BlueCross BlueShield Federal Employee Program

TAMILFU
(oseltamivir)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Tamiflu (oseltamivir phosphate), an antiviral drug, is an ethyl ester prodrug requiring ester hydrolysis for conversion to the active form, oseltamivir carboxylate. Oseltamivir carboxylate is an inhibitor of influenza virus neuraminidase affecting release of viral particles. Efficacy of oseltamivir in patients who begin treatment after 48 hours of symptoms has not been established (1).

Oseltamivir is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) (1).

Regulatory Status

FDA-approved indication: Tamiflu is an influenza neuraminidase inhibitor (NAI) indicated for: (1)

1. Treatment of acute, uncomplicated influenza A and B in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours
2. Prophylaxis of influenza A and B in patients 1 year and older

Limitations of Use: (1)

- Not a substitute for annual influenza vaccination.
- Consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use
- Not recommended for patients with end-stage renal disease not undergoing dialysis.

Persons at high risk of complications from influenza should be considered for antiviral therapy. There is data to suggest that the highest risk of both mortality and serious morbidity (e.g. hospitalization) occurs for severely immunocompromised patients (e.g. hematopoietic stem cell transplant patients) and very elderly (age >85 years). Residents of nursing homes and infants aged <24 months also have high hospitalization rates but lower case-fatality rates than do the other 2 groups (2).

Examples of persons at high risk of complications would be (2):

- Unvaccinated infants aged 12-24 months
- Persons with asthma or other chronic pulmonary diseases, such as cystic fibrosis in children or chronic obstructive pulmonary disease in adults.

- Persons with hemodynamically significant cardiac disease
- Persons who have immunosuppressive disorders or who are receiving immunosuppressive therapy
- HIV-infected persons
- Persons with sickle cell anemia and other hemoglobinopathies
- Persons with diseases that require long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Persons with chronic renal dysfunction
- Persons with cancer
- Persons with chronic metabolic disease, such as diabetes mellitus
- Persons with neuromuscular disorders, seizure disorders, or cognitive dysfunction that may compromise the handling of respiratory secretions
- Adults aged >65 years
- Residents of any age of nursing homes or other long-term care institutions

Per the CDC, chemoprophylaxis is recommended for control of outbreaks in institutional settings (e.g. long-term care facilities for elderly persons and children) and hospitals. CDC recommends antiviral chemoprophylaxis for a minimum of 2 weeks, and continuing up to 1 week after the last known case was identified. Antiviral chemoprophylaxis is recommended for all residents, including those who have received the influenza vaccination (3).

Summary

Tamiflu (oseltamivir phosphate), an antiviral drug, is an ethyl ester prodrug requiring ester hydrolysis for conversion to the active form, oseltamivir carboxylate. Oseltamivir carboxylate is an inhibitor of influenza virus neuraminidase affecting release of viral particles. Oseltamivir is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) (1). Persons at high risk of complications from influenza should be considered for antiviral therapy. There is data to suggest that the highest risk of both mortality and serious morbidity (e.g. hospitalization) occurs for severely immunocompromised patients (e.g. hematopoietic stem cell transplant patients) and very elderly (age >85 years). Residents of nursing homes and infants aged <24 months also have high hospitalization rates but lower case-fatality rates than do the other 2 groups (2).

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Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Tamiflu while maintaining optimal therapeutic outcomes.

References

1. Tamiflu [package insert]. South San Francisco, CA: Genentech, Inc; August 2019.
2. IDSA Seasonal Influenza in Adults and Children – Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America. Clin Infect Dis. (2009) 48 (8): 1003-1032. http://cid.oxfordjournals.org/content/48/8/1003.1/F3.expansion.html.
3. Influenza Antiviral Medications: Summary for Clinicians (2018-2019 influenza season). Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm#dosage.