1.3 Limitations of Use

Oseltamivir Phosphate is not a substitute for early influenza vaccination on an annual basis as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices.

Influenza viruses change over time. Emergence of resistance substitutions could

Prepared Pharmaceuticals Inc.
OSELTAMIVIR PHOSPHATE—oseltamivir phosphate for suspension

1 INDICATIONS AND USAGE

FULL PRESCRIBING INFORMATION: CONTENTS

1 INDICATIONS AND USAGE

1.1 Treatment of Influenza

Oseltamivir Phosphate for Oral Suspension is indicated for the treatment of acute, uncomplicated illness due to influenza A and B infection in patients 2 weeks of age and older who have been symptomatic for no more than 48 hours.

1.2 Prophylaxis of Influenza

Oseltamivir Phosphate for Oral Suspension is indicated for the prophylaxis of influenza A and B in patients 2 years of age and older who have been symptomatic for no more than 48 hours.

1.3 Limitations of Use

Oseltamivir Phosphate is an influenza neuraminidase inhibitor (NAI) indicated for:

Recent Major Changes

15 PATIENT COUNSELING INFORMATION

16 HOW SUPPLIED/STORAGE AND HANDLING

14.2 Prophylaxis of Influenza

14.1 Treatment of Influenza

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

12.4 Microbiology

12.3 Pharmacokinetics

12.1 Mechanism of Action

12.2 Preclinical Pharmacology

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7 DRUG INTERACTIONS

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5 ADVERSE REACTIONS

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3 WARNINGS AND PRECAUTIONS

2 DOSAGE AND ADMINISTRATION

1 DOSAGE FORMS AND STRENGTHS

Full Prescribing Information: Contents*
2.1 Dosage and Administration Overview

Administer oseltamivir phosphate for oral suspension for the treatment of influenza in patients 2 weeks of age or older (see Dosage and Administration (2.2)) or for prophylaxis of influenza in patients 1 year and older (see Dosage and Administration (2.3)) using:

- Oseltamivir phosphate for oral suspension (supplied as a powder). This is the preferred formulation (6 mg per mL) for patients who cannot swallow capsules.
- Oseltamivir phosphate for oral suspension (6 mg per mL) prepared from the powder. This is produced by mixtures of 45 mg of oseltamivir phosphate powder with water to produce the oral suspension (see Dosage and Administration (2.5)).

The oral suspension may be taken with or without food; however, tolerability may be enhanced if oseltamivir phosphate for oral suspension is taken with food.

Adjust the oseltamivir phosphate for oral suspension dosage in patients with moderate or severe renal impairment (see Dosage and Administration (2.4)).

For patients who cannot swallow capsules, oseltamivir phosphate for oral suspension is the preferred formulation.

2.2 Recommended Dosage for Treatment of Influenza

Initiate treatment with oseltamivir phosphate for oral suspension within 48 hours of influenza symptom onset.

Adults and Adolescents (13 years of age and older)
The recommended oral dosage of oseltamivir phosphate for oral suspension for treatment of influenza in adults and adolescents 13 years and older is 75 mg twice daily (32.5 mL of oral suspension twice daily) for 5 days.

Pediatric Patients (2 weeks of age through 12 years of age)
Table 1 displays the recommended dosage of oseltamivir phosphate for oral suspension for treatment of influenza in pediatric patients 2 weeks of age through 12 years of age and provides information about prescribing the formulation for oral suspension.

2.3 Recommended Dosage for Prophylaxis of Influenza

Initiate post-exposure prophylaxis with oseltamivir phosphate for oral suspension within 48 hours following close contact with an infected individual. Initiate seasonal prophylaxis with oseltamivir phosphate for oral suspension during a community outbreak.

Adults and Adolescents (13 years of age and older)
The recommended dosage of oseltamivir phosphate for oral suspension for prophylaxis of influenza in adults and adolescents 13 years and older is 75 mg orally once daily (32.5 mL of oral suspension once daily) for at least 10 days following close contact with an infected individual and up to 6 weeks during a community outbreak. In immunocompromised patients, oseltamivir phosphate for oral suspension may be continued for up to 12 weeks (see Use in Specific Populations (8.6)). The duration of protection lasts for as long as oseltamivir phosphate for oral suspension is continued.

Pediatric Patients (2 weeks of age through 12 years of age)
Table 1 displays the recommended oral dosage of oseltamivir phosphate for oral suspension for prophylaxis of influenza in pediatric patients 2 weeks of age through 12 years of age and provides information about prescribing the formulation for oral suspension.

Table 1: Oseltamivir Phosphate for Oral Suspension Dosage Recommendations in Pediatric Patients for Treatment and Prophylaxis of Influenza

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Treatment Prophylaxis Dosage Recommendations</th>
<th>Volume of Oral Suspension (6 mL/g)</th>
<th>Number of Bottles of Oral Suspension to Dispense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients 2 Weeks to less than 1 Year of Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any weight</td>
<td>1 mg/kg twice daily</td>
<td>0.5 mL/kg</td>
<td>1 bottle</td>
</tr>
<tr>
<td>Patients 1 to 12 Years of Age Based on Body Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 kg or less</td>
<td>10 mg once daily</td>
<td>5 mL</td>
<td>1 bottle</td>
</tr>
<tr>
<td>15.1 kg to 22 kg</td>
<td>15 mg once daily</td>
<td>45 mg once daily</td>
<td>5 mL</td>
</tr>
<tr>
<td>23 kg to 40 kg</td>
<td>30 mg once daily</td>
<td>10 mL</td>
<td>1 bottle</td>
</tr>
<tr>
<td>40.1 kg or more</td>
<td>75 mg once daily</td>
<td>30 mL</td>
<td>3 bottles</td>
</tr>
</tbody>
</table>

Table 2: Recommended Dosage Modifications for Treatment and Prophylaxis of Influenza in Adult Patients with Renal Impairment or End Stage Renal Disease (ESRD) on Dialysis

<table>
<thead>
<tr>
<th>Renal Impairment (Creatinine Clearance)</th>
<th>Recommended Treatment Regimen</th>
<th>Recommended Prophylaxis Regimen†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt;30 mL/min/1.73 m²)</td>
<td>75 mg twice daily for 5 days</td>
<td>75 mg once daily</td>
</tr>
<tr>
<td>Moderate (&gt;30-60 mL/min/1.73 m²)</td>
<td>30 mg twice daily for 5 days</td>
<td>30 mg once daily</td>
</tr>
<tr>
<td>Severe (&gt;10-30 mL/min/1.73 m²)</td>
<td>30 mg once daily</td>
<td>30 mg every other day</td>
</tr>
<tr>
<td>ESRD Patients on Hemodialysis (≥160 mL/min)</td>
<td>30 mg immediately and then 30 mg after every hemodialysis cycle (a total of 60 mg every other day)</td>
<td>30 mg immediately and then 30 mg after every hemodialysis cycle</td>
</tr>
<tr>
<td>ESRD Patients on Continuous Ambulatory Peritoneal Dialysis (CAPD)</td>
<td>A single 30 mg dose administered immediately</td>
<td>30 mg immediately and then 30 mg on alternate days</td>
</tr>
<tr>
<td>ESRD Patients not on Dialysis</td>
<td>Oseltamivir Phosphate for Oral Suspension is not recommended</td>
<td>Oseltamivir Phosphate for Oral Suspension is not recommended</td>
</tr>
</tbody>
</table>

† Oseltamivir phosphate for oral suspension can be used for 20 mL daily dosing. The recommended duration of post-exposure prophylaxis is at least 10 days and the recommended duration for community outbreak prophylaxis is up to 12 weeks (or up to 6 weeks in immunocompromised patients). Data derived from studies in continuous ambulatory peritoneal dialysis (CAPD) patients.

2.5 Preparation and Storage of Constituted Oseltamivir Phosphate for Oral Suspension

Prior to dispensing to the patient, constitute oseltamivir phosphate for oral suspension (supplied as powder) as follows:

1. Tap the closed bottle containing the oseltamivir phosphate powder several times to loosen the powder.
2. Measure 55 mL of water in a graduated cylinder.
3. Add the total amount of water to constitute the bottle.
4. Cap the bottle with child-resistant cap tightly and shake the closed bottle well for 15 seconds.
5. Label the bottle with instructions for Shake Well Before Use.
6. The constituted oral suspension contains 360 mg of oseltamivir base per 60 mL of volume (6 mg per mL) and is white, tutti-fruits-flavored. Use the constituted oral suspension within 17 days of preparation when stored under refrigeration, 2° to 8°C (36° to 46°F), or within 10 days if stored at controlled room temperature, 25°
Oseltamivir phosphate (16%) compared to placebo (8%).

5.1 Serious Skin/Hypersensitivity Reactions
Cases of anaphylaxis and serious skin reactions including toxic epidermal necrolysis, Stevens-Johnson Syndrome, and erythema multiforme have been reported in postmarketing experience with oseltamivir phosphate. Stop oseltamivir phosphate for oral suspension immediately and seek medical attention if a patient develops symptoms consistent with a serious skin reaction.

5.2 Neuropsychiatric Events
Serious neuropsychiatric events, including delirium, hallucinations, and delusions, have been reported in pediatric and adult subjects. Oseltamivir phosphate for oral suspension is contraindicated in patients with known serious hypersensitivity to oseltamivir phosphate (see Contraindications (4) and Adverse Reactions (6.2)).

5.3 Risk of Bacterial Infections
Because children are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse Reactions from Treatment and Prophylaxis Trials in Adult and Adolescent Subjects 13 Years of Age and Older

The overall safety profile of oseltamivir phosphate is based on data from 2,464 adult and adolescent subjects that received the recommended dosage of 75 mg orally twice daily for 5 days for treatment of influenza and 1,943 adult and adolescent subjects that received the recommended dosage of 75 mg orally once daily for up to 8 weeks for prophylaxis of influenza in clinical trials.

The most common adverse reactions in the pooled treatment and pooled prophylaxis trials in adults and adolescents are displayed in Table 5. The majority of these adverse reactions were reported on a single occasion, occurred on either the first or second treatment day and resolved spontaneously within 1-2 days. This summary includes otherwise healthy adults/adolescents and subjects "at risk" (subjects at higher risk of developing complications associated with influenza, e.g., elderly patients and patients with chronic cardiac or respiratory disease). In general, the safety profile in the subjects "at risk" was qualitatively similar to that in otherwise healthy adults/adolescents.

Table 5: Adverse Reactions (6.2)

<table>
<thead>
<tr>
<th>System/Class</th>
<th>Oseltamivir Phosphate 75 mg twice daily (n = 2468)</th>
<th>Placebo (n = 1977)</th>
<th>Oseltamivir Phosphate 75 mg once daily (n = 1943)</th>
<th>Placebo (n = 1586)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10%</td>
<td>8%</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Headache</td>
<td>8%</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2%</td>
<td>1%</td>
<td>17%</td>
<td>16%</td>
</tr>
<tr>
<td>Other Disorders</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

Adverse Reactions from Treatment and Prophylaxis Trials in Pediatric Subjects 3 years of age and older

A total of 1,453 pediatric subjects (including otherwise healthy pediatric subjects aged 3 years of age and older and pediatric subjects admitted to hospitals for the treatment of influenza) participated in clinical trials of oseltamivir phosphate given for the treatment of influenza. A total of 838 pediatric subjects received treatment with oseltamivir phosphate for oral suspension twice at 4 mg per kg twice daily for 5 days or weight-based dosing. Vomiting was the only adverse reaction reported at a frequency of ≥1% in subjects receiving oseltamivir phosphate (16%) compared to placebo (8%).

Adverse Reactions from Treatment and Prophylaxis Trials in Immunocompromised Subjects

In a 12-week seasonal prophylaxis study in 475 immunocompromised subjects, including 138 pediatric subjects aged 1 to 12 years of age, the safety profile in the 238 subjects receiving oseltamivir phosphate 75 mg once daily was consistent with that observed in other pediatric and adult subjects.
previously observed in other oseltamivir phosphate prophylaxis clinical trials (see Clinical Studies [14.2]).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of oseltamivir phosphate. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to oseltamivir phosphate exposure.

General disorders and administration site conditions: Swelling of the face or tongue, allergy, anaphylaxis/anaphylactoid reactions, hypotension
Skin and subcutaneous tissue disorders: Skin rash, urticaria, angioedema, toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme (see Warnings and Precautions [5.12])
Gastrointestinal Disorders: Gastrointestinal bleeding, hemorraghic colitis
Cardiac
Hepatobiliary Disorders: Hepatitis, liver function tests abnormal
Nervous System Disorders: Seizure
Metabolism and Nutrition Disorders: Aggravation of diabetes
Psychiatric Disorders: Abnormal behavior, delirium, including symptoms such as hallucinations, agitation, anxiety, altered level of consciousness, confusion, hallucinations, delirium (see Warnings and Precautions [5.12])

7 DRUG INTERACTIONS

7.1 Influenza Vaccines

There are no adequate and well-controlled studies with oseltamivir phosphate for oral suspension in pregnant women to inform a drug-associated risk of adverse development outcomes. Available published epidemiological data suggest that oseltamivir phosphate for oral suspension, taken in any trimester, is not associated with an increased risk of birth defects. However, these studies individually are limited by small sample sizes, use of different comparison groups, and some lacked information on maternal infection status.

Risk Summary

No dose adjustments are needed for either oseltamivir or the concomitant drug when coadministering oseltamivir with amoxicillin, azithromycin, aspirin, cinemol, and ticlopidine (see Clinical Pharmacology [12.3]).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with oseltamivir phosphate for oral suspension in pregnant women to inform a drug-associated risk of adverse development outcomes. Available published epidemiological data suggest that oseltamivir phosphate for oral suspension, taken in any trimester, is not associated with an increased risk of birth defects. However, these studies individually are limited by small sample sizes, use of different comparison groups, and some lacked information on maternal infection status.

Risk Summary

There is no evidence from animal studies that oseltamivir and oseltamivir carboxylate are embryotoxic or teratogenic at systemic drug exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the maximum recommended human dose (MRHD) of oseltamivir phosphate (75 mg twice a day) in the rabbit study. Embryo-fetal effects consisting of an increased incidence of minor skeletal abnormalities and variants were observed at maternally toxic doses (150 mg/kg/day; toxic endpoint: maternal toxicity) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the maximum recommended human dose (MRHD) of oseltamivir phosphate (75 mg twice a day) in the rabbit study. Embryo fetal effects consisting of an increased incidence of minor skeletal abnormalities and variants were observed at maternally toxic doses (150 mg/kg/day; toxic endpoint: maternal toxicity) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day).

In prenatal and postnatal development studies in rats, oseltamivir was administered orally at doses ≤500 mg/kg/day, resulting in systemic drug exposures (based on AUC for oseltamivir carboxylate) 44 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day). In the rabbit study, Embryo-fetal effects consisting of an increased incidence of minor skeletal malformations were observed at a maternally toxic dose (150 mg/kg/day) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the maximum recommended human dose (MRHD) of oseltamivir phosphate (75 mg twice a day) in the rabbit study. Embryo fetal effects consisting of an increased incidence of minor skeletal abnormalities and variants were observed at maternally toxic doses (150 mg/kg/day; toxic endpoint: maternal toxicity) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day). No adverse maternal or offspring effects were observed at clinically relevant exposures (see Data).

The background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage is 2–4% and 15–20%, respectively.

Clinical Considerations

Disease Associated Maternal and/or Embryofetal Risk

Pregnant women are at higher risk of severe complications from influenza, which may lead to adverse pregnancy and/or fetal outcomes including maternal death, stillbirth, preterm delivery, low birth weight and small for gestational age.

Data

Human Data

Published prospective and retrospective observational studies of more than 5,000 pregnant women exposed to oseltamivir phosphate during pregnancy including more than 1,000 women exposed in the first trimester suggest that the observed rate of congenital malformations was not increased above the rate in the general companion population, regardless of when therapy was administered. However, individually, none of these studies had adequate sample sizes and some lacked information on dose which preclude a definitive assessment of the risk.

Animal Data

Oseltamivir was administered orally during organogenesis to pregnant rats (at 50, 250, or 1500 mg/kg/day) on gestation days 6 to 17 and rabbits (at 50, 150, or 550 mg/kg/day) on gestation days 6 to 18. In both species, the incidence of skeletal anomalies was increased at maternally toxic doses (150 mg/kg/day; toxic endpoint: maternal toxicity) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 44 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day). In the rabbit study, embryofetal effects consisting of an increased incidence of minor skeletal abnormalities and variants were observed at maternally toxic doses (150 mg/kg/day; toxic endpoint: maternal toxicity) resulting in systemic exposures (based on AUC for oseltamivir carboxylate) 190 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day).

In prenatal and postnatal development studies in rats, oseltamivir was administered orally at doses ≤500 mg/kg/day, resulting in systemic drug exposures (based on AUC for oseltamivir carboxylate) 44 times human exposures at the MRHD of oseltamivir phosphate (75 mg twice a day).

8.2 Lactation

Risk Summary

Based on limited published data, oseltamivir and oseltamivir carboxylate have been shown to be present in human milk at low levels considered unlikely to lead to toxicity in the breastfed infant. Postmarketing experience has not reported any information to suggest serious adverse effects of oseltamivir exposure via breast milk in infants. It is not known if oseltamivir affects human milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for oseltamivir phosphate and any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.

8.3 Pediatric Use

Treatment of Infection

The safety and efficacy of oseltamivir phosphate for the treatment of influenza in pediatric patients less than 2 weeks of age have not been established. 

Efficacy in Pediatric Patients

A pediatric open-label trial of oseltamivir phosphate in 54 pediatric patients 2 weeks to less than 1 year of age was supported by adequate and well-controlled trials in adults and adolescents treated with oseltamivir phosphate in a study of treatment and prophylaxis.

1 year to 17 years of age: Safety and efficacy in adolescent patients 13 to 17 years of age was supported by adequate and well-controlled trials in adults and adolescents treated with oseltamivir phosphate in a study of treatment and prophylaxis.

The safety and efficacy of oseltamivir phosphate for the treatment of influenza in pediatric patients less than 2 weeks of age have not been established.
Prophylaxis of Influenza

The safety and efficacy of oseltamivir phosphate for prophylaxis of influenza in pediatric patients 1 year to 17 years of age has been established (see Dosage and Administration (2.3), Clinical Pharmacology (12.3), and Clinical Studies (14.2)) and is based on:

- 13 to 17 years of age: Prophylaxis in adolescent patients 13 to 17 years of age is supported by one randomized, placebo-controlled post-exposure household prophylaxis trial of oseltamivir phosphate 75 mg taken orally once daily for 7 days in household contacts including 257 adolescents (see Clinical Studies (14.2)).
- 1 year to 12 years of age: Oseltamivir phosphate for prophylaxis in pediatric patients 1 year to 12 years of age is supported by one randomized, open-label, post-exposure household prophylaxis trial including pediatric subjects 3 years to 12 years of age who received 330 mg oseltamivir phosphate for oral suspension once daily for 7 days and a community outbreak safety study in 49 patients 1 year to 12 years of age.

The safety and efficacy of oseltamivir phosphate for influenza have not been established for pediatric patients less than 1 year of age.

8.5 Geriatric Use

Treatment of Influenza

Of the 4,765 adults in clinical trials of oseltamivir phosphate for the treatment of influenza, 948 (20%) were 65 years and older, while 328 (7%) were 75 years and older. In these double-blind, placebo-controlled trials the treatment of influenza in patients at least 65 years old that enrolled 741 subjects (374 received placebo and 362 oseltamivir phosphate), no overall differences in safety or effectiveness were observed between these subjects and younger subjects, and reported clinical experience has not identified differences in responses between the elderly and younger subjects (see Clinical Studies (14.1)).

Prophylaxis of Influenza

Of the 4,615 adults in clinical trials of oseltamir phosphate for the prophylaxis of influenza, 1,146 (22%) were 65 years and older, while 781 (16%) were 75 years and older. In a randomized, placebo-controlled trial in elderly residents of nursing homes who took oseltamivir phosphate for up to 42 days for the prophylaxis of influenza (oseltamivir phosphate n=276, placebo n=272), no overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger subjects (see Clinical Studies (14.2)).

8.6 Renal Impairment

Patients with renal impairment had higher blood levels of oseltamivir carboxylate compared to patients with normal renal function which may increase the risk of oseltamivir phosphate-associated adverse reactions. Therefore, dosage adjustment is recommended for patients with a serum creatinine clearance between 10 and 60 mL/minute and for patients with end-stage renal disease (ESRD) undergoing routine hemodialysis or continuous peritoneal dialysis treatment (see Dosage and Administration (2.7) and Clinical Pharmacology (12.7)).

8.7 Hepatic Impairment

No dosage adjustment is required in patients with mild to moderate hepatic impairment. The safety and pharmacokinetics in patients with severe hepatic impairment have not been evaluated (see Clinical Pharmacology (12.3)).

8.8 Use in Patients with Chronic Conditions

Efficacy of oseltamivir phosphate in the treatment of influenza in patients with chronic cardiac disease and/or respiratory disease was evaluated in one randomized, placebo-controlled, double-blind trial in patients with influenza A and B (H3N2) infection and a history of chronic cardiac disease and/or respiratory disease. No new safety signals were identified (see Clinical Studies (14.2)).

8.9 Immunocompromised Patients

Efficacy of oseltamivir phosphate for the treatment or prophylaxis of influenza has not been established in immunocompromised patients (see Clinical Studies (14.2)). Safety of oseltamivir phosphate for prophylaxis of influenza in immunocompromised patients has not been established (see Adverse Reactions (6.1)).

10 OVERDOSAGE

Reports of overdoses with oseltamivir phosphate have been received from clinical trials and during postmarketing experience. In the majority of cases reporting overdoses, no adverse reactions were reported. Adverse reaction reported following overdose were similar in nature to those observed with therapeutic doses of oseltamivir phosphate (see Adverse Reactions (6)).

11 DESCRIPTION

Oseltamivir phosphate for Oral Suspension, an influenza neuraminidase inhibitor (NAI), is available as a powder for oral suspension, which when constituted with water as directed contains 6 mg per mL oseltamivir base.

In addition to the active ingredient, the powder for oral suspension contains sorbitol, titanium dioxide, xanthan gum, sodium benzoate, monosodium citrate, tutti-frutti flavoring, and saccharin sodium.

Oseltamivir phosphate is a white crystalline solid with the chemical name (S)-1-(2-carboxyethyl)-2-(3-fluoro-4-(4-methyl-5-(1H-tetrazol-5-yl)-1H-pyridin-2-yl)phenyl)ethanamine hydrochloride. The chemical formula is C22H20F3N4O6·HCl (free base). The molecular weight is 632.4 for oseltamivir free base and 642.4 for oseltamivir phosphate salt. The structural formula is as follows:

![Chemical Structure of Oseltamivir Phosphate](https://example.com/structure.png)

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oseltamivir is an antiviral drug with activity against influenza virus (see Microbiology (12.4)).

12.2 Pharmacokinetics

Absorption and Bioavailability

Oseltamivir is absorbed from the gastrointestinal tract after oral administration of oseltamivir phosphate and is extensively converted predominantly by hepatic esterases to oseltamivir carboxylate in the systemic circulation and to a lesser extent as oseltamivir phosphate and less than 5% of the oral dose reaches the systemic circulation as oseltamivir (see Table 6).

### Table 6 Mean (± SD) Pharmacokinetic Parameters of Oseltamivir and Oseltamivir Carboxylate Following Multiple Dosing of 75 mg Capsules Twice Daily (n=20)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oseltamivir</th>
<th>Oseltamivir Carboxylate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>65 (26)</td>
<td>348 (128)</td>
</tr>
<tr>
<td>AUC0-24 (ng·h/mL)</td>
<td>112 (55)</td>
<td>7718 (267)</td>
</tr>
</tbody>
</table>

Plasma concentrations of oseltamivir carboxylate are proportional to doses up to 500 mg given twice daily (10-20 times the maximum recommended oseltamivir phosphate dosage) (see Dosage and Administration (2.3)).

Coadministration with food had no significant effect on the peak plasma concentration (Cmax) ng/mL, under fed conditions and 44% ng/mL, under fasted conditions) and the area under the plasma concentration time curve (AUC) ng·h/mL, under fed conditions and 60% ng·h/mL, under fasted conditions) of oseltamivir carboxylate. Distribution

The volume of distribution (Vd) of oseltamivir carboxylate, following intravenous administration in 24 subjects (oseltamivir phosphate is not available as an IV formulation), ranged between 23 and 26 liters.
The binding of oseltamivir carboxylate to human plasma protein is low (3%). The binding of oseltamivir to human plasma protein is 42%, which is insufficient to cause significant displacement-based drug interactions.

Elimination

Absorbed oseltamivir is primarily (>90%) eliminated by conversion to the active metabolite, oseltamivir carboxylate. Plasma concentrations of oseltamivir declined with a half-life of 1 to 3 hours in most subjects after oral administration. Oseltamivir carboxylate is not further metabolized and is eliminated unchanged in the urine. Plasma concentrations of oseltamivir carboxylate declined with a half-life of 6 to 10 hours in most subjects after oral administration.

Metabolism

Oseltamivir is extensively converted to the active metabolite, oseltamivir carboxylate, by esterases located predominantly in the liver. Oseltamivir Carboxylate is not further metabolized. Neither oseltamivir nor oseltamivir carboxylate is a substrate for, or inhibitor of, cytochrome P450 isozymes.

Excretion

Oseltamivir carboxylate is eliminated entirely (>99%) by renal excretion. Renal clearance (13.8 L/h) exceeds glomerular filtration rate (7.5 L/h), indicating that tubular secretion (via organic anion transporter) occurs in addition to glomerular filtration. Less than 20% of an orally administered dose is eliminated in feces.

Specific Populations

Renal impairment

Administration of 100 mg of oseltamivir phosphate twice daily (about 1.3 times the maximum recommended dosage) for 5 days to subjects with various degrees of renal impairment showed that exposure to oseltamivir carboxylate is inversely proportional to declining renal function. Population-derived pharmacokinetic parameters were determined for patients with varying degrees of renal function including ESRD patients on hemodialysis. Median simulated exposures of oseltamivir carboxylate for recommended treatment and prophylactic regimens are provided in Table 7. The pharmacokinetics of oseltamivir have not been studied in ESRD patients not undergoing dialysis (see Indications and Usage (1.3), and Use in Specific Populations (8.6)).

<table>
<thead>
<tr>
<th>Renal Function/Impairment</th>
<th>Normal Creatinine</th>
<th>Mild Impairment</th>
<th>Moderate Impairment</th>
<th>Severe Impairment</th>
<th>ESRD Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK exposure parameter</td>
<td>75 mg</td>
<td>75 mg</td>
<td>30 mg</td>
<td>30 mg every 12 h</td>
<td>30 mg every 12 h</td>
</tr>
<tr>
<td>推荐 [ng/l]</td>
<td>145</td>
<td>221</td>
<td>100</td>
<td>145</td>
<td>100</td>
</tr>
<tr>
<td>AUC [ng/ml]</td>
<td>5947</td>
<td>209</td>
<td>353</td>
<td>353</td>
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Population-derived pharmacokinetic parameters were determined for patients with varying degrees of renal function including ESRD patients on hemodialysis. Median simulated exposures of oseltamivir carboxylate for recommended treatment and prophylactic regimens are provided in Table 7.

Hepatic Impairment

In clinical studies, oseltamivir carboxylate exposure was not altered in subjects with mild or moderate hepatic impairment (see Use in Specific Populations (8.7)).

Pregnant Women

A pooled population pharmacokinetic analysis indicates that the oseltamivir phosphate dosage regimen resulted in lower exposure to the active metabolite in pregnant women compared with non-pregnant women undergoing the same dosage regimen (see Use in Specific Populations (8.8)). Oseltamivir carboxylate is not expected to have activity against susceptible influenza virus strains and there are insufficient pharmacokinetics and safety data to recommend a dose adjustment for pregnant women (see Use in Specific Populations (8.1)).

Pediatric Subjects

The pharmacokinetics of oseltamivir and oseltamivir carboxylate have been evaluated in a single-dose pharmacokinetic study in pediatric subjects aged 5 to 14 years (n=18) and in a small number of pediatric subjects aged 3 to 12 years (n=5) enrolled in a clinical trial of younger pediatric subjects treated both the postinfluenza the active metabolite faster than adult subjects resulting in a lower exposure for a given mg/kg dose. For oseltamivir, the peak concentration in pediatric subjects were similar to those in adults. For oseltamivir carboxylate, peak concentrations in pediatric subjects were similar to those in adults, with the exception of 2 children aged 3 to 6 years (n=2) who had higher oseltamivir carboxylate concentrations than adults, likely due to differences in renal function and urine excretion. The pharmacokinetics of oseltamivir in pediatric subjects over 12 years of age were similar to those in adult subjects (see Use in Specific Populations (8.6)).

Pediatric Subjects (1 year to 12 years of age)
The pharmacokinetics of oseltamivir and oseltamivir carboxylate have been evaluated in two open-label studies of pediatric subjects less than one year of age (n=122) infected with influenza virus. The pharmacokinetics of oseltamivir in pediatric subjects over 12 years of age were similar to those in adults (see Use in Specific Populations (8.6)).

Exposure to oseltamivir carboxylate at steady-state was 25 to 35% higher in geriatric subjects (age range 65 to 75 years) compared to young adults. Based on drug exposure and tolerability, dose adjustments are not recommended for geriatric patients (see Use in Specific Populations (8.7)).

Drug-Interaction Studies

Oseltamivir is extensively converted to oseltamivir carboxylate by esterases, located predominately in the liver. Drug interactions involving competition for excretion have not been formally evaluated. However, in vitro studies indicate that neither oseltamivir nor oseltamivir carboxylate suggests that the probability of drug displacement is low. In vivo studies demonstrate that neither oseltamivir nor oseltamivir carboxylate is a substrate for P-gp-mediated drug interactions for conversion to the active form, oseltamivir carboxylate. Oseltamivir carboxylate is an inhibitor of influenza virus neuraminidase affecting release of viral particles. The median IC50 values of oseltamivir against influenza A(H1N1), influenza A(H3N2), and influenza B clinical isolates were 2.5 nM (range 0.3 to 5.16 nM, N=74), 0.96 nM (range 0.1 to 7.95 nM, N=74), and 60 nM (range 0.25-250 nM, N=236), respectively, in a neuraminidase assay with a fluorescently labeled MUNANA substrate.

12.4 Microbiology

Mechanism of Action

Oseltamivir phosphate is an ethyl ester prodrug requiring enter hydrolysis for conversion to the active form, oseltamivir carboxylate. Oseltamivir carboxylate is an inhibitor of influenza virus neuraminidase affecting release of viral particles. The median IC50 values of oseltamivir against influenza A(H1N1), influenza A(H3N2), and influenza B clinical isolates were 2.5 nM (range 0.3 to 5.16 nM, N=74), 0.96 nM (range 0.1 to 7.95 nM, N=74), and 60 nM (range 0.25-250 nM, N=236), respectively, in a neuraminidase assay with a fluorescently labeled MUNANA substrate.

Toxicology

The antiviral activity of oseltamivir carboxylate against laboratory strains and clinical isolates of influenza virus was determined in cell culture. The concentrations of oseltamivir carboxylate required for inhibition of influenza virus in cell culture were highly variable depending on the assay method used and the virus strain. The 50% and 90%
**14.2 Treatment of Influenza**

**Adults**

Two randomized, placebo-controlled, double-blind clinical trials of oseltamivir phosphate were conducted in adults between 18 and 65 years old, one in the U.S. and one outside the U.S., for the treatment of acute uncomplicated influenza. Eligible subjects had fever of at least 100°F, accompanied by at least one respiratory symptom (cough, nasal symptoms, or sore throat) and at least one systemic symptom (myalgia, chills, weakness, fatigue, headache, or dyspnea), and influenza virus was shown to be circulating in the community at the time of enrollment. Subjects were randomized to receive placebo or oseltamivir phosphate twice daily for 5 days. All enrolled subjects were admitted to take fever-reducing medications. Oseltamivir phosphate was found to be non-mutagenic in the Ames test and the human lymphocyte transformation assays with and without enzymatic activation and negative in the mouse micronucleus test. The recommendation was in favor of oral medication. Cough, nasal symptoms, or sore throat, and at least one systemic symptom (myalgia, chills, weakness, fatigue, headache), and influenza were shown to be circulating in the community at the time of enrollment. Oseltamivir phosphate was found to be non-mutagenic in the Ames test and the human lymphocyte transformation assay with and without enzymatic activation and negative in the mouse micronucleus test.

### Immune Response

No influenza vaccine/oseltamivir interaction study has been conducted. In studies of naturally acquired and experimental influenza, treatment with oseltamivir phosphate did not impair normal humoral antibody response to infection.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In 2-year carcinogenicity studies in mice and rats given daily oral doses of the prodrug oseltamivir phosphate up to 400 mg/kg and 500 mg/kg, respectively, the prodrug and the active form oseltamivir phosphate induced no statistically significant increases in tumors. In mice, the 2-year oral dose level of oseltamivir phosphate producing a maximum of 13% of the recommended clinical dose based on AUC comparisons. The respective safety margins of the exposure to the active oseltamivir phosphate in the 25- and 50-fold. Oseltamivir was found to be non-mutagenic in the Ames test and the human lymphocyte transformation assays with and without enzymatic activation and negative in the mouse micronucleus test. It was found to be positive in a Syrian Hamster Embryo (SHE) cell transformation test. Oseltamivir carboxylate was non-mutagenic in the Ames test and the L5178Y mouse lymphoma assay with and without enzymatic activation and negative in the SHE cell transformation test. In a fertility and early embryonic development study in rats, doses of oseltamivir at 50, 250, and 1000 mg/kg/day were administered to females for 3 weeks before mating, during mating and until day 6 of pregnancy. Males were dosed for 4 weeks before mating, during mating, and for 3 weeks after mating. There were no effects on fertility, mating performance or early embryonic development at any dose level. The highest dose in this study was approximately 105 times the human systemic exposure of C0.005 of oseltamivir carboxylate that occurs after administration of the maximum recommended human dose.

### 14 CLINICAL STUDIES

#### 14.2 Treatment of Influenza

Adults

Two randomized, placebo-controlled, double-blind clinical trials of oseltamivir phosphate were conducted in adults between 18 and 65 years old, one in the U.S. and one outside the U.S., for the treatment of acute uncomplicated influenza. Eligible subjects had fever of at least 100°F, accompanied by at least one respiratory symptom (cough, nasal symptoms, or sore throat) and at least one systemic symptom (myalgia, chills, weakness, fatigue, headache), and influenza virus was shown to be circulating in the community at the time of enrollment. Subjects were randomized to receive placebo or oseltamivir phosphate twice daily for 5 days. All enrolled subjects were admitted to take fever-reducing medications. Oseltamivir phosphate was found to be non-mutagenic in the Ames test and the human lymphocyte transformation assays with and without enzymatic activation and negative in the mouse micronucleus test. It was found to be positive in a Syrian Hamster Embryo (SHE) cell transformation test. Oseltamivir carboxylate was non-mutagenic in the Ames test and the L5178Y mouse lymphoma assay with and without enzymatic activation and negative in the SHE cell transformation test. In a fertility and early embryonic development study in rats, doses of oseltamivir at 50, 250, and 1000 mg/kg/day were administered to females for 3 weeks before mating, during mating and until day 6 of pregnancy. Males were dosed for 4 weeks before mating, during mating, and for 3 weeks after mating. There were no effects on fertility, mating performance or early embryonic development at any dose level. The highest dose in this study was approximately 105 times the human systemic exposure of C0.005 of oseltamivir carboxylate that occurs after administration of the maximum recommended human dose.

**Adolescents and Adults with Chronic Cardiac or Respiratory Disease**

A double-blind, placebo-controlled, multicenter trial was unable to demonstrate efficacy...
of oseltamivir phosphate (75 mg twice daily for 5 days) in the treatment of influenza in adult and adolescent subjects (13 years or older) with chronic cardiac (excluding chronic atrial fibrillation) or respiratory disease as measured by time to alleviation of all symptoms. However, in patients treated with oseltamivir phosphate there was a more rapid cessation of febrile illness. No difference in the incidence of influenza complications was observed between the treatment and placebo groups in this population.

Geriatric Subjects
Three double-blind placebo-controlled treatment trials were conducted in subjects who were at least 65 years of age in three consecutive seasons. The enrollment criteria were similar to that of adult trials with the exception of fever being defined as higher than 39.5°C. Of 745 subjects enrolled, 476 (65%) subjects were influenza-infected of these, 95% were infected with influenza type A and 5% with influenza type B.

In the pooled analysis, there was a 5-day reduction in the median time to improvement in influenza-infected subjects who received oseltamivir phosphate 75 mg twice daily for 5 days compared to those who received placebo (p<0.001). See Use in Specific Populations (8.5).

Some seasonal variability was noted in the clinical efficacy outcomes.

Pediatric Subjects (1 year to 12 years of age)
One double-blind placebo-controlled treatment trial was conducted in pediatric subjects aged 1 year to 12 years (median age 5 years) who had fever (at least 38°C) plus one respiratory symptom (cough or coryza) when influenza virus was known to be circulating in the community. A total of 385 subjects were enrolled and 370 subjects were randomized to receive oseltamivir phosphate treatment of 7 mg per kg twice daily, started within 48 hours of onset of symptoms, reduced the total composite time to freedom from illness by 5.5 days compared to placebo. Subgroup analysis by gender showed no differences in the treatment effect of oseltamivir phosphate in male and female pediatric subjects.

Pediatric Subjects (2 weeks to less than 1 year of age)
Two open-label trials evaluated the safety and pharmaco kinetics of oseltamivir and oseltamivir carboxylate in influenza-infected pediatric subjects 2 weeks to less than 1 year of age (including premature infants) at least 36 weeks post conceptionsal age. Subjects received oseltamivir phosphate at doses ranging from 2 to 3.5 mg per kg twice daily for 5 days depending on the subject age. These clinical trials were not designed to evaluate clinical efficacy or virologic response.

Of the 136 subjects under the age of 1 year enrolled and dosed in the trials, the majority of the subjects were male (55%), white (79%), non-Hispanic (74%), term (76%) and infected with influenza A (86%). Pharmacokinetic data indicated that a dose of 3 mg per kg twice daily in pediatric subjects 2 weeks to less than 1 year of age provided similar exposure as adults and children treated with the approved dose of oseltamivir phosphate in the pediatric population. However, coadministration of oseltamivir phosphate and other non-absorbable medications or foods was not studied and may result in decreased oseltamivir phosphate exposure.

14.2 Prophylaxis of Influenza

Adult and Adolescent Subjects (13 years of age and older)
The efficacy of oseltamivir phosphate in preventing naturally occurring influenza illness has been demonstrated in three seasonal prophylaxis (community out break) clinical trials and one post exposure prophylaxis trial in household contacts. The efficacy endpoint for all of these trials was the incidence of laboratory-confirmed clinical influenza in the treatment group following criteria (all signs and symptoms must have been recorded within 24 hours):

- Oral temperature greater than or equal to 99°F (37.2°C),
- At least one respiratory symptom (cough, sore throat, nasal congestion),
- At least one constitutional symptom (aches and pains, fatigue, headache, chills, fever), and
- Either a positive virus isolation or a four-fold increase in virus antibody titers from baseline.

In a pooled analysis of two seasonal prophylaxis trials in healthy unvaccinated adults aged 18 to 65 years, oseltamivir phosphate 75 mg once daily was taken for 42 days during a community outbreak, reduced the incidence of laboratory-confirmed clinical influenza from 5% (23/101) for the placebo group to 1% (1/101) for the oseltamivir phosphate group.

In the seasonal community outbreak prophylaxis trial in elderly residents of skilled nursing homes, about 80%, 43%, and 14% of the subjects were vaccinated, had cardiac disorders, and had chronic airway obstructive disorders, respectively. In this trial, subjects were randomized to oseltamivir phosphate 75 mg once daily or placebo taken orally only was administered within 48 hours of onset of symptoms in the index case and continued for 7 days (index cases did not receive oseltamivir phosphate treatment). The incidence of laboratory-confirmed clinical influenza was 12% (24/200) in the placebo-treated subjects compared to 1% (2/200) for the oseltamivir phosphate-treated subjects.

Pediatric Subjects (1 year to 12 years of age)
The efficacy of oseltamivir phosphate in preventing naturally occurring influenza illness was demonstrated in a randomized, open-label post-exposure prophylaxis trial in household contacts that included pediatric subjects aged 1 year to 12 years, both as index cases and as family contacts. All index cases in this trial received oseltamivir phosphate for oral suspension 50 to 60 mg taken orally once daily for 10 days. The efficacy parameter was the incidence of laboratory-confirmed clinical influenza in the household. Laboratory-confirmed clinical influenza was defined as meeting all of the following criteria:

- Oral temperature at least 100°F (37.8°C),
- Cough and/or coryza recorded at least 48 hours, and
- Either a positive virus isolation or a four-fold increase in virus antibody titers from baseline or at illness visits.

Among household contacts 1 year to 12 years of age not already shedding virus at baseline, the incidence of laboratory-confirmed clinical influenza was lower in the group who received oseltamivir phosphate prophylaxis (3% [3%]) compared to the group who did not receive oseltamivir phosphate prophylaxis (11% [11%]).

Immunocompromised Subjects
A double-blind, placebo-controlled trial was conducted for seasonal prophylaxis of influenza in 475 immunocompromised subjects (including 18 pediatric subjects 1 year to 12 years of age) who had received solid organ (>100) and hematopoietic stem cell transplants (n=27). Median time since transplant for solid organ transplant recipients was 1,155 days for the placebo group and 1,379 days for the oseltamivir phosphate group. Median time since transplant for the hematopoietic stem cell transplant recipients was 424 days for the placebo group and 367 days for the oseltamivir phosphate group. Approximately 45% of subjects received influenza vaccine prior to entering the study. The primary efficacy endpoint was the incidence of laboratory-confirmed clinical influenza in the placebo and oseltamivir phosphate groups during the study period. The incidence of laboratory confirmed influenza was 4% (2/47) in the placebo-treated group compared to 1% (1/47) in the oseltamivir phosphate-treated group. The difference was not statistically significant. A secondary analysis was performed using the same clinical symptoms and RT-PCR for laboratory confirmation of influenza infection. Among subjects who were not already shedding virus at baseline, the incidence of RT-PCR confirmed clinical influenza infection was 3% (2/61) in the placebo group and <1% (1/21) in the oseltamivir phosphate group.

15 HOW SUPPLIED/STORAGE AND HANDLING

Oseltamivir Phosphate for Oral Suspension (Suspended in Powder)
Supplied as a white to light yellow powder blended in a glass bottle with a child-resistant closure. After composition, the powder blend produces a white to light yellow tutti-fruity flavored oral suspension. After composition with 55 mL of water, each bottle delivers a usable volume of 60 mL of oral suspension equivalent to 360 mg oseltamivir base (6 mg/mL). [See Dosage and Administration (2.5)]. [NDC 0088-7650-04].

Storage
Store dry powder at 25°C (77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

Store constituted oral suspension under refrigeration for up to 17 days at 2°C to 8°C (36° to 46°F). Do not freeze. Alternatively, store constituted suspension for up to 10 days at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION
Oseltamivir phosphate for oral suspension may cause serious side effects, including:

Serious Skin/Hypersensitivity Reactions

Advise patients and/or caregivers of the risk of severe allergic reactions (including anaphylaxis) or serious skin reactions. Instruct patients and/or caregiver to stop oseltamivir phosphate for oral suspension and seek immediate medical attention if an allergic-like reaction occurs or is suspected (5.2).

Neuropsychiatric Events

Advise patients and/or caregivers of the risk of neuropsychiatric events in oseltamivir phosphate-treated patients with influenza and instruct patients to contact their healthcare provider if they experience any signs of abnormal behavior while receiving oseltamivir phosphate for oral suspension (See Warnings and Precautions (5.3)).

Important Dosing Information

Instruct patients to begin treatment with oseltamivir phosphate for oral suspension as soon as possible from the first appearance of flu symptoms, within 48 hours of onset of symptoms. Similarl, instruct patients to start taking oseltamivir phosphate for treatment of LAIV within 2 weeks or 48 hours after oseltamivir phosphate administration, unless medically necessary (See Drug Interactions (7.1)).

Fructose Intolerance

Inform patients with hereditary fructose intolerance that one dose of 75 mg oseltamivir phosphate for oral suspension (supplied as powder) delivers 2 grams of sorbitol. Inform patients with hereditary fructose intolerance that this is below the daily maximum limit of sorbitol and may cause dyspepsia and diarrhea (see Warnings and Precautions (5.4)).

Oseltamivir Phosphate for Oral Suspension

Manufactured by:

Nesher Pharmaceuticals (USA) LLC.
St. Louis, MO 63044

Distributed by:

Zydus Pharmaceuticals USA Inc.
Pennington, NJ 08534
PI008-1
Rev. 06/2020

Revised By: Preferred Pharmaceuticals Inc.

PATIENT INFORMATION

Oseltamivir phosphate for oral suspension (os-el-TAM-ih-veer)

What is Oseltamivir Phosphate for Oral Suspension?

Oseltamivir phosphate for oral suspension is a prescription medicine used to:

• treat the flu (influenza) in people 2 weeks of age and older who have had flu symptoms for no more than 2 days,
• prevent the flu in people who are 1 year of age and older.

It is not known if oseltamivir phosphate for oral suspension is:

• effective in people who start treatment after 2 days of developing flu symptoms,
• effective for the treatment of the flu in people with long-time (chronic) heart problems or breathing problems,
• effective for the treatment or prevention of flu in people who have weakened immune systems (immuno-compromised),
• safe and effective for the treatment of the flu in children less than 2 weeks of age.
• safe and effective in the prevention of the flu in children less than 1 year of age.

Oseltamivir phosphate for oral suspension does not treat or prevent illness that is caused by infections other than the influenza virus.

Oseltamivir phosphate for oral suspension does not prevent bacterial infections that may happen with the flu.

Oseltamivir phosphate for oral suspension is not recommended for people with end-stage renal disease (ESRD) who are not receiving dialysis.

Oseltamivir phosphate for oral suspension does not take the place of receiving a flu vaccination. Talk to your healthcare provider about when you should receive an annual flu vaccination.

Who should not take Oseltamivir phosphate for oral suspension?

Do not take oseltamivir phosphate for oral suspension if you are allergic to oseltamivir phosphate or any of the ingredients in oseltamivir phosphate for oral suspension. See the end of this leaflet for a complete list of ingredients in oseltamivir phosphate for oral suspension.

What should I tell my healthcare provider before taking oseltamivir phosphate for oral suspension?

Before you take oseltamivir phosphate for oral suspension, tell your healthcare provider if you:

• have kidney problems,
• have a history of fructose (fruit sugar) intolerance. Oseltamivir phosphate for oral suspension contains sorbitol and may cause stomach upset and diarrhea in people who are fructose intolerant,
• have any other medical conditions,
• are pregnant or plan to become pregnant. Available information indicate that oseltamivir phosphate for oral suspension does not increase the risk of birth defects.
• are breastfeeding or plan to breast feed. Oseltamivir phosphate can pass into breast milk in small amounts.

Tell your healthcare provider about all the medicines you take, including prescription or over-the-counter medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take Oseltamivir phosphate for oral suspension?

• Take oseltamivir phosphate for oral suspension exactly as your healthcare provider tells you to.
• Take oseltamivir phosphate for oral suspension with food or without food. There is less chance of stomach upset if you take oseltamivir phosphate for oral suspension with food.
• If you miss a dose of oseltamivir phosphate for oral suspension, take it as soon as you remember, 18 to 2 hours or less before your next dose, do not take the missed dose, and continue to take your regular dose at your scheduled time.

What are the possible side effects of oseltamivir phosphate for oral suspension?

Oseltamivir phosphate for oral suspension may cause serious side effects, including:

• Serious skin and allergic reactions. Oseltamivir phosphate for oral suspension can cause serious skin and allergic reactions. Stop taking oseltamivir phosphate for oral suspension and get medical help right away if you get any of the following symptoms:

  • skin rash or hives
  • your skin, lips, tongue, and eyes are red
  • hives or swelling in your mouth
  • itching
  • swelling of your face, eyes, lips, tongue, or throat
  • trouble breathing
  • chest pain or tightness

• Change in behavior. People, especially children, who have the flu can develop nervous system problems and abnormal behavior that can lead to death. During treatment with oseltamivir phosphate for oral suspension, tell your healthcare provider right away if you or your child have confusion, speech problems, shaky movements, seizures, or start hearing voices or seeing things that are not really
The most common side effects of oseltamivir phosphate for oral suspension when used for treatment of the flu include nausea, vomiting, and headache.

The most common side effect of oseltamivir phosphate for oral suspension when used for prevention of the flu include nausea, vomiting, headache, and pain.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of oseltamivir phosphate for oral suspension.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Oseltamivir Phosphate for Oral Suspension?

- Store oseltamivir phosphate for oral suspension in the refrigerator for up to 17 days between 36°F to 46°F (2°C to 8°C). Do not freeze.
- Store oseltamivir phosphate for oral suspension for up to 10 days at room temperature between 68°F to 77°F (20°C to 25°C).
- Discard any oseltamivir phosphate for oral suspension that is out of date or no longer needed.

Oseltamivir phosphate for oral suspension comes in a child-resistant package.

Keep oseltamivir phosphate for oral suspension and all medicines out of the reach of children.

General information about the safe and effective use of oseltamivir phosphate for oral suspension.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use oseltamivir phosphate for oral suspension for a condition for which it was not prescribed. Do not give oseltamivir phosphate for oral suspension to other people, even if they have the same symptoms you have. It may harm them.

If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about oseltamivir phosphate for oral suspension that is written for health professionals. For more information, contact Zydus Pharmaceuticals at 1-877-993-8779.

What are the ingredients in oseltamivir phosphate for oral suspension?

Active ingredient: oseltamivir phosphate

Inactive ingredients:

Oseltamivir Phosphate for Oral Suspension: sorbitol, monosodium citrate, xanthan gum, titanium dioxide, tutti-frutti flavoring, sodium benzoate, sodium saccharin and water.

Manufactured by: Nesher Pharmaceuticals USA LLC
St. Louis, MO 63144

Distributed by: Zydus Pharmaceuticals USA Inc.
Pennington, NJ 08534

Relabeled By: Preferred Pharmaceuticals Inc.

These are not all of the possible side effects of oseltamivir phosphate for oral suspension.

Oseltamivir phosphate for oral suspension comes in a child-resistant package.
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**Labeler** - Preferred Pharmaceuticals Inc. (791119022)

**Registrant** - Preferred Pharmaceuticals Inc. (791119022)

**Establishment**

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