EMA/72987/2021

European Medicines Agency decision

P/0064/2021

of 18 February 2021

on the acceptance of a modification of an agreed paediatric investigation plan for exenatide (Byetta, Bydureon), (EMEA-000689-PIP01-09-M11) 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.

European Medicines Agency decision

P/0064/2021

of 18 February 2021

on the acceptance of a modification of an agreed paediatric investigation plan for exenatide (Byetta, Bydureon), (EMEA-000689-PIP01-09-M11) 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/237/2009 issued on 30 November 2009, the decision P/12/2010 issued on 20 January 2010, the decision P/21/2011 issued on 25 January 2011, the decision P/224/2011 issued on 27 September 2011, the decision P/0217/2013 issued on 6 September 2013, the decision P/0197/2014 issued on 8 August 2014, the decision P/0130/2016 issued on 20 May 2016, the decision P/0244/2017 issued on 4 September 2017, the decision P/0297/2018 issued on 12 September 2018, the decision P/0017/2020 issued on 6 January 2020 and the decision P/0353/2020 issued on 9 September 2020,

Having regard to the application submitted by AstraZeneca AB on 22 October 2020 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 29 January 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 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for exenatide (Byetta, Bydureon), solution for injection, powder and solvent for prolonged-release suspension for injection, solution for injection in pre-filled injector, subcutaneous 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 AstraZeneca AB, SE 151 85 Södertälje, Sweden.

EMA/PDCO/577753/2020
Amsterdam, 29 January 2021

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

EMEA-000689-PIP01-09-M11

Scope of the application

Active substance(s):

Exenatide

Invented name:

Byetta

Bydureon

Condition(s):

Treatment of type 2 diabetes mellitus

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Powder and solvent for prolonged-release suspension for injection

Solution for injection in pre-filled injector

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

AstraZeneca AB

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted to the European Medicines Agency on 22 October 2020 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/237/2009 issued on 30 November 2009, the decision P/12/2010 issued on 20 January 2010, the decision P/21/2011 issued on 25 January 2011, the decision P/224/2011 issued on 27 September 2011, the decision P/0217/2013 issued on 6 September 2013, the decision P/0197/2014 issued on 8 August 2014, the decision P/0130/2016 issued on 20 May 2016, the decision P/0244/2017 issued on 4 September 2017, the decision P/0297/2018 issued on 12 September 2018, the decision P/0017/2020 issued on 6 January 2020 and the decision P/0353/2020 issued on 9 September 2020.

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

The procedure started on 1 December 2020.

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 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 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(s)

Treatment of type 2 diabetes mellitus

The waiver applies to:

- the paediatric population from birth to less than 10 years;
- solution for injection, powder and solvent for prolonged-release suspension for injection, solution for injection in pre-filled injector, subcutaneous 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.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of type 2 diabetes mellitus

2.1.1. Indication(s) targeted by the PIP

Treatment of type 2 diabetes mellitus as monotherapy or in combination with metformin, and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies, or in combination with insulin with or without other oral antidiabetic agents.

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

From 10 to less than 18 years

2.1.3. Pharmaceutical form(s)

Solution for injection

Powder and solvent for prolonged-release suspension for injection

Solution for injection in pre-filled injector

2.1.4. Studies

Area	**Number of studies**	**Description**
Quality	0	Not applicable
Non-clinical	2	**Study 1** Juvenile toxicity study in male rats to investigate potential effects of Bydureon on sexual maturation

		Study 2 Juvenile toxicity study in female rats to investigate potential effects of Bydureon on sexual maturation
Clinical	3	**Study 3** Randomised, single-blind, dose-escalating, placebo-controlled crossover study to evaluate the pharmacokinetics, pharmacodynamics and tolerability of exenatide in adolescent patients with type 2 diabetes mellitus (2993-124) **Study 4** Double-blind, placebo-controlled, randomized, multi-center parallel study of the safety and efficacy of exenatide twice daily (as monotherapy and adjunctive therapy to oral antidiabetic agents) in children and adolescents with type 2 diabetes mellitus (H8O-MC-GWBQ) **Study 5** Double-blind, placebo-controlled, randomized, multi-center parallel study of the safety and efficacy of exenatide once weekly (bydureon), as monotherapy and adjunctive therapy to oral antidiabetic agents and/or insulin, in children and adolescents with type 2 diabetes mellitus
Extrapolation, modelling and simulation studies	0	**Study 6** Study deleted during procedure EMEA-000689-PIP01-09-M06 **Study 7** Study deleted during procedure EMEA-000689-PIP01-09-M11. **Study 8** Study deleted during procedure EMEA-000689-PIP01-09-M06. **Study 9** Study deleted during procedure EMEA-000689-PIP01-09-M07
Other studies	0	Not applicable
Other measures	0	Not applicable

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 2020
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:

- Bydureon is indicated in adults 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medicinal products including basal insulin, when the therapy in use, together with diet and exercise, does not provide adequate glycaemic control.
- Byetta is indicated for treatment of type 2 diabetes mellitus in combination with:
  - metformin
  - sulphonylureas
  - thiazolidinediones
  - metformin and a sulphonylurea
  - metformin and a thiazolidinedione

  in adults who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

  Byetta is also indicated as adjunctive therapy to basal insulin with or without metformin and/or pioglitazone in adults who have not achieved adequate glycaemic control with these medicinal products.

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Subcutaneous use