

EMA/26024/2011

## European Medicines Agency decision

P/19/2011

of 25 January 2011

on the acceptance of a modification of an agreed paediatric investigation plan for sitagliptin (phosphate monohydrate) (Januvia) (EMA-000470-PIP01-08-M03) 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.**

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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/61/2009 issued on 27 March 2009, the decision P/211/2009 issued on 30 October 2009, and decision P/171/2010 issued on 6 September 2010,

Having regard to the application submitted by Merck Sharp and Dohme (Europe), Inc. on 4 October 2010 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 10 December 2010, 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.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

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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 sitagliptin (phosphate monohydrate) (Januvia) film-coated tablet, oral use, 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 Merck Sharp and Dohme (Europe), Inc., 5 Clos du Lynx, Brussels, 1200, Belgium.

Done at London, 25 January 2011

For the European Medicines Agency  
Andreas Pott  
Acting Executive Director  
(Signature on file)



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/PDCO/661588/2010

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

EMA-000470-PIP01-08-M03

### Scope of the application

**Active substance(s):**

Sitagliptin (phosphate monohydrate)

**Invented name:**

Januvia

**Condition(s):**

Type 2 diabetes mellitus

**Authorised indication(s):**

See Annex II

**Pharmaceutical form(s):**

Film-coated tablet

**Route(s) of administration:**

Oral use

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

Merck Sharp and Dohme (Europe), Inc.

**Information about the authorised medicinal product:**

See Annex II



## **Basis for opinion**

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp and Dohme (Europe), Inc. submitted to the European Medicines Agency on 4 October 2010 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/61/2009 issued on 27 March 2009, the decision P/211/2009 issued on 30 October 2009, and the decision P/171/2010 issued on 6 September 2010.

The applicant proposed modifications to the paediatric investigation plan and to the deferral.

The procedure started on 13 October 2010.

## **Scope of the modification**

Some measures and timelines of the original Opinion 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 Icelandic and the Norwegian Paediatric Committee member(s) agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset of the paediatric population and conditions covered by the waiver 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.

London, 10 December 2010

On behalf of the Paediatric Committee  
Dr Daniel Brasseur, Chairman  
(Signature on file)

## **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**

# 1. Waiver

Treatment of Type 2 diabetes mellitus

# 2. Waiver

## 2.1. Condition

Type 2 diabetes mellitus

The waiver applies to:

- the paediatric population from birth to less than 10 years,
- for film-coated tablets, oral use,
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets.

# 3. Paediatric Investigation Plan

## 3.1. Type 2 diabetes mellitus

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

Treatment of Type 2 diabetes mellitus

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

From 10 to less than 18 years of age

### 3.1.3. Pharmaceutical form(s)

Film-coated tablets, oral use, 25 mg, 50 mg and 100 mg

### 3.1.4. Studies

| Area         | Number of studies | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality      |                   | Not applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Non-clinical |                   | Not applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Clinical     | 2                 | <p>1. Randomized, double-blind, placebo-controlled, single-dose trial to evaluate the pharmacokinetics of sitagliptin in children from 10 to less and 18 years of age, with type 2 diabetes mellitus.</p> <p>2. Multicenter, double-blind, randomized, placebo- and metformin-controlled trial to evaluate the safety and efficacy of sitagliptin in children from 10 to less than 18 years of age, with type 2 diabetes mellitus with inadequate glycaemic control.</p> |

#### **4. Follow-up, completion and deferral of PIP**

|                                                                                                   |                 |
|---------------------------------------------------------------------------------------------------|-----------------|
| Measures to address long term follow-up of potential safety issues in relation to paediatric use: | Yes             |
| Date of completion of the paediatric investigation plan:                                          | By October 2018 |
| 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 type 2 diabetes mellitus

Authorised indications:

- In adults for the treatment of type 2 diabetes mellitus as monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.
- In adults for the treatment of type 2 diabetes mellitus as dual oral therapy in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control.
- In adults for the treatment of type 2 diabetes mellitus as dual oral therapy in combination a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance.
- In adults for the treatment of type 2 diabetes mellitus as dual therapy in combination a peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ) agonist (i.e. a thiazolidinedione) when use of a PPAR $\gamma$  agonist is appropriate and when diet and exercise plus the PPAR $\gamma$  agonist alone do not provide adequate glycaemic control.
- In adults for the treatment of type 2 diabetes mellitus as triple oral therapy in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.
- In adults for the treatment of type 2 diabetes mellitus as triple oral therapy in combination with a PPAR $\gamma$  agonist and metformin when use of a PPAR $\gamma$  agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.
- In adults for the treatment of type 2 diabetes mellitus as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.

| EU Number       | (Invented) name | Strength | Pharmaceutical Form | Route of Administration | Packaging                                      | Package size |
|-----------------|-----------------|----------|---------------------|-------------------------|------------------------------------------------|--------------|
| EU/1/07/383/001 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 14           |
| EU/1/07/383/002 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 28           |
| EU/1/07/383/003 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 56           |
| EU/1/07/383/004 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 84           |
| EU/1/07/383/005 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 98           |
| EU/1/07/383/006 | Januvia         | 25 mg    | Film-coated tablet  | Oral use                | perforated unit dose blister (PVC/PE/PVDC/alu) | 50 x 1       |
| EU/1/07/383/007 | Januvia         | 50 mg    | Film-coated tablet  | Oral use                | blister (PVC/PE/PVDC/alu)                      | 14           |

|                 |         |        |                    |          |                                                |        |
|-----------------|---------|--------|--------------------|----------|------------------------------------------------|--------|
| EU/1/07/383/008 | Januvia | 50 mg  | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 28     |
| EU/1/07/383/009 | Januvia | 50 mg  | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 56     |
| EU/1/07/383/010 | Januvia | 50 mg  | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 84     |
| EU/1/07/383/011 | Januvia | 50 mg  | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 98     |
| EU/1/07/383/012 | Januvia | 50 mg  | Film-coated tablet | Oral use | perforated unit dose blister (PVC/PE/PVDC/alu) | 50 x 1 |
| EU/1/07/383/013 | Januvia | 100 mg | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 14     |
| EU/1/07/383/014 | Januvia | 100 mg | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 28     |
| EU/1/07/383/015 | Januvia | 100 mg | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 56     |
| EU/1/07/383/016 | Januvia | 100 mg | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 84     |
| EU/1/07/383/017 | Januvia | 100 mg | Film-coated tablet | Oral use | blister (PVC/PE/PVDC/alu)                      | 98     |
| EU/1/07/383/018 | Januvia | 100 mg | Film-coated tablet | Oral use | perforated unit dose blister (PVC/PE/PVDC/alu) | 50 x 1 |