EMA/643855/2014

European Medicines Agency decision

P/0295/2014

of 30 October 2014

on the acceptance of a modification of an agreed paediatric investigation plan for ticagrelor (Brilique), (EMEA-000480-PIP01-08-M07) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

P/0295/2014

of 30 October 2014

on the acceptance of a modification of an agreed paediatric investigation plan for ticagrelor (Brilique), (EMEA-000480-PIP01-08-M07) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/199/2009 issued on 2 October 2009, the decision P/30/2011 issued on 28 January 2011, the decision P/239/2011 issued on 30 September 2011, the decision P/0020/2012 issued on 27 January 2012, and the decision P/0255/2012 issued on 26 October 2012,

Having regard to the application submitted by Astrazeneca AB on 17 July 2014 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 October 2014, 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 waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the waiver.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for ticagrelor (Brilique), film-coated tablet, granules for oral suspension, tablet, age-appropriate oral dosage form, oral use, including changes to the waiver, 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 AstraZeneca AB, Building 411A, Floor 4, 5-15185 – Sodertalje, Sweden.

Done at London, 30 October 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/459242/2014

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

EMEA-000480-PIP01-08-M07

Scope of the application

Active substance(s):

Ticagrelor

Invented name:

Brilique

Condition(s):

Prevention of thromboembolic events

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Granules for oral suspension

Tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Astrazeneca AB

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Astrazeneca AB submitted to the European Medicines Agency on 17 July 2014 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/199/2009 issued on 2 October 2009, the decision P/30/2011 issued on 28 January 2011, the decision P/239/2011 issued on 30 September 2011, the decision P/0020/2012 issued on 27 January 2012, and the decision P/0255/2012 issued on 26 October 2012.

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

The procedure started on 13 August 2014.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. The waiver has been removed.

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 waiver in the scope set out in the Annex I of this opinion.

   The Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 10 October 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 (PIP)

1. Waiver

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition

Prevention of thromboembolic events

2.1.1. Indication(s) targeted by the PIP

Prevention of vaso-occlusive crises in paediatric patients with sickle cell disease

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

From birth to less than 18 years

2.1.3. Pharmaceutical form(s)

Granules for oral suspension, tablet, age-appropriate oral dosage form

2.1.4. Measures

Area	Number of studies	Description
Quality	1	Study 1 Development of granules for oral suspension at strengths supporting appropriate dosing for oral use for paediatric patients from 2 years to less than 18 years Study 11 Development of tablet at strengths and size (‘mini tablet’) supporting appropriate dosing for oral use for paediatric patients from 2 years to less than 18 years Study 16 Development of an age-appropriate dosage form for the age range from birth to less than 24 months
Non-clinical	4	Study 2 Dose Range-Finding Study in Suckling Rats Study 3 Definitive study in Suckling Rats Study 4

		Definitive Study in Weaning Rats Study 5 Suckling rat lung function study
Clinical	5	Study 12 A two part study with part A multi-centre, open-label, randomised, PK and PD dose-ranging study to determine dose and part B double-blind, parallel-group, placebo-controlled, 4-week extension in patients with sickle cell disease from 2 to less than 18 years of age. (D5136C00007) Study 13 Multi-centre, double-blind, randomised, placebo-controlled study of ticagrelor with 2 dose levels to determine the efficacy of ticagrelor in prevention of vaso-occlusive crises in paediatric patients with sickle cell disease from 2 to less than 18 years of age. (D5136C00009) Study 14 Multi-centre, open label, single dose study to investigate the pharmacokinetics of ticagrelor in paediatric patients from birth to less than 24 months of age with sickle cell disease. (D5136C00010 Study 15 Open-label, randomised, 3-period, 3-treatment, crossover, single-centre, single-dose study to assess the relative bioavailability of ticagrelor granule for oral suspension and the mini ticagrelor tablet to the commercial ticagrelor tablet in healthy adult subjects

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 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. Prevention of thromboembolic events

Authorised indication(s):

- Brilique, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with Acute Coronary Syndromes (unstable angina, non ST elevation Myocardial Infarction [NSTEMI] or ST elevation Myocardial Infarction [STEMI]); including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery by-pass grafting (CABG).

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use