**MHRA**
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

**gov.uk/mhra**

# Decision Cover Letter

## Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100884-PIP01-23-M01

# Scope of the Application

## Active Substance(s)

SACUBITRIL; VALSARTAN

## Condition(s)

Treatment of Heart failure

## Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate solid oral dosage form

## Route(s) of Administration

ORAL USE

## Name / Corporate name of the PIP applicant

Novartis Pharmaceuticals UK Limited

## Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novartis Pharmaceuticals UK Limited submitted to the licensing authority on 20/02/2023 14:50 GMT an application for a Modification

The procedure started on 07/03/2023 11:01 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

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

This decision is forwarded to the applicant, together with its annex and appendix.

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# Final Decision Letter

MHRA-100884-PIP01-23-M01

Of 16/03/2023 11:15 GMT

On the adopted decision for SACUBITRIL; VALSARTAN (MHRA-100884-PIP01-23-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for SACUBITRIL; VALSARTAN, Film-coated tablet; Age-appropriate solid oral dosage form , ORAL USE .

This decision is addressed to Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, UNITED KINGDOM, W12 7FQ

## ANNEX I

### 1. Waiver

### 1.1 Condition:

| |
|---|
| Treatment of heart failure The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 month of age Pharmaceutical form(s): Film-coated tablet Age-appropriate solid oral dosage form Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe. |

### 2. Paediatric Investigation Plan:

### 2.1 Condition(s):

| |
|---|
| Treatment of heart failure |

## 2.2 Indication(s) targeted by the PIP:

| |
|---|
| Treatment of heart failure |

## 2.3 Subset(s) of the paediatric population concerned by the paediatric development:

| |
|---|
| The paediatric population from 1 month to less than 18 years of age |

## 2.4 Pharmaceutical Form(s):

| |
|---|
| Film-coated tablet Age-appropriate solid oral dosage form |

## 2.5 Studies:

| Study Type | Number of Studies | Study Description |
|---|---|---|
| **Quality Measures** | 1 | Study 1 Development of an age-appropriate solid oral dosage form. |
| **Non-Clinical Studies** | 3 | Study 2 Mechanistic in-vitro study (1170517). Study 3 4-week dose range-finding juvenile rabbit bone toxicity study (1170514). Study 4 4-week investigative bone study in juvenile rats (1170516). |
| **Clinical Studies** | 3 | Study 5 (CLCZ696 B2126) Open-label, randomised, single-dose, multiple treatment period study to determine the relative bioavailability of LCZ696 paediatric formulation relative to the LCZ696 200 mg Final Market Image (FMI) tablet in healthy adult subjects. Study 6 (CLCZ696B2319 Part 1) Open-label, multi-centre study to evaluate the safety/tolerability, pharmacokinetics and pharmacodynamics of LCZ696 in paediatric patients from one month to less than 18 years of age with heart failure. Study 7 (CLCZ696B2319 Part 2) Double-blind, randomised, multi–centre, active controlled, parallel group study to evaluate the safety and efficacy of LCZ696 vs. enalapril in paediatric patients from one month to less than 18 years of age with symptomatic left ventricular systolic dysfunction and heart failure. |
| **Extrapolation, Modeling & Simulation Studies** | 0 | Not applicable. |

| | | |
|---|---|---|
| **Other Studies** | 0 | Not applicable. |
| **Other Measures** | 0 | Not applicable. |

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

| | |
|---|---|
| **Concerns on potential long term safety and efficacy issues in relation to paediatric use:** | Yes |
| **Date of completion of the paediatric investigation plan:** | 31/03/2022 |
| **Deferral of one or more studies contained in the paediatric investigation plan:** | Yes |