

December 1, 2009

IMPORTANT TAMIFLU SUPPLY INFORMATION

Dear Healthcare Professional:

Increased Supply of Tamiflu Now Available for Pediatric Patients

Roche is pleased to announce there is increased supply of pediatric dosing formulations of Tamiflu now available. The company is confident that there is ample supply of Tamiflu for use in children and adults to meet current demand. This increased supply provides healthcare providers the flexibility they need to meet the needs of their pediatric influenza patients.

An initial supply of Tamiflu Oral Suspension was shipped to wholesalers and pharmacies in early December 2009. This is in addition to the significant quantities of Tamiflu Small Capsules (30 mg and 45 mg) shipped in November. Roche expects to provide Tamiflu Oral Suspension and Small Capsules (30mg, 45mg) through the remainder of this year and throughout the 2009/2010 influenza season.

Flexibility of Tamiflu for Healthcare Providers*

The multiple formulations and mixing options of Tamiflu available provide healthcare providers the flexibility to treat those pediatric influenza patients who can and cannot swallow capsules:

- For those pediatric patients that **can** swallow capsules, Tamiflu is provided in the following strengths:
 - 30mg and 45mg capsules (Tamiflu Small Capsules)
 - 75mg capsules (patients >88lbs)
- For those pediatric and adult patients that **cannot** swallow capsules, the following options are available:
 - Tamiflu Oral Suspension
 - Tamiflu 30mg, 45mg and 75mg capsules mixed at home with a sweetened liquid
 - Pharmacy compounding of Tamiflu 75mg capsules into an oral suspension

Important Information for Physicians*

When prescribing Tamiflu for your patients, please remember to include the following important information on the prescription form:

- Tamiflu dosage in **mg**, based on patient's weight
- Tamiflu formulation: oral suspension or capsules (capsules available as 30mg, 45 mg, and 75 mg strengths)
- Frequency (treatment: twice daily, prophylaxis: once daily)
- Length of therapy (treatment: 5 days, prophylaxis: typically 10 days (please refer to prescribing information for more details))

**Please see accompanying complete Prescribing Information*

Indications

TAMIFLU is indicated for the treatment of uncomplicated influenza caused by viruses types A and B in patients 1 year 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.

TAMIFLU is not a substitute for early and annual vaccination as recommended by the Centers for Disease Control's Advisory Committee on Immunization Practices (ACIP).

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 benefits of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use TAMIFLU.

Safety Information

Vaccination is considered the first line of defense against influenza.

There is no evidence for efficacy against any illness caused by agents other than influenza types A and B.

Treatment efficacy in subjects with chronic cardiac 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 at imminent risk of requiring hospitalization.

Efficacy of TAMIFLU has not been established in immunocompromised patients.

Safety and efficacy of repeated treatment or prophylaxis courses have not been studied.

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.

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.

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. Patients with influenza should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.

In postmarketing experience, rare cases of anaphylaxis and serious skin reactions, including toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme, have been reported with TAMIFLU.

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%), bronchitis (2%, 2%)
- Treatment in pediatrics – vomiting (15%, 9%), abdominal pain (5%, 4%), epistaxis (3%, 3%), ear disorder (2%, 1%)
- Prophylaxis of adults – headache (18%, 18%), 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%)

Sincerely,



Hal Barron, MD

Executive Vice President
Head Global Development
Chief Medical Officer