Tamiflu 30 mg, 45 mg, 75mg hard capsules

Therapeutic indications

Treatment of influenza: Tamiflu is indicated for adults and children, including full-term newborns, who exhibit typical symptoms of influenza at the time when the influenza virus is circulating in the population. The efficacy has been demonstrated when treatment is initiated within two days from the onset of symptoms.

Prevention of influenza: After exposure to a clinically diagnosed case of influenza in individuals aged 1 year or older at the time when the influenza virus is circulating in the population.

The appropriate use of Tamiflu for the prevention of influenza should be determined on a case-by-case basis, guided by the circumstances and the population in need of protection. In exceptional cases (e.g., when the circulating virus strain does not match the vaccine strain and during a pandemic), seasonal prevention may be considered in individuals aged 1 year or older.

Tamiflu is indicated for the prevention of influenza after exposure in infants younger than 1 year during a pandemic influenza outbreak (

Tamiflu is not a substitute for influenza vaccination.
The use of antiviral drugs for the treatment and prevention of influenza should be determined based on official recommendations. When making decisions regarding the use of oseltamivir for treatment and prophylaxis, consideration should be given to what is known about the characteristics of circulating influenza viruses, available information on seasonal sensitivity patterns of influenza to drugs, and the consequences of the disease in different geographic areas and patient populations .

Dosage and administration

Dosage: Tamiflu hard capsules and Tamiflu suspension are bioequivalent preparations. Doses of 75 mg can be taken as follows:

- One 75 mg capsule
- One 30 mg capsule plus one 45 mg capsule
- One 30 mg dose plus one 45 mg dose of suspension.

Commercially produced Tamiflu powder for oral suspension (6 mg/ml) is the preferred product for pediatric and adult patients who have difficulty swallowing capsules or require lower doses.

Adults and adolescents aged 13 years and older: Treatment: The recommended oral dosage is 75 mg oseltamivir twice daily for 5 days for adolescents (13 to 17 years) and adults.

Body weight Recommended dosage for 5 days Recommended dosage for 10 days*

Immunocompromised patients: 40 kg 75 mg twice daily 75 mg twice daily

*The recommended treatment duration in immunocompromised adult and adolescent patients is 10 days. See Special populations, Immunocompromised patients for more information.

Treatment should be initiated as soon as possible within the first two days after the onset of influenza symptoms.

Prevention after exposure: The recommended dosage for the prevention of influenza after close contact with an infected person is 75 mg oseltamivir once daily for 10 days for adolescents (13 to 17 years) and adults.

Body weight Recommended dosage for 10 days Recommended dosage for 10 days

Immunocompromised patients: 40 kg 75 mg once daily 75 mg once daily

Treatment should be initiated as soon as possible within two days after exposure to an infected person.

Prevention during an influenza epidemic among the population: The recommended dosage for the prevention of influenza during an outbreak among the population is 75 mg oseltamivir once daily for a period of up to 6 weeks (or up to 12 weeks in immunocompromised patients.

Pediatric patients

Children aged 1 to 12 years: Tamiflu 30 mg, 45 mg, and 75 mg capsules and oral suspension are available for infants and children aged 1 year or older.

Treatment: The following weight-based dosage recommendations are recommended for infants and children aged 1 year or older: Body weight Recommended dosage for 5 days Recommended dosage for 10 days*

Body weight	**Dosage for 5 days**	**Dosage for 10 days** Immunocompromised patients
10 kg t/m 15 kg	30 mg twice daily	30 mg twice daily
> 15 kg t/m 23 kg	45 mg twice daily	45 mg twice daily
> 23 kg t/m 40 kg	60 mg twice daily	60 mg twice daily
> 40 kg	70 mg twice daily	70 mg twice daily

The recommended treatment duration in immunocompromised children (≥ 1 year) is 10 days. See Special populations, Immunocompromised patients for more information. Treatment should be initiated as soon as possible within the first two days after the onset of influenza symptoms.

Prevention after exposure: The recommended preventive dosage of Tamiflu after exposure is as follows: Body weight Recommended dosage for 10 days Recommended dosage for 10 days

Body weight	**Dosage for 5 days**	**Dosage for 10 days** Immunocompromised patients
10 kg t/m 15 kg	30 mg twice daily	30 mg twice daily
> 15 kg t/m 23 kg	45 mg twice daily	45 mg twice daily
> 23 kg t/m 40 kg	60 mg twice daily	60 mg twice daily
> 40 kg	70 mg twice daily	70 mg twice daily

Prevention during an influenza epidemic among the population: Prevention during an influenza epidemic has not been studied in children under 12 years of age.

Babies aged 0-12 months

Treatment: The recommended dosage for treating babies aged 0-12 months is 3 mg/kg twice daily. This is based on pharmacokinetic and safety data demonstrating that this dosage in babies aged 0-12 months achieves plasma concentrations of the prodrug and active metabolite expected to be clinically effective with a safety profile similar to that seen in older children and adults (see section 5.2). The following dosage recommendation is recommended for treating babies aged 0-12 months:

Body weight* Recommended dosage for 5 days

Recommended dosage for 10 days**

Body weight	**Dosage for 5 days**	**Dosage for 10 days** Immunocompromised patients
3 kg	9 mg twice daily	9 mg twice daily
4 kg	12 mg twice daily	12 mg twice daily
5 kg	15 mg twice daily	15 mg twice daily
6 kg	18 mg twice daily	18 mg twice daily
7 kg	21 mg twice daily	21 mg twice daily
8 kg	24 mg twice daily	24 mg twice daily
9 kg	27 mg twice daily	27 mg twice daily
10 kg	30 mg twice daily	30 mg twice daily

*This table does not include all possible weights for this population. For all patients under 1 year of age, 3 mg/kg should be used to determine the dose regardless of the patient's weight.Treatment should be initiated as soon as possible within the first two days after the onset of influenza symptoms.

** The recommended treatment duration in immunocompromised babies (0-12 months) is 10 days. See Special populations, Immunocompromised patients for more information.

This dosage recommendation is not intended for premature infants, i.e., babies with a post-conceptual age of less than 36 weeks. Insufficient data are available for these patients, in whom different dosages may be required due to the immaturity of their physiological functions.

Prevention after exposure: The recommended prophylactic dosage for babies younger than 1 year during a pandemic influenza outbreak is half of the daily treatment dosage. This is based on clinical data in babies and children aged 1 year or older and adults showing that a prophylactic dosage equal to half of the daily treatment dosage is clinically effective for the prevention of influenza. The following prophylactic age-dependent dosage recommendation is recommended for babies aged 0-12 months (see section 5.2 for exposure simulation):

Age Recommended dosage for 10 days Recommended dosage for 10 days

Age	**Recommended Dosage for 10 days**	**Recommended Dosage for 10 days** Immunocompromised patients
0-12 months	3 mg/kg once daily	3 mg/kg once daily

This dosage recommendation is not intended for premature infants, i.e., babies with a post-conceptual age of less than 36 weeks. Insufficient data are available for these patients, in whom different dosages may be required due to the immaturity of their physiological functions.

Prevention during an influenza epidemic among the population: Prevention during an influenza epidemic has not been studied in babies aged 0-12 months.

Special populations

Impaired liver function: No dosage adjustment is necessary for patients with liver disease, either in treatment or prevention. No studies have been conducted in children with liver disease.

Impaired renal function: Treatment of influenza: Dosage adjustment is recommended for adults and adolescents (13 to 17 years old) with moderate or severe renal impairment. The recommended dosages are further described in the table below. Creatinine clearance Recommended dosage for treatment

Creatinine clearance	Recommended dosage during treatment
60 (ml/min)	30 mg (suspension or capsules) twice daily
30 to 60 (ml/min)	30 mg (suspension or capsules) once daily
10 to 30 (ml/min)	Not recommended (no data available)
Hemodialysis patients	30 mg after each hemodialysis session
Peritoneal dialysis patients	30 mg (suspension or capsules) single dose

Prevention of influenza: Dosage adjustment is recommended for adults and adolescents (13 to 17 years old) with moderate or severe renal impairment, as further described in the table below.

Creatinine clearance	Recommended dosage during treatment
60 (ml/min)	30 mg (suspension or capsules) once daily
30 to 60 (ml/min)	30 mg (suspension or capsules) every other day
10 to 30 (ml/min)	Not recommended (no data available)
Hemodialysis patients	30 mg after every second hemodialysis session
Peritoneal dialysis patients	30 mg (suspension or capsules) once per week

Elderly patients: No dosage adjustment is necessary unless there are clear indications of moderate or severe renal impairment.

Immunocompromised patients : Treatment: The recommended duration of influenza treatment in immunocompromised patients is 10 days. No dosage adjustment is needed. Treatment should be initiated as soon as possible within the first two days after the onset of influenza symptoms.

Seasonal prophylaxis: Extended duration of seasonal prophylaxis up to 12 weeks has been evaluated in immunocompromised patients

Method of administration

Oral use: Patients unable to swallow capsules can receive the appropriate doses of Tamiflu suspension.

Contraindications

Special warnings and precautions for use

Oseltamivir is only effective against disease caused by influenza viruses. There is no evidence of the efficacy of oseltamivir against any disease caused by agents other than influenza viruses.

Tamiflu is not a substitute for influenza vaccination. The use of Tamiflu should not influence the evaluation of individuals for annual influenza vaccination. Protection against influenza lasts only as long as Tamiflu is taken. Tamiflu should only be used for the treatment and prevention of influenza when reliable epidemiological data indicate that influenza is prevalent in the population.

The sensitivity of circulating influenza virus strains to oseltamivir appears to be highly variable (see section 5.1). Therefore, prescribers should consider the most up-to-date information on oseltamivir susceptibility patterns of circulating viruses when making the decision to use Tamiflu or not.

Severe underlying disease: Regarding the safety and efficacy of oseltamivir, there is no information available regarding patients with any disease that is so severe or unstable that they are at risk of being hospitalized.

Immunocompromised patients: The efficacy of oseltamivir in both the treatment and prophylaxis of influenza in immunocompromised patients has not been clearly established.

Cardiac/respiratory disease: The efficacy of oseltamivir in the treatment of individuals with chronic cardiac or respiratory disease has not been established. There was no difference in the incidence of complications observed between the treatment group and the placebo group in this population.

Pediatric patients: Currently, there are no available data that allow dosage recommendations in premature infants (<36 weeks post-conceptual age).

Severely impaired renal function: Dosage adjustment is recommended for both treatment and prevention in adolescents (13 to 17 years) and adults with severely impaired renal function. Insufficient clinical data are available to provide a dosage recommendation for the use in infants and children (1 year or older) with impaired renal function.

Neuropsychiatric adverse reactions: Neuropsychiatric adverse reactions have been reported during the administration of Tamiflu to patients with influenza, particularly in children and adolescents. These reactions have also been observed in patients with influenza who did not receive oseltamivir. Patients should be closely monitored for behavioral changes, and the benefits and risks of continuing treatment should be carefully assessed on an individual basis.

The use of Tamiflu can be considered during pregnancy if necessary, after weighing the available safety and benefit information (see section 5.1 'Treatment of influenza in pregnant women' for data on benefits in pregnant women) and the pathogenicity of the circulating influenza virus strain.

Breastfeeding: In lactating rats, oseltamivir and its active metabolite were excreted in milk. Very limited information is available on infants who were breastfed by mothers using oseltamivir and on the excretion of oseltamivir in breast milk. Limited data showed that oseltamivir and its active metabolite were found in breast milk, although in low amounts, which could result in a subtherapeutic dose for the child. Based on this information, the pathogenicity of the circulating influenza virus strain, and the underlying condition of the breastfeeding mother, administration of oseltamivir may be considered if there are clear potential benefits for breastfeeding mothers.

Fertility: Based on preclinical data, there is no evidence that Tamiflu has an effect on male or female fertility.

Influence on the ability to drive and use machines: Tamiflu does not affect the ability to drive or operate machinery.

Adverse effects:

In adults/adolescents, the most commonly reported adverse effects were nausea and vomiting in the treatment studies and nausea in the prevention studies. The majority of these adverse effects were reported as isolated incidents on either the first or second day of treatment and resolved on their own within 1-2 days. In children, the most commonly reported adverse effect was vomiting. These adverse effects did not lead to discontinuation of Tamiflu treatment in the majority of patients.

The following serious adverse effects have been rarely reported since the marketing of oseltamivir: anaphylactic and anaphylactoid reactions, liver disorders (fulminant hepatitis, impaired liver function, and jaundice), angioedema, Stevens-Johnson syndrome and toxic epidermal necrolysis, gastrointestinal bleeding, and neuropsychiatric disorders. (Regarding neuropsychiatric disorders, see section 4.4).

List of adverse effects in summary table
The adverse effects in the tables below are classified into the following categories: Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), and very rare (<1/10,000). Adverse effects are added to the corresponding category in the tables based on the pooled analysis of clinical studies.

Treatment and prevention of influenza in adults and adolescents
The most frequent adverse effects observed in studies for the treatment and prevention of influenza in adults/adolescents with the recommended dose (75 mg twice daily for 5 days for treatment and 75 mg once daily for a duration of up to 6 weeks for prophylaxis) are shown in Table 1.

The reported safety profile of Tamiflu in individuals receiving the recommended prophylaxis dosage (75 mg once daily for a duration of up to 6 weeks) was qualitatively comparable to the safety profile in individuals from the treatment studies, despite a longer duration of dosing in the prophylaxis studies.

Adverse effects observed in studies investigating Tamiflu for the treatment and prevention of influenza in adults and adolescents, or through post-marketing surveillance.

- **Infections and parasitic diseases: Common:** Herpes simplex, Nasopharyngitis, Upper respiratory tract infections, Sinusitis.
- **Blood and lymphatic system disorders: Rare:** Thrombocytopenia.
- **Immune system disorders: Uncommon:** Hypersensitivity reaction Rare: Anaphylactic reactions, Anaphylactoid reactions.
- **Psychiatric disorders: Rare:** Agitation, Abnormal behavior, Anxiety, Confusion, Delusions, Delirium, Hallucinations, Nightmares, Self-injury.
- **Nervous system disorders: Very common:** Headache. **Common:** Insomnia, **Uncommon:** Altered level of **consciousness, Convulsions.**
- **Eye disorders: Very rare:** Visual disturbances.
- **Cardiac disorders: Common:** Cardiac arrhythmia.
- **Respiratory thoracic, and mediastinal disorders: Common:** Cough, Sore throat, Rhinorrhea.
- **Gastrointestinal disorders: Very common:** Nausea **Common:** Vomiting, Abdominal pain (including upper abdominal pain),Dyspepsia. **Very rare:** Gastrointestinal bleeding, Hemorrhagic colitis
- **Hepatobiliary disorders: Rare:** Elevated liver enzyme levels **Very rare:** Fulminant hepatitis,Liver failure, Hepatitis.
- **Skin and subcutaneous tissue disorders: Rare:** Eczema, Dermatitis, Skin rash, Urticaria **Very rare:** Angioedema, Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis.
- **General disorders and administration site conditions: Common:** Pain, Dizziness (including vertigo), Fatigue, Pyrexia,Pain in the limbs

Treatment and prevention of influenza in children
A total of 1,473 children (including otherwise healthy children aged 1-12 years and asthmatic children aged 6-12 years) participated in clinical studies with oseltamivir for the treatment of influenza. Among these children, 851 were treated with oseltamivir suspension. A total of 158 children received the recommended dose of Tamiflu per day in a post-exposure prophylaxis study in households (n=99), a 6-week seasonal prophylaxis study in children (n=49), and a 12-week seasonal prophylaxis study in immunocompromised children (n=10).

Table 2 shows the most commonly reported adverse reactions from clinical studies in children.
Table 2 Adverse reactions observed in studies investigating Tamiflu for the treatment and prevention of influenza in children (age/weight-based dosing [30 mg to 75 mg once daily])

- **Infections and parasitic conditions: Common:** Otitis media.
- **Nervous system disorders: Common:** Headache.
- **Eye disorders: Common:** Conjunctivitis (including red eyes, eye discharge, and eye pain).
- **Ear and labyrinth disorders: Common:** Ear pain **Rare:** Tympanic membrane disorders.
- **Respiratory, thoracic, and mediastinal disorders: Very common:** Cough, Nasal congestion **Common:** Rhinorrhea.
- **Gastrointestinal disorders: Very common:** Vomiting **Common:** Abdominal pain (including upper abdominal pain), Dyspepsia, Nausea.
- **Skin and subcutaneous tissue disorders: Common:** Dermatitis, (including allergic and atopic dermatitis)

Description of selected adverse effects

Psychiatric disorders and nervous system disorders: Influenza can be associated with various neurological and behavioral symptoms, including events such as hallucinations, delirium, and abnormal behavior, in some cases leading to fatal outcomes. These events can occur in cases of encephalitis or encephalopathy but can also occur without clear evidence of a severe illness.

Among patients with influenza receiving Tamiflu, there have been post-marketing reports of seizures and delirium (including symptoms such as altered level of consciousness, confusion, abnormal behavior, delusions, hallucinations, agitation, anxiety, and nightmares). In a very small number of cases, this has led to self-injury or fatal outcomes. These events were mainly reported in children and adolescents, often occurring abruptly and resolving rapidly. The contribution of Tamiflu to these events is unknown. Such neuropsychiatric adverse effects have also been reported in patients with influenza who did not receive Tamiflu.

Liver and biliary disorders: Liver and biliary disorders, including hepatitis and elevated liver enzymes, have been reported in patients with influenza-like illness. These reports include fatal fulminant hepatitis/liver failure.

Other special populations: Pediatric patients (infants younger than 1 year)

Two studies characterized the pharmacokinetics, pharmacodynamics, and safety profile of oseltamivir treatment in 135 children younger than 1 year infected with influenza. In these studies, the safety profile among age cohorts was similar, with vomiting, diarrhea, and diaper rash being the most frequently reported adverse effects (see section 5.2). Insufficient data are available for infants with a post-conceptual age of less than 36 weeks.

Available safety data on oseltamivir administered for the treatment of influenza in infants younger than 1 year, from prospective and retrospective observational studies (in more than 2,400 infants in this age group), epidemiological database research, and post-marketing reports, show that the safety profile for infants younger than 1 year is comparable to the established safety profile for children aged 1 year and older.

Elderly individuals and patients with chronic heart and/or respiratory disorders

Studies on Tamiflu for the treatment of influenza include a population of otherwise healthy adults/adolescents and patients "at risk" (patients who are more likely to experience complications associated with influenza, such as elderly individuals and patients with chronic heart or respiratory diseases). Overall, the safety profile in patients "at risk" was qualitatively comparable to that of otherwise healthy adults/adolescents.

Immunocompromised patients: The treatment of influenza has been evaluated in two studies involving immunocompromised patients treated with the standard dosage or higher doses (double or triple dose) of Tamiflu (see section 5.1). The safety profile of Tamiflu in these studies was consistent with that observed in previous clinical studies where Tamiflu was administered for the treatment of influenza in immunocompetent patients of all age groups (patients who were otherwise healthy or patients "at risk" [i.e., with respiratory and/or cardiac comorbidities]). The most commonly reported adverse effect in immunocompromised children was vomiting (28%).

In a 12-week prophylaxis study involving 475 immunocompromised patients, including 18 children aged 1 to 12 years and older, the safety profile of 238 patients receiving oseltamivir was consistent with what was previously observed in clinical studies where Tamiflu was administered for prophylaxis.

Children with pre-existing bronchial asthma
In general, the adverse effect profile in children with pre-existing bronchial asthma is qualitatively comparable to that of otherwise healthy children.

Overdose: Cases of overdose with Tamiflu have been reported in clinical studies and during post-marketing experience. Most reports of overdose did not include any adverse effects. Adverse effects reported after overdose were similar in nature and distribution to those observed with therapeutic doses of Tamiflu, as described in section 4.8 Adverse Reactions.

Pediatric patients: Overdose is more frequently reported in children than in adults and adolescents. Caution should be exercised in the preparation of Tamiflu oral suspension and administration of Tamiflu products to children.

How to

- pharmacy-prepared suspension: Stable for 10 days if stored below 25°C.
- Capsules: Store below 25°C.

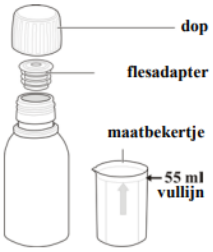
Taking the Tamiflu oral suspension involves 2 steps.

Step 1: Preparing a new medication bottle

Step 2: Measuring and administering the correct dose

Shake the suspension well and draw the recommended dose into the dispenser. See the second part of the instructions. Repeat this step every time you need a dose.

Step 1: Preparing a new medication bottle



You will need:

- The bottle of Tamiflu powder (included in the medication package)
- The screw cap (included in the medication package)
- A plastic measuring cup (included in the medication package)
- The plastic bottle adapter (included in the medication package)
- Water

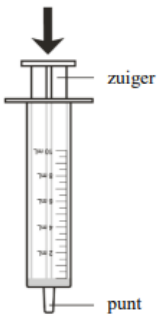
1. Tap the closed bottle gently several times to loosen the powder.
2. Use the measuring cup to measure 55 ml of water
3. Fill the measuring cup with water up to the indicated level.
4. Add all the water, close the bottle, and shake it
5. Pour all the water from the measuring cup into the bottle onto the powder.
6. Always use 55 ml of water, regardless of the dose you need.
7. Replace the cap on the bottle. Shake the bottle well for 15 seconds.
8. Attach the bottle adapter
9. Close the bottle

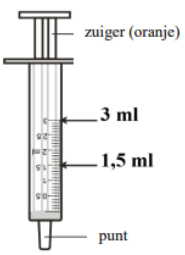
Step 2: Measuring and administering the correct dose

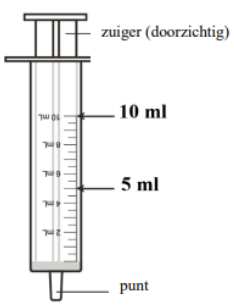
You will need:

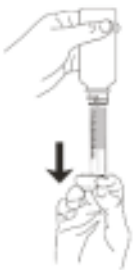
- A bottle of prepared Tamiflu oral suspension
- Depending on the required dose, you will need either the 3 ml oral dosing dispenser (orange plunger, 0.1 ml graduation) or the 10 ml oral dosing dispenser (transparent plunger, 0.5 ml graduation) from the medication package.
- For doses from 1.0 ml to 3.0 ml, use the 3 ml oral dosing dispenser.
- For doses above 3.0 ml up to 10 ml, use the 10 ml oral dosing dispenser.

1. Shake the bottle
2. Prepare the oral dosing dispenser for use
3. Push the plunger all the way down toward the tip of the dispenser.
4. plunger (orange) plunger (transparent)
5. Fill the dispenser with the correct dose
6. Loosen the cap of the bottle.
7. Insert the tip of the dispenser into the opening of the bottle adapter.
8. Then invert the entire unit (bottle and dispenser together).
9. Slowly pull the plunger back to draw the medication into the dispenser.
10. Stop at the marked line indicating the required dose.
11. Return the entire unit to an upright position.
12. Remove the dispenser from the bottle.
13. Administer the medication into the mouth
14. Directly inject the suspension into the mouth by pushing the plunger of the dispenser downward. Ensure that the medication is swallowed.
15. You may eat and drink after taking the medication.
16. Close the bottle, store it properly
17. Replace the cap on the bottle.









Immediately after administration, disassemble the dispenser and rinse both parts under running tap water. Do not boil the dispenser as it may damage it. Allow the dispenser to air dry before using it again. If you have lost or damaged the dispenser, contact your doctor or pharmacist. They will advise you on how to take your medication.