suspected[®] หรือ confirmed cases[®] ดังต่อไปนี้

1. ผู้ป่วยที่มีอาการรุนแรง
 2. ผู้ป่วยกลุ่มเสี่ยงต่อโรครุนแรง
 3. ผู้ป่วยที่อาการไม่ดีขึ้นหลัง 48 ชม. นับตั้งแต่เริ่มป่วย
 4. ผู้ป่วยอื่นๆ ตามแนวทางเวชปฏิบัติในดุลยพินิจของแพทย์ผู้ดูแลรักษา
- การให้ยา Oseltamivir ขนาดสูง 2 เท่าของปกติมีผลการศึกษาเบื้องต้นพบว่าไม่มีประสิทธิภาพดีกว่าขนาดปกติที่แนะนำ ส่วนการใช้ยาระยะนานกว่า 5 วันนั้น ให้พิจารณาตามความจำเป็นและเหมาะสมตามดุลยพินิจของแพทย์ผู้ดูแล

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3.2 อาการไม่พึงประสงค์จากยา Oseltamivir

- ผลข้างเคียงที่พบบ่อยได้แก่ คลื่นไส้ อาเจียน ปวดท้อง ปวดศีรษะ ท้องเสีย
- การให้ยาหรืออาหารจะทำให้มีอาการคลื่นไส้ อาเจียน ปวดท้อง ลดลง
- การแพ้ยาอาจเกิดขึ้น เช่น ผื่นลมพิษ

3.3 การเก็บยา

- ยาแคปซูลเก็บที่อุณหภูมิสูงกว่า 25 องศาเซลเซียส ยาน้ำเก็บในตู้เย็น

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Should Adjunctive Therapy Be Administered to Patients With Suspected or Confirmed Influenza?

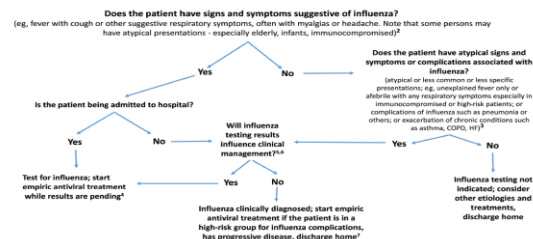
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- Clinicians should not routinely administer immunomodulation using immunoglobulin preparations such as intravenous immunoglobulin for treatment of adults or children with suspected or confirmed seasonal influenza (A-III).

Hu Y, et al. Lancet 2013; 381:2273–9.
Lee N, et al. Clin Infect Dis 2008; 46:1323–4.
Giannella M, et al. Clin Microbiol Infect 2011; 17:1160–5.
Lee N, et al. J Infect Dis 2009; 200:492–500.
Linko R, et al. Acta Anaesthesiol Scand 2011; 55:971–9.
Viasus D, et al. J Infect 2011; 62:193–9.
Martin-Loeches I, et al. Intensive Care Med 2011; 37:272–83.

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Figure 1. Guide for considering influenza testing when influenza viruses are circulating in the community (regardless of influenza vaccination history)



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Who Should Be Considered for Antiviral Chemoprophylaxis to Prevent Influenza in the Absence of Exposure or an Institutional Outbreak (Preexposure Chemoprophylaxis)?

Recommendations

- Antiviral drugs should not be used for routine or widespread chemoprophylaxis outside of institutional outbreaks;
- Antiviral chemoprophylaxis can be considered in certain situations:
 - Clinicians can consider antiviral chemoprophylaxis for the duration of the influenza season for **adults and children aged ≥3 months who are at very high risk of developing complications from influenza** and for whom **influenza vaccination is contraindicated, unavailable, or expected to have low effectiveness** (eg, persons who are severely immunocompromised) (C-II).
 - Clinicians can consider antiviral chemoprophylaxis for the duration of the influenza season for **adults and children aged ≥3 months who have the highest risk of influenza-associated complications**, such as recipients of hematopoietic stem cell transplant in the first 6–12 months posttransplant and lung transplant recipients (B-II).

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Who Should Be Considered for Antiviral Chemoprophylaxis to Prevent Influenza in the Absence of Exposure or an Institutional Outbreak (Preexposure Chemoprophylaxis)?

- Clinicians can consider **short-term antiviral chemoprophylaxis** in conjunction with prompt administration of inactivated influenza vaccine for unvaccinated adults and children aged ≥3 months who are at high risk of developing complications from influenza in whom influenza vaccination is expected to be effective (but not yet administered) when influenza activity has been detected in the community (C-II).
- Clinicians can consider short-term antiviral chemoprophylaxis for
 - Unvaccinated adults, including healthcare personnel,
 - Children aged ≥3 months who are in close contact with persons at high risk of developing influenza complication during periods of influenza activity when influenza **vaccination is contraindicated or unavailable** and these high-risk persons are unable to take antiviral chemoprophylaxis (C-III).
- Clinicians can consider educating patients and parents of patients to arrange for early empiric initiation of antiviral

• IDSA Influenza Clinical Guidelines 2018 • CID 2019:68 (15 March) • e7 treatment as an alternative to antiviral chemoprophylaxis (C-III).

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Which Antiviral Drugs Should Be Used for Preexposure Chemoprophylaxis for Influenza? Recommendation

- 37. Clinicians should use an **NAI (oral oseltamivir or inhaled zanamivir)** if preexposure chemoprophylaxis for influenza is administered rather than an adamantane antiviral (A-II).

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What Is the Duration of Pre-exposure Antiviral Chemoprophylaxis to Prevent Influenza?

Recommendations

- Clinicians should administer preexposure antiviral chemoprophylaxis for
 - Adults and children aged ≥3 months who are at very high risk of developing complications from influenza (eg, severely immunocompromised persons such as hematopoietic stem cell transplant recipients) for whom influenza vaccination is
 - Contraindicated,
 - Unavailable
 - Expected to have low effectiveness, as soon as influenza activity is detected in the community and continued for the duration of community influenza activity (A-II).
- Clinicians should test for influenza and switch to antiviral treatment dosing in persons receiving preexposure antiviral chemoprophylaxis who become symptomatic, preferably with an antiviral drug with a different resistance profile if not contraindicated (A-II).

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Which Asymptomatic Persons Exposed to Influenza Should Be Considered for Postexposure Antiviral Chemoprophylaxis in a Noninstitutional Setting?

Recommendations

1. Clinicians can consider postexposure antiviral chemoprophylaxis for asymptomatic adults and children aged ≥3 months who are at very high risk of developing complications from influenza (eg, severely immunocompromised persons) and for whom influenza vaccination is
 - Contraindicated,
 - Unavailable, or expected to have low effectiveness,
 - After household exposure to influenza (C-II).
2. Clinicians can consider postexposure antiviral chemoprophylaxis (in conjunction with influenza vaccination) for
 - Adults and children aged ≥3 months who are unvaccinated and are household contacts of a person at very high risk of complications from influenza (eg, severely immunocompromised persons), after exposure to influenza (C-II).
3. Clinicians can consider educating patients and arranging for early empiric initiation of antiviral treatment as an alternative to postexposure antiviral chemoprophylaxis (C-III).

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When Should Postexposure Antiviral Chemoprophylaxis Be Started?

Recommendations

1. Clinicians should administer
 - Postexposure antiviral chemoprophylaxis as soon as possible after exposure, ideally no later than 48 hours after exposure (A-III).
2. Clinicians should not administer once-daily postexposure antiviral chemoprophylaxis if >48 hours has elapsed since exposure.
- Full-dose empiric antiviral treatment should be initiated as soon as symptoms occur, if treatment is indicated (A-III).

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How Long Should Postexposure Antiviral Chemoprophylaxis Be Given?

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Recommendations

- Should administer postexposure antiviral chemoprophylaxis in a nonoutbreak setting for 7 days after the most recent exposure to a close contact with influenza (A-III).
- Clinicians should test for influenza and switch to antiviral treatment dosing in persons receiving postexposure antiviral chemoprophylaxis who become symptomatic, preferably with an antiviral drug with a different resistance profile if not contraindicated (A-III).

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Which Antiviral Drugs Should Be Used for Post exposure Chemoprophylaxis?

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Recommendation

- NAI (inhaled zanamivir or oral oseltamivir) if postexposure chemoprophylaxis for influenza is given, rather than an adamantane antiviral (A-II).

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Control Measures for Managing Institutional Influenza Outbreaks

Resident level	
	<ul style="list-style-type: none"> • Identify and isolate all ill residents or patients with suspected or laboratory-confirmed influenza; encourage ill residents to stay in their rooms as much as possible • Ask ill residents or patients with suspected or laboratory-confirmed influenza to wear facemasks when out of their rooms • Promptly identify influenza virus infection in residents and initiate antiviral treatment in suspected or confirmed influenza cases as soon as possible • Encourage and facilitate frequent hand washing • Educate residents or patients and their families on respiratory etiquette • Arrange beds in rooms housing >1 resident to maximize distance between the heads of beds to at least 2 meters or approximately 6 feet • Once an influenza outbreak is declared (when 2 cases of laboratory-confirmed influenza are identified within 72 hours of each other in residents or patients of the same ward or unit), start empiric antiviral treatment of newly symptomatic residents with a neuraminidase inhibitor as soon as possible

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Control Measures for Managing Institutional Influenza Outbreaks

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Ward/unit level

- Implement droplet precautions when providing care for ill residents or patients, in addition to standard precautions already in place regardless of symptoms.
- Cohort ill residents by rooming together, or in group activities such as dining or recreation
- Post signs diverting nonessential visits
- Minimize or restrict staff working on affected wards from working on nonaffected wards
- Post signs to remind staff and visitors to wash hands, wear facemasks, and to adhere to standard, contact, and droplet precautions when entering rooms of ill residents or patients
- Add distance between individuals during mealtimes and activities, eg, eating just outside of or in their rooms rather than a common dining area
- Keep residents on their wards; prohibit or, as feasible, limit and do not overlap movement of residents of affected wards to nonaffected wards or common areas

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Control Measures for Managing Institutional Influenza Outbreaks

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- Once an outbreak is declared, administer empiric antiviral chemoprophylaxis with a neuraminidase inhibitor as soon as possible to asymptomatic exposed residents on the affected ward or unit
 - Close affected wards to new admissions
 - Once an influenza outbreak is declared, consider whether to offer empiric antiviral chemoprophylaxis with a neuraminidase inhibitor to unvaccinated staff on the affected ward/unit, including staff with influenza vaccine contraindications or immunocompromised staff (who are expected to have poor immune response to vaccination) for the duration of the outbreak
 - If there is substantial antigenic drift between circulating influenza viruses and influenza vaccine virus strains, consider whether to extend empiric antiviral chemoprophylaxis with a neuraminidase inhibitor to all staff on the affected ward/unit with an influenza outbreak, regardless of influenza vaccination status
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Control Measures for Managing Institutional Influenza Outbreaks

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- Have annual influenza vaccination programs in place for residents or patients and healthcare personnel
- Have policies and procedures for identification and management of an influenza outbreak, including occupational health aspects (eg, which staff should receive antiviral treatment or chemoprophylaxis, be referred for influenza testing and antiviral treatment; policies for sick leave and return to work)
- Have mechanisms in place for rapid collection and handling of respiratory specimens from ill residents or patients and healthcare personnel for influenza testing, preferably by molecular assays. If influenza molecular assays are negative, test specimens for other respiratory pathogens, since noninfluenza respiratory viruses and bacteria infections have also been associated with respiratory disease outbreaks in healthcare and long-term care facilities; the nonpharmaceutical control measures apply to these as well
- Implement active daily surveillance for any new respiratory illness (eg, fever, increased work of breathing, coughing, or sneezing) among residents or patients and staff. Respiratory symptoms, even without fever, should trigger suspicion for influenza, especially in elderly individuals. Nonrespiratory manifestations, such as altered mental status, may also be a sign of influenza virus infection in elderly patients

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Control Measures for Managing Institutional Influenza Outbreaks

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- Collect respiratory specimens for influenza testing (preferably by molecular assay such as RT-PCR, if available) from all new symptomatic residents or patients to facilitate identification of the end of the outbreak and inform the extent (units or wards affected) and duration of outbreak control interventions.
 - Any ill staff who develop respiratory symptoms should don a facemask and promptly be excluded from the facility and, if indicated, be offered or referred for empiric antiviral treatment or have influenza testing performed. Institute a policy where ill staff do not return to work until afebrile >24 hours without antipyretic treatment and with improvement in respiratory symptoms or no earlier than 5 days after illness onset, because lack of fever does not necessarily mean lack of infectiousness
 - Post and display information about influenza illness signs and symptoms, facility policies related to influenza prevention and control, influenza vaccine recommendations, outbreak activity, and precautions for visitors and staff
 - Have procedures in place to actively screen all visitors for any illness signs and symptoms, and prohibit anyone with any illness from visiting
 - Offer influenza vaccination to unvaccinated staff members and residents or patients, and oseltamivir chemoprophylaxis to staff for 14 days after influenza vaccination. If influenza vaccine is not available, antiviral chemoprophylaxis can be offered to all unvaccinated staff for the duration of an institutional outbreak
 - Notify local public health authorities as soon as possible of a suspected or confirmed influenza outbreak
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Control Measures for Managing Institutional Influenza Outbreaks

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- Notify local public health authorities as soon as possible of a suspected or confirmed influenza outbreak

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Vaccine

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Recommended composition of influenza virus vaccines for use in the 2019 SOUTHERN HEMISPHERE influenza season

- 27 September 2018
- It is recommended that egg based quadrivalent vaccines for use in the 2019 southern hemisphere influenza season contain the following:
 - an A/Michigan/45/2015 (H1N1)pdm09-like virus;
 - an A/Switzerland/8060/2017 (H3N2)-like virus;
 - a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and
 - a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).
- It is recommended that the A(H3N2) component of NON-EGG-BASED vaccines for use in the 2019 southern hemisphere influenza season be an A/Singapore/INFIMH-16-0019/2016-like virus together with the other vaccine components as indicated above.

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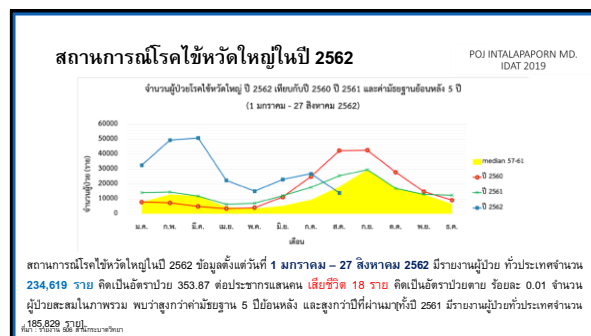
Recommended composition of influenza virus vaccines for use in the **2019 SOUTHERN HEMISPHERE** influenza season
27 September 2018

It is recommended that **egg based** quadrivalent vaccines for use in the 2019 southern hemisphere influenza season contain the following:

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- an A/Switzerland/8060/2017 (H3N2)-like virus;
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It is recommended that the A(H3N2) component of **NON-EGG-BASED** vaccines for use in the 2019 southern hemisphere influenza season be an A/Singapore/INFIMH-16-0019/2016-like virus together with the other vaccine components as indicated above.

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รายงานการเปลี่ยนแปลงสายพันธุ์ไข้หวัดใหญ่ระหว่าง ม.ค. - ส.ค. 2562
โดย ศูนย์ไข้หวัดใหญ่แห่งชาติ สถาบันวิจัยวิทยาศาสตร์สาธารณสุข กรมวิทยาศาสตร์การแพทย์
วันที่ 30 กันยายน 2562

สายพันธุ์ที่เฝ้าระวังในประเทศไทยระหว่างเดือนมกราคม - สิงหาคม 2562					
pdmA(H1N1)	ร้อยละ	A (H3N2)	ร้อยละ	B	ร้อยละ
A/Michigan/45/2015 (H1N1)pdm09	100	A/Switzerland/8060/2017 (H3N2)	14.81	B/Brisbane/60/2008 (Victoria lineage)	3.37
		A/Singapore/INFIMH-16-0019/2016 (H3N2)	85.19	B/Colorado/06/2017 (2 aa deletion in HA) (Victoria lineage)	3.67
				B/Colorado/06/2017 (3 aa deletion in HA) (Victoria lineage)	90.92
				B/Phuket/3073/2013 (Yamagata lineage)	2.04

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Recommended composition of influenza virus vaccines for use in the **2019-2020 northern hemisphere** influenza season
21 February 2019 (updated on 21 March 2019)

It is recommended that quadrivalent vaccines for use in the 2019-2020 northern hemisphere influenza season contain the following:

- an A/Brisbane/02/2018 (H1N1)pdm09-like virus;
- an A/Kansas/14/2017 (H3N2)-like virus;
- a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and
- a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).

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Thank You

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