EMA/18986/2022

# European Medicines Agency decision

P/0024/2022

of 31 January 2022

on the acceptance of a modification of an agreed paediatric investigation plan for vadadustat (EMEA-001944-PIP01-16-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[1],

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

Having regard to the European Medicines Agency's decision P/0035/2017 issued on 31 January 2017, decision P/0074/2020 issued on 21 March 2020 and the decision P/0401/2020 issued on 23 October 2020,

Having regard to the application submitted by Otsuka Pharmaceutical Development & Commercialisation Europe GmbH on 13 September 2021 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 17 December 2021, 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.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for vadadustat, tablet, age-appropriate oral formulation, 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 Otsuka Pharmaceutical Development & Commercialisation Europe GmbH, Europa-Allee 52, 60327 - Frankfurt am Main, Germany.

EMA/PDCO/530259/2021
Amsterdam, 17 December 2021

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

EMEA-001944-PIP01-16-M03

## Scope of the application

**Active substance(s):**

Vadadustat

**Condition(s):**

Treatment of anaemia due to chronic disorders

**Pharmaceutical form(s):**

Tablet

Age-appropriate oral formulation

**Route(s) of administration:**

Oral use

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

Otsuka Pharmaceutical Development & Commercialisation Europe GmbH

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Otsuka Pharmaceutical Development & Commercialisation Europe GmbH submitted to the European Medicines Agency on 13 September 2021 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/0035/2017 issued on 31 January 2017, decision P/0074/2020 issued on 21 March 2020 and the decision P/0401/2020 issued on 23 October 2020.

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

The procedure started on 19 October 2021.

## 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 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 and the subset(s) of the paediatric population and condition(s) 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 annex 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

## *1.1. Condition*

Treatment of anaemia due to chronic disorders

The waiver applies to:

- the paediatric population from birth to less than 4 months of age;
- tablet and age appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

# 2. Paediatric investigation plan

## *2.1. Condition*

Treatment of anaemia due to chronic disorders

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

Treatment of anaemia secondary to chronic kidney disease

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

From 4 months to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Tablet

Age appropriate oral formulation

### 2.1.4. Measures

| Area | Number of measures | Description |
|---|---|---|
| Quality-related studies | 1 | **Study 1**<br>Development of an age-appropriate oral dosage form. |
| Non-clinical studies | 2 | **Study 2**<br>Pilot oral gavage study in juvenile rats<br>**Study 3**<br>*This study was deleted as a result of procedure EMEA-001944-PIP01-16-M01.* |

| | | |
|---|---|---|
| | | **Study 9**<br><br>*(added in procedure EMEA-001944-PIP01-16-M02)*<br><br>Definitive study in juvenile rats to determine the potential toxicity of vadadustat when administered daily to juvenile rats and to investigate the progression and/or reversibility of any treatment-related effects after a 6-week treatment free (recovery) period. |
| Clinical studies | 4 | **Study 4**<br><br>Open-label, single-arm, externally controlled trial to evaluate the activity, safety, tolerability, PK and PD of oral vadadustat for the correction of anaemia in children from 4 months to less than 18 years of age with anaemia secondary to chronic kidney disease (CKD).<br><br>**Study 5**<br><br>Medical record review study to assess the activity and safety of ESA treatment to correct and maintain haemoglobin levels in children from 4 months to less than 18 years of age with anaemia secondary to CKD and naïve to ESA treatment.<br><br>**Study 6**<br><br>Open-label, single-arm, externally controlled trial to evaluate the activity, safety, tolerability, PK and PD of oral vadadustat for the maintenance treatment of anaemia in children from 4 months to less than 18 years of age with anaemia secondary to CKD receiving ESA treatment.<br><br>**Study 7**<br><br>Medical record review study to assess the activity and safety of ESA treatment to maintain haemoglobin levels in children from 4 months to less than 18 years of age with anaemia secondary to CKD receiving ESA treatment. |
| Extrapolation, modelling and simulation studies | 1 | **Study 8**<br><br>Modelling and simulation study to develop PK/PD simulations for the prediction of exposure and selection of doses to be used in children from 4 months to less than 18 years of age with anaemia secondary to CKD naïve to ESA treatment or receiving ESA treatment. |
| Other studies | 0 | Not applicable. |
| Other measures | 0 | Not applicable. |

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

| | |
|---|---|
| Concerns on potential long term safety/efficacy issues in relation to paediatric use: | Yes |
| Date of completion of the paediatric investigation plan: | By May 2027 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |