CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

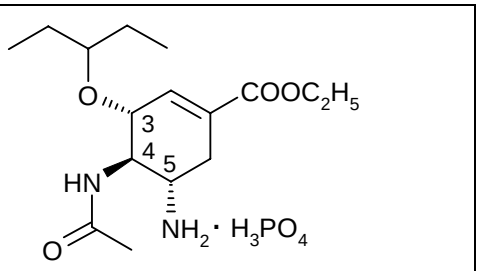
021246Orig1s045 and 021087Orig1s062

CHEMISTRY REVIEW(S)

ONDQA Pre-Marketing Assessment Division II
Quality Assessment for Efficacy Supplement

Tamiflu (oseltamavir phosphate) For Suspension, 6 mg/mL **Roche**
NDA 21-246 / S-045 (EDR-032; SD-369
Submission Date: June 21, 2012
PDUFA Date: Dec 21, 2012

Tamiflu (oseltamavir phosphate) Capsules, 30, 45 and 75 mg
NDA 21-087 / S-062 (EDR-009; SD-875)



Oseltamavir Phosphate

Summary:
This efficacy supplement provides for expanded patient population (treatment) and revised dosing recommendations for children with post conceptual ages of (b) (4) weeks to 1 year, based on two clinical studies (CASG114 and WP22849). The proposed dosage is 3 mg/kg twice a day for 5 days.

No new facilities are listed on the 356h form, nor is there any info on manufacturing facilities in Section 1.1.2. No CMC information is included in Module 2, and there is no Module 3.

The draft labeling available on Dec 19, 2012 was review from the CMC perspective, and the labeling in the last Annual Report (Dec 2011) was also consulted. There are no changes to the Description or How Supplied sections of the Prescribing Information, and no CMC-related edits to the Patient Counseling Information. No container labels are provided.

The only CMC-related changes to the Patient Information section relate to the storage recommendations. Because the sponsor declined to accept the recommendations from the Medical Policy reviewer (Dr. Latonia Ford) the following clarification was sent:

We hope the following will clarify the reasoning behind our requests for the storage language in the Patient Instructions.

In the Prescribing Information we use language that is appropriate for pharmacists and others with technical expertise. The capsules can be stored under USP controlled room

conditions (a common approach for US marketed product), and the oral suspension can be stored for up to 10 days at USP controlled room temperature, or up to 17 days under refrigeration.

In the Patient Instructions, CDER recommends using simplified language, mentioning "room temperature", and including a temperature range that is a reasonable approximation of room temperature (with the deg F listed first). The 15-30 deg range for short-term excursions was felt to be too wide, so we have been recommending 20-25 deg C for approximately the last year. So, where Section 16 of the Prescribing Information calls for USP Controlled Room Temperature, we recommend for the Patient Instructions the statement that we conveyed previously:

- Store [product name] at room temperature between 68°F to 77°F (20°C to 25°C).

This is the reason we recommend the following language:

- Store TAMIFLU capsules at room temperature between 68°F to 77°F (20°C to 25°C).
- Store TAMIFLU for oral suspension in the refrigerator for up to 17 days between 36ºF to 46ºF (2ºC to 8ºC)
- Store TAMIFLU for oral suspension for up to 10 days at room temperature between 68°F to 77°F (20°C to 25°C).
- Safely throw away any unused TAMIFLU that is out of date or no longer needed.

The Patient Instructions were revised per FDA recommendations in the labeling submitted Dec 20, 2012.

In Section 1.12, the applicant requests a categorical exclusion from the requirements to prepare an Environmental Assessment. Although some increase in use of the drug may result from the change in labeling, the supplement meets the requirements of a categorical exclusion under:

- 21 CFR §25.31(b) because the estimated concentration of the active drug substance at the point of entry, referred to as the Expected Introduction Concentration (EIC), into the aquatic environment will be below 1 part per billion (ppb). To the best of the firm's knowledge, no extraordinary circumstances exist in regards to this action.

Conclusions:
This supplement is recommended for approval from the CMC perspective. The only CMC issue is the categorical exclusion from the requirement to perform an environmental assessment. This should be granted, since the applicant has provided an appropriate claim per 21 CFR §25.31.

Stephen P. Miller, Ph.D.
CMC-Lead

See DARRTS
Date

Thomas F. Oliver, Ph.D.
Branch Chief

See DARRTS
Date

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/s/

STEPHEN MILLER
12/21/2012

THOMAS F OLIVER
12/21/2012

ONDQA Pre-Marketing Assessment Division II
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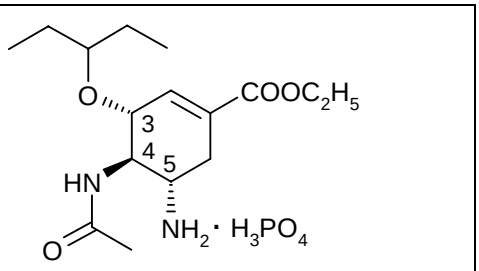

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Stephen P. Miller, Ph.D.	*See DARRTS*
CMC-Lead	Date
Thomas F. Oliver, Ph.D.	*See DARRTS*
Branch Chief	Date

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/s/

STEPHEN MILLER
07/31/2012

THOMAS F OLIVER
08/06/2012