



IMPORTANT PRESCRIBING INFORMATION

January 22, 2013

Dear Pharmacist:

Genentech is pleased to announce that TAMIFLU for Oral Suspension 6 mg/mL is now indicated for the treatment of acute, uncomplicated illness due to influenza in patients 2 weeks of age and older who have been symptomatic for no more than 2 days.

TAMIFLU is already indicated for the treatment and prophylaxis of uncomplicated influenza caused by viruses types A and B in patients 1 year and older. Please see information on the full Indication with Limitations of Use, and important safety information below.

Safety and efficacy have not been established for prophylaxis of influenza in pediatric patients less than 1 year old and have not been established for treatment of influenza in pediatric patients less than 2 weeks of age.

The recommended dose of TAMIFLU Oral Suspension for treatment of influenza in pediatric patients 2 weeks of age to less than 1 year of age is 3 mg/kg twice daily for 5 days.

Please note the following dispensing details:

- Small volumes will be involved when dispensing for patients less than 1 year of age
- Remove the 10 mL dosing device from packaging when dispensing to patients less than 1 year of age.
- Provide an appropriate dosing device that can accurately measure and administer these smaller volumes

With regard to dosing TAMIFLU for treatment of influenza, please note the following:

- For pediatric patients 2 weeks to less than 1 year of age, use dosing of 3 mg/kg twice daily as shown in the attached dosing table
- For pediatric patients 1 to 12 years of age, please use weight-based dosing as shown in the attached dosing table
- For adults and adolescents ≥ 13 years of age, use 75 mg twice daily for 5 days
- For patients with renal impairment, please refer to the Full Prescribing Information for dosing instructions for these patients

Please see Important Safety Information below, and refer to the Full Prescribing Information for complete information of the most serious and most common risks associated with Tamiflu. In the clinical studies evaluating the tolerability and absorption of TAMIFLU for treatment of influenza in pediatric patients younger than 1 year of age, the safety observed was consistent with that seen in subjects aged 1 year and above, with diarrhea, vomiting and diaper rash being the most frequently reported adverse events.

For more information about TAMIFLU, please visit us at <http://www.tamiflu.com/hcp>. Full Prescribing Information is accompanying this letter, and can be downloaded at <http://www.gene.com/gene/products/information/tamiflu/pdf/pi.pdf>.

With this latest approval, TAMIFLU is now indicated for the treatment of influenza in infants to the elderly.

Sincerely,



Bruce Cooper
Head, U.S. Medical Affairs
Genentech, Inc.

Please see Important Safety Information below.

Treatment and Prophylaxis Dosing of TAMIFLU for Influenza in Pediatric Patients¹

Weight (kg)	Treatment Dosing for 5 days	Prophylaxis Dosing for 10 days ²	Volume of Oral Suspension (6 mg/mL) for each Dose ^{**}	Number of Bottles of Oral Suspension to Dispense	Number of Capsules and Strength to Dispense [§]
Patients from 2 Weeks to less than 1 Year of Age					
Any weight	3 mg/kg twice daily	Not applicable [*]	0.5 mL/kg [†]	1 bottle	Not applicable
Patients 1-12 Years of Age Based on Body Weight					
15 kg or less	30 mg twice daily	30 mg once daily	5 mL	1 bottle	10 Capsules 30 mg
15.1 kg thru 23 kg	45 mg twice daily	45 mg once daily	7.5 mL	2 bottles	10 Capsules 45 mg
23.1 kg thru 40 kg	60 mg twice daily	60 mg once daily	10 mL	2 bottles	20 Capsules 30 mg
40.1 kg or more	75 mg twice daily	75 mg once daily	12.5 mL ^{‡‡}	3 bottles	10 Capsules 75 mg

¹ Treatment should begin within 2 days of onset of symptoms, and prophylaxis should begin within 2 days of exposure to an infected individual.

² Dose adults and adolescents (13 years and older) following close contact with an infected individual for at least 10 days. Dosing in both adult and pediatric patients (1 to 12 years of age) during a community outbreak is up to 6 weeks in immunocompetent patients.

^{*} TAMIFLU is not approved for prophylaxis of patients less than 1 year of age

^{**} A 10 mL oral dosing dispenser is provided with the oral suspension. In the event that the dispenser provided is lost or damaged, another dosing dispenser may be used to deliver the volumes.

[†]For patients less than 1 year of age, remove the provided 10 mL oral dosing dispenser from the packaging, and provide an appropriate dosing device that can accurately measure and administer small volumes

^{‡‡}Delivery of this TAMIFLU for Oral Suspension dose requires administering 10 mL followed by another 2.5 mL.

[§]Oral Suspension is the preferred formulation for patients who cannot swallow capsules.

Indication and Limitations of Use

TAMIFLU is indicated for the treatment of acute, uncomplicated illness due to influenza infection in patients 2 weeks of age and older who have been symptomatic for no more than 2 days.

TAMIFLU is also indicated for the prophylaxis of influenza in patients 1 year and older.

- Efficacy of TAMIFLU in patients who begin treatment after 48 hours of symptoms has not been established.
- TAMIFLU is not a substitute for early and annual vaccination as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices.
- There is no evidence for efficacy of TAMIFLU in any illness caused by agents other than influenza viruses types A and B.
- Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use TAMIFLU.

Important Safety Information

Severe Allergic Reactions

- TAMIFLU is contraindicated in patients who have had severe allergic reactions such as anaphylaxis or serious skin reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme to any component of TAMIFLU.
- In postmarketing experience, cases of anaphylaxis and serious skin reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome and erythema multiforme, have been reported with TAMIFLU. TAMIFLU should be stopped and appropriate treatment instituted if an allergic-like reaction occurs or is suspected.

Neurologic Symptoms

- Influenza can be associated with a variety of neurologic and behavioral symptoms, which can include events such as hallucinations, delirium and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease.
- There have been postmarketing reports (mostly from Japan) of delirium and abnormal behavior leading to injury, and in some cases resulting in fatal outcomes, in patients with influenza who were receiving TAMIFLU. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made but they appear to be uncommon based on TAMIFLU usage data. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of TAMIFLU to these events has not been established. Closely monitor patients with influenza for signs of abnormal behavior. If neuropsychiatric symptoms occur, evaluate the risks and benefits of continuing treatment for each patient.

Bacterial Infections

- Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. TAMIFLU has not been shown to prevent such complications.

Limitations of Populations Studied

- Efficacy of TAMIFLU in the treatment of influenza in patients with chronic cardiac disease and/or respiratory disease has not been established. No difference in the incidence of complications was observed between the treatment and placebo groups in this population. No information is available regarding treatment of influenza in patients with any medical condition sufficiently severe or unstable to be considered at imminent risk of requiring hospitalization.
- Efficacy of TAMIFLU for treatment or prophylaxis of influenza has not been established in immunocompromised patients.
- Safety and efficacy of TAMIFLU for treatment of influenza in pediatric patients less than 2 weeks of age have not been established.
- Safety and efficacy of TAMIFLU for prophylaxis of influenza have not been established for pediatric patients less than 1 year of age.

Concurrent Use with Live Attenuated Influenza Vaccine

- The concurrent use of TAMIFLU with live attenuated influenza vaccine (LAIV) intranasal has not been evaluated. However, because of the potential for interference between these products, LAIV should not be administered within 2 weeks before or 48 hours after administration of TAMIFLU, unless medically indicated.

Most Common Adverse Reactions

- The safety profile observed in pediatric patients 2 weeks to less than 1 year of age was consistent with the established safety profile of pediatric subjects aged 1 year and above, with vomiting, diarrhea and diaper rash being the most frequently reported adverse reactions.
- Adverse events that occurred more frequently in patients treated with TAMIFLU than in patients taking placebo and occurred in $\geq 2\%$ of patients were (TAMIFLU %, placebo %):
 - Treatment in adults—nausea (10%, 6%), vomiting (9%, 3%)
 - Treatment in pediatrics—vomiting (15%, 9%), abdominal pain (5%, 4%), ear disorder (2%, 1%)
 - Prophylaxis of adults—nausea (7%, 3%), diarrhea (3%, 2%), vomiting (2%, 1%), abdominal pain (2%, 1%)
 - Prophylaxis of pediatrics—vomiting (10%, 2%), abdominal pain (3%, 0%), nausea (4%, 1%)

Please see accompanying full Prescribing Information.