EMA/153113/2024

European Medicines Agency decision

P/0137/2024

of 6 May 2024

on the acceptance of a modification of an agreed paediatric investigation plan for avatrombopag maleate (Doptelet), (EMEA-001136-PIP01-11-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/0309/2011 issued on 20 December 2011, the decision P/0373/2019 issued on 22 November 2019 and the decision P/0010/2023 issued on 31 January 2023,

Having regard to the application submitted by Swedish Orphan Biovitrum AB on 14 December 2023 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 22 March 2024, 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.

[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 avatrombopag maleate (Doptelet), film-coated tablet, 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 Swedish Orphan Biovitrum AB, Tomtebodavägen 23A, Solna, SE-112 76 – Stockholm, Sweden.

EMA/PDCO/7725/2024
Amsterdam, 22 March 2024

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

EMEA-001136-PIP01-11-M03

Scope of the application

Active substance(s):

Avatrombopag maleate

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of idiopathic thrombocytopenic purpura

Treatment of thrombocytopenic purpura secondary to liver disease

Pharmaceutical form(s):

Film-coated tablet

Powder for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Swedish Orphan Biovitrum AB

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Swedish Orphan Biovitrum AB submitted to the European Medicines Agency on 14 December 2023 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/0309/2011 issued on 20 December 2011, the decision P/0373/2019 issued on 22 November 2019 and the decision P/0010/2023 issued on 31 January 2023.

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

The procedure started on 22 January 2024.

Scope of the modification

Some measures and 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 Paediatric Committee member of Norway 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 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

1.1. Condition:

Treatment of idiopathic thrombocytopenic purpura

The waiver applies to:

- infants from birth to less than 1 years of age;
- film-coated tablet, powder for oral suspension, 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 subset(s).

1.2. Condition:

Treatment of thrombocytopenic purpura secondary to liver disease

The waiver applies to:

- all paediatric subsets from birth to less than 18 years of age;
- film-coated tablet, powder for oral suspension, 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 idiopathic thrombocytopenic purpura

2.1.1. Indication(s) targeted by the PIP

Treatment of thrombocytopenia in patients aged 1 year to less than 18 years with chronic immune (idiopathic) thrombocytopenic purpura (ITP), who have had insufficient response to at least one prior ITP treatment.

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

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film coated tablet

Powder for oral suspension

2.1.4. Studies

Area	Description
Quality	**Study 1:** Development of an age appropriate pharmaceutical form for oral use. **Study 2:** Bioavailability study in healthy adults.
Non-clinical	**Study 3:** 4-week dose range finding oral toxicity study in juvenile rats. **Study 4:** 10-week oral toxicity study in juvenile rats followed by a 4-week recovery period.
Clinical	**Study 5 (AVA-PED-301):** Randomized, double-blind, placebo-controlled, parallel group trial to assess efficacy, PK/PD, tolerability and safety of avatrombopag (maleate) in children with chronic idiopathic thrombocytopenic purpura.
Extrapolation, modelling and simulation studies	**Study 6 (AVA-PKPD-PED-ITP-003):** Population Pharmacokinetic/ Pharmacodynamic (PopPKPD) study to predict initial paediatric doses to be used in further clinical studies. This study was introduced during modification EMEA-001136-PIP01-11-M01.

3. Follow-up, completion and deferral of PIP

Concerns on potential long-term safety and efficacy issues in relation to paediatric use:	No.
Date of completion of the paediatric investigation plan:	By December 2023.
Deferral for one or more studies contained in the paediatric investigation plan:	Yes.

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of idiopathic thrombocytopenic purpura:

Authorised indication(s):

- Doptelet is indicated for the treatment of primary chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).
  - Invented name(s): Doptelet
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Treatment of thrombocytopenia purpura secondary to liver disease:

Authorised indication(s):

- Doptelet is indicated for the treatment of severe thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo an invasive procedure.
  - Invented name(s): Doptelet
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure