



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/163780/2017

## European Medicines Agency decision

P/0108/2017

of 11 April 2017

on the acceptance of a modification of an agreed paediatric investigation plan for oseltamivir (phosphate) (Tamiflu), (EMEA-000365-PIP01-08-M08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

### **Disclaimer**

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

**Only the English text is authentic.**



# European Medicines Agency decision

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004<sup>1</sup>,

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/192/2009 issued on 2 October 2009, the decision P/29/2011 issued on 28 January 2011, the decision P/0206/2012 issued on 17 September 2012, P/0133/2013 issued on 7 June 2013, the decision P/0062/2014 issued on 7 March 2014 and the decision P/0267/2015 issued on 27 November 2015,

Having regard to the application submitted by Roche Registration Limited on 12 December 2016 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 February 2017, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

- (1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

**Article 1**

Changes to the agreed paediatric investigation plan for oseltamivir (phosphate) (Tamiflu), capsule, hard, powder for oral suspension, oral use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

**Article 2**

This decision is addressed to Roche Registration Limited, 6 Falcon Way, Shire Park, AL7 1TW - Welwyn Garden City, United Kingdom.

EMA/PDCO/859953/2016  
London, 24 February 2017

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMA-000365-PIP01-08-M08

### Scope of the application

**Active substance(s):**

Oseltamivir (phosphate)

**Invented name:**

Tamiflu

**Condition(s):**

Treatment and prevention of influenza

**Authorised indication(s):**

See Annex II

**Pharmaceutical form(s):**

Capsule, hard

Powder for oral suspension

**Route(s) of administration:**

Oral use

**Name / corporate name of the PIP applicant:**

Roche Registration Limited

**Information about the authorised medicinal product:**

See Annex II

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration Limited submitted to the European Medicines Agency on 12 December 2016 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/192/2009 issued on 2 October 2009, the decision P/29/2011 issued on 28 January 2011, the decision P/0206/2012 issued on 17 September 2012, P/0133/2013 issued on 7 June 2013, the decision P/0062/2014 issued on 7 March 2014 and the decision P/0267/2015 issued on 27 November 2015.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 3 January 2017.

## Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

## Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:
  - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

## **Annex I**

**The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)**

## 1. Waiver

Not applicable.

## 2. Paediatric Investigation Plan

### 2.1. Condition

Treatment and prevention of influenza

#### 2.1.1. Indication(s) targeted by the PIP

Treatment and prevention of influenza in healthy and immunocompromised patients from birth to less than 18 years of age.

#### 2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age

#### 2.1.3. Pharmaceutical form(s)

Hard capsules for oral use

Powder for oral suspension for oral use

#### 2.1.4. Measures

| Area                    | Number of studies | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality-related studies | 0                 | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Non-clinical studies    | 0                 | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Clinical studies        | 5                 | <p>Measure 1: Open-label, non-randomised, PK / PD and safety trial to evaluate oseltamivir in children less than 24 months of age with confirmed influenza infection.</p> <p>Measure 2: Randomized, double-blind, multi-centre, stratified trial to evaluate efficacy, safety, tolerability and resistance of oseltamivir conventional and high dose for the treatment of immunocompromised paediatric patients from 1 year to less than 18 years of age (and in adults) with influenza.</p> <p>Measure 4: Open label, non-randomized, multiple dose PK / PD and safety trial of oseltamivir in the treatment of infants from birth to less than 12 months of age with confirmed influenza infection.</p> |

|                                                 |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------------------------------|---|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                 |   | <p>Measure 5: Open label, randomized, two-arm multi-centre trial to evaluate pharmacokinetics and pharmacodynamics of two doses of oseltamivir in the treatment of influenza in immunocompromised paediatric patients from birth to less than 13 years of age</p> <p>Measure 6: Open label, prospective, multi-centre, observational study to evaluate safety, anti-viral activity and clinical outcomes of oseltamivir for treatment of immunocompromised children from at least 37 weeks of gestational age to less than 18 years</p> |
| Extrapolation, modelling and simulation studies | 1 | Measure 3: To simulate multi-dose administration of oseltamivir in immunocompromised children from birth to less than 18 year of age for treatment and prophylaxis of influenza.                                                                                                                                                                                                                                                                                                                                                        |
| Other studies                                   | 0 | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Other measures                                  | 0 | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

### 3. Follow-up, completion and deferral of the PIP

|                                                                                         |                  |
|-----------------------------------------------------------------------------------------|------------------|
| Concerns on potential long term safety / efficacy issues in relation to paediatric use: | Yes              |
| Date of completion of the paediatric investigation plan:                                | By February 2019 |
| Deferral for one or more studies contained in the paediatric investigation plan:        | Yes              |

## **Annex II**

### **Information about the authorised medicinal product**

## Condition(s) and authorised indication(s):

### 1. Treatment of influenza

Authorised indications:

- *Treatment of influenza*

Tamiflu is indicated in adults and children including full term neonates who present with symptoms typical of influenza, when influenza virus is circulating in the community. Efficacy has been demonstrated when treatment is initiated within two days of first onset of symptoms.

### 2. Prevention of influenza

Authorised indications:

- *Prevention of influenza*

- Post-exposure prevention in individuals 1 year of age or older following contact with a clinically diagnosed influenza case when influenza virus is circulating in the community.
- The appropriate use of Tamiflu for prevention of influenza should be determined on a case by case basis by the circumstances and the population requiring protection. In exceptional situations (e.g. in case of a mismatch between the circulating and vaccine virus strains, and a pandemic situation) seasonal prevention could be considered in individuals one year of age or older.
- Tamiflu is indicated for post-exposure prevention of influenza in infants less than 1 year of age during a pandemic influenza outbreak (see section 5.2).

Tamiflu is not a substitute for influenza vaccination.

## Authorised pharmaceutical form(s):

Capsule, hard

Powder for oral suspension

## Authorised route(s) of administration:

Oral use