



# **Beyond the Vaccine**

## **The Role of Antivirals in the Prophylaxis and Treatment of Influenza**

These slides are meant to be used as an accompaniment to the presentation for note taking purposes, they are not intended as a standalone reference.

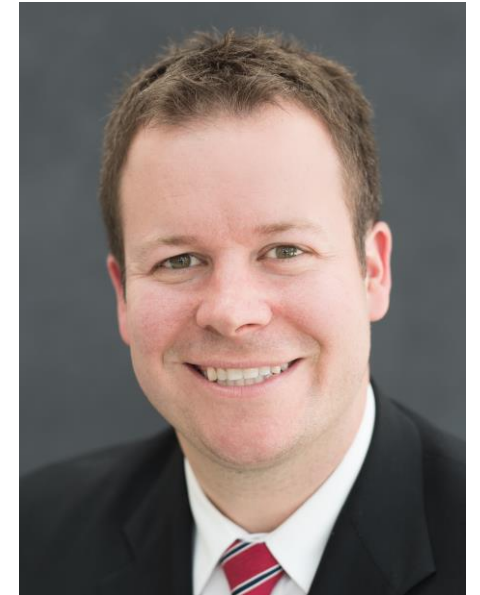


This educational activity is sponsored by Postgraduate Healthcare Education, LLC and supported by an educational grant from Genentech, a member of the Roche Group.

# Faculty

## **Clark Kebodeaux, PharmD, BCACP**

Clinical Associate Professor Pharmacy Practice and Science  
University of Kentucky College of Pharmacy  
Lexington, Kentucky



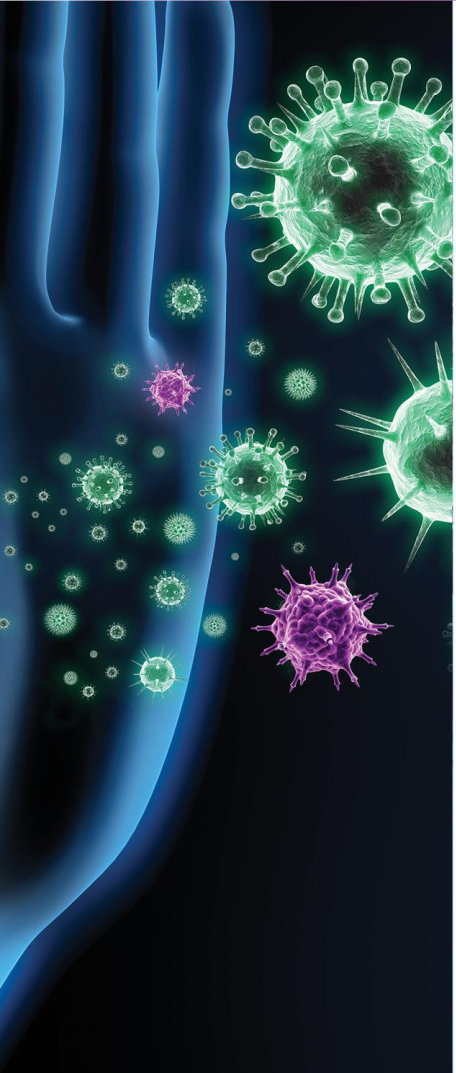
**Dr. Kebodeaux** serves as a Clinical Associate Professor of Pharmacy Practice and Science and Program Director for the PGY1 Community-Based Pharmacy Residency Program at the University of Kentucky College of Pharmacy and a Clinical Ambulatory Care Pharmacist at the Bluegrass Community Health Center in Lexington, Kentucky. He received his PharmD from the University of Kansas School of Pharmacy in Lawrence, Kansas. Dr. Kebodeaux is board certified in ambulatory care.

# Disclosures

**Dr. Kebodeaux** has disclosed that he has no relevant affiliations or financial relationships with a commercial interest to disclose.

The clinical reviewer, **Kyle A. Davis, PharmD**, hereby states that he has no relevant affiliation or financial relationship or relationship to products or devices with a commercial interest related to the content of this activity to disclose.

Susanne Batesko, RN, BSN, Robin Soboti, RPh, and Susan R. Grady, MSN, RN, as well as the planners, managers, and other individuals, not previously disclosed, who are in a position to control the content of Postgraduate Healthcare Education, LLC (PHE) continuing education activities, hereby state that they have no relevant conflicts of interest and no financial relationships or relationships to products or devices during the past 12 months to disclose in relation to this activity. PHE is committed to providing participants with a quality learning experience and to improve clinical outcomes without promoting the financial interests of a proprietary business.



# Accreditation



Postgraduate Healthcare Education, LLC is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

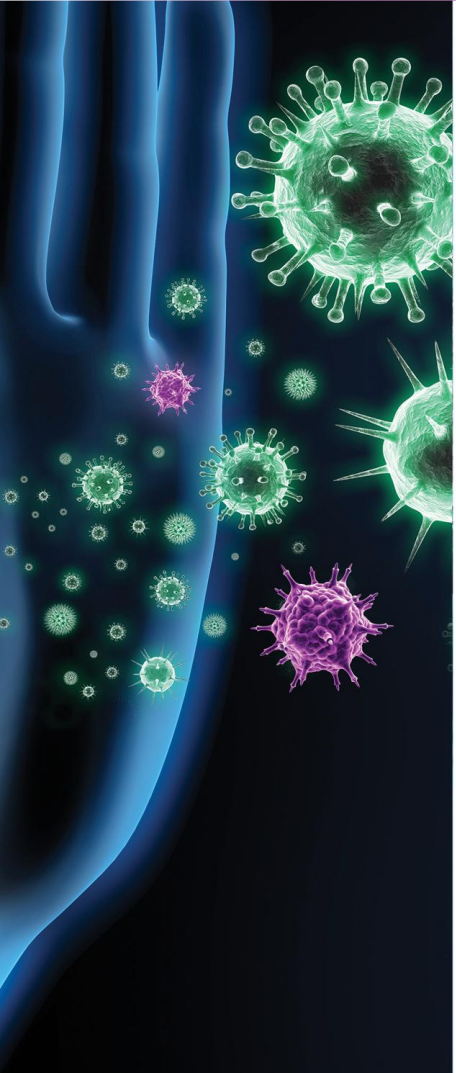
**UAN:** 0430-0000-21-028-H01-P

**Credits:** 1.00 hour (0.1 CEU)

**Type of Activity:** Application

# Learning Objectives

- **Describe** the burden of disease related to influenza
- **Differentiate** the indications for use, dosage regimens, and administration issues among the influenza antivirals
- **Explain** efficacy and safety data of the antivirals for prophylaxis and/or treatment of influenza

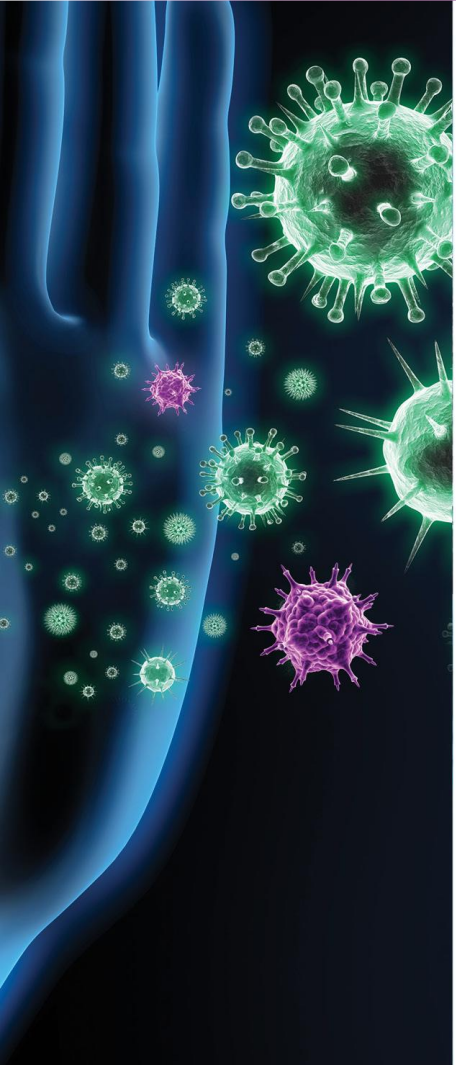


# Influenza

- Influenza is an RNA virus with a varied clinical presentation
  - Ranges from mild, symptomatic disease to severe disease, including death
- Influenza is a respiratory illness primarily spread via droplets
- Most effective method of prevention is annual vaccination
  - Diagnosed influenza is treated with antiviral medications

# Epidemiology

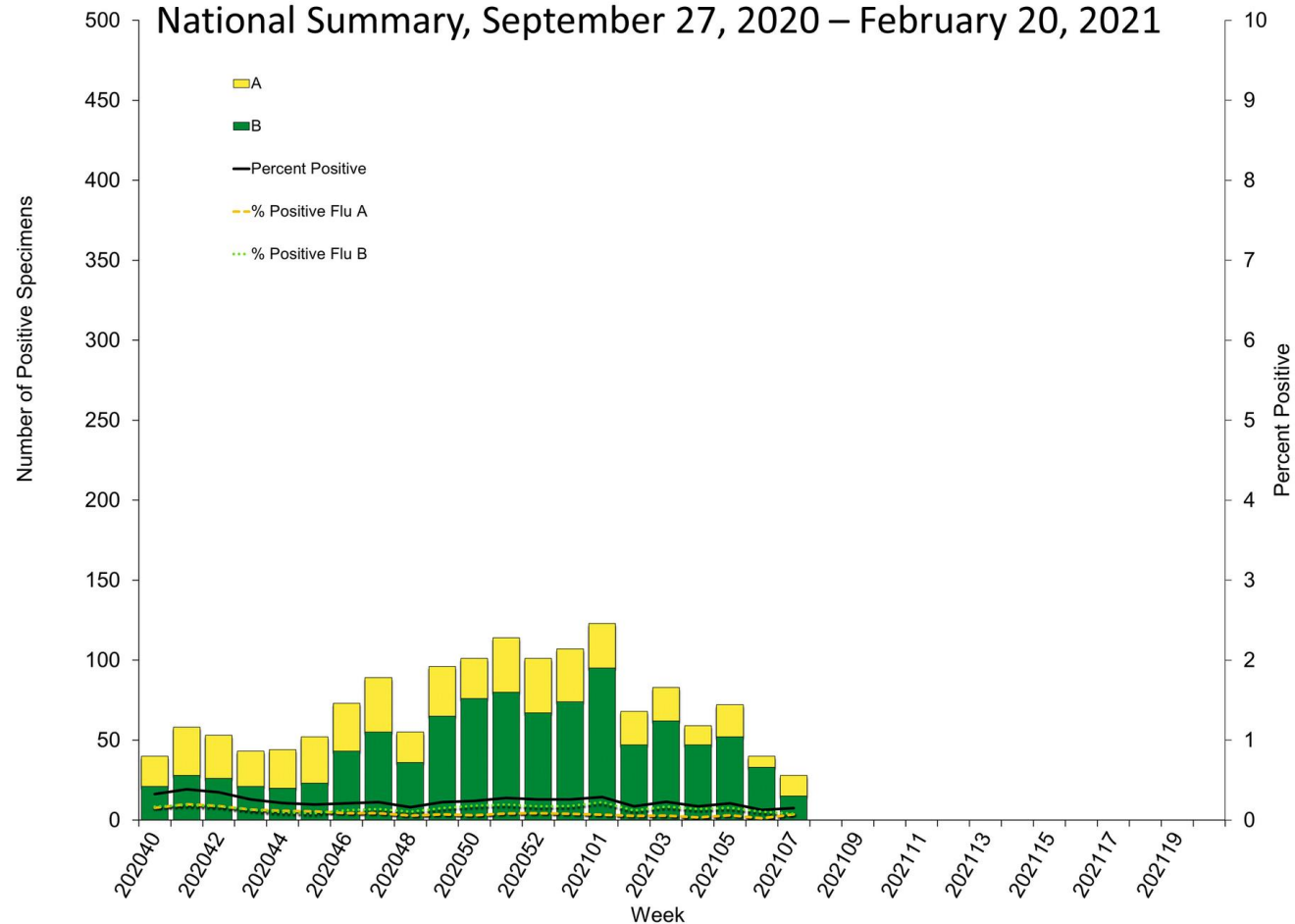
- Symptomatic influenza affects 8% of Americans on average each year
  - Range of 3% to 11%, according to a 2018 Centers for Disease Control and Prevention (CDC) analysis
- Risk increases with age and severity of influenza season





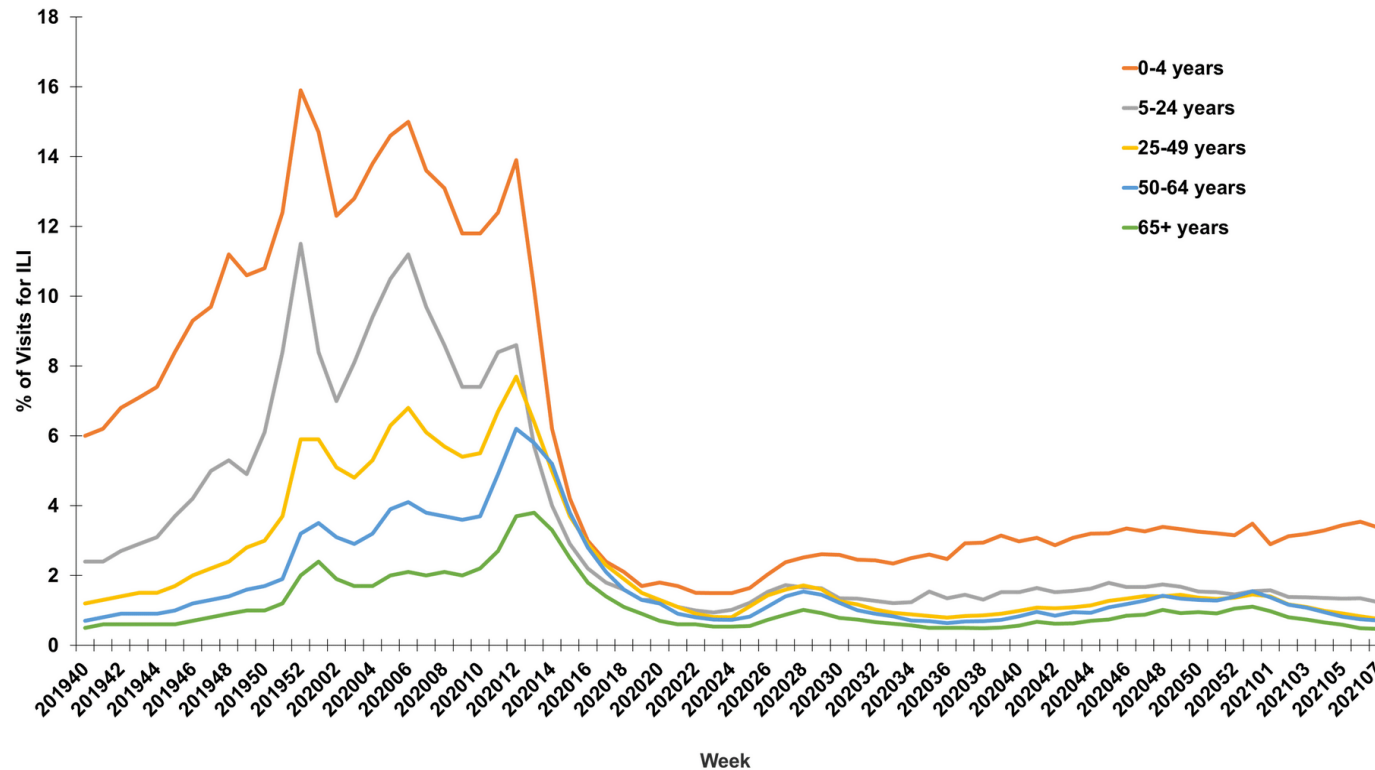
# Epidemiology

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories,  
National Summary, September 27, 2020 – February 20, 2021



# Epidemiology

Percentage of Visits for Influenza-Like Illness (ILI) by Age Group  
Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet),  
Weekly National Summary, 2019-2020 and 2020-2021 Seasons



# Burden of Disease

- Mitigation efforts to contain the COVID-19 pandemic have had a significant impact on influenza activity in the United States
- As of February 20, 2021, the hospitalization rate was 0.6 per 100,000
  - Influenza hospitalization in the 2011-2012 was 2.2x higher
- In the 2019-2020 influenza season, approximately 38 million symptomatic cases of influenza, 18 million office visits, 400,000 hospitalizations, and 22,000 deaths were reported to have occurred in the US

# Pathophysiology

- RNA virus based on antigen presentation
  - Types A, B, and C
- Type A influenza (H\_N\_)
  - Hemagglutinin (HA)
  - Neuraminidase (NA)
- Influenza is named according to the type, location of initial isolation, strain designation, and year of isolation
  - Example (2020-2021):  
A/Brisbane/02/2018 (H1N1)pdm09-like virus

# Clinical Presentation

- Seasonal presentation: Fall-Winter (October-March)
  - Peak: December-February
- Signs/symptoms: Acute presentation
  - Fever or chills
  - Cough, sore throat
  - Runny or stuffy nose
  - Muscle aches, headaches
  - Fatigue
  - Vomiting/diarrhea

# Clinical Presentation

- Complications
  - Sinusitis, ear infections
  - Pneumonia
  - Myocarditis, encephalitis, rhabdomyolysis
  - Serious inflammatory disease and death
- Risk factors
  - 65 years and older
  - Chronic medical conditions
  - Pregnant women
  - Children <5 years old

# Symptoms of Influenza and COVID-19


Influenza	COVID-19
Fever or chills	Fever or chills
Cough	Cough
Sore throat	Sore throat
Runny or stuffy nose	Runny or stuffy nose
Muscle aches	Muscle aches
Headaches	Headaches
Fatigue	Fatigue
Vomiting/diarrhea	<b>Change in or loss of taste or smell</b>

# Comparison of Influenza and COVID-19

	Influenza	COVID-19
<b>Symptom Presentation and Duration</b>	1-4 days postinfection	~5 days postinfection (range 2-14 days)
<b>Contagiousness and Spread</b>	3-4 days	Unknown
<b>Complications</b>	Pneumonia, respiratory, cardiac injury, worsening chronic conditions	Similar to influenza; multisystem inflammatory syndrome in children (MIS-C)

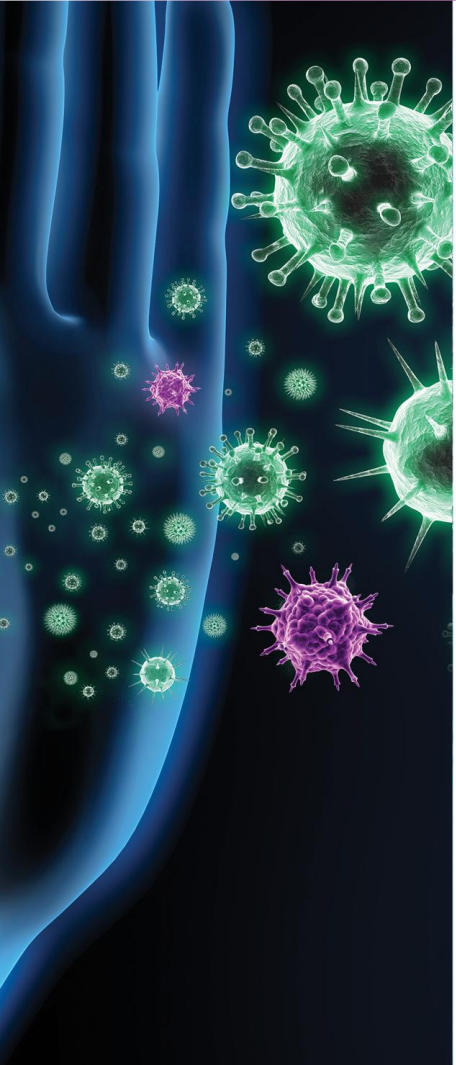


# Role of Vaccination

- 
- An illustration on the left side of the slide shows a human hand in a blue, semi-transparent style. The hand is positioned as if about to be washed. Surrounding the hand are several glowing, spherical virus particles of various colors (green, purple, pink) with spiky surfaces, representing pathogens. The background is dark, making the glowing elements stand out.
- Advisory Committee on Immunization Practices (ACIP) recommends annual influenza vaccination to all patients 6 months of age or older without a valid contraindication for vaccination
  - Significant impact on illness, medical visits, and severe disease
  - Vaccination with personal and systematic actions can impact spread of disease
    - Handwashing, masks, ventilation

# Diagnosis


- Various testing methods
  - Molecular assay (RT-PCR)
  - Rapid influenza diagnostic tests (RIDTs)
  - Rapid molecular assay (nucleic acid/viral RNA)
  - Rapid cell culture
  - Rapid viral culture
- Influenza types A and B
  - CLIA-waived (RIDT and rapid molecular assay)



# Diagnosis

- Rapid influenza diagnostic tests (RIDTs)
- Sensitivity and specificity
  - Compared to RT-PCR
  - Improved with the use of analyzer device
- Important to accurately interpret results with clinical picture
  - False negatives

# Influenza Antivirals

- 
- An illustration of a human hand in shades of blue and purple, with several glowing, spiky virus particles in green and purple floating around it. The background is dark, making the glowing viruses stand out.
- Six FDA-approved antiviral medications
    - Amantadine
    - Rimantadine
    - Oseltamivir (Tamiflu®)
    - Zanamivir (Relenza®)
    - Peramivir (Rapivab®)
    - Baloxavir marboxil (Xofluza®)
  - Amantadine and rimantadine are **not** recommended for use in the US during influenza season

# Oseltamivir

- Neuraminidase inhibitor
- Indication
  - Treatment of acute, uncomplicated influenza in patients 2 weeks of age and older who have been symptomatic for no more than 2 days
  - Prophylaxis of influenza in patients 1 year and older
- Recommended by the CDC and American Academy of Pediatrics (AAP) for chemoprophylaxis in children 3 months to 1 year of age
- Available as a generic

# Oseltamivir

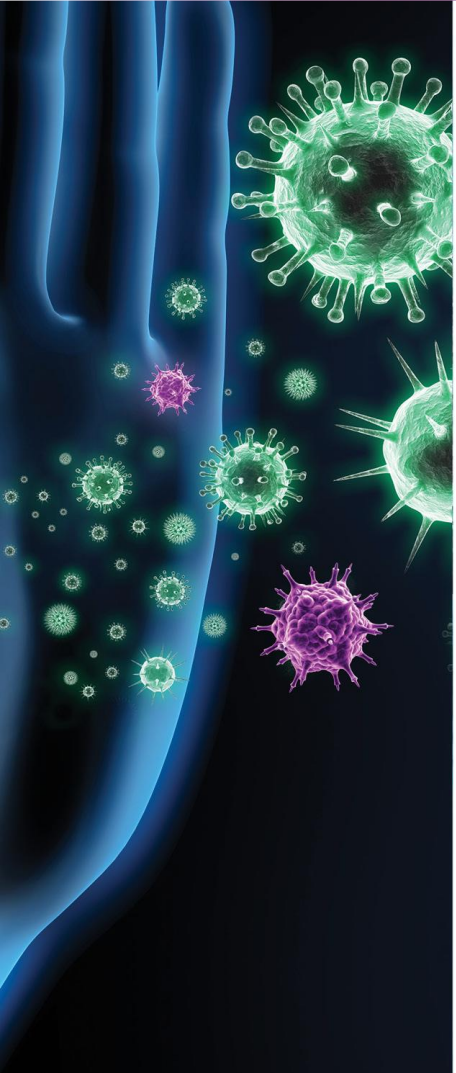
- Dosage/administration
  - 30-mg, 45-mg, 75-mg capsules
  - 6-mg/mL oral suspension
- Adverse events
  - Nausea
  - Vomiting
  - Headache

# Zanamivir

- Neuraminidase inhibitor
- Indication
  - Treatment of influenza in patients aged 7 years and older who have been symptomatic for no more than 2 days
  - Prophylaxis of influenza in patients aged 5 years and older
- Avoid in COPD, respiratory disease
  - History of lactose or milk protein allergy

# Zanamivir

- Dosage/administration
  - Relenza Diskhaler
    - 5 mg/blister
- Adverse events
  - Sinusitis
  - Bronchospasm
  - Dizziness



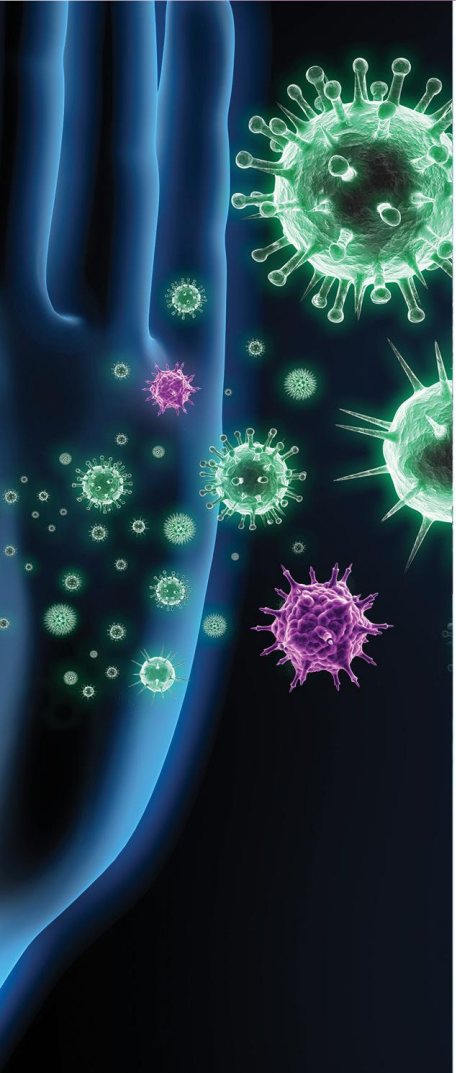


# Peramivir

- Neuraminidase inhibitor
  - Intravenous
- Indication
  - Treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days
  - Not recommended for prophylaxis
- Adverse events
  - Diarrhea
  - Skin reactions/neuropsychiatric events (postmarketing)

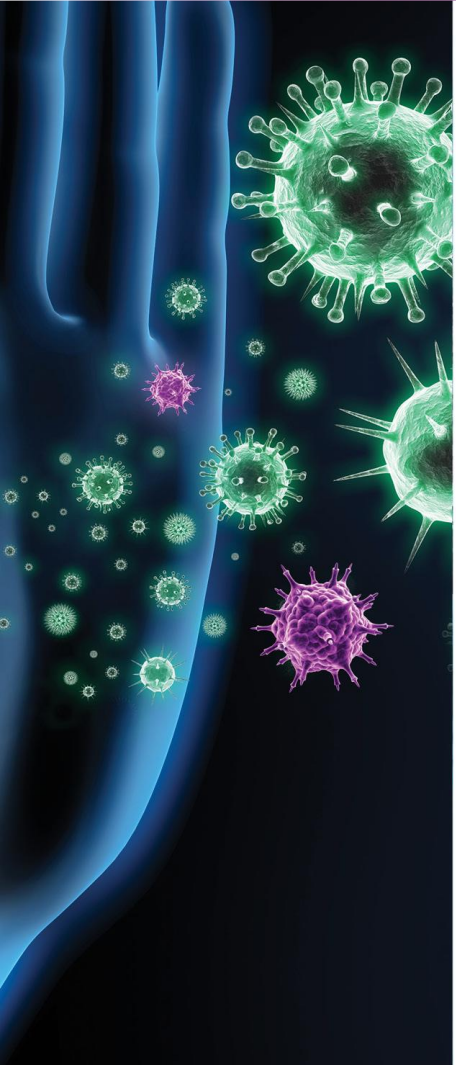
# Peramivir

- Dosage/administration
  - 600 mg infused over 15 minutes
    - 200 mg in 20 mL (10 mg/mL) single use vials
- Adverse events
  - Diarrhea
  - Skin reactions/neuropsychiatric events (postmarketing)



# Baloxavir Marboxil

- Polymerase acidic (PA) endonuclease inhibitor
- Indication
  - Treatment of acute uncomplicated influenza in patients 12 years of age and older who have been symptomatic for no more than 2 days for both healthy individuals and those at high risk for influenza-related complications
  - Postexposure prophylaxis (PEP) of influenza in patients 12 years of age and older following contact with an individual who has influenza



# Baloxavir Marboxil

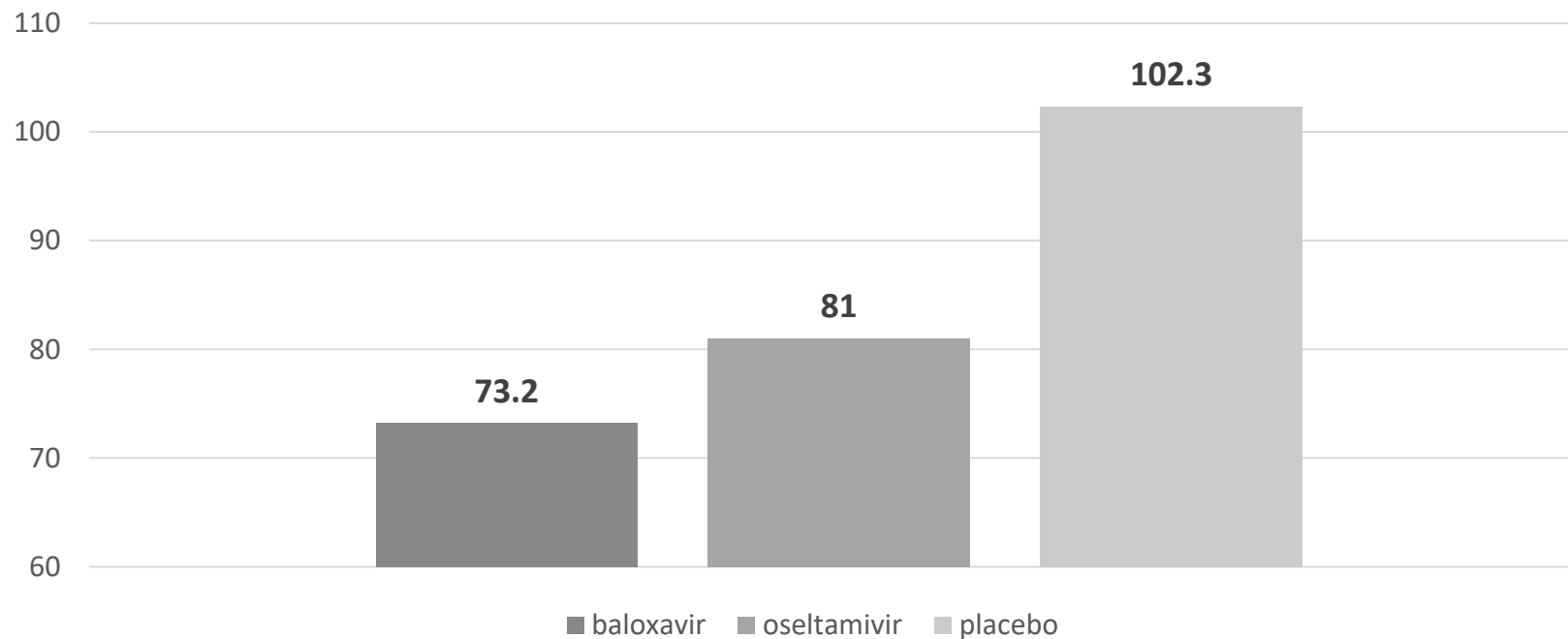
- Dosage/administration
  - Tablet therapy pack
    - 20 mg, 40 mg (x2 for total dose)
- Adverse events
  - Not significant compared to placebo (diarrhea, bronchiolitis, headache)
  - Hypersensitivity

# CAPSTONE-2

- Phase III trial
  - High-risk adolescent and adult outpatients with uncomplicated influenza
- 2184 patients
  - Randomized 1:1:1 (baloxavir:placebo:oseltamivir)
- Baloxavir and oseltamivir have similar efficacy versus placebo in treatment of influenza symptoms with similar safety concerns
  - Supports early intervention for high-risk patients

# CAPSTONE-2


Results: Time to improvement of influenza symptoms (TTIS) in hours



# Influenza Treatment

- Patients at high risk for influenza, with severe disease, or who are hospitalized should be treated with antiviral treatment empirically
  - Suspected influenza within 48 hours of symptom onset (outpatient)
- Outpatient
  - Oseltamivir (Tamiflu)
  - Zanamivir (Relenza)
  - Peramivir (Rapivab)
  - Baloxavir marboxil (Xofluza)
- Inpatient/severe disease
  - Oseltamivir (Tamiflu)

# Influenza Chemoprophylaxis

- 
- An illustration on the left side of the slide shows a human hand in a blue, semi-transparent style. The hand is positioned as if about to touch or hold something. Surrounding the hand are several glowing, spherical virus particles. Some are green with prominent spikes, while others are purple and more irregular in shape. The background behind the hand is dark, making the glowing particles stand out.
- Influenza vaccination
    - Neuraminidase inhibitors are 70% to 90% effective at prevention of influenza disease in addition to routine vaccination
  - Target patient populations: Adults and children >3 months of age
    - Immunocompromised (immunosuppressant medications)
    - Contraindication to influenza vaccine
    - High-risk for complications



# Influenza Treatment and Prophylaxis

	Oseltamivir	Zanamivir	Peramivir	Baloxavir
Treatment (Adults)	75 mg <u>twice</u> daily x 5 days Renal Dosing: CrCl 31-60 mL/min: 30 mg twice daily CrCl 11-30 mL/min: 30 mg once daily	10 mg (two 5-mg inhalations) <u>twice</u> daily x 5 days	>13 y: One 600 mg dose IV for minimum of 15 min x 1 day CrCl 30-49 mL/min: 200 mg CrCl 10-29 mL/min: 100 mg	>12 y: <80 kg: One 40 mg dose ≥80 kg: One 80 mg dose x 1 day
Treatment (Children)	<12 mo: 3 mg/kg/dose twice daily >12 mo: ≤15 kg: 30 mg twice daily >15 to 23 kg: 45 mg twice daily >23 to 40 kg: 60 mg twice daily >40 kg: 75 mg twice daily x 5 days	>7 y: 10 mg (two 5-mg inhalations) twice daily x 5 days	2-12 y: One 12 mg/kg dose, up to 600 mg max, IV for minimum of 15 min x 1 day	See adult dosage
Chemoprophylaxis (Adults)	75 mg <u>once</u> daily x 7 days	10 mg (two 5-mg inhalations) <u>once</u> daily x 7 days	N/A	>12 y: <80 kg: One 40 mg dose ≥80 kg: One 80 mg dose x 1 day
Chemoprophylaxis (Children)	>3 mo & <1 y: 3 mg/kg/dose once daily >12 mo: ≤15 kg: 30 mg once daily >15 to 23 kg: 45 mg once daily >23 to 40 kg: 60 mg once daily >40 kg: 75 mg once daily x 7 days	>5 y: 10 mg (two 5-mg inhalations) once daily x 7 days	N/A	See adult dosage

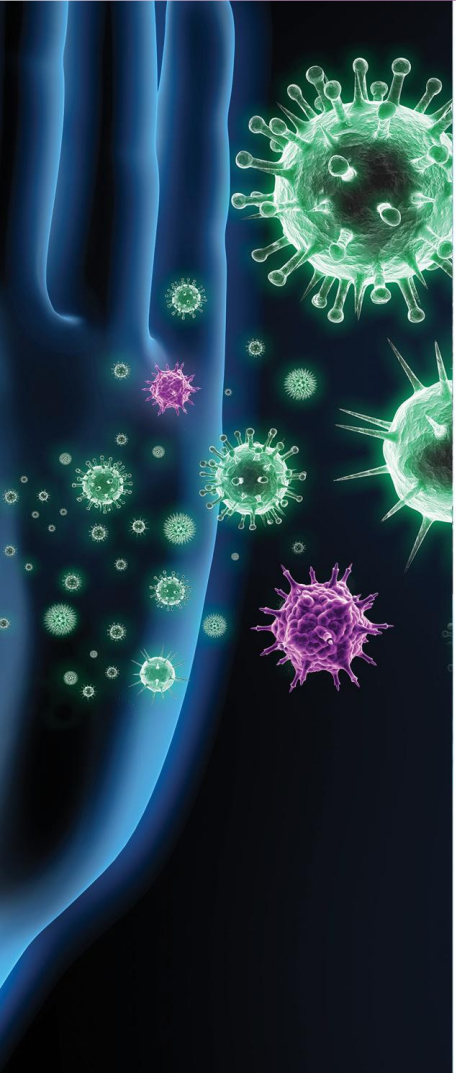
# IDSA Guidelines

- When influenza is active in each community\*:
  - Test for high-risk patients if testing will influence management
    - Elderly
    - Infants
    - Immunocompromised
  - Patients who present with acute onset of respiratory symptoms with or without fever
    - Complication or exacerbation of chronic disease
  - Those not as high risk but may still be indicated for antiviral therapy or chemoprophylaxis

\*Outpatient settings.

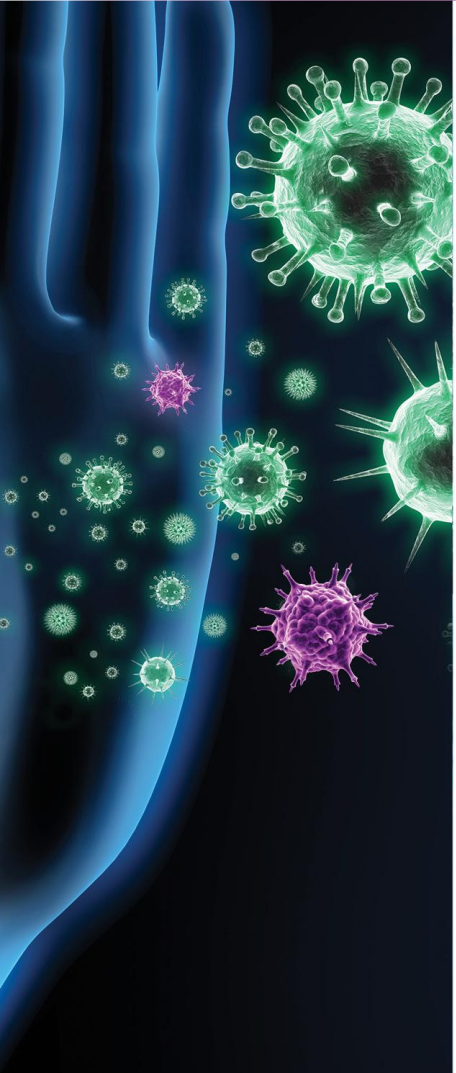
# Pharmacist Considerations

- Appropriateness and adverse effects of influenza treatment
- Chemoprophylaxis and reducing influenza spread
- Access
  - State laws and regulations
  - Point-of-care testing (POCT)
  - Rapid diagnosis and treatment



# Conclusion

- Multiple options exist to improve efficacy and reduce barriers (including adherence)
- Screening and testing are important tools for reducing community spread of influenza disease
- Pharmacists can have significant impact on influenza treatment and prevention through the appropriateness of antiviral treatment



A hand in a blue glove is shown on the left side of the image. The background is dark blue with various colorful virus particles (green, purple, and pink) scattered throughout. A semi-transparent white horizontal band is overlaid across the center of the image, containing the text "Questions & Answers".

# Questions & Answers