EMA/314183/2016

European Medicines Agency decision

P/0157/2016

of 15 June 2016

on the acceptance of a modification of an agreed paediatric investigation plan for clostridium botulinum neurotoxin type A (150 kD), free of complexing proteins (Xeomin, Bocouture), (EMEA-001039-PIP01-10-M02) 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 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/0042/2012 issued on 28 February 2012 and, the decision P/0067/2015 issued on 1 April 2015,

Having regard to the application submitted by Merz Pharmaceuticals GmbH on 08 February 2016 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 April 2016, 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 clostridium botulinum neurotoxin type A (150 kD), free of complexing proteins (Xeomin, Bocouture), powder for solution for injection, solution for injection in pre-filled syringe, intramuscular 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 Merz Pharmaceuticals GmbH, Eckenheimer Landstr. 100, 60318 - Frankfurt (Main), Germany.

Done at London, 15 June 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/103336/2016
London, 29 April 2016

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

EMEA-001039-PIP01-10-M02

Scope of the application

Active substance(s):

Clostridium Botulinum neurotoxin type A (150 kD), free of complexing proteins

Invented name:

Xeomin

Bocouture

Condition(s):

Treatment of muscle spasticity

Treatment of dystonia

Treatment of muscle-induced wrinkles

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for solution for injection

Solution for injection in pre-filled syringe

Route(s) of administration:

Intramuscular use

Name/corporate name of the PIP applicant:

Merz Pharmaceuticals GmbH

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merz Pharmaceuticals GmbH submitted to the European Medicines Agency on 08 February 2016 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/0042/2012 issued on 28 February 2012 and, the decision P/0067/2015 issued on 1 April 2015.

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

The procedure started on 1 March 2016.

Scope of the modification

A new pharmaceutical form has been added and the scope of the waiver has 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 waiver 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:

Treatment of muscle spasticity

The waiver applies to:

- preterm newborn infants, term newborn infants (from birth to less than 28 days) and infants and toddlers (from 28 days to less than 24 months);
- powder for solution for injection, solution for injection in pre-filled syringe, intramuscular use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

1.2. Condition:

Treatment of dystonia

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- powder for solution for injection, solution for injection in pre-filled syringe, intramuscular use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

1.3. Condition:

Treatment of muscle-induced wrinkles

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- powder for solution for injection, solution for injection in pre-filled syringe, intramuscular use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subsets.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of muscle spasticity

2.1.1. Indication(s) targeted by the PIP:

Treatment of muscle spasticity in cerebral palsy

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

From 2 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for solution for injection, solution for injection in pre-filled syringe

2.1.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	2	**Study 1:** Prospective, multicentre, randomised, double-blind, parallel-group, three dose superiority controlled trial to evaluate dose-response efficacy of Clostridium Botulinum neurotoxin type A (150 kD), (high versus low dose and mid versus low dose) for the treatment of lower limb (LL) spasticity in children from 2 years to less than 18 years with cerebral palsy (CP). (MRZ60201_3070_1) **Study 2:** Open-label, non-controlled, multicenter long-term trial to evaluate the safety of Clostridium Botulinum neurotoxin type A (150 kD) for the treatment of spasticity in the upper and/or lower limb in children from 2 years to less than 18 years of age with cerebral palsy (CP). (MRZ60201_3071_1)

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 October 2018
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 muscle spasticity

Authorised indications:

- treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adult patients.

2. Treatment of dystonia

Authorised indications:

- treatment of cervical dystonia of a predominantly rotational form (spasmodic torticollis) in adult patients;
- treatment of blepharospasmus in adult patients.

3. Treatment of muscle-induced wrinkles

Authorised indications:

- treatment of upper facial lines in adults below 65 years when the severity of these lines has an important psychological impact for the patient:
  - moderate to severe vertical lines between the eyebrows seen at maximum frown (glabellar frown lines) and/or
  - moderate to severe lateral periorbital lines seen at maximum smile (crow's feet lines) and/or
  - moderate to severe horizontal forehead lines seen at maximum contraction.

Authorised pharmaceutical form(s):

Powder for solution for injection

Authorised route(s) of administration:

Intramuscular use